779 mRNA COVID-19 Vaccine Adverse Event Annotated References (With Abstracts): by General Category

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Immune issues/Auto immunity/Guillain-Barre Syndrome

Abicic, A., et al. (2022). "New-Onset Ocular Myasthenia Gravis After Booster Dose of COVID-19 Vaccine." Cureus **14**(7): e27213.

Coronavirus disease 2019 (COVID-19) vaccines have been reported as possible triggers of the production of antibodies pathogenic to the peripheral nerve and neuromuscular junction. We report on a patient who experienced vertical diplopia three weeks after the booster dose of the Pfizer-BioNTech vaccine (Comirnaty(R)). The diagnosis of myasthenia gravis (MG) was established based on highly positive antibodies to the nicotinic acetylcholine receptor (nAChR). Treatment with pyridostigmine and prednisone was started with gradually raising doses. On a follow-up exam two months after treatment initiation, clinical improvement was noted with an almost normal bulbomotor examination. The occurrence of diplopia following COVID-19 vaccination should raise suspicion of new-onset ocular MG and testing for anti-nAChR antibodies is advised.

Ajmera, K. M. (2021). "Fatal Case of Rhabdomyolysis Post-COVID-19 Vaccine." Infect Drug Resist **14**: 3929-3935.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or COVID-19 pandemic has taken away the lives of many people (>4 million per WHO) around the world as of July 2021. With the advancement of the vaccine against COVID-19, in less than a year since the start of the pandemic, the infection rate has come under control in certain regions but is still rising in many more. However, with time, we are also learning a lot more about the adverse events related to the vaccine. This report documents the first fatal case of rhabdomyolysis potentially associated with the COVID-19 vaccine and supports the possibility that autoimmunity is a major risk factor for covid vaccine-related rhabdomyolysis.

Akinosoglou, K., I. Tzivaki and M. Marangos (2021). "Covid-19 vaccine and autoimmunity: Awakening the sleeping dragon." Clin Immunol **226**: 108721.

Al-Rasbi, S., et al. (2022). "Myocarditis, Pulmonary Hemorrhage, and Extensive Myositis with Rhabdomyolysis 12 Days After First Dose of Pfizer-BioNTech BNT162b2 mRNA COVID-19 Vaccine: A Case Report." Am J Case Rep **23**: e934399.

BACKGROUND The COVID-19 pandemic is a current global crisis, and there are hundreds of millions of individuals being vaccinated worldwide. At present, there have been few reports of COVID-19 vaccine-induced autoimmune processes manifested as myositis, thrombocytopenia, and myocarditis. CASE REPORT A 37-year-old man presented to the Emergency Department (ED) with a 3-day history of back pain and a 1-day history of left upper limb swelling with paresthesia and shortness of breath, 12-days after receiving the first dose of Pfizer/BioNTech BNT162b2 mRNA COVID-19 vaccine. He was diagnosed with severe myositis complicated with rhabdomyolysis and non-oliguric acute kidney injury, thrombocytopenia, myocarditis with pulmonary edema, and pulmonary hemorrhage. Screens for potential toxic, infectious, paraneoplastic, and autoimmune disorders were

unremarkable. The patient was treated with a 5-day course of intravenous methylprednisolone and intravenous immunoglobulin, with a good response. He was hospitalized for 16 days and discharged home on a tapering dose of oral prednisolone for 6 weeks. CONCLUSIONS The case describes a possible link between Pfizer/BioNTech BNT162b2 mRNA COVID-19 vaccine and immune-mediated myocarditis, pulmonary vasculitis, myositis, and thrombocytopenia. However, further data are required to confirm such an association.

Asaduzzaman, M., et al. (2022). "COVID-19 mRNA vaccine-associated encephalopathy, myocarditis, and thrombocytopenia with excellent response to methylprednisolone: A case report." J Neuroimmunol **368**: 577883.

INTRODUCTION: Large-scale vaccination is considered one of the most effective strategies to control the pandemic of COVID-19. Since its start, different complications have been described thought to be related to vaccination. Here, we present a rare case where encephalopathy, myocarditis, and thrombocytopenia developed simultaneously following the second dose of Pfizer-BioNTech mRNA vaccine (BNT162b2). CASE PRESENTATION: A 15-years-old female presented with fever, altered consciousness, and convulsions after taking the second shot of the vaccine. Clinical and laboratory workup was notable for the presence of thrombocytopenia and myocarditis. No alternative causes of encephalitis were found. The patient responded significantly to methylprednisolone suggesting underlying immune pathogenesis responsible for the clinical features. The diagnostic criteria for possible autoimmune encephalitis were also fulfilled. CONCLUSION: Although rare, the clinician should be aware of the possible adverse events following COVID-19 vaccination. Further research with large pooled data is needed to get more insight into its pathogenesis and causal relationship.

Ashkenazi, S. (2023). "Autoimmunity, COVID-19, Post-COVID19 Syndrome and COVID-19 Vaccination." Isr Med Assoc J **25**(2): 161-162.

Ballout, A. A., et al. (2022). "A Single-Health System Case Series of New-Onset CNS Inflammatory Disorders Temporally Associated With mRNA-Based SARS-CoV-2 Vaccines." Front Neurol **13**: 796882.

BACKGROUND: Since 2020, over 250 million doses of mRNA-based SARS-CoV-2 vaccines have been administered in the United States and hundreds of millions worldwide between the Pfizer-BioNTech and Moderna SARS-CoV-2 vaccines. To date, there have been rare reports associating mRNA-based SARS-CoV-2 vaccines with episodes of inflammatory and autoimmune CNS disorders. We report a case series of five patients with new-onset neurological disorders of inflammatory or immunological origin temporally associated with these vaccines. METHODS: A case-series of five patients within a single 23-hospital health system who developed new-onset CNS inflammatory disease within 2 weeks of receiving a dose of an mRNA-based SARS-CoV-2 vaccine. RESULTS: Five cases of post-vaccination CNS disorders of immune origin (fatal ADEM; n = 1, new-onset NMOSD; n = 2, new-clinical onset MS-like syndrome but with preexisting clinically silent mild demyelination; n = 1, meningoencephalitis; n = 1) observed within 2

weeks of inoculation with either the first or second dose of mRNA-based SARS-CoV-2 vaccines (Moderna = 3, Pfizer = 2). DISCUSSION: To our knowledge, these are among the emerging cases of CNS adverse events of immunological or inflammatory origin. These findings should be interpreted with great caution as they neither prove a mechanistic link nor imply a potential long-term increased risk in post-vaccination CNS autoimmunity. Larger prospective studies assessing the potential association between mRNA-based vaccination and the development of neurological adverse events of suspected immune origin, particularly among those with underlying CNS or systemic autoimmune disorders, are needed. The use of mRNA-based SARS-CoV-2 vaccines should continue to be strongly encouraged given their high efficacy in overcoming this pandemic.

Banamah, T. A., et al. (2022). "Severe Rhabdomyolysis Complicated With Acute Kidney Injury Required Renal Replacement Therapy After Pfizer COVID-19 Vaccine " Cureus **14**(5): e25199.

The adverse effects of coronavirus disease 2019 (COVID-19) vaccines are somewhat common but rarely life-threatening. Diagnosing life-threatening vaccine-related adverse effects is heavily dependent on history taking and ruling out the other possible causes. Vaccine-related complications vary, so awareness of possible complications can lead to efficient management. We present the case of a 58-year-old woman with a history of schizophrenia who received the COVID-19 Pfizer vaccine and developed severe rhabdomyolysis. She required renal replacement therapy and fully recovered with possible transient autoimmune activity. This case highlights the importance of early awareness of adverse effects following vaccine administration and careful history taking and monitoring to avoid life-threatening conditions.

Becker, E. C., et al. (2023). "Type 1 Autoimmune Pancreatitis Unmasked by COVID-19 Vaccine." ACG Case Rep J **10**(1): e00950.

Autoimmune pancreatitis is a rare fibro-inflammatory disease with 2 distinct subtypes of which each has their own clinical presentation, risk factors, and histopathological patterns. We present a case of newly diagnosed type 1 autoimmune pancreatitis in a symptomatic 54-year-old man with stable ulcerative colitis 1 month after COVID-19 vaccination. Previous reports have indicated that vaccinations can trigger autoimmune disease in predisposed individuals. This case discusses the occurrence of autoimmune pancreatitis triggered after COVID-19 vaccination.

Bellucci, M., et al. (2022). "Case Report: Post-COVID-19 Vaccine Recurrence of Guillain-Barre Syndrome Following an Antecedent Parainfectious COVID-19-Related GBS." Front Immunol **13**: 894872.

Guillain-Barre syndrome (GBS) is an autoimmune neurological disorder often preceded by viral illnesses or, more rarely, vaccinations. We report on a unique combination of postcoronavirus disease 2019 (COVID-19) vaccine GBS that occurred months after a parainfectious COVID-19-related GBS. Shortly after manifesting COVID-19 symptoms, a 57-year-old man developed diplopia, right-side facial weakness, and gait instability that, together with electrophysiology and cerebrospinal fluid examinations, led to a diagnosis

of post-COVID-19 GBS. The involvement of cranial nerves and IgM seropositivity for ganglioside GD1b were noteworthy. COVID-19 pneumonia, flaccid tetraparesis, and autonomic dysfunction prompted his admission to ICU. He recovered after therapy with intravenous immunoglobulins (IVIg). Six months later, GBS recurred shortly after the first dose of the Pfizer/BioNTech vaccine. Again, the GBS diagnosis was confirmed by cerebrospinal fluid and electrophysiology studies. IgM seropositivity extended to multiple gangliosides, namely for GM3/4, GD1a/b, and GT1b IgM. An IVIg course prompted complete recovery. This case adds to other previously reported observations suggesting a possible causal link between SARS-CoV-2 and GBS. Molecular mimicry and anti-idiotype antibodies might be the underlying mechanisms. Future COVID-19 vaccinations/revaccinations in patients with previous para-/post-COVID-19 GBS deserve a reappraisal, especially if they are seropositive for ganglioside antibodies.

Bidari, A., et al. (2023). "Immune thrombocytopenic purpura secondary to COVID-19 vaccination: A systematic review." Eur J Haematol **110**(4): 335-353.

INTRODUCTION: This systematic review aimed to retrieve patients diagnosed with de novo immune thrombocytopenic purpura (ITP) after COVID-19 immunization to determine their epidemiological characteristics, clinical course, therapeutic strategies, and outcome. MATERIALS AND METHODS: We conducted the review using four major databases, comprising PubMed, Scopus, Web of Science, and the Cochrane library, until April 2022. A systematic search was performed in duplicate to access eligible articles in English. Furthermore, a manual search was applied to the chosen papers' references to enhance the search sensitivity. Data were extracted and analyzed with the SPSS 20.1 software. RESULTS: A total of 77 patients with de novo COVID-19 vaccine-associated ITP were identified from 41 studies, including 31 case reports and 10 case series. The median age of patients who developed COVID-19 vaccine-associated ITP was 54 years (IQR 36-72 years). The mRNA-based COVID-19 vaccines, including BNT16B2b2 and mRNA-1273, were most implicated (75.4%). Those were followed by the adenovirus vector-based vaccines, inclusive of ChAdOx1 nCoV-19 and vAd26.COV2.S. No report was found relating ITP to other COVID-19 vaccines. Most cases (79.2%) developed ITP after the first dose of COVID-19 vaccination. 75% of the patients developed ITP within 12 days of vaccination, indicating a shorter lag time compared to ITP after routine childhood vaccinations. Sixty-seven patients (87%) patients were hospitalized. The management pattern was similar to primary ITP, and systemic glucocorticoids, IVIg, or both were the basis of the treatment in most patients. Most patients achieved therapeutic goals; only two individuals required a secondary admission, and one patient who presented with intracranial hemorrhage died of the complication. CONCLUSIONS: De novo ITP is a rare complication of COVID-19 vaccination, and corresponding reports belong to mRNA-based and adenovirus vector-based vaccines, in order of frequency. This frequency pattern may be related to the scale of administration of individual vaccines and their potency in inducing autoimmunity. The more the COVID-19 vaccine is potent to induce antigenic challenge, the shorter the lag time would be. Most patients had a benign course and responded to typical treatments of primary ITP.

Bril, F. (2021). "Autoimmune hepatitis developing after coronavirus disease 2019 (COVID-19) vaccine: One or even several swallows do not make a summer." J Hepatol **75**(5): 1256-1257.

Brito, S., et al. (2021). "A Case of Autoimmune Hemolytic Anemia Following COVID-19 Messenger Ribonucleic Acid Vaccination." Cureus **13**(5): e15035.

Autoimmune hemolytic anemia (AIHA) is a condition characterized by the increased destruction of red blood cells (RBCs) mediated by anti-erythrocyte autoantibodies with or without complement activation. Its clinical presentation is heterogeneous, ranging from asymptomatic to severe forms with fatal outcomes, and it can be either idiopathic or secondary to a coexisting disorder. In this report, we present a case of a patient who suffered from acute and severe AIHA after receiving the second dose of the coronavirus disease 2019 (COVID-19) messenger ribonucleic acid (mRNA) vaccine.

Camacho-Dominguez, L., et al. (2022). "COVID-19 vaccine and autoimmunity. A new case of autoimmune hepatitis and review of the literature." J Transl Autoimmun **5**: 100140.

Autoimmunity following COVID-19 vaccination has been reported. Herein, a 79-year-old man with clinical and immunological features of autoimmune hepatitis type 1 after ChAdOx1 nCoV-19 vaccination is presented. Clinical manifestations rapidly remitted after the instauration of immunomodulatory management. This case, together with a comprehensive review of the literature, illustrates the association between COVID-19 vaccines and the development of autoimmune conditions.

Chamling, B., et al. (2021). "Occurrence of acute infarct-like myocarditis following COVID-19 vaccination: just an accidental co-incidence or rather vaccination-associated autoimmune myocarditis?" Clin Res Cardiol **110**(11): 1850-1854.

Chaturvedi, H. T., et al. (2023). "New acute onset of ocular myasthenia gravis after COVID-19 vaccine: A case report." J Family Med Prim Care **12**(2): 394-396.

Reports have shown the association of coronavirus disease 2019 (COVID-19) with several neuromuscular disorders. Myasthenia gravis (MG) is an autoimmune disease in which antibodies bind to acetyl choline receptors in the postsynaptic membrane at the neuromuscular junction. The characteristic clinical feature of the disease is weakness of the ocular muscle, bulbar muscle, and extremity muscles; when the weakness is limited to the ocular muscle only, the condition is known as ocular myasthenia gravis. Diagnosis is usually confirmed by the acetylcholine receptor antibodies. Symptoms of MG may be aggravated by various types of infections and medications. Here, we are presenting a rare case of a new and acute onset of ocular MG presented after administration of Covishield vaccine.

Costa, R., et al. (2022). "Brown-Sequard syndrome in a patient with spondyloarthritis after COVID-19 vaccine: a challenging differential diagnosis." ARP Rheumatol **1**(3): 257-259.

A 41-year-old woman with pre-radiographic axial and peripheric spondyloarthritis, taking adalimumab since 2010, started motor impairment of the right limbs and numbness of the left leg seven days after the administration of COVID-19 mRNA vaccine. Adalimumab

was taken 47 days before clinical onset. A comprehensive study for infectious, autoimmune and neoplastic causes were unremarkable. MRI depicted an acute inflammatory lesion at C2 level with gadolinium enhancement. The patient started methylprednisolone with clinical improvement. Three scenarios should be considered: primary CNS inflammatory disorder or a secondary manifestation of the underlying rheumatologic disease; immune-mediated inflammatory lesion triggered by vaccine; demyelinating event due to adalimumab.

Elrashdy, F., et al. (2021). "Autoimmunity roots of the thrombotic events after COVID-19 vaccination." Autoimmun Rev **20**(11): 102941.

Although vaccination represents the most promising way to stop or contain the coronavirus disease 2019 (COVID-19) pandemic and safety and effectiveness of available vaccines were proven, a small number of individuals who received anti-SARS-CoV-2 vaccines developed a prothrombotic syndrome. Vaccine-induced immune thrombotic thrombocytopenia (VITT) can be triggered by the adenoviral vector-based vaccine, whereas lipid nanoparticle-mRNA-based vaccines can induce rare cases of deep vein thrombosis (DVT). Although the main pathogenic mechanisms behind this rare phenomenon have not yet been identified, both host and vaccine factors might be involved, with pathology at least in part being related to the vaccine-triggered autoimmune reaction. In this review, we are considering some aspects related to pathogenesis, major risk factors, as well as peculiarities of diagnosis and treatment of this rare condition.

Erard, D., et al. (2022). "Autoimmune hepatitis developing after COVID 19 vaccine: Presumed guilty?" Clin Res Hepatol Gastroenterol **46**(3): 101841.

Etuk, A. S., I. N. Jackson and H. Panayiotou (2022). "A Rare Case of Myocarditis After the First Dose of Moderna Vaccine in a Patient With Two Previous COVID-19 Infections." Cureus **14**(5): e24802.

Myocarditis is the inflammation of the cardiac muscle caused by a variety of factors ranging from infections to autoimmune diseases. Most cases of vaccine-induced myocarditis occur after the second dose of vaccination; however, a few cases have been reported following the first dose of vaccination with or without previous coronavirus disease 2019 (COVID-19) infection. A case of myocarditis occurring about three weeks after the first dose of the Moderna vaccine has been reported in a patient with one previous COVID-19 infection. However, there have not been any documented cases of myocarditis after the first dose of the Moderna vaccine in a patient with two prior COVID-19 infections. Our index patient had already experienced two COVID-19 infections in the past and was diagnosed with myocarditis eight hours after receiving the first dose of the Moderna vaccine. The susceptibility to developing this likely stems from the possible production of antibodies to the viral antigen from previous COVID-19 infections. Furthermore, the fact that our patient developed symptoms eight hours after receiving the vaccine suggests a possible additive effect of antibodies produced from the two previous COVID-19 infections. This case report suggests that individuals repeatedly

infected with COVID-19 may be at increased risk of myocarditis following the administration of the Moderna vaccine.

Farley, S., et al. (2021). "Autoimmunity after Coronavirus Disease 2019 (COVID-19) Vaccine: A Case of Acquired Hemophilia A." Thromb Haemost **121**(12): 1674-1676.

Fitzsimmons, W. E. (2022). "COVID-19 vaccine associated transverse myelitis-Evusheld as an option when vaccination is not recommended due to severe adverse events." Hum Vaccin Immunother **18**(5): 2068338.

Individuals who experience severe COVID-19-vaccine-related adverse reactions such as transverse myelitis may be precluded from receiving further vaccination to protect from SARS-CoV-2 infection. Although the mechanism of autoimmune spinal cord inflammation resulting in transverse myelitis is unclear, it may be safe to administer antibody therapy for preventing COVID-19. Recently, Evusheld, tixagevimab with cilgavimab, two spike-protein directed monoclonal antibodies were authorized by the U.S. FDA and U.K. MHRA for administration to individuals when vaccination is not recommended. We report the safe administration of Evusheld to a patient who experienced transverse myelitis 11 months previously as a result of receiving the Moderna mRNA vaccine. This patient has experienced no adverse events to Evusheld. Additional experience and data collection are warranted to determine the safety of this prophylactic therapy.

Frontiers Production, O. (2023). "Erratum: Effect of SARS-CoV-2 BNT162b2 mRNA vaccine on thyroid autoimmunity: a twelve-month follow-up study." Front Endocrinol (Lausanne) **14**: 1257424.

Gao, J. J., et al. (2021). "Acute Transverse Myelitis Following COVID-19 Vaccination." Vaccines (Basel) **9**(9).

An increasing number of people are undergoing vaccination for COVID-19 because of the ongoing pandemic. The newly developed, genetically engineered mRNA vaccines are critical for controlling the epidemic disease. However, major adverse effects, including neuroimmunological disorders, are being attributed to this vaccine. For instance, several cases of acute transverse myelitis (ATM) after COVID-19 vaccination have been reported in clinical trials. Here, we report an exceedingly rare case of longitudinally extensive transverse myelitis (LETM), a rare subtype of ATM involving three or more vertebral segments, that occurred shortly after vaccination with the Moderna COVID-19 (mRNA-1273) vaccine, with a comorbidity of vitamin B12 deficiency. The findings of subsequent investigations suggest the possibility that autoimmune responses are triggered by the reactions between anti-SARS-CoV-2 spike protein antibodies and tissue proteins, as well as the interaction between spike proteins and angiotensin-converting enzyme 2 receptors.

Garrido, I., et al. (2021). "Autoimmune hepatitis after COVID-19 vaccine - more than a coincidence." J Autoimmun **125**: 102741.

The COVID-19 pandemic is still raging across the world and vaccination is expected to lead us out of this pandemic. Although the efficacy of the vaccines is beyond doubt, safety still remains a concern. We report a case of a 65-year-old woman who experienced acute severe autoimmune hepatitis two weeks after receiving the first dose of Moderna-COVID-19 vaccine. Serum immunoglobulin G was elevated and antinuclear antibody was positive (1:100, speckled pattern). Liver histology showed a marked expansion of the portal tracts, severe interface hepatitis and multiple confluent foci of lobular necrosis. She started treatment with prednisolone, with a favorable clinical and analytical evolution. Some recent reports have been suggested that COVID-19 vaccination can lead to the development of autoimmune diseases. It is speculated that the vaccine can disturb self-tolerance and trigger autoimmune responses through cross-reactivity with host cells. Therefore, healthcare providers must remain vigilant during mass COVID-19 vaccination.

Giuffrida, G., et al. (2022). "Immune-mediated thrombotic thrombocytopenic purpura following administration of Pfizer-BioNTech COVID-19 vaccine." Haematologica **107**(4): 1008-1010.

Giuffrida, G., et al. (2022). "Relapse of immune-mediated thrombotic thrombocytopenic purpura following mRNA COVID-19 vaccination: a prospective cohort study." Haematologica **107**(11): 2661-2666.

Immune-mediated thrombotic thrombocytopenic purpura (iTTP) is a rare and life-threatening disease. Vaccination has been reported to be a trigger of onset and relapse of autoimmune diseases. We evaluated after mRNA COVID-19 vaccination 32 adult patients previously diagnosed with iTTP by means of weekly monitoring of complete blood count and ADAMTS13 testing. Thirty of 32 patients received at least one dose of Pfizer-BioNTech, the remaining two received Moderna. A total of five patients, all vaccinated with Pfizer-BioNTech, had a biochemical relapse at a median post-vaccination time of 15 days following the second or third vaccine dose, presenting without measurable ADAMTS13 activity and a median anti- ADAMTS13 autoantibody value of 34 U/mL. Four of five cases had concomitant clinical relapse and were treated with corticosteroids alone or daily sessions of plasma exchange and caplacizumab, while one patient was closely monitored with ADAMTS13 with no onset of anemia and thrombocytopenia. Although the benefits of vaccination exceed its potential risks, clinicians should be aware that iTTP relapse might follow COVID-19 vaccination. Therefore, laboratory and clinical monitoring of iTTP patients should be done in the first post-vaccination month, in order to promptly diagnose and treat any relapse.

Goldman, M. and C. Hermans (2021). "Thrombotic thrombocytopenia associated with COVID-19 infection or vaccination: Possible paths to platelet factor 4 autoimmunity." PLoS Med **18**(5): e1003648.

Michel Goldman and Cedric Hermans discuss thrombotic mechanisms in COVID-19 and rare adverse reactions to SARS-CoV-2 vaccinations.

Gonzalez-Enriquez, J. O. (2022). "[Bell's Palsy Secondary to COVID-19 Vaccine Pfizer: Case report]." Rev Med Inst Mex Seguro Soc **60**(2): 224-228.

BACKGROUND: BNT162b2 (Pfizer-BioNTech) is a nucleosidemodified mRNA vaccine formulated with lipid nanoparticles for the prevention of COVID-19 disease caused by SARSCoV-2 infection. In early December 2020, BNT162b2 received an emergency use authorization, initial efficacy and safety data have been released, consumer / patient information sheets for vaccines distributed in North America do not warn of Bell's palsy as a possible adverse effect. We reported the case of a patient who developed Bell's palsy on the right side in less than 3 hours after the application of the first dose of the Pfizer-BioNTech COVID-19 vaccine. CLINICAL CASE: 32-year-old latina woman who developed right facial paralysis after receiving the first dose of the BNT162b2 mRNA vaccine on April 7, 2021; with right facial paresis, absence of forehead wrinkles, lip-buccal sulcus and nasolabial fold; spasms of the facial and periorbital muscles, laterocervical pain; possible etiologies were ruled out, prednisone, gabapentin and topiramate. CT without alterations, achieving gradual improvement; until full functional recovery after 15 days. With benign evolution, congruent with the natural history of the disease, classifying it as idiopathic Bell's palsy. CONCLUSIONS: Although a causal relationship cannot be established, the time and mode of appearance of the paralysis suggested a relationship with the application of the BNT162b2 vaccine. Given the recommendation of the health authorities to monitor the cases of Bell's palsy, and the surveillance of events supposedly attributable to vaccination (ESAVI) and as it is the first case reported in the literature, in the mexican population, we believe that this case should be shared with the scientific community in a timely manner.

Hamedi, K. R., et al. (2023). "Comparison of COVID-19 Vaccine-Associated Myocarditis and Viral Myocarditis Pathology." Vaccines (Basel) **11**(2).

The COVID-19 pandemic has led to significant loss of life and severe disability, justifying the expedited testing and approval of messenger RNA (mRNA) vaccines. While found to be safe and effective, there have been increasing reports of myocarditis after COVID-19 mRNA vaccine administration. The acute events have been severe enough to require admission to the intensive care unit in some, but most patients fully recover with only rare deaths reported. The pathways involved in the development of vaccine-associated myocarditis are highly dependent on the specific vaccine. COVID-19 vaccine-associated myocarditis is believed to be primarily caused by uncontrolled cytokine-mediated inflammation with possible genetic components in the interleukin-6 signaling pathway. There is also a potential autoimmune component via molecular mimicry. Many of these pathways are similar to those seen in viral myocarditis, indicating a common pathophysiology. There is concern for residual cardiac fibrosis and increased risk for the development of cardiomyopathies later in life. This is of particular interest for patients with congenital heart defects who are already at increased risk for fibrotic cardiomyopathies. Though the risk for vaccine-associated myocarditis is important to consider, the risk of viral myocarditis and other injury is far greater with COVID-19 infection. Considering these relative risks, it is still recommended that the general public

receive vaccination against COVID-19, and it is particularly important for congenital heart defect patients to receive vaccination for COVID-19.

Hamid, R., et al. (2022). "Potential Association Between COVID-19 Vaccination and Facial Palsy: Three Cases With Neuroimaging Findings." Ear Nose Throat J: 1455613221113818.

Acute onset Facial palsy was reported in four vaccinated participants in the BNT162b2 (Pfizer-BioNTech) vaccine clinical trials published on December 10, 2020. So far, few cases of Facial palsy among the mRNA vaccine groups have been previously documented in the literature. Facial palsy is cited as medically attended adverse event following immunization on April 12, 2021, after the first dose of the approved Pfizer-BioNTech COVID-19 vaccines for preventive immunization for SARS-CoV-2 is administrated to the population in Turkey. This study is aimed to describe clinical and magnetic resonance imaging features of three patients, who developed acute onset peripheral facial paralysis after administration of the BNT162b2 vaccine, without any previous medical condition. The first patient presented with right sided facial palsy within the same day following the vaccine was administrated, while the second patient presented with left sided facial palsy 2 months after vaccination. The third patient, on the other hand, presented with right sided facial palsy and abducens nerve (CN VI) paralysis two days after vaccine was administrated.

Hermel, M., et al. (2022). "COVID-19 Vaccination Might Induce Postural Orthostatic Tachycardia Syndrome: A Case Report." Vaccines (Basel) **10**(7).

We report a case of new-onset postural orthostatic tachycardia syndrome in a healthy 46-year-old female after a single dose of the BNT162b2 (Pfizer-BioNTech) SARS-CoV-2 vaccine. There have been three prior reports of new-onset postural orthostatic tachycardia syndrome after COVID-19 vaccination. Predominant symptoms noted included fatigue, brain fog, headache, sinus tachycardia, and dizziness. Management includes noninvasive therapies, behavioral approaches, and pharmacologic regimens. Here, the patient presented with fatigue, palpitations, dizziness, and presyncope, with symptoms beginning 7 days after vaccination. Presenting vitals included temperature within normal limits, inappropriate tachycardia, up to 120 beats per minute, blood pressure of 128/87 mm of mercury, and 100% saturation in room air. Her management included lifestyle changes, dietary supplements, and ivabradine. Further studies are needed to evaluate prevalence, etiology, and optimal management.

Hines, A., et al. (2021). "Immune thrombocytopenic purpura and acute liver injury after COVID-19 vaccine." BMJ Case Rep **14**(7).

A 26-year-old woman was sent to the emergency room by her primary care physician for a new petechial rash and thrombocytopenia 2 weeks after receiving the Moderna mRNA-1273 SARS-CoV-2 vaccine. Her hospital course was complicated by transaminitis. Her platelet count improved to normal on hospital day 5 after receiving intravenous steroids and intravenous immunoglobulin to treat her suspected diagnosis of immune thrombocytopenic purpura. Extensive workup for her thrombocytopenia and transaminitis was unremarkable including ruling out infectious, autoimmune and toxic

causes. A liver biopsy was unrevealing and her transaminitis was improved on discharge. Although not proven, the temporal relationship of her vaccination with thrombocytopenia and abnormal liver enzymes points towards the Moderna mRNA-1273 SARS-CoV-2 vaccine as the most likely inciting factor.

Hinterseher, J., M. Hertl and D. Didona (2023). "Autoimmune skin disorders and SARS-CoV-2 vaccination - a meta-analysis." J Dtsch Dermatol Ges **21**(8): 853-861.

BACKGROUND AND OBJECTIVES: The coronavirus SARS-CoV-2, which is the cause of COVID-19 disease in infected patients, has led to an ongoing worldwide pandemic. Although SARS-CoV-2 vaccination had a dramatic positive effect on the course of COVID-19, there has been increasing evidence of adverse effects after SARS-CoV-2 vaccination. This meta-analysis highlights the association between SARS-CoV-2 vaccination and de novo induction or aggravation of inflammatory and autoimmune skin diseases. MATERIAL AND METHODS: A systematic meta-analysis of the literature on new onset or worsening of inflammatory and autoimmune diseases after SARS-CoV-2 vaccination was performed according to the PRISMA guidelines. The search strategy included following terms: "COVID-19/SARS-CoV-2 vaccine bullous pemphigoid/pemphigus vulgaris/systemic lupus erythematosus/dermatomyositis/lichen planus/leukocytoclastic vasculitis." Moreover, we describe representative cases from our dermatology department. RESULTS: The database-search in MEDLINE identified 31 publications on bullous pemphigoid, 24 on pemphigus vulgaris, 65 on systemic lupus erythematosus, nine on dermatomyositis, 30 on lichen planus, and 37 on leukocytoclastic vasculitis until June 30th, 2022. Severity and response to treatment varied among the described cases. CONCLUSIONS: Our meta-analysis highlights a link between SARS-CoV-2 vaccination and new onset or worsening of inflammatory and autoimmune skin diseases. Moreover, the extent of disease exacerbation has been exemplified by cases from our dermatological department.

Hirose, S., et al. (2021). "Acute autoimmune transverse myelitis following COVID-19 vaccination: A case report." Medicine (Baltimore) **100**(51): e28423.

RATIONALE: Transverse myelitis is an infectious or noninfectious inflammatory spinal cord syndrome. We report a rare case of transverse myelitis following vaccination against COVID-19. PATIENT CONCERNS: A 70-year-old male presented with progressive sensorimotor dysfunction of the bilateral lower limbs 7 days after receiving the mRNA-1273 vaccine against COVID-19. Spinal magnetic resonance imaging revealed intramedullary lesions with gadolinium enhancement on the Th1/2 and Th5/6 vertebral levels. Cerebrospinal fluid (CSF) testing showed a mildly increased level of total protein and positive oligoclonal bands (OCB). DIAGNOSIS: The patient was diagnosed with acute transverse myelitis. INTERVENTION: The patient received 5 days of intravenous methylprednisolone pulse (1000 mg/day) followed by oral prednisolone (30 mg/day with gradual tapering). OUTCOMES: The patient fully recovered from muscle weakness of the lower limbs. He was discharged from our hospital and able to independently walk without unsteadiness. LESSON: This is a rare case of transverse myelitis following COVID-19 vaccination. Positive OCB in CSF in the present case highlights the possibility of

autoimmune processes, including polyclonal activation of B lymphocytes, following vaccination.

Hodl, I., et al. (2023). "Altered cellular immune response to vaccination against SARS-CoV-2 in patients suffering from autoimmunity with B-cell depleting therapy." Microbes Infect **25**(4): 105103.

B-cell depleting therapies result in diminished humoral immunity following vaccination against COVID-19, but our understanding on the impact on cellular immune responses is limited. Here, we performed a detailed analysis of cellular immunity following mRNA vaccination in patients receiving B-cell depleting therapy using ELISpot assay and flow cytometry. Anti-SARS-CoV-2 spike receptor-binding domain antibody assays were performed to elucidate B-cell responses. To complement our cellular analysis, we performed immunophenotyping for T- and B-cell subsets. We show that SARS-CoV-2 vaccination using mRNA vaccines elicits cellular T-cell responses in patients under B-cell depleting therapy. Some facets of this immune response including TNFalpha production of CD4(+) T-cells and granzyme B production of CD8(+) T-cells, however, are distinctly diminished in these patients. Consequently, it appears that the finely coordinated process of T-cell activation with a uniform involvement of CD4(+) and CD8(+) T-cells as seen in HCs is disturbed in autoimmune patients. In addition, we observed that immune cell composition does impact cellular immunity as well as sustainability of anti-spike antibody titers. Our data suggest disturbed cellular immunity following mRNA vaccination in patients treated with B-cell depleting therapy. Immune cell composition may be an important determinant for vaccination efficacy.

Hoshina, Y., C. Sowers and V. Baker (2022). "Myasthenia Gravis Presenting after Administration of the mRNA-1273 Vaccine." Eur J Case Rep Intern Med **9**(7): 003439.

The mRNA-1273 SARS-CoV-2 vaccine received emergency use authorization in December 2021. We present a case of myasthenia gravis (MG) which became clinically apparent following vaccination against SARS-CoV-2. A 30-year-old man developed acute onset diplopia, 2 days after receiving his first mRNA-1273 vaccination against SARS-CoV-2. He reported blurred vision with horizontally displaced images, which worsened with increased eye strain. Diplopia resolved when one eye was covered. He also had fatigable arm weakness, but denied dysphagia, dysarthria, dysphonia or dyspnoea. On examination, he had left-sided ptosis and esotropia at rest which worsened with sustained upward gaze and prolonged focus. He also had fatigable weakness of neck flexion and extension (4+/5), and generalized, fatigable weakness (4/5). His single-breath count was 38. Cranial nerves, sensory examination and deep tendon reflexes were normal. A 2-min ice-pack test and neostigmine test temporarily improved his diplopia and ptosis. The acetylcholine receptor (AChR) antibody was borderline high and muscle-specific tyrosine kinase (MuSK) antibody was negative. Chest CT and brain MRI with contrast were unremarkable. The patient was diagnosed with MG and oral pyridostigmine and prednisone therapy were initiated. We present a case of newly diagnosed MG after administration of mRNA-1273 vaccination against SARS-CoV-2. Although there has been long-standing discussion regarding the potential for vaccines to

exacerbate autoimmune conditions, data remain sparse and consensus has not been reached. Consequently, this case is important to make providers aware of potential side effects of a novel vaccine, and may also help guide the selection of vaccination candidates and monitoring parameters. LEARNING POINTS: We present a case of newly diagnosed myasthenia gravis after administration of the mRNA-1273 SARS-CoV-2 vaccine.mRNA-1273 vaccination against SARS-CoV-2 may exacerbate subclinical cases of myasthenia gravis.Recognition of new vaccine side effects may guide the selection of vulnerable patients.

Ju, H. J., et al. (2023). "Risk of autoimmune skin and connective tissue disorders after mRNA-based COVID-19 vaccination." J Am Acad Dermatol.

BACKGROUND: Data on the association between the development of autoimmune diseases and COVID-19 vaccination are limited. OBJECTIVE: To investigate the incidence and risk of autoimmune connective tissue disorders following mRNA-based COVID-19 vaccination. METHODS: This nationwide population-based study was conducted in South Korea. Individuals who received vaccination between September 8, 2020-December 31, 2021, were identified. Historical prepandemic controls were matched for age and sex in 1:1 ratio. The incidence rate and risk of disease outcomes were compared. RESULTS: A total of 3,838,120 vaccinated individuals and 3,834,804 controls without evidence of COVID-19 were included. The risk of alopecia areata, alopecia totalis, primary cicatricial alopecia, psoriasis, vitiligo, anti-neutrophil cytoplasmic antibody-associated vasculitis, sarcoidosis, Behcet disease, Crohn disease, ulcerative colitis, rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, Sjogren syndrome, ankylosing spondylitis, dermato/polymyositis, and bullous pemphigoid was not significantly higher in vaccinated individuals than in controls. The risk was comparable according to age, sex, type of mRNA-based vaccine, and cross-vaccination status. LIMITATIONS: Possible selection bias and residual confounders. CONCLUSION: These findings suggest that most autoimmune connective tissue disorders are not associated with a significant increase in risk. However, caution is necessary when interpreting results for rare outcomes due to limited statistical power.

Kang, S. H., et al. (2022). "Autoimmune Hepatitis Following Vaccination for SARS-CoV-2 in Korea: Coincidence or Autoimmunity?" J Korean Med Sci **37**(15): e116.

Autoimmune hepatitis (AIH) is a chronic, autoimmune disease of the liver that occurs when the body's immune system attacks liver cells, causing the liver to be inflamed. AIH is one of the manifestations of a coronavirus disease 2019 (COVID-19), as well as an adverse event occurring after vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Few cases of AIH have been described after vaccination with two messenger RNA (mRNA)-based vaccines-BTN162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna)-against SARS-CoV-2. Herein, we report a case of AIH occurring after Pfizer-BioNTech COVID-19 vaccine. A 27-year-old female presented with jaundice and hepatomegaly, appearing 14 days after receiving the second dose of Pfizer-BioNTech vaccine. Her laboratory results showed abnormal liver function with high total immunoglobulin G level. She was diagnosed with AIH with histologic finding and

successfully treated with oral prednisolone. We report an AIH case after COVID-19 vaccination in Korea.

Karabulut, K., A. Andronikashvili and A. H. Kapici (2021). "Recurrence of Thrombotic Thrombocytopenic Purpura after mRNA-1273 COVID-19 Vaccine Administered Shortly after COVID-19." Case Rep Hematol **2021**: 4130138.

Thrombotic thrombocytopenic purpura (TTP) is a potentially life-threatening consumptive coagulopathy requiring emergent diagnosis and timely treatment. It is characterized by microangiopathic hemolytic anemia and thrombocytopenia with the development of microthrombi caused by inherited or acquired deficiency of the von Willebrand factor-cleaving protease ADAMTS13 and resulting end-organ damage. Most of the cases are the result of acquired deficiency of ADAMTS13, for which the exact etiology is unknown but reported to be related to various autoimmune disorders, infections, and medications. Our case report features of a patient with a history of idiopathic thrombocytopenic purpura and thrombotic thrombocytopenic purpura, who developed a recurrence of TTP 5 days after his first dose of the mRNA Coronavirus disease 2019 (COVID-19) vaccine (mRNA-1273 vaccine) in the setting of recent COVID-19. The close temporal association between vaccine administration, recent COVID-19, and relapse of remitted TTP raises concern for an enhanced immune reaction to COVID-19 vaccine in the setting of recent COVID-19 and underlying autoimmune disease. The association is not absolute, but given the novelty of COVID-19 and the mRNA COVID-19 vaccine and the relapse timing, it leads us to pose this hypothesis. Vaccine distribution to a larger and more diverse population will allow for an increased rate of adverse event reporting. This case report exemplifies potential safety issues that may be encountered with new vaccine administration in patients with recent COVID-19 and underlying autoimmune disease. There are no specific recommendations for COVID-19 vaccine administration in such patients.

Kc, O., et al. (2022). "A Rare Case of Longitudinally Extensive Transverse Myelitis Following Pfizer-BioNTech COVID-19 Vaccination with a Favourable Outcome." Eur J Case Rep Intern Med **9**(9): 003553.

INTRODUCTION: mRNA COVID-19 vaccines are very safe, but rare adverse events such as transverse myelitis have been reported after COVID-19 vaccination. CASE DESCRIPTION: We report the case of 50-year-old man who presented with progressive lower extremity weakness, back pain and urinary retention after his second dose of the Pfizer COVID-19 vaccine. MRI of the spine revealed longitudinally extensive transverse myelitis (LETM). He recovered completely after treatment with intravenous methylprednisone and physical therapy. DISCUSSION: This case highlights the rare association between LETM and COVID-19 vaccines and encourages clinicians to maintain a high index of suspicion for prompt diagnosis and treatment. LEARNING POINTS: Longitudinally extensive transverse myelitis (LETM) is rare adverse events after mRNA COVID-19 vaccination.Clinicians should maintain a high index of suspicion for prompt diagnosis of vaccine-induced transverse myelitis.Vaccine-induced LETM should show marked clinical improvement after appropriate treatment.

Keshavarz, P., et al. (2022). "Myocarditis Following COVID-19 Vaccination: Cardiac Imaging Findings in 118 Studies." Tomography **8**(4): 1959-1973.

We reviewed the reported imaging findings of myocarditis in the literature following COVID-19 vaccination on cardiac imaging by a literature search in online databases, including Scopus, Medline (PubMed), Web of Science, Embase (Elsevier), and Google Scholar. In total, 532 cases of myocarditis after COVID-19 vaccination were reported (462, 86.8% men and 70, 13.2% women, age range 12 to 80) with the following distribution: Pfizer-BioNTech: 367 (69%), Moderna: 137 (25.8%), AstraZeneca: 12 (2.3%), Janssen/Johnson & Johnson: 6 (1.1%), COVAXIN: 1 (0.1%), and unknown mRNA vaccine: 9 (1.7%). The distribution of patients receiving vaccine dosage was investigated. On cardiac MR Imaging, late intravenous gadolinium enhancement (LGE) was observed mainly in the epicardial/subepicardial segments (90.8%, 318 of 350 enhancing segments), with the dominance of inferolateral segment and inferior walls. Pericardial effusion was reported in 13.1% of cases. The vast majority of patients (94%, 500 of 532) were discharged from the hospital except for 4 (0.7%) cases. Post-COVID-19 myocarditis was most commonly reported in symptomatic men after the second or third dose, with CMRI findings including LGE in 90.8% of inferior and inferolateral epicardial/subepicardial segments. Most cases were self-limited.

Kim, K. H., et al. (2022). "Onset of various CNS inflammatory demyelination diseases following COVID-19 vaccinations." Mult Scler Relat Disord **68**: 104141.

BACKGROUND: Since the start of COVID-19 vaccination worldwide, there have been several reports of inflammatory demyelinating diseases of the central nervous system (CNS-IDDs) following vaccination. METHODS: We prospectively collected cases of new-onset CNS-IDDs with a temporal relationship between disease onset and COVID-19 vaccination and investigated their proportion among newly registered cases of CNS-IDD over the past year. RESULTS: Among 117 cases, 10 (8.5%) had their first disease manifestation within one month following COVID-19 vaccination: 2 multiple sclerosis, 2 neuromyelitis optica spectrum disorder, 3 MOG antibody-associated disease, and 3 unclassified CNS-IDDs. CONCLUSION: This observation suggests that COVID-19 vaccination may trigger the onset of various CNS-IDDs in susceptible individuals.

Kobayashi, K., et al. (2023). "Multisystem inflammatory syndrome and lymphohistiocytic myocarditis after Covid-19 vaccine in a middle-aged woman." ESC Heart Fail **10**(2): 1435-1439.

We describe a 51-year-old otherwise healthy woman hospitalized for hypotension, fever, and weakness 4 days after the second-dose Covid-19 mRNA vaccine. Elevated inflammatory markers, natriuretic peptide levels and troponin levels, and slightly reduced left ventricular ejection fraction of 50% were noted. We also found the multiple organ damage, including mucocutaneous, gastrointestinal, and neurologic systems. In addition, we revealed the positive results for anti-nucleocapsid SARS-CoV-2 IgG, albeit negative for SARS-CoV-2 polymerase chain reaction testing, suggesting the prior asymptomatic Covid-19 infection. We finally diagnosed her as multisystem inflammatory syndrome after vaccination. Of note, we obtained myocardial specimen from the

patients and demonstrated the lymphohistiocytic myocarditis, which is a rare form of myocarditis.

Lai, Y. W., et al. (2022). "Autoimmune Rheumatic Disease Flares with Myocarditis Following COVID-19 mRNA Vaccination: A Case-Based Review." Vaccines (Basel) **10**(10).

Since the introduction of coronavirus disease 2019 (COVID-19) messenger ribonucleic acid (mRNA) vaccines, there have been multiple reports of post-vaccination myocarditis (mainly affecting young healthy males). We report on four patients with active autoimmune rheumatic diseases (ARDs) and probable or confirmed myocarditis following COVID-19 mRNA vaccination managed at a tertiary hospital in Singapore; we reviewed the literature on post-COVID-19 mRNA vaccination-related myocarditis and ARD flares. Three patients had existing ARD flares (two had systemic lupus erythematosus (SLE), one had eosinophilic granulomatosis polyangiitis (EGPA)), and one had new-onset EGPA. All patients recovered well after receiving immunosuppressants comprising high-dose glucocorticoids, cyclophosphamide, and rituximab. Thus far, only one case of active SLE with myocarditis has been reported post-COVID-19 mRNA vaccination in the literature. In contrast to isolated post-COVID-19 mRNA vaccination myocarditis, our older-aged patients had myocarditis associated with ARD flares post-COVID-19 vaccination (that occurred after one dose of an mRNA vaccine), associated with other features of ARD flares, and required increased immunosuppression to achieve myocarditis resolution. This case series serves to highlight the differences in clinical and therapeutic aspects in ARD patients, heighten the vigilance of rheumatologists for this development, and encourage the adoption of risk reduction strategies in this vulnerable population.

Lee, H. Y. and W. C. Lien (2023). "Effects of COVID-19 vaccine type on Guillain-Barre syndrome: Two cases and a literature review." Hum Vaccin Immunother **19**(1): 2171231.

Guillain-Barre syndrome (GBS) is a rare but severe complication of COVID-19 vaccination. We report two cases of GBS following vaccination with the adenovirus vector vaccine ChAdOx1 nCoV-19 (Vaxzevria, AstraZeneca) and review the relevant literature. Relevant studies published between December 2020 and May 2022 including 881 patients with GBS were reviewed. GBS incidence and the need for mechanical ventilation were reported at a higher level among patients receiving Vaxzevria (n = 400). However, incidence cannot be accurately estimated from case reports. Thus, the true GBS rates following COVID-19 vaccination should be determined by population-based data.

Lee, M. L. and J. M. P. Bautista (2023). "Guillain-Barre Syndrome Following the Administration of Adenovirus Vector-Based COVID-19 Vaccine." Cureus **15**(7): e42316.

Li, L., et al. (2022). "Effect of Inactivated SARS-CoV-2 Vaccine on Thyroid Function and Autoimmunity Within 28 Days After the Second Dose." Thyroid **32**(9): 1051-1058.

Lo, H. K., et al. (2023). "mRNA-1273 COVID-19 vaccine-induced Steven-Johnson syndrome." QJM **116**(3): 247-249.

Lodato, F., et al. (2021). "An unusual case of acute cholestatic hepatitis after m-RNABNT162b2 (Comirnaty) SARS-CoV-2 vaccine: Coincidence, autoimmunity or drug-related liver injury." J Hepatol **75**(5): 1254-1256.

Lopez Romero-Salazar, F., et al. (2022). "SARS-CoV-2 vaccine, a new autoimmune hepatitis trigger?" Rev Esp Enferm Dig **114**(9): 567-568.

SARS-CoV2 infection and vaccination against this virus have been related to the development of autoimmune diseases. We report a case of autoimmune hepatitis (AIH) after SARS-COV2 vaccine. Male, 76 years old, with a history of hepatic cirrhosis secondary to primary biliary cholangitis (PBC), compensated, treated with ursodeoxycholic acid and obeticholic acid. The patient received the third dose of the SARS-CoV2 vaccine (BioNTech/Pfizer) in December 2021. In subsequent analytical control, the patient presented altered liver test, with elevation of ALT and AST. Ultrasound was performed, without alterations, and viral causes were ruled out. IgG elevation and positive antinuclear antibodies were observed. A liver biopsy was performed, with findings of intense interface and lobular hepatitis and areas of centrilobular necrosis. The inflammation was predominantly lymphoplasmacytic. The patient was diagnosed with AIH and initiated therapy with steroids and azathioprine, currently with an adequate response. AIH is an immune-mediated disease of uncertain etiology. Cases of AIH with SARS-CoV2 vaccination as a possible trigger have recently been published, with characteristics similar to ours. Some of them had a history of autoimmune pathology, such as this case (PBC). Therefore, it is suggested that vaccination can induce the development of autoimmune pathology in patients at risk. Our reported case reinforces the hypothesis of an association between AIH and the SARS-CoV2 vaccine.

Maisch, B. (2023). "SARS-CoV-2, vaccination or autoimmunity as causes of cardiac inflammation. Which form prevails?" Herz **48**(3): 195-205.

The causes of cardiac inflammation during the COVID-19 pandemic are manifold and complex, and may have changed with different virus variants and vaccinations. The underlying viral etiology is self-evident, but its role in the pathogenic process is diverse. The view of many pathologists that myocyte necrosis and cellular infiltrates are indispensable for myocarditis does not suffice and contradicts the clinical criteria of myocarditis, i.e., a combination of serological evidence of necrosis based on troponins or MRI features of necrosis, edema, and inflammation based on prolonged T1 and T2 times and late gadolinium enhancement. The definition of myocarditis is still debated by pathologists and clinicians. We have learned that myocarditis and pericarditis can be induced by the virus via different pathways of action such as direct viral damage to the myocardium through the ACE2 receptor. Indirect damage occurs via immunological effector organs such as the innate immune system by macrophages and cytokines, and then later the acquired immune system via T cells, overactive proinflammatory cytokines, and cardiac autoantibodies. Cardiovascular diseases lead to more severe courses of SARS-CoV-2 disease. Thus, heart failure patients have a double risk for

complicated courses and lethal outcome. So do patients with diabetes, hypertension, and renal insufficiency. Independent of the definition, myocarditis patients benefitted from intensive hospital care, ventilation, if needed, and cortisone treatment. Postvaccination myocarditis and pericarditis affect primarily young male patients after the second RNA vaccine. Both are rare events but severe enough to deserve our full attention, because treatment according to current guidelines is available and necessary.

Martora, F., et al. (2023). "Herpes zoster and alopecia areata following mRNA BNT162b2 COVID-19 vaccine: Controversial immune effects." J Cosmet Dermatol **22**(1): 36-38.

Mathew, M., et al. (2023). "COVID-19 vaccine triggered autoimmune hepatitis: case report." Eur J Hosp Pharm.

May Lee, M., et al. (2022). "Alopecia areata following COVID-19 vaccination: vaccine-induced autoimmunity?" Int J Dermatol **61**(5): 634-635.

McCullough, J., et al. (2022). "Posterior Reversible Encephalopathy Syndrome Onset Within 24 Hours Following Moderna mRNA Booster COVID-19 Vaccination: Vaccine Adverse Event Vs. Hypertension?" Cureus **14**(5): e24919.

We present a case of a female who presented with the acute onset of neurological changes within 24 hours of receiving her third, or booster, dose of the mRNA Moderna (Cambridge, Massachusetts) coronavirus disease 2019 (COVID-19) vaccination. Her clinicoradiological findings were most consistent with posterior reversible encephalopathy syndrome (PRES). Although PRES has been reported with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, this raised suspicion of a possible vaccine-induced PRES with her only confounder being hypertension managed with a beta-blocker. Extensive workup for other entities associated with PRES, including infection, autoimmune, paraneoplastic syndrome, and alcohol were unrevealing. Thus far, there have not been any reports of PRES post mRNA vaccination. We encourage providers to report similar cases with neurological manifestations post mRNA vaccination to the vaccine adverse event reporting system (VAERS). Timely diagnosis and treatment of PRES may help minimize any irreversible neurological sequelae.

McShane, C., et al. (2021). "The mRNA COVID-19 vaccine - A rare trigger of autoimmune hepatitis?" J Hepatol **75**(5): 1252-1254.

Mekritthikrai, K., et al. (2022). "Autoimmune Hepatitis Triggered by COVID-19 Vaccine: The First Case From Inactivated Vaccine." ACG Case Rep J **9**(7): e00811.

We report a case of a 52-year-old woman without previous underlying liver disease, presenting with progressive jaundice and diagnosed with autoimmune hepatitis after 2 doses of an inactivated coronavirus disease 2019 (CoronaVac) vaccine. All serology and histology were compatible with autoimmune hepatitis. Symptoms were improved and liver function tests were normalized after treatment with steroids and azathioprine.

Morita, S., et al. (2023). "Effect of SARS-CoV-2 BNT162b2 mRNA vaccine on thyroid autoimmunity: A twelve-month follow-up study." Front Endocrinol (Lausanne) **14**: 1058007.

OBJECTIVES: Graves' disease (GD) has been highlighted as a possible adverse effect of the respiratory syndrome coronavirus-2 (SARS-CoV-2) vaccine. However, it is unknown if the SARS-CoV-2 vaccine disrupts thyroid autoimmunity. We aimed to present long-term follow-up of thyroid autoimmunity after the SARS-CoV-2 BNT162b2 mRNA vaccine. METHODS: Serum samples collected from seventy Japanese healthcare workers at baseline, 32 weeks after the second dose (pre-third dose), and 4 weeks after the third dose of the vaccine were analyzed. The time courses of anti-SARS-CoV-2 spike immunoglobulin G (IgG) antibody, thyroid-stimulating hormone receptor antibody (TRAb), and thyroid function were evaluated. Anti-thyroglobulin antibodies (TgAb) and anti-thyroid peroxidase antibodies (TPOAb) were additionally evaluated in thirty-three participants. RESULTS: The median age was 50 (IQR, 38-54) years and 69% were female. The median anti-spike IgG antibody titer was 17627 (IQR, 10898-24175) U/mL 4 weeks after the third dose. The mean TRAb was significantly increased from 0.81 (SD, 0.05) IU/L at baseline to 0.97 (SD, 0.30) IU/L 4 weeks after the third dose without functional changes. An increase in TRAb was positively associated with female sex (beta = 0.32, P = 0.008) and low basal FT4 (beta = -0.29, P = 0.02) and FT3 (beta = -0.33, P = 0.004). TgAb was increased by the third dose. Increase in TgAb was associated with history of the thyroid diseases (beta = 0.55, P <0.001). CONCLUSIONS: SARS-CoV-2 BNT162b2 mRNA vaccine can disrupt thyroid autoimmunity. Clinicians should consider the possibility that the SARS-CoV-2 vaccine may disrupt thyroid autoimmunity.

Mungmunpuntipantip, R. and V. Wiwanitkit (2022). "Correspondence on 'COVID-19 vaccine triggered autoimmune hepatitis: case report' by Mathew et al." Eur J Hosp Pharm.

Nakano, H., et al. (2022). "Acute transverse myelitis after BNT162b2 vaccination against COVID-19: Report of a fatal case and review of the literature." J Neurol Sci **434**: 120102.

Parry, P. I., et al. (2023). "'Spikeopathy': COVID-19 Spike Protein Is Pathogenic, from Both Virus and Vaccine mRNA." Biomedicines **11**(8).

The COVID-19 pandemic caused much illness, many deaths, and profound disruption to society. The production of 'safe and effective' vaccines was a key public health target. Sadly, unprecedented high rates of adverse events have overshadowed the benefits. This two-part narrative review presents evidence for the widespread harms of novel product COVID-19 mRNA and adenovectorDNA vaccines and is novel in attempting to provide a thorough overview of harms arising from the new technology in vaccines that relied on human cells producing a foreign antigen that has evidence of pathogenicity. This first paper explores peer-reviewed data counter to the 'safe and effective' narrative attached to these new technologies. Spike protein pathogenicity, termed 'spikeopathy', whether from the SARS-CoV-2 virus or produced by vaccine gene codes, akin to a 'synthetic virus', is increasingly understood in terms of molecular biology and pathophysiology. Pharmacokinetic transfection through body tissues distant from the injection site by lipid-nanoparticles or viral-vector carriers means that 'spikeopathy' can affect many

organs. The inflammatory properties of the nanoparticles used to ferry mRNA; N1-methylpseudouridine employed to prolong synthetic mRNA function; the widespread biodistribution of the mRNA and DNA codes and translated spike proteins, and autoimmunity via human production of foreign proteins, contribute to harmful effects. This paper reviews autoimmune, cardiovascular, neurological, potential oncological effects, and autopsy evidence for spikeopathy. With many gene-based therapeutic technologies planned, a re-evaluation is necessary and timely.

Petr, V., et al. (2023). "First Booster of SARS-COV-2 mRNA Vaccine Is Not Associated With Alloimmunization and Subclinical Injury of Kidney Allograft." Transplantation **107**(2): e62-e64.

Picod, A., et al. (2022). "Immune-mediated thrombotic thrombocytopenic purpura following COVID-19 vaccination." Blood **139**(16): 2565-2569.

Pinazo-Bandera, J. M., et al. (2022). "Acute hepatitis with autoimmune features after COVID-19 vaccine: coincidence or vaccine-induced phenomenon?" Gastroenterol Rep (Oxf) **10**: goac014.

Pomara, C., et al. (2021). "COVID-19 Vaccine and Death: Causality Algorithm According to the WHO Eligibility Diagnosis." Diagnostics (Basel) **11**(6).
The current challenge worldwide is the administration of anti-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccines. Even if rarely, severe vascular adverse reactions temporally related to vaccine administration have induced diffidence in the population at large. In particular, researchers worldwide are focusing on the so-called "thrombosis and thrombocytopenia after COVID-19 vaccination". This study aims to establish a practical workflow to define the relationship between adverse events following immunization (AEFI) and COVID-19 vaccination, following the basic framework of the World Health Organization (WHO). Post-mortem investigation plays a pivotal role to support this causality relationship when death occurs. To demonstrate the usefulness and feasibility of the proposed workflow, we applied it to two exemplificative cases of suspected AEFI following COVID-19 vaccination. Based on the proposed model, we took into consideration any possible causality relationship between COVID-19 vaccine administration and AEFI. This led us to conclude that vaccination with ChAdOx1 nCov-19 may cause the rare development of immune thrombocytopenia mediated by platelet-activating antibodies against platelet factor 4 (PF4), which clinically mimics heparin-induced autoimmune thrombocytopenia. We suggest the adoption of the proposed methodology in order to confirm or rule out a causal relationship between vaccination and the occurrence of AEFI.

Reddy, S., S. Reddy and M. Arora (2021). "A Case of Postural Orthostatic Tachycardia Syndrome Secondary to the Messenger RNA COVID-19 Vaccine." Cureus **13**(5): e14837.
Postural orthostatic tachycardia syndrome (POTS) is an impaction of the autonomic nervous system initiating orthostatic tachycardia. There are numerous triggers for POTS including viruses, vaccines, and an autoimmune basis. This case report is clinically relevant to better understand the pathophysiology behind the messenger RNA (mRNA)

coronavirus disease 2019 (COVID-19) vaccine and the mechanism that triggers autonomic nervous system dysfunction. Furthermore, the overall goal of this case study is to report a unique side effect associated with the novel mRNA COVID-19 vaccine. A 42-year-old male, with no prior symptoms of sinus tachycardia and presyncope episodes, is diagnosed with POTS secondary to the first dose of the mRNA COVID-19 vaccine. Symptoms to this date include sinus tachycardia, dizziness, headaches, and fatigue that are often triggered after a large meal or standing for a longer duration. Numerous diagnostic tests and images failed to confirm any other diagnosis other than POTS. There was a sequential connection between the onset of symptoms approximately one week after taking the first dose of the mRNA COVID-19 vaccine. Currently, POTS in this patient is controlled by lifestyle modification. This case report has broader implications as it can help us understand how the mRNA vaccine works on the body relative to the immune system. Our theory is that the development of antibodies activates an autoimmune reaction that triggers POTS disease. The prevalence of the POTS dysautonomia post-vaccination will be clearer as more data and research are conducted on the side effects from the innovative mRNA vaccines created to combat severe acute respiratory syndrome coronavirus 2.

Rivera-Tenorio, A., et al. (2022). "Drug-induced liver injury after covid-19 mRNA vaccine: case report." Colomb Med (Cali) **53**(3): e5005187.

CASE DESCRIPTION: A 22-year-old female patient received the first dose of Pfizer-BioNTech vaccine (RNAm) against COVID-19; 6 days later, she presented abdominal pain located in the right hypochondrium and epigastrium, associated with emetic episodes. Re-consultation 21 days later due to the same symptoms; three days after the second dose of the vaccine was administered. CLINICAL FINDINGS: Pain on palpation in the right hypochondrium. Laboratories reported hepatocellular lesion and cholestasis, with negative amylase, hepatotropic virus and autoimmune hepatitis tests. Liver and biliary tract ultrasound and cholangioresonance were normal. TREATMENT AND RESULTS: Hyoscine and intravenous fluids as support therapy. She presented improvement in abdominal pain and progressive decrease of transaminases and bilirubin levels until normalization, and was discharged on the fifth day of hospitalization. A drug-associated hepatotoxicity (DILI) diagnosis was considered probable, in this case, secondary to vaccination against COVID-19. CLINICAL RELEVANCE: The current SARS CoV-2 pandemic has spurred the development of new vaccines, the safety of which remains a concern. There is a likely causal relationship between vaccination and liver involvement in this clinical case, rather than simply a sporadic occurrence.

Root-Bernstein, R. (2021). "COVID-19 coagulopathies: Human blood proteins mimic SARS-CoV-2 virus, vaccine proteins and bacterial co-infections inducing autoimmunity: Combinations of bacteria and SARS-CoV-2 synergize to induce autoantibodies targeting cardiolipin, cardiolipin-binding proteins, platelet factor 4, prothrombin, and coagulation factors." Bioessays **43**(12): e2100158.

Severe COVID-19 is often accompanied by coagulopathies such as thrombocytopenia and abnormal clotting. Rarely, such complications follow SARS-CoV-2 vaccination. The

cause of these coagulopathies is unknown. It is hypothesized that coagulopathies accompanying SARS-CoV-2 infections and vaccinations result from bacterial co-infections that synergize with virus-induced autoimmunity due to antigenic mimicry of blood proteins by both bacterial and viral antigens. Coagulopathies occur mainly in severe COVID-19 characterized by bacterial co-infections with Streptococci, Staphylococci, Klebsiella, Escherichia coli, and Acinetobacter baumannii. These bacteria express unusually large numbers of antigens mimicking human blood antigens, as do both SARS-CoV-2 and adenoviruses. Bacteria mimic cardiolipin, prothrombin, albumin, and platelet factor 4 (PF4). SARS-CoV-2 mimics complement factors, Rh antigens, platelet phosphodiesterases, Factors IX and X, von Willebrand Factor (VWF), and VWF protease ADAMTS13. Adenoviruses mimic prothrombin and platelet factor 4. Bacterial prophylaxis, avoidance of vaccinating bacterially infected individuals, and antigen deletion for vaccines may reduce coagulopathy risk. Also see the video abstract here: https://youtu.be/zWDOsghrPg8.

Roy, A., et al. (2022). "Immune-mediated liver injury following COVID-19 vaccination: A systematic review." Hepatol Commun **6**(9): 2513-2522.

Immune-mediated liver injury (ILI) following coronavirus disease 2019 (COVID-19) vaccination is not well-characterized. Therefore, we systematically reviewed the literature on ILI after COVID-19 vaccination. We searched PubMed, Cochrane, Ovid, Embase, and gray literature to include articles describing ILI following COVID-19 vaccination. Reports without confirmatory evidence from liver biopsy were excluded. Descriptive analysis, and study quality were reported as appropriate. Of the 1,048 articles found, 13 (good/fair quality; 23 patients) were included. Studies were primarily from Europe (n = 8), America (n = 2), Asia (n = 2), or Australia (n = 1). Patients were predominantly females (62.5%) of age 55.3 years (49.1-61.4), with an antecedent exposure to Moderna messenger RNA (mRNA)-1273 (47.8%), Pfizer-BioNTech BNT162b2 mRNA (39.2%), or ChAdOx1 nCoV-19 vaccine (13%). Pre-existing comorbidities (69.6%) were common, including liver disease in 26.1% and thyroid disorders in 13% of patients. About two-thirds of the patients were on concurrent medications (paracetamol, levothyroxine, statins, and non-steroidal anti-inflammatory drugs). Jaundice was the most common symptom (78.3%). Peak bilirubin, alanine aminotransferase, and alkaline phosphatase levels were 10.8 (6.8-14.8) mg/dl, 1,106.5 (757.0-1,702.5) U/L, and 229 (174.6-259.6) U/L, respectively. Histological findings were intense portal lymphoplasmacytic infiltrate with interface hepatitis. Steroids were used in 86.9% of patients, and complete response, recovering course, and death were reported in 56.5%, 39.1%, and 4.3% of patients, respectively. ILI following COVID-19 vaccination is rare. The diagnosis is established on temporal correlation, biochemical findings, and histopathology. Prognosis is excellent with corticosteroids. Causality establishment remains a challenge.

Ruggeri, R. M., L. Giovanellla and A. Campenni (2022). "SARS-CoV-2 vaccine may trigger thyroid autoimmunity: real-life experience and review of the literature." J Endocrinol Invest **45**(12): 2283-2289.

PURPOSE: SARS-CoV-2 infection can be associated with destructive thyroiditis and triggers thyroid autoimmunity. More recent evidence suggests that SARS-CoV-2 vaccines may also be associated with permanent or transient thyroid dysfunction in susceptible individuals. METHODS: We observed three patients who developed/exacerbated autoimmune thyroid diseases (AITDs) shortly after receiving mRNA-based vaccines against SARS-CoV2. Clinical histories are reported, and relevant literature in the field is summarized. RESULTS: Our case series gives a description of the full spectrum of autoimmune disorders that may occur after SARS-CoV-2 vaccines administration, ranging from a case of new-onset Graves' disease to autoimmune hypothyroidism in two patients with pre-existing AITDs. Our three patients had a personal and/or family history of autoimmune disorders, suggesting that genetic predisposition is an important risk factor for the development of AITDs following vaccination. Moreover, our real-life experience demonstrates that persistent hypothyroidism may occur in the long run and should be overlooked; subjects with a previous AITDs are at risk of developing it. Reviewing the pertinent literature up to date Graves' disease is the most common vaccine-related AITDs with up to 51 cases reported in the literature, occurring mainly in female patients with no personal history of AIDTs, while only a case of autoimmune hypothyroidism has been reported so far. CONCLUSIONS: SARS-CoV-2 vaccines can trigger autoimmune reactions and the present case series contributes to make clinicians aware of full spectrum of AITDs that may occur following vaccination. Thyroid function monitoring is recommended, mainly in subjects with a personal/family history of AITDs.

Saeed, S., et al. (2023). "Case Report: A case of multisystem inflammatory syndrome in an 11-year-old female after COVID-19 inactivated vaccine." Front Pediatr **11**: 1068301.

BACKGROUND: Multisystem inflammatory syndrome in children (MIS-C), also known as pediatric inflammatory, multisystem syndrome temporally associated with SARS-CoV-2, is a rare but serious complication of SARS-CoV-2 infection in children that typically occurs 2-6 weeks after SARS-CoV-2 infection. The pathophysiology of MIS-C is unknown. MIS-C, first recognized in April 2020, is characterized by fever, systemic inflammation, and multi-system organ involvement. Post-vaccination adverse effects have increased with COVID-19 vaccinations, and MIS linked to immunization with COVID-19 vaccines has also been observed. CASE REPORT: An 11-year-old Chinese girl presented with a high-grade fever, rash, and dry cough for 2 days. She had her 2nd SARS-CoV-2 inactivated vaccination dose five days before hospital admission. On day 3 & 4, she experienced bilateral conjunctivitis, hypotension (66/47 mmHg), and a high CRP level. She was diagnosed with MIS-C. The patient's condition deteriorated rapidly, necessitating intensive care unit admission. The patient's symptoms improved after intravenous immunoglobulin, methylprednisolone, and oral aspirin therapy. She was discharged from the hospital after 16 days as her general condition, and laboratory biomarkers returned to normal. CONCLUSION: Inactivated Covid-19 vaccination might trigger MIS-C. Further research is needed to evaluate whether a correlation exists between COVID-19 vaccination and MIS-C development.

Safary, A., et al. (2023). "SARS-CoV-2 vaccine-triggered autoimmunity: Molecular mimicry and/or bystander activation of the immune system." Bioimpacts **13**(4): 269-273.

Induced autoimmunity or autoinflammatory-like conditions as a rare vaccine-related adverse event have been reported following COVID-19 vaccination. Such inadvertent adverse reactions have raised somewhat concerns about the long-term safety of the developed vaccines. Such multifactorial phenomena may be related to the cross-reactivity between the viral-specific antigens with the host self-proteins through molecular mimicry mechanism and/or nonspecific bystander activation of the non-target antigen-independent immunity by the entities of the vaccine products. However, due to the low incidence of the reported/identified individuals and insufficient evidence, autoimmunity following the COVID-19 vaccination has not been approved. Thereby, it seems that further designated studies might warrant post-monitoring of the inevitable adverse immunologic reactions in the vaccinated individuals, especially among hypersensitive cases, to address possible immunological mechanisms induced by the viral vaccines, incorporated adjuvants, and even vaccine delivery systems.

Saluja, P., et al. (2022). "Thrombotic thrombocytopenic purpura (TTP) after COVID-19 vaccination: A systematic review of reported cases." Thromb Res **214**: 115-121.

INTRODUCTION: With the advent of COVID-19 vaccines, hospitalization rates and progression to severe COVID-19 disease have reduced drastically. Most of the adverse events reported by the vaccine recipients were minor. However, autoimmune hematological complications such as vaccine-induced immune thrombotic thrombocytopenia (VITT), immune thrombocytopenic purpura (ITP) and TTP have also been reported post-COVID-19 vaccination. Given this, we sought to reflect on the existing cases of TTP, whether de novo or relapsing, reported after COVID-19 vaccination to further gain insight into any association, if present, and outcomes. METHODS: We searched PubMed, Embase, and Ebsco databases for published individual case reports on the occurrence or relapse of TTP after receiving any COVID-19 vaccine. A total of 23 articles (27 patients) were included in this qualitative analysis. RESULTS: The mean age for the patients who developed de novo TTP post-COVID-19 vaccination was 51.3 years. TTP episodes were seen mostly after BNT162b2 vaccine, followed by mRNA-1273 vaccine. All patients with immune TTP except one received plasma exchange (PLEX) and steroids. One patient passed away after two days of hospitalization, likely due to a sudden cardiovascular event. CONCLUSION: Our review underscores the importance of in-depth anamnesis before vaccination and outlines characteristics of predisposed individuals. Evaluation of post-vaccine thrombocytopenia must include the possibility of TTP given the associated fatality with this condition.

Salunkhe, M., et al. (2023). "Spectrum of various CNS inflammatory demyelination diseases following COVID-19 vaccinations." Acta Neurol Belg.

BACKGROUND AND PURPOSE: Although rare, neurological adverse events have been reported post-COVID-19 vaccination. This study reports 16 patients diagnosed with CNS inflammatory demyelinating diseases (CNS-IDD) within 6 weeks of COVID-19 vaccine administration. METHODOLOGY: A prospective observational study was conducted from

June 2021 to May 2022. All patients were diagnosed according to the latest international guidelines with CNS-IDD within 6 weeks of COVID-19 vaccine exposure. Data regarding the demographic profile, clinical features, type of COVID-19 vaccination, radiological findings and occurrence of symptoms were noted and further analysed using descriptive statistics. RESULTS: We reported 16 cases (median age 40 years) of CNS demyelination: fourteen occurred in temporal association with ChAdOx1-S vaccine and two in association with BBV152 vaccine. Median time duration of presenting symptoms after vaccination was 19 days (3-40 days). The most common presentation was myelitis (7/16 patients), followed by optic neuritis (6/16 patients). Demyelination events were reported after first and second dose in thirteen and five patients respectively, although two patients reported such events after both vaccine dosages. Myelin oligodendrocyte glycoprotein (MOG) IgG antibodies were positive in eight patients. Tumefactive demyelination was seen in four patients. Management included high-dose methylprednisolone, PLEX, IVIG or a combination of those, with a favourable outcome in the majority of cases. CONCLUSION: Although a rare event, awareness regarding potential demyelinating episodes post-COVID-19 vaccination can help in early diagnosis. The presence of increased MOG-IgG antibodies with temporal association in post-COVID vaccine patients raises a possibility of an immunogenic phenomenon leading to demyelinating disorders.

Schinas, G., et al. (2023). "Immune-mediated liver injury following COVID-19 vaccination." World J Virol **12**(2): 100-108.

Liver injury secondary to vaccination is a rare adverse event that has recently come under attention thanks to the continuous pharmacovigilance following the widespread implementation of coronavirus disease 2019 (COVID-19) vaccination protocols. All three most widely distributed severe acute respiratory syndrome coronavirus 2 vaccine formulations, e.g., BNT162b2, mRNA-1273, and ChAdOx1-S, can induce liver injury that may involve immune-mediated pathways and result in autoimmune hepatitis-like presentation that may require therapeutic intervention in the form of corticosteroid administration. Various mechanisms have been proposed in an attempt to highlight immune checkpoint inhibition and thus establish causality with vaccination. The autoimmune features of such a reaction also prompt an in-depth investigation of the newly employed vaccine technologies. Novel vaccine delivery platforms, e.g., mRNA-containing lipid nanoparticles and adenoviral vectors, contribute to the inflammatory background that leads to an exaggerated immune response, while patterns of molecular mimicry between the spike (S) protein and prominent liver antigens may account for the autoimmune presentation. Immune mediators triggered by vaccination or vaccine ingredients per se, including autoreactive antibodies, cytokines, and cytotoxic T-cell populations, may inflict hepatocellular damage through well-established pathways. We aim to review available data associated with immune-mediated liver injury associated with COVID-19 vaccination and elucidate potential mechanisms underlying its pathogenesis.

Schmitt, P., et al. (2021). "Acute Myocarditis after COVID-19 vaccination: A case report." Rev Med Interne **42**(11): 797-800.

INTRODUCTION: The etiology of myocarditis often remains undetermined. A large variety of infectious agents, systemic diseases, drugs, and toxins can cause the disease. We report the case of a 19-year-old man who developed myocarditis three days after Pfizer-BioNTech COVID-19 booster vaccination. CASE REPORT: A 19-year-old man, presenting with troponin-positive acute chest pain, was referred to our department. He had received the Pfizer-BioNTech COVID-19 vaccine three days prior to his admission. The diagnosis of acute myocarditis was confirmed by cardiovascular magnetic resonance imaging. Patient hemodynamic status remained stable during hospitalization. The left ventricular ejection fraction was preserved during hospital stay and at one-month follow-up. We found no evidence for another infectious or autoimmune etiology. CONCLUSION: Although imputability of the vaccine cannot be formally established on the basis of this case report, the findings raise the possibility of an association between mRNA COVID-19 vaccination and acute myocarditis.

Shahrani, S., et al. (2022). "Autoimmune hepatitis (AIH) following coronavirus (COVID-19) vaccine-No longer exclusive to mRNA vaccine?" Liver Int **42**(10): 2344-2345.

Shirah, B., I. Mulla and Y. Aladdin (2023). "Optic Neuritis Following the BNT162b2 mRNA COVID-19 Vaccine in a Patient with Systemic Lupus Erythematosus Uncovering the Diagnosis of Neuromyelitis Optica Spectrum Disorders." Ocul Immunol Inflamm **31**(6): 1213-1215.

COVID-19 vaccinations have been given worldwide to save the lives of millions. However, several complications following different types of COVID-19 vaccinations were reported previously in the literature. Previous articles have reported multiple ocular complications following different types of COVID-19 vaccinations. In this article, we report a unique case in which the diagnosis of neuromyelitis optica spectrum disorders (NMOSD) was unveiled following vaccination with BNT162b2 mRNA COVID-19 vaccine and manifesting as acute optic neuritis in a patient with systemic lupus erythematosus (SLE). The temporal association of acute optic neuritis after receiving the BNT162b2 mRNA COVID-19 vaccine along with the serological evidence of NMOSD support this theory. The risk of triggering an occult autoimmune disorder in patients with an overactive immune system such as this patient should be studied to calibrate the benefits and risks of vaccination against COVID-19. Screening for aquaporin-4 antibodies in patients with SLE prior to vaccination against COVID-19 may be considered to prevent potentially devastating neurological disability in patients with premorbid occult NMOSD.

Shouman, K., et al. (2021). "Autonomic dysfunction following COVID-19 infection: an early experience." Clin Auton Res **31**(3): 385-394.

PURPOSE: Post-COVID-19 syndrome is a poorly understood aspect of the current pandemic, with clinical features that overlap with symptoms of autonomic/small fiber dysfunction. An early systematic analysis of autonomic dysfunction following COVID-19 is lacking and may provide initial insights into the spectrum of this condition. METHODS: We conducted a retrospective review of all patients with confirmed history of COVID-19

infection referred for autonomic testing for symptoms concerning for para-/postinfectious autonomic dysfunction at Mayo Clinic Rochester or Jacksonville between March 2020 and January 2021. RESULTS: We identified 27 patients fulfilling the search criteria. Symptoms developed between 0 and 122 days following the acute infection and included lightheadedness (93%), orthostatic headache (22%), syncope (11%), hyperhidrosis (11%), and burning pain (11%). Sudomotor function was abnormal in 36%, cardiovagal function in 27%, and cardiovascular adrenergic function in 7%. The most common clinical scenario was orthostatic symptoms without tachycardia or hypotension (41%); 22% of patients fulfilled the criteria for postural tachycardia syndrome (POTS), and 11% had borderline findings to support orthostatic intolerance. One patient each was diagnosed with autoimmune autonomic ganglionopathy, inappropriate sinus tachycardia, vasodepressor syncope, cough/vasovagal syncope, exacerbation of preexisting orthostatic hypotension, exacerbation of sensory and autonomic neuropathy, and exacerbation of small fiber neuropathy. CONCLUSION: Abnormalities on autonomic testing were seen in the majority of patients but were mild in most cases. The most common finding was orthostatic intolerance, often without objective hemodynamic abnormalities on testing. Unmasking/exacerbation of preexisting conditions was seen. The temporal association between infection and autonomic symptoms implies a causal relationship, which however cannot be proven by this study.

Sogbe, M., et al. (2023). "Systemic lupus erythematosus myocarditis after COVID-19 vaccination." Reumatol Clin (Engl Ed) **19**(2): 114-116.

INTRODUCTION: Cases of acute myocarditis have been after administration of the BNT162b2 and Ad26.COV2.S vaccine. OBJECTIVE: Describe another possible mechanism of myocarditis after COVID-19 vaccination. CASE PRESENTATION: We describe the clinical case of a 72-year-old female with pleuritic chest pain one week after the third of the BNT162b2 mRNA vaccine. Serological tests for cardiotropic pathogens were negative, and autoimmunity screening was positive with anti-nuclear antibody (ANA) in 1:160 dilution, Anti-double-stranded DNA (anti-dsDNA), and anti-histone antibodies. (18)F-fluoro-deoxy-glucose (FDG) positron emission tomography/computed tomography (PET/CT) showed a focal myocardial and pericardial inflammatory process in the cardiac apex. RESULTS AND DISCUSSION: Systemic lupus erythematosus (SLE) diagnosis was made with myocardial affection. As far as we know, this is the first report of a case of lupus myocarditis after the COVID-19 vaccine. CONCLUSION: Given the pathogenic rationales, the association between SLE and myocarditis should be considered.

Sookaromdee, P. and V. Wiwanitkit (2022). "COVID-19 vaccine and autoimmune hepatitis." Rev Esp Enferm Dig **114**(10): 631.

We would like to correspond and share ideas on the publication "SARS-CoV-2 vaccine, a new autoimmune hepatitis trigger?." Lopez Romero-Salazar reported a case of autoimmune hepatitis (AIH) after receiving SARS-COV2 vaccine. Lopez Romero-Salazar et al noted that "vaccination can induce the development of autoimmune pathology in patients at risk." The possibility of a link between AIH and the SARS-CoV2 vaccine is explored. We agree that the COVID-19 vaccination has the potential to create clinical

problems. The aberrant immune response could lead to a variety of health issues, including hepatitis. The vaccine recipient in this case had hepatitis, but there is no information about his or her health or liver function prior to inoculation. Other probable causes of hepatitis should be considered.

Sprow, G., et al. (2022). "Autoimmune Skin Disease Exacerbations Following COVID-19 Vaccination." Front Immunol **13**: 899526.

BACKGROUND: Vaccination against COVID-19 reduces the risk of severe COVID-19 disease and death. However, few studies have examined the safety of the COVID-19 vaccine in patients with autoimmune skin disease. OBJECTIVES: We sought to determine the incidence of disease exacerbation in this population following COVID-19 vaccination as well as the associated factors. METHODS: We performed a chart review of all patients seen in the autoimmune skin disease clinic of the principal investigator during the study period. All patients included for analysis were systematically and prospectively asked about COVID-19 vaccination status, manufacturers, vaccine dates, autoimmune symptoms after the vaccine, and timing of symptom onset using a standardized template as part of their visit. Demographics and autoimmune disease diagnosis were also collected. Analysis used Chi-square and Fisher's exact tests. RESULTS: 402 subjects were included for analysis. 85.6% of patients were fully vaccinated, with 12.9% unvaccinated and 1.5% partially vaccinated. 14.8% of fully vaccinated patients reported worsening autoimmune signs and symptoms after the vaccine. Fully vaccinated dermatomyositis patients were more likely to report worsening autoimmune signs and symptoms after the vaccine (22.7%) than fully vaccinated lupus erythematosus patients (8.6%) (p=0.009). Patients fully vaccinated with the Moderna vaccine trended towards an increased likelihood of reporting worsening autoimmune signs and symptoms after the vaccine (19.1%) than those with the Pfizer-BioNTech vaccine (12.0%) (p=0.076). Of the patients who had autoimmune symptoms after vaccination, 20% had symptoms after the 1st dose, 82% after the 2nd dose, and 4% after the 3rd dose with median onset (95% confidence interval) of 7 (2,14), 14 (14,21), and 18 (7,28) days later, respectively. CONCLUSIONS: More fully vaccinated dermatomyositis patients had exacerbation of autoimmune signs and symptoms after the vaccine than fully vaccinated lupus erythematosus patients. However, given the risks of COVID-19, clinicians should still promote vaccination in most patients with autoimmune skin disease.

Sumantri, S., M. A. Haryanto and E. S. A. Widyastuti (2023). "Risk of adverse events following CoronaVac's COVID-19 vaccination in women with and without autoimmunity." Clin Epidemiol Glob Health **20**: 101249.

INTRODUCTION: Adverse Events Following Immunization (AEFI) of the COVID-19 vaccine is one of the important considerations, especially in patients with autoimmunity. This study aims to compare the number of CoronaVac AEFIs in women with and without autoimmunity. METHODOLOGY: This is a retrospective cohort study with an unpaired comparative analytic design with a retrospective cohort method. We recruited 602 volunteers, 182 women with autoimmunity and 420 without autoimmunity. We included women who received the CoronaVac vaccine, aged 17-65 years. Data were analyzed

using the chi-square or fisher exact method as an alternative. RESULTS: We found a generally increased risk for AEFI in women with autoimmunity (RR = 1.179; 95% CI 1.059-1.313; p = 0.007) compared to women without autoimmunity, especially for systemic (RR = 1.1271; 95% CI 1.045-1.545; p = 0.025), allergic (RR = 2.052; 95% CI 1.070-3.932; p = 0.045), fever (RR = 2.163 95%; CI 1.093-4.282; p = 0.039), fatigue (RR = 2.182 95%; CI 1.558-3.056; p = 0.001), and headache (RR = 1.619 95%; CI 1.164-2.251; p = 0.006). On the other hand, we found no increased risk for the overall severity of AEFI (RR = 0.851 95% CI; 0.655-1.105; p = 0.256). We also found a relapse of autoimmune condition in 10.4% (n = 19) after CoronaVac vaccination. CONCLUSIONS: There is an increased risk of AEFI after CoronaVac vaccination in women with autoimmunity compared to those without the condition. Although the severity of AEFIs and risk of autoimmune relapse were relatively low.

Swierkot, J., et al. (2022). "The Risk of Autoimmunity Development following mRNA COVID-19 Vaccination." Viruses **14**(12).

The broad spectrum of interactions between autoimmune diseases and the SARS-CoV-2 vaccination is not fully understood. This study aims to evaluate the prevalence of anti-nuclear antibodies (ANA), anti-ENA, anticardiolipin antibodies (ACL), and anti-beta-2 glycoprotein I antibodies (anti-beta2GPI) before and after the SARS-CoV-2 mRNA vaccination in a real-life setting in healthcare professionals. The identification of risk factors associated with vaccine immunogenicity was evaluated. The study group consisted of employees of two hospitals (354 individuals). Samples for antibody assays were collected before vaccination and at 7-9 months after complete immunisation. There was no significant increase in the prevalence of ANA, ACL or anti-beta2GPI antibodies, or autoimmune diseases in subjects who were vaccinated 7-9 months after complete immunisation. In terms of detected anti-ENA, the anti-DFS70 antibodies were found in 6 times more subjects than before vaccination at the second blood draw (in 18 and 3 subjects, respectively) (p = 0.001). There were no significant relationships between a SARS-CoV-2 infection history, humoral response, cellular response, subject category, smoking, sex, body weight, ANA, anti-ENA, ACL, or anti-beta2GPI. This study revealed a possible association between the severity of vaccine adverse events (VAEs) and ANA titre. Individuals with more severe VAEs (>10 points) after the second dose of the vaccine had significantly higher ANA titre after complete immunization. When analysing the significance of time between the ANA, anti-ENA, ACL, and anti- beta2GPI assays and complete immunisation antibody values, no qualitative result was statistically significant. There was correlation between the time since complete immunization and ANA after.

Tagliaferri, A. R., et al. (2021). "A Case of COVID-19 Vaccine Causing a Myasthenia Gravis Crisis." Cureus **13**(6): e15581.

Myasthenia gravis is a rare disease of the neuromuscular junction subsequently affecting the bulbar, respiratory, and extremity skeletal muscles. It is an autoimmune disease in which antibodies target the acetylcholine receptor (AChR), preventing transmission of the excitatory cascade during muscle contraction. Myasthenia gravis is typically well controlled using acetylcholinesterase inhibitors, steroids, immunosuppressant agents,

and/or thymectomies. However, exacerbations can be induced by infection or medications. This is particularly important during the coronavirus disease 2019 (COVID-19) pandemic in which myasthenia gravis patients have been known to have poorer outcomes. We report a very rare presentation of a myasthenia gravis crisis induced by the Moderna COVID-19 vaccine.

Trontzas, I. P., et al. (2022). "Vaccine-Related Autoimmune Hepatitis: Emerging Association with SARS-CoV-2 Vaccination or Coincidence?" Vaccines (Basel) **10**(12).

BACKGROUND: There is an increasing number of liver injury cases resembling autoimmune hepatitis (AIH) following SARS-CoV-2 vaccination; however, an association has not yet been established. METHODS/MATERIALS: A literature review was performed to identify articles regarding the association of AIH with vaccination, emphasizing on SARS-CoV-2 vaccines, and the proposed mechanisms. We then performed a literature search for AIH-like cases following SARS-CoV-2 vaccination, and we evaluated the included cases for AIH diagnosis using simplified diagnostic criteria (SDC), and for vaccination causality using the Naranjo score for adverse drug reactions. RESULTS: We identified 51 AIH-like cases following SARS-CoV-2 vaccination. Forty cases (80%) were characterized as "probable", "at least probable", or "definite" for AIH diagnosis according to SDC. Forty cases (78.4%) were characterized as "probable", four (7.8%) as "possible", and three (5.8%) as "definite" for vaccine-related AIH according to the Naranjo score. CONCLUSION: SARS-CoV-2 vaccine-related AIH carries several phenotypes and, although most cases resolve, immunosuppressive therapy seems to be necessary. Early diagnosis is mandatory and should be considered in any patient with acute or chronic hepatitis after SARS-CoV-2 vaccination, especially in those with pre-existing liver disease.

Tsai, T. F. and C. Y. Ng (2023). "COVID-19 vaccine-associated vitiligo: A cross-sectional study in a tertiary referral center and systematic review." J Dermatol **50**(8): 982-989.

As the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus continues to infect patients globally, vaccination remains one of the primary methods to combat this prolonged pandemic. However, there are growing reports of coronavirus disease 2019 (COVID-19) vaccines possibly triggering autoimmunity, irrespective of the vaccine's design. This phenomenon has been observed in patients with vitiligo, with a rising number of cases reporting new-onset or worsening vitiligo following COVID-19 vaccinations. In this study, the authors present the most extensive case series of COVID-19 vaccine-associated vitiligo to date, along with a systematic review of the literature. The aim is to assist physicians in the clinical evaluation of patients with vitiligo with regard to future vaccinations.

Tv, P., et al. (2023). "Postural orthostatic tachycardia syndrome-like symptoms following COVID-19 vaccination: An overview of clinical literature." Hum Antibodies **31**(1-2): 9-17.

BACKGROUND: Postural Orthostatic Tachycardia Syndrome (POTS) is a common condition affecting more than 170 people per 100,000 population. However, POTS following COVID-19 vaccination remains a rare reporting in the medical literature.

OBJECTIVE: We, herein, summarize and highlight the evidence that has been reported regarding POTS-like symptoms following COVID-19 vaccination. METHODS: We conducted a literature search and summarized the findings in the form of a narrative commentary. All types of publications (case reports/series, original articles, letters to editors, brief communications etc.) in English language were included. RESULTS: Whilst the exact pathogenetic mechanism behind POTS is yet to elucidated, there has been increasing evidence pointing towards an autoimmune dysfunction. Females were found to be predominantly affected (72%) with age range from 17 years to 52 years. Additionally, it seems that POTS-like symptoms could be triggered after immunization with Pfizer- BioNTech, Moderna, and Oxford-AstraZeneca COVID-19 vaccines. The symptoms typically appear within the first week, depending upon previous exposure to the virus and presence of other systemic conditions. In some patients, the condition is self-resolving. However, in others, non-pharmacological interventions coupled with negative ionotropic medications can be used for symptomatic management of the patients. CONCLUSIONS: Timely diagnosis and proper treatment are quintessential for ensuring early alleviation (and in some cases complete resolution) of symptoms. Furthermore, there may be episodes of relapse. Overall prognosis of the new-onset POTS-like symptoms is difficult to predict based on current literature.

Zarafshani, M., et al. (2023). "IgM nephropathy in a patient with dermatomyositis following COVID-19 vaccination: A case report." Int J Rheum Dis.

BACKGROUND: Dermatomyositis (DM) is a systemic autoimmune disease characterized by distinct skin lesions and a clinically heterogeneous constellation of systemic manifestations. This disease poses a challenge to clinicians because of its rarity, diverse clinical presentations, and variable organ involvement, resulting from an autoimmune attack on affected organs, which could be triggered by environmental factors in genetically susceptible individuals. Renal involvement is rare, with immunoglobulin M (IgM) nephropathy yet to be reported in patients with DM. CASE PRESENTATION: A 38-year-old man was admitted to Shariati Hospital, affiliated with Tehran University of Medical Sciences, with proximal weakness of the upper and lower extremities that had developed in the preceding month after receiving the Sinopharm COVID-19 vaccine. The patient was diagnosed with DM based on the heliotrope rash, Gottron's papules, progressive proximal muscle weakness, and paraclinical findings. IgM nephropathy developed subsequently, diagnosed by light and immunofluorescence microscopy. CONCLUSION: We describe the first case of IgM nephropathy in a DM patient following COVID-19 vaccination. This phenomenon requires further investigation into the possible crosslinks between the pathogenesis of IgM nephropathy with DM and the COVID-19 vaccine. Diagnosing renal complications in DM patients promptly and accurately can help to achieve the best outcomes.

Zhou, H. and Q. Ye (2023). "Clinical Features of COVID-19 Vaccine-Associated Autoimmune Hepatitis: A Systematic Review." Diseases **11**(2).

Autoimmune hepatitis (AIH) is an inflammatory liver disease wherein the body's immune system instigates an attack on the liver, causing inflammation and hepatic impairment.

This disease usually manifests in genetically predisposed individuals and is triggered by stimuli or environments such as viral infections, environmental toxins, and drugs. The causal role of COVID-19 vaccination in AIH remains uncertain. This review of 39 cases of vaccine-related AIH indicates that female patients above the age of 50 years or those with potential AIH risk factors may be susceptible to vaccine-related AIH, and the clinical features of vaccine-associated AIH are similar to those of idiopathic AIH. These features commonly manifest in patients after the first dose of vaccination, with symptom onset typically delayed by 10-14 days. The incidence of underlying liver disease in patients with potential health conditions associated to liver disease is similar to that of patients without preexisting illnesses. Steroid administration is effective in treating vaccine-related AIH-susceptible patients, with most patients experiencing improvement in their clinical symptoms. However, care should be taken to prevent bacterial infections during drug administration. Furthermore, the possible pathogenic mechanisms of vaccine-associated AIH are discussed to offer potential ideas for vaccine development and enhancement. Although the incidence of vaccine-related AIH is rare, individuals should not be deterred from receiving the COVID-19 vaccine, as the benefits of vaccination significantly outweigh the risks.

Zhou, M., et al. (2023). "Case report: Coronavirus Disease 2019 (COVID-19) modified RNA vaccination-induced Adult-Onset Still's Disease with fulminant myocarditis as initial presentation." Front Cardiovasc Med **10**: 1066699.

Myocarditis is a rare complication of Coronavirus Disease 2019 (COVID-19) vaccination. We report a case of an elderly female who presented initially with acute myocarditis, fulminant heart failure, and atrial fibrillation after receiving a modified ribonucleic acid (mRNA) vaccine (BNT162b2). Unlike other patients with vaccine-induced myocarditis, she developed persistent fever, sore throat, polyarthralgia, diffuse macular rash, and lymphadenopathy. After extensive investigation, she was diagnosed with post-vaccination Adult-Onset Still's Disease. The systemic inflammation gradually subsided after the use of non-steroidal anti-inflammatory drugs and systemic steroids. She was discharged from hospital with stable hemodynamics. Methotrexate was subsequently given to maintain long-term remission.

Myopericarditis

Abbate, A., et al. (2021). "Fulminant myocarditis and systemic hyperinflammation temporally associated with BNT162b2 mRNA COVID-19 vaccination in two patients." Int J Cardiol **340**: 119-121.

Immune-mediated myocardial injury following Severe Acute Respiratory Syndrome Coronavirys-2 (SARS-CoV2) infection has been described in adults and children. Cases of myocarditis following immunization for SARS-CoV2 have recently been documented, mostly associated with mild severity and spontaneous recovery. We herein report two cases of fulminant myocarditis following BNT162b2 mRNA Covid-19 vaccination associated with systemic hyperinflammatory syndrome and refractory shock requiring support with veno-arterial extracorporeal membrane oxygenation.

Abraham, N., et al. (2022). "Myocarditis and/or pericarditis risk after mRNA COVID-19 vaccination: A Canadian head to head comparison of BNT162b2 and mRNA-1273 vaccines." Vaccine **40**(32): 4663-4671.

BACKGROUND: Canadian and international data suggest the risk of myocarditis and/or pericarditis is elevated during the week after mRNA COVID-19 vaccination, particularly in younger age groups, in males, and after second doses. OBJECTIVES: This article examines whether there is a product-specific difference in the risk for myocarditis and/or pericarditis between the two mRNA vaccines administered in Canada: BNT162b2 (Pfizer-BioNTech Comirnaty) and mRNA-1273 (Moderna Spikevax). MATERIALS AND METHODS: Reporting rates of myocarditis and/or pericarditis were calculated from reports received by the Canadian Adverse Events Following Immunization Surveillance System from December 2020-March 2022. Excess cases and attributable incidence among individuals aged 18-39 were estimated for each vaccine in comparison with background rates from 2015 to 2019. Head-to-head comparisons used Poisson regression, conditioned on week of vaccine administration, to estimate rate ratios for the week after mRNA-1273 vaccination versus the week after BNT162b2, by age and sex as well as overall. Analyses were restricted to May 30-March 13, 2021, when heightened media awareness was unlikely to have affected reporting rates for the two products differentially. RESULTS: In 18-29 year-old males who received a second dose of mRNA COVID-19 vaccine, attributable risk of myocarditis and/or pericarditis was found to be 5.69 (95% CI: 4.07 - 7.95; $p < 0.001$) times higher among mRNA-1273 recipients (n = 106) as compared to BNT162b2 recipients (n = 33). In the same group, Poisson regression modelling estimated that the risk of myocarditis and/or pericarditis was 4.72 (p-value = <0.001) times higher after mRNA-1723 compared to BNT162b2 vaccination. CONCLUSIONS: The risk of myocarditis and/or pericarditis is higher after mRNA-1723 vaccination than BNT162b2 vaccination in those aged 18-39 years, especially in males aged 18-29 years, where the risk is several times higher.

Abu Mouch, S., et al. (2021). "Myocarditis following COVID-19 mRNA vaccination." Vaccine **39**(29): 3790-3793.

BACKGROUND: Clinical trials of the BNT162b2 vaccine, revealed efficacy and safety. We report six cases of myocarditis, which occurred shortly after BNT162b2 vaccination. METHODS: Patients were identified upon presentation to the emergency department with symptoms of chest pain/discomfort. In all study patients, we excluded past and current COVID-19. Routine clinical and laboratory investigations for common etiologies of myocarditis were performed. Laboratory tests also included troponin and C-reactive protein levels. The diagnosis of myocarditis was established after cardiac MRI. FINDINGS: Five patients presented after the second and one after the first dose of the vaccine. All patients were males with a median age of 23 years. Myocarditis was diagnosed in all patients, there was no evidence of COVID-19 infection. Laboratory assays excluded concomitant infection; autoimmune disorder was considered unlikely. All patients responded to the BNT162b2 vaccine. The clinical course was mild in all six patients. INTERPRETATION: Our report of myocarditis after BNT162b2 vaccination may be possibly considered as an adverse reaction following immunization. We believe our information should be interpreted with caution and further surveillance is warranted.

Ahmed, H. O., M. M. Ahmed and O. Elrasheid (2022). "A Case Series of Myocarditis Related to the COVID-19 Vaccine." Cureus **14**(10): e29892.

Perimyocarditis related to the coronavirus disease 2019 (COVID-19) vaccine is one of the rare adverse events that emerged in April 2021 and then the number of cases commensurably increased as the number of vaccinated people rose. This is a case series of myocarditis/pericarditis related to the messenger RNA (mRNA) COVID-19 vaccine in which we identified four cases with different presentations and outcomes. A short-term follow-up period of five months revealed a full recovery of three cases within one to 12 weeks and persistent left ventricular systolic dysfunction in the fourth case which will require further follow-up to assess long-term outcomes.

Ahmed, S. K. (2022). "Myocarditis after BNT162b2 and mRNA-1273 COVID-19 vaccination: A report of 7 cases." Ann Med Surg (Lond) **77**: 103657.

BACKGROUND AND OBJECTIVES: According to some reports, there is a link between the development of myocarditis and the administration of messenger RNA (mRNA) vaccines against coronavirus disease (COVID-19). Here, we report seven cases that developed myocarditis after receiving a second dose of mRNA COVID-19 vaccine. METHODS: This is a multi-center case series study. In this study, we present 7 patients diagnosed with myocarditis following BNT162b2 and mRNA-1273 COVID-19 vaccinations on March 7, 2021, and March 3, 2022. RESULTS: All seven patients were males and hemodynamically stable. The median age was 24.5 years, ranging from 16 to 36 years old. All patients received the second dose of a messenger RNA (mRNA) vaccine between one and four days before being admitted to the hospital (5 received BNT162b2 [Pfizer-BioNTech] and 2 received mRNA-1273 [Moderna]). The electrocardiograms of all seven patients were abnormal, and their troponin levels were elevated. Moreover, all patients were treated with colchicine and NSAIDs. The average length of stay in the hospital was 2.4 days, and all of the patients' symptoms had resolved by the time they were discharged. CONCLUSION: The results of the current study raise the possibility of an association

between BNT162b2 [Pfizer-BioNTech] or mRNA-1273 [Moderna] COVID-19 vaccination and myocarditis.

Ahmed, S. K., et al. (2022). "Global reports of myocarditis following COVID-19 vaccination: A systematic review and meta-analysis." Diabetes Metab Syndr **16**(6): 102513.

BACKGROUND AND AIMS: Recent media reports of myocarditis after receiving COVID-19 vaccines, particularly the messenger RNA (mRNA) vaccines, are causing public concern. This review summarizes information from published case series and case reports, emphasizing patient and disease characteristics, investigation, and clinical outcomes, to provide a comprehensive picture of the condition. METHODS: A systematic literature search of PubMed and Google scholar was conducted from inception to April 27, 2022. Individuals who develop myocarditis after receiving the COVID-19 vaccine, regardless of the type of vaccine and dose, were included in the study. RESULTS: Sixty-two studies, including 218 cases, participated in the current systematic review. The median age was 29.2 years; 92.2% were male and 7.8% were female. 72.4% of patients received the Pfizer-BioNTech (BNT162b2) vaccine, 23.8% of patients received the Moderna COVID-19 Vaccine (mRNA-1273), and the rest of the 3.5% received other types of COVID-19 vaccine. Furthermore, most myocarditis cases (82.1%) occurred after the second vaccine dose, after a median time interval of 3.5 days. The most frequently reported symptoms were chest pain, myalgia/body aches and fever. Troponin levels were consistently elevated in 98.6% of patients. The admission ECG was abnormal in 88.5% of cases, and the left LVEF was lower than 50% in 21.5% of cases. Most patients (92.6%) resolved symptoms and recovered, and only three patients died. CONCLUSION: These findings may help public health policy to consider myocarditis in the context of the benefits of COVID-19 vaccination.

Aikawa, T., et al. (2022). "Non-infectious endocarditis and myocarditis after COVID-19 mRNA vaccination." Eur Heart J Case Rep **6**(1): ytab533.

Al-Rasbi, S., et al. (2022). "Myocarditis, Pulmonary Hemorrhage, and Extensive Myositis with Rhabdomyolysis 12 Days After First Dose of Pfizer-BioNTech BNT162b2 mRNA COVID-19 Vaccine: A Case Report." Am J Case Rep **23**: e934399.

BACKGROUND The COVID-19 pandemic is a current global crisis, and there are hundreds of millions of individuals being vaccinated worldwide. At present, there have been few reports of COVID-19 vaccine-induced autoimmune processes manifested as myositis, thrombocytopenia, and myocarditis. CASE REPORT A 37-year-old man presented to the Emergency Department (ED) with a 3-day history of back pain and a 1-day history of left upper limb swelling with paresthesia and shortness of breath, 12-days after receiving the first dose of Pfizer/BioNTech BNT162b2 mRNA COVID-19 vaccine. He was diagnosed with severe myositis complicated with rhabdomyolysis and non-oliguric acute kidney injury, thrombocytopenia, myocarditis with pulmonary edema, and pulmonary hemorrhage. Screens for potential toxic, infectious, paraneoplastic, and autoimmune disorders were unremarkable. The patient was treated with a 5-day course of intravenous methylprednisolone and intravenous immunoglobulin, with a good response. He was

hospitalized for 16 days and discharged home on a tapering dose of oral prednisolone for 6 weeks. CONCLUSIONS The case describes a possible link between Pfizer/BioNTech BNT162b2 mRNA COVID-19 vaccine and immune-mediated myocarditis, pulmonary vasculitis, myositis, and thrombocytopenia. However, further data are required to confirm such an association.

Alami, A., et al. (2023). "Myocarditis and Pericarditis Post-mRNA COVID-19 Vaccination: Insights from a Pharmacovigilance Perspective." J Clin Med **12**(15).

Concerns remain regarding the rare cardiovascular adverse events, myocarditis and pericarditis (myo/pericarditis), particularly in younger individuals following mRNA COVID-19 vaccination. Our study aimed to comprehensively assess potential safety signals related to these cardiac events following the primary and booster doses, with a specific focus on younger populations, including children as young as 6 months of age. Using the Vaccine Adverse Events Reporting System (VAERS), the United States national passive surveillance system, we conducted a retrospective pharmacovigilance study analyzing spontaneous reports of myo/pericarditis. We employed both frequentist and Bayesian methods and conducted subgroup analyses by age, sex, and vaccine dose. We observed a higher reporting rate of myo/pericarditis following the primary vaccine series, particularly in males and mainly after the second dose. However, booster doses demonstrated a lower number of reported cases, with no significant signals detected after the fourth or fifth doses. In children and young adults, we observed notable age and sex differences in the reporting of myo/pericarditis cases. Males in the 12-17 and 18-24-year-old age groups had the highest number of cases, with significant signals for both males and females after the second dose. We also identified an increased reporting for a spectrum of cardiovascular symptoms such as chest pain and dyspnea, which increased with age, and were reported more frequently than myo/pericarditis. The present study identified signals of myo/pericarditis and related cardiovascular symptoms after mRNA COVID-19 vaccination, especially among children and adolescents. These findings underline the importance for continued vaccine surveillance and the need for further studies to confirm these results and to determine their clinical implications in public health decision-making, especially for younger populations.

Alania-Torres, E., et al. (2021). "Case Report: Probable Myocarditis After Covid-19 mRNA Vaccine in a Patient With Arrhythmogenic Left Ventricular Cardiomyopathy." Front Cardiovasc Med **8**: 759119.

Arrhythmogenic left ventricular cardiomyopathy (ALVC) is a rare heritable heart-muscle disorder characterized by a progressive loss of left ventricular myocardium and its replacement by fibrofatty tissue. Myocarditis is an inflammatory disease of the heart that may occur secondary to infections, immune system activation or exposure to drugs. Hot phases of ALVC present with chest pain and troponin rise, mimicking acute viral myocarditis and indicate a progression of the disease. Recently, myocarditis has also been described as an infrequent complication of coronavirus disease 2019 (Covid-19) mRNA vaccines. We herein report for the first time a case of probable myocarditis induced by Covid-19 vaccine in a patient with previous medical history of ALVC. We aim

to highlight the common characteristics of ALVC and Covid-19 vaccine myocarditis and work through the differential diagnosis of these two entities.

Albert, E., et al. (2021). "Myocarditis following COVID-19 vaccination." Radiol Case Rep **16**(8): 2142-2145.

The coronavirus disease 2019 (COVID-19) vaccination frequently leads to minor side-effects, that may be more intense after the second dose, but more serious side effects have been reported. We report a case of a 24-year-old man who presented to the hospital with acute substernal chest pain, 4 days after his second COVID-19 Moderna vaccination. Laboratory studies revealed elevated troponins and negative viral serologies. Cardiac magnetic resonance imaging (cMRI) demonstrated edema and delayed gadolinium enhancement of the left ventricle in a midmyocardial and epicardial distribution. The patient was diagnosed with myocarditis following Moderna vaccination. Our case report raises concern that myocarditis is a rare side effect of COVID-19 vaccine. Despite our report, it appears that there is a significantly higher risk of cardiac involvement from COVID-19 infection compared to COVID-19 vaccination.

Aldana-Bitar, J., et al. (2022). "Serial Changes in Troponin I in COVID-19 Vaccine-Associated Myocarditis." Cardiol Res **13**(4): 250-254.

A 63-year-old woman presented with atypical chest pain after a third dose of the coronavirus disease 2019 (COVID-19) messenger ribonucleic acid (mRNA) vaccine. Serial cardiac troponin measurements were performed to evaluate the trajectory of her time-concentration curve which showed a typical myocarditis curve with rapid normalization. The diagnosis of myocarditis was confirmed by cardiac magnetic resonance imaging and follow-up imaging showed resolution. All symptoms resolved with weeks.

Alizadeh, L. S., et al. (2022). "A case of myocarditis after COVID-19 vaccination: incidental or consequential?" Heliyon **8**(6): e09537.

Vaccination represents one of the fundamentals in the fight against SARS-CoV-2. Myocarditis has been reported as a rare but possible adverse consequence of different vaccines, and its clinical presentation can range from mild symptoms to acute heart failure. We report a case of a 29-year-old man who presented with fever and retrosternal pain after receiving SARS-CoV-2 vaccine. Cardiac magnetic resonance imaging and laboratory data revealed typical findings of acute myocarditis.

Aljohani, O. A., et al. (2022). "Myocarditis in children after COVID-19 vaccine." Ann Pediatr Cardiol **15**(3): 280-283.

Three healthy adolescents presented with myocarditis confirmed on cardiac magnetic resonance imaging after receiving Pfizer-BioNTech COVID-19 vaccine. All patients were hemodynamically stable and had good short-term outcomes. Long-term outcomes are yet to be determined. Larger studies are needed to determine whether an association between Pfizer-BioNTech COVID-19 vaccine and myocarditis exists.

Ameratunga, R., et al. (2022). "First Identified Case of Fatal Fulminant Necrotizing Eosinophilic Myocarditis Following the Initial Dose of the Pfizer-BioNTech mRNA COVID-19 Vaccine (BNT162b2, Comirnaty): an Extremely Rare Idiosyncratic Hypersensitivity Reaction." J Clin Immunol **42**(3): 441-447.

RATIONALE: Transient myopericarditis has been recognised as an uncommon and usually mild adverse event predominantly linked to mRNA-based COVID-19 vaccines. These have mostly occurred in young males after the second dose of mRNA COVID-19 vaccines. OBJECTIVES: Fulminant necrotising eosinophilic myocarditis triggered by a variety of drugs or vaccines is an extremely rare hypersensitivity reaction carrying a substantial mortality risk. Early recognition of this medical emergency may facilitate urgent hospital admission for investigation and treatment. Timely intervention can lead to complete cardiac recovery, but the non-specific clinical features and rarity make early diagnosis challenging. FINDINGS: The clinical and pathological observations from a case of fatal fulminant necrotising myocarditis in a 57-year-old woman, following the first dose of the Pfizer-BioNTech vaccine, are described. Other causes have been discounted with reasonable certainty. CONCLUSION: These extremely rare vaccine-related adverse events are much less common than the risk of myocarditis and other lethal complications from COVID-19 infection. The benefits of vaccination far exceed the risks of COVID-19 infection.

Amir, G., et al. (2022). "CMR Imaging 6 Months After Myocarditis Associated with the BNT162b2 mRNA COVID-19 Vaccine." Pediatr Cardiol **43**(7): 1522-1529.

Temporal association between BNT162b2 mRNA COVID-19 vaccine and myocarditis (PCVM) has been reported. We herein present early and 6-month clinical follow-up and cardiac magnetic resonance imaging (CMR) of patients with PVCM. A retrospective collection of data from 15 patients with PCVM and abnormal CMR was performed. Clinical manifestation, laboratory data, hospitalizations, treatment protocols, and imaging studies were collected early (up to 2 months) and later. In nine patients, an additional CMR evaluation was performed 6 months after diagnosis. PCVM was diagnosed in 15 patients, mean age 17 +/- 1 (median 17.2, range 14.9-19 years) years, predominantly in males. Mean time from vaccination to onset of symptoms was 4.4 +/- 6.7 (median 3, range 0-28) days. All patients had CMR post diagnosis at 4 +/- 3 (median 3, range 1-9) weeks, 4/5 patients had hyper enhancement on the T2 sequences representing edemaQuery, and 12 pathological Late glandolinium enhancement. A repeat scan performed after 5-6 months was positive for scar formation in 7/9 patients. PCVM is a rare complication, affecting predominantly males and appearing usually within the first week after administration of the second dose of the vaccine. It usually is a mild disease, with clinical resolution with anti-inflammatory treatment. Late CMR follow up demonstrated resolution of the edema in all patients, while some had evidence of residual myocardial scarring.

Ammirati, E. and L. T. Cooper, Jr. (2022). "Recovery from mRNA COVID-19 vaccine-related myocarditis." Lancet Child Adolesc Health **6**(11): 749-751.

Ammirati, E., et al. (2023). "Outcome and Morphofunctional Changes on Cardiac Magnetic Resonance in Patients With Acute Myocarditis Following mRNA COVID-19 Vaccination." Circ Heart Fail **16**(6): e010315.

Amodio, D., et al. (2023). "Relapsing myocarditis following initial recovery of post COVID-19 vaccination in two adolescent males - Case reports." Vaccine X **14**: 100318.

Whilst there has been significant public health benefits associated with global use of COVID-19 spike protein vaccines, potential serious adverse events following immunization have been reported. Acute myocarditis is a rare complication of COVID19 vaccines and often it is self-limiting. We describe two cases experiencing recurrent myocarditis following mRNA COVID-19 vaccine despite a prior episode with full clinical recovery. Between September 2021-September 2022 we observed two male adolescents with recurrent myocarditis related to mRNA-based-COVID19 vaccine. During the first episode both patients presented with fever and chest pain few days after their second dose of BNT162b2 mRNA Covid-19 Vaccine (Comirnaty(R)). The blood exams showed increased cardiac enzymes. In addition, complete viral panel was run, showing HHV7 positivity in a single case. The left ventricular ejection fraction (LVEF) was normal at echocardiogram but cardiac magnetic resonance scanning (CMR) was consistent with myocarditis. They were treated with supportive treatment with full recovery. The 6 months follow-up demonstrated good clinical conditions with normal cardiological findings. The CMR showed persistent lesions in left ventricle 's wall with LGE. After some months the patients presented at emergency department with fever and chest pain and increased cardiac enzymes. No decreased LVEF was observed. The CMR showed new focal areas of edema in the first case report and stable lesions in the second one. They reached full recovery with normalization of cardiac enzymes after few days. These case reports outline the need of strict follow-up in patients with CMR consistent with myocarditis after mRNA-based-COVID19 vaccine. More efforts are necessary to depict the underlying mechanisms of myocarditis after SARS-CoV2 vaccination to understand the risk of relapsing and the long-term sequelae.

Amodio, D., et al. (2023). "Similarities and differences between myocarditis following COVID-19 mRNA vaccine and multiple inflammatory syndrome with cardiac involvement in children." Clin Immunol: 109751.

Despite the multiple benefits of vaccination, cardiac adverse Events Following COVID-19 Immunization (c-AEFI) have been reported. These events as well as the severe cardiac involvement reported in Multisystem inflammatory syndrome in children (MIS-C) appear more frequent in young adult males. Herein, we firstly report on the inflammatory profiles of patients experiencing c-AEFI in comparison with age, pubertal age and gender matched MIS-C with cardiac involvement. Proteins related to systemic inflammation were found higher in MIS-C compared to c-AEFI, whereas a higher level in proteins related to myocardial injury was found in c-AEFI. In addition, higher levels of DHEAS, DHEA, and cortisone were found in c-AEFI which persisted at follow-up. No anti-heart muscle and anti-endothelial cell antibodies have been detected. Overall current comparative data showed a distinct inflammatory and androgens profile in c-AEFI

patients which results to be well restricted on heart and to persist months after the acute event.

Anastassopoulou, C., et al. (2022). "Temporal relationship of myocarditis and pericarditis following COVID-19 vaccination: A pragmatic approach." Int J Cardiol **358**: 136-139.
BACKGROUND: Complications following COVID-19 vaccination, particularly with mRNA vaccines, rarely include myocarditis and pericarditis. This work principally aimed at defining a realistic temporal relationship between vaccination and myocarditis/pericarditis development. METHODS: All relevant cases reported from week 52/2020 through week 41/2021 in the VAERS database were retrieved and analyzed for licensed vaccines. These included BNT162b2, mRNA-1273, and AD26.COV2.S. Incidence rates were calculated using the corresponding administered vaccine doses as denominators. Additionally, analyzed parameters included demographics, dose series, hospitalization length and outcome. RESULTS: Overall, 2016 myocarditis and 1380 pericarditis cases, (4.96/10(6) and 3.40/10(6) administered vaccine doses, respectively), were recorded. Most myocarditis cases occurred following BNT162b2 (5.60/10(6) doses) in males <30 years. Pericarditis affected predominantly males <40, both sexes >40 years, and was most common post AD26.COV2.S (4.78/10(6) doses). Hospitalization was required for 40.3% and 27.2% of myocarditis and pericarditis cases, respectively. A bimodal pattern was found for both myocarditis and pericarditis, with two peaks that coincided temporally, but were reversed in intensity. The first peak was recorded 1-3 days post-vaccination and was more pronounced in myocarditis, while the second was recorded 15-30 days post-vaccination and was more intense in pericarditis. CONCLUSIONS: Myocarditis/pericarditis after COVID-19 vaccination is rare and depicts a bimodal pattern.

Angeli, F., et al. (2023). "Hypertension and myocarditis following COVID-19 vaccination. Two sides of the coin?" Eur J Intern Med **113**: 107-109.

Ansari, U., et al. (2022). "Case Report: Transient Increase of CMR T1 Mapping Indices in a Patient With COVID-19 mRNA Vaccine Induced Acute Myocarditis." Front Cardiovasc Med **9**: 880717.
BACKGROUND: Acute myocarditis is commonly associated with viral infections, including severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Myocarditis following mRNA COVID-19 vaccination has also been reported, however this is rare and usually resolves within days or weeks. We present a case of acute myocarditis reported after vaccination with mRNA-1273 COVID-19 vaccine (Moderna) diagnosed using cardiac magnetic resonance imaging (CMR). This report describes the utility of CMR in the diagnosis and follow-up of such patients using parameters which could suggest the clinical course of myocarditis. CASE SUMMARY: A 23-year-old male presented in the emergency department with complaints of chest pain radiating to the left arm following vaccination with the second dose of COVID-19 mRNA-1273 vaccine (Moderna). Patient's history revealed an incidence of myocarditis in the past. CMR showed a mid-range left ventricular ejection fraction (38%) and subepicardial late gadolinium enhancement (LGE) in the inferolateral and apical myocardial segments with diffuse elevation of native T1

mapping relaxation times in all myocardial segments. The patient was admitted briefly in the intensive care unit and after a favorable clinical course was discharged from the hospital in stable condition. A follow-up CMR after 3 months revealed normalization of LVEF (57%) and native T1- times in most segments. Scarred myocardium reflecting chronic myocarditis continued to show elevated T1 times. CONCLUSIONS: Our patient presenting with acute myocarditis after recent COVID-19 mRNA vaccination reported a favorable clinical course. CMR revealed increased T1 mapping relaxation times diffusely spread across the myocardium and an impairment of the left ventricular function (LVEF) during the acute phase. However, the LVEF as well as the T1 times normalized at follow-up in all segments except for myocardium affected by chronic myocarditis.

Anthony, J. A., T. Echeverry and R. D. Fishberg (2022). "The Rise of mRNA COVID-19 Vaccine-Associated Myocarditis and Its Implications on the Future Use of This New Vaccine Platform." Cureus **14**(6): e25631.

Vaccine-associated myocarditis is becoming increasingly documented as a complication of the messenger ribonucleic acid (mRNA) vaccination platform. This complication so far has been found to predominantly affect the younger male population within seven days of receiving the second dose of an mRNA vaccine. We present a case of a 45-year-old male found to have clinical, biochemical, and radiological evidence of myocarditis three days after receipt of the second dose of the Moderna COVID-19 vaccine. Troponin I and inflammatory marker trends, in addition to the use of cardiac MRI imaging, was important in making the diagnosis. Symptom resolution was achieved after two months of colchicine and anti-heart failure medications. We highlight the occurrence of this rare vaccine complication in an endeavor to stress the need for further research to better understand this condition so that better guidance can be provided to the medical community on how best to screen and manage it.

Asaduzzaman, M., et al. (2022). "COVID-19 mRNA vaccine-associated encephalopathy, myocarditis, and thrombocytopenia with excellent response to methylprednisolone: A case report." J Neuroimmunol **368**: 577883.

INTRODUCTION: Large-scale vaccination is considered one of the most effective strategies to control the pandemic of COVID-19. Since its start, different complications have been described thought to be related to vaccination. Here, we present a rare case where encephalopathy, myocarditis, and thrombocytopenia developed simultaneously following the second dose of Pfizer-BioNTech mRNA vaccine (BNT162b2). CASE PRESENTATION: A 15-years-old female presented with fever, altered consciousness, and convulsions after taking the second shot of the vaccine. Clinical and laboratory workup was notable for the presence of thrombocytopenia and myocarditis. No alternative causes of encephalitis were found. The patient responded significantly to methylprednisolone suggesting underlying immune pathogenesis responsible for the clinical features. The diagnostic criteria for possible autoimmune encephalitis were also fulfilled. CONCLUSION: Although rare, the clinician should be aware of the possible adverse events following COVID-19 vaccination. Further research with large pooled data is needed to get more insight into its pathogenesis and causal relationship.

Augustin, M., M. Hallek and S. Nitschmann (2022). "[Myocarditis and pericarditis after COVID-19 mRNA vaccination]." Inn Med (Heidelb) **63**(12): 1323-1326.

Aviram, G., et al. (2022). "Myocarditis Associated With COVID-19 Booster Vaccination." Circ Cardiovasc Imaging **15**(2): e013771.

Awaya, T., et al. (2022). "Response to: Note the distinction between myocarditis, novel coronavirus myocarditis and COVID-19 vaccine-associated myocarditis." QJM **115**(10): 696.

Aye, Y. N., et al. (2023). "Acute myocardial infarction and myocarditis following COVID-19 vaccination." QJM **116**(4): 279-283.

Emerging reports raise concerns on the potential association between the COVID-19 vaccines and cardiac manifestations. We sought to evaluate cardiac complications associated with COVID-19 vaccination in a pooled analysis from our institution's cohort study and systematic review. Consecutive patients admitted to a tertiary hospital in Singapore between 1 January 2021 and 31 March 2021, with the onset of cardiac manifestations within 14 days following COVID-19 vaccination, were studied. Furthermore, a systematic review was performed, with PubMed, Embase, Research Square, MedRxiv and LitCovid databases accessed from inception up to 29 June 2021. Relevant manuscripts reporting individual patient data on cardiac complications following COVID-19 vaccination were included. Thirty patients were included in the study cohort, with 29 diagnosed with acute myocardial infarction (AMI) and 1 with myocarditis. Five patients developed heart failure, two had cardiogenic shock, three intubated, and one had cardiovascular-related mortality. In the systematic review, 16 studies were included with 41 myocarditis and 6 AMI cases. In the pooled analysis of the study cohort and the systematic review, 35 patients had AMI and 42 had myocarditis. Majority were men, and myocarditis patients were younger than AMI patients. Myocarditis patients tended to present 72 h postvaccination, while AMI patients were older and typically presented 24 h postvaccination. Majority with AMI or myocarditis developed symptoms after the first and second vaccination dose, respectively. This pooled analysis of patients presenting with cardiac manifestations following COVID-19 vaccination highlights the differences between myocarditis and AMI presentations in temporal association with the vaccination.

Azir, M., et al. (2021). "STEMI Mimic: Focal Myocarditis in an Adolescent Patient After mRNA COVID-19 Vaccine." J Emerg Med **61**(6): e129-e132.

BACKGROUND: In May 2021, the U.S. Food and Drug Administration expanded the Emergency Use Authorization for the Pfizer-BioNTech mRNA Coronavirus disease 2019 (COVID-19) Vaccine (BNT162b2) to include adolescents 12-15 years of age. As vaccine administration continues to increase, potential adverse outcomes, to include myocarditis, are being reported to the Vaccine Adverse Event Reporting System. CASE REPORT: This case report describes a 17-year-old male patient who developed focal myocarditis mimicking an ST-segment elevation myocardial infarction (STEMI) 3 days

after administration of an mRNA COVID-19 vaccine. Why Should an Emergency Physician Be Aware of This? Myocarditis is a rare complication in adolescents receiving mRNA COVID-19 vaccines. Focal myocarditis may demonstrate localizing electrocardiographic changes consistent with a STEMI. Overall, complications of the mRNA COVID-19 vaccines are extremely rare. The vaccine continues to be recommended by public health experts, as the benefits of vaccinations greatly outweigh the rare side effects.

Bae, D. H., et al. (2022). "Simultaneous Occurrence of Immune-Mediated Thrombocytopenia and Myocarditis After mRNA-1273 COVID-19 Vaccination: A Case Report." J Korean Med Sci **37**(21): e169.

With the global spread of severe acute respiratory syndrome coronavirus 2, several vaccines were developed; messenger RNA (mRNA) vaccines have recently been widely used worldwide. However, the incidence of myocarditis following mRNA vaccination is increasing; although the cause of myocarditis has not yet been clearly identified, it is presumed to be caused by a problem in the innate immune system. Immune-mediated thrombocytopenia (ITP) after vaccination is rare but has been reported and is also assumed to occur by the same mechanism. We report the first case of simultaneous myocarditis and ITP after mRNA vaccination. A 38-year-old woman presented with chest pain, mild dyspnea, and sweating after vaccination with mRNA-1273 vaccine (Moderna) 4 days prior to admission. Upon admission to the emergency department, cardiac enzymes were elevated; blood test performed 5 months ago showed normal platelet count, but severe thrombocytopenia was observed upon admission. After administration of intravenous immunoglobulin, the platelet count improved; subsequently, myocarditis was observed on endomyocardial biopsy. Thus, myocarditis and ITP were judged to have occurred simultaneously due to the expression of the innate immune system markers after mRNA vaccination. The patient was discharged on day 6 of admission.

Bansal, M., A. Mehta and M. Pandey (2023). "Myocarditis post-COVID-19 vaccination." Postgrad Med J.

There has been much interest in the possible adverse events associated with available anti-coronavirus disease of 2019 (COVID-19) vaccines, given the rapid pace at which they had to be developed during the pandemic. One such adverse event is myocarditis post-COVID-19 vaccination. Several pathophysiological mechanisms have been proposed that might help us understand the relationship between the messenger ribonucleic acid (mRNA) vaccine and the occurrence of myocarditis, though we are yet to ascertain the causal link between them. Although the actual absolute incidence of myocarditis post-COVID-19 vaccination remains low among the large, general population that has been vaccinated, there has been a high relative incidence of this adverse event. We aim to review the existing literature and bring to light what we have so far understood with respect to the association between COVID-19 vaccination and myocarditis. This will help in better understanding the burden of the pathology along with alleviating apprehensions associated with it.

Barda, N., et al. (2021). "Safety of the BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting." N Engl J Med **385**(12): 1078-1090.

BACKGROUND: Preapproval trials showed that messenger RNA (mRNA)-based vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) had a good safety profile, yet these trials were subject to size and patient-mix limitations. An evaluation of the safety of the BNT162b2 mRNA vaccine with respect to a broad range of potential adverse events is needed. METHODS: We used data from the largest health care organization in Israel to evaluate the safety of the BNT162b2 mRNA vaccine. For each potential adverse event, in a population of persons with no previous diagnosis of that event, we individually matched vaccinated persons to unvaccinated persons according to sociodemographic and clinical variables. Risk ratios and risk differences at 42 days after vaccination were derived with the use of the Kaplan-Meier estimator. To place these results in context, we performed a similar analysis involving SARS-CoV-2-infected persons matched to uninfected persons. The same adverse events were studied in the vaccination and SARS-CoV-2 infection analyses. RESULTS: In the vaccination analysis, the vaccinated and control groups each included a mean of 884,828 persons. Vaccination was most strongly associated with an elevated risk of myocarditis (risk ratio, 3.24; 95% confidence interval [CI], 1.55 to 12.44; risk difference, 2.7 events per 100,000 persons; 95% CI, 1.0 to 4.6), lymphadenopathy (risk ratio, 2.43; 95% CI, 2.05 to 2.78; risk difference, 78.4 events per 100,000 persons; 95% CI, 64.1 to 89.3), appendicitis (risk ratio, 1.40; 95% CI, 1.02 to 2.01; risk difference, 5.0 events per 100,000 persons; 95% CI, 0.3 to 9.9), and herpes zoster infection (risk ratio, 1.43; 95% CI, 1.20 to 1.73; risk difference, 15.8 events per 100,000 persons; 95% CI, 8.2 to 24.2). SARS-CoV-2 infection was associated with a substantially increased risk of myocarditis (risk ratio, 18.28; 95% CI, 3.95 to 25.12; risk difference, 11.0 events per 100,000 persons; 95% CI, 5.6 to 15.8) and of additional serious adverse events, including pericarditis, arrhythmia, deep-vein thrombosis, pulmonary embolism, myocardial infarction, intracranial hemorrhage, and thrombocytopenia. CONCLUSIONS: In this study in a nationwide mass vaccination setting, the BNT162b2 vaccine was not associated with an elevated risk of most of the adverse events examined. The vaccine was associated with an excess risk of myocarditis (1 to 5 events per 100,000 persons). The risk of this potentially serious adverse event and of many other serious adverse events was substantially increased after SARS-CoV-2 infection. (Funded by the Ivan and Francesca Berkowitz Family Living Laboratory Collaboration at Harvard Medical School and Clalit Research Institute.).

Bart, N. K. (2023). "Editorial for "Cardiac Magnetic Resonance Imaging Findings in COVID-19 Vaccine-Related Myocarditis: A Pooled Analysis of 468 Patients"." J Magn Reson Imaging **57**(5): 1531-1532.

Bautista Garcia, J., et al. (2021). "Acute myocarditis after administration of the BNT162b2 vaccine against COVID-19." Rev Esp Cardiol (Engl Ed) **74**(9): 812-814.

Behers, B. J., et al. (2022). "Myocarditis Following COVID-19 Vaccination: A Systematic Review of Case Reports." Yale J Biol Med **95**(2): 237-247.

Introduction: COVID-19, the infectious disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), often presents with a spectrum of symptoms at varying levels of severity, ranging from asymptomatic patients to those with fatal complications, such as myocarditis. With increased availability of COVID-19 vaccines, the awareness of possible side effects has expanded as reports surface. This study reviewed cases of myocarditis following COVID-19 vaccination and with existing literature on COVID-19 infection-induced myocarditis to compare clinical courses and analyze possible mechanisms of action. Methods: A systematic review of literature was conducted to identify published case reports (as of February 3, 2022) pertaining to the development of myocarditis following COVID-19 vaccination with either Pfizer or Moderna for an in-depth analysis. Additional subgroup analyses were conducted based on age, past medical history, vaccine manufacturer, and dose number. Results: There were 53 eligible case reports that were included in this study. Patients were mostly male with a median age of 24 years, and the most reported symptom upon presentation was chest pain. Seventy percent of the cases involved the Pfizer vaccine with a majority of myocarditis developing subsequent to second dose. Resolution of symptoms was achieved in all but one patient. Clinical severity, as measured primarily by left ventricular ejection fraction, appeared to be worse among adult patients than pediatric, as well as for patients with comorbidities. Conclusion: This study revealed an observable association between COVID-19 vaccines and myocarditis. However, the clinical course and prognosis seem favorable and less prevalent than those conferred from natural infection.

Bellamoli, M., et al. (2023). "Acute myocarditis after a first dose of COVID-19 mRNA vaccination: an uncommon but potentially serious adverse effect." J Cardiovasc Med (Hagerstown) **24**(2): 154-158.

Bellos, I., V. Karageorgiou and D. Viskin (2022). "Myocarditis following mRNA Covid-19 vaccination: A pooled analysis." Vaccine **40**(12): 1768-1774.

BACKGROUND: Post-marketing surveillance studies have raised concerns of increased myocarditis rates following coronavirus disease-19 (Covid-19) mRNA vaccines. The present study aims to accumulate the published mRNA Covid-19 vaccine-associated myocarditis cases, describe their clinical characteristics and determine the factors predisposing to critical illness. METHODS: Medline, Scopus, Web of Science, CENTRAL and Google Scholar were systematically searched from inception. Studies reporting adult myocarditis cases following BNT162b2 or mRNA-1273 vaccination were included. Individual participant data coming from case reports/series were pooled. Proportional random-effects meta-analysis was conducted by combining the pooled cohort and observational studies with aggregated data. RESULTS: Overall, 39 studies were included with a total of 129 patients. Most cases occurred in young males after the second vaccine dose. Myocarditis after the first dose was significantly associated with prior Covid-19 (p-value: 0.025). The most common electrocardiographic finding was ST-segment elevation, while late gadolinium enhancement was invariably observed in cardiac magnetic reasoning. Logistic regression analysis demonstrated that signs of heart failure were predictive of subsequent critical illness (Odds ratio: 19.22, 95% confidence

intervals-CI: 5.57-275.84). Proportion meta-analysis indicated that complete resolution of symptoms is achieved in 80.5% of patients (95% CI: 59.3-92.1), while the proportion of participants necessitating intensive care unit admission is 7.0% (95% CI: 3.8-12.9). CONCLUSIONS: Myocarditis following mRNA Covid-19 vaccination is typically mild, following an uncomplicated clinical course with rapid improvement of symptoms. Future research is needed to define its exact incidence, clarify its pathophysiology and determine the optimal management plan depending on its severity. Protocol registration: dx.https://doi.org/10.17504/protocols.io.bxwtppen.

Beshai, R. and J. J. Lee (2022). "Unusual Case of Takotsubo Cardiomyopathy Secondary to COVID-19 Vaccine: Case Report and Literature Review." Cureus **14**(5): e25398.

COVID-19 is a serious disease with high morbidity and mortality around the globe. We present a case of a 45-year-old male who presents with substernal chest pain three days after receiving the second dose of his COVID-19 mRNA (Moderna) vaccine. A transthoracic echo showed reduced left ventricular ejection fraction of 25-30% with akinesis of the mid to distal anterior, anteroseptal, anterolateral, inferolateral, inferoseptal, and inferior walls. Patient symptoms improved significantly during his hospitalization. Repeat trans-thoracic echo four days after his hospitalization showed ejection fraction recovery without segmental wall motion abnormalities. This case demonstrates the importance of recognizing Takotsubo cardiomyopathy as a complication of COVID-19 vaccine.

Bollano, E., et al. (2022). "Somatostatin receptor positron emission tomography/computed tomography in myocarditis following mRNA COVID-19 vaccination." Eur Heart J Case Rep **6**(4): ytac117.

Bolze, A., et al. (2022). "Decoding the Human Genetic and Immunological Basis of COVID-19 mRNA Vaccine-Induced Myocarditis." J Clin Immunol **42**(7): 1354-1359.

Bouchaala, A., et al. (2023). "Post-vaccine COVID-19 acute myocarditis: case reports and literature review." Pan Afr Med J **44**: 192.

COVID-19 vaccines have reduced both lethality and hospitalization rates of the novel coronavirus disease. Nevertheless, multiple side effects have been reported in the literature, most often are harmless. We report two cases of acute myocarditis, hospitalized in the emergency department for chest pain occurring after the second dose of mRNA vaccine AstraZeneca. The SARS-Cov-2 infection was ruled out in both patients with a negative PCR obtained by nasal swabs and normal thoracic CT scans. Both patients had high levels of high-sensitive cardiac troponin I. Acute coronary syndromes were excluded with cardiac catheterization. Cardiac Magnetic resonance imaging (MRI) showed signs in favor of acute myocarditis. The evolution was favorable for both patients after being put on anti-inflammatory treatment. The universality and accumulation of reports concerning acute myocarditis following COVID vaccination, in the absence of any other diagnostic element that could explain the myocardial injury,

establish a strong causal link, although the etiopathogenesis of such injury remains poorly elucidated.

Boursier, C., et al. (2022). "(68)Ga-DOTATOC digital-PET imaging of inflammatory cell infiltrates in myocarditis following COVID-19 vaccination." Eur J Nucl Med Mol Imaging **49**(4): 1433-1434.

Cadegiani, F. A. (2022). "Catecholamines Are the Key Trigger of COVID-19 mRNA Vaccine-Induced Myocarditis: A Compelling Hypothesis Supported by Epidemiological, Anatomopathological, Molecular, and Physiological Findings." Cureus **14**(8): e27883.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) mRNA vaccine-induced myocarditis is a rare but well-documented complication in young males. The increased incidence of sudden death among athletes following vaccination has been reported and requires further investigation. Whether the risk of myocarditis, a known major cause of sudden death in young male athletes, also increases after coronavirus disease 2019 (COVID-19) infection is unknown. The severity and implications of these critical adverse effects require a thorough analysis to elucidate their key triggering mechanisms. The present review aimed to evaluate whether there is a justification to hypothesize that catecholamines in a "hypercatecholaminergic" state are the key trigger of SARS-CoV-2 mRNA vaccine-induced myocarditis and related outcomes and whether similar risks are also present following COVID-19 infection. A thorough, structured scoping review of the literature was performed to build the hypothesis through three pillars: detection of myocarditis risk, potential alterations and abnormalities identified after SARS-CoV-2 mRNA vaccination or COVID-19 infection and consequent events, and physiological characteristics of the most affected population. The following terms were searched in indexed and non-indexed peer review articles and recent preprints (<12 months): agent, "SARS-CoV-2" or "COVID-19"; event, "myocarditis" or "sudden death(s)" or "myocarditis+sudden death(s)" or "cardiac event(s)"; underlying cause, "mRNA" or "spike protein" or "infection" or "vaccine"; proposed trigger, "catecholamine(s)" or "adrenaline" or "epinephrine" or "noradrenaline" or "norepinephrine" or "testosterone"; and affected population, "young male(s)" or "athlete(s)." The rationale and data that supported the hypothesis were as follows: SARS-CoV-2 mRNA vaccine-induced myocarditis primarily affected young males, while the risk was not observed following COVID-19 infection; independent autopsies or biopsies of patients who presented post-SARS-CoV-2 mRNA vaccine myocarditis in different geographical regions enabled the conclusion that a primary hypercatecholaminergic state was the key trigger of these events; SARS-CoV-2 mRNA was densely present, and SARS-CoV-2 spike protein was progressively produced in adrenal medulla chromaffin cells, which are responsible for catecholamine production; the dihydroxyphenylalanine decarboxylase enzyme that converts dopamine into noradrenaline was overexpressed in the presence of SARS-CoV-2 mRNA, leading to enhanced noradrenaline activity; catecholamine responses were physiologically higher in young adults and males than in other populations; catecholamine responses and resting catecholamine production were higher in male athletes than in non-athletes; catecholamine responses to stress and its sensitivity were enhanced in the presence of androgens; and catecholamine expressions in young male

athletes were already high at baseline, were higher following vaccination, and were higher than those in non-vaccinated athletes. The epidemiological, autopsy, molecular, and physiological findings unanimously and strongly suggest that a hypercatecholaminergic state is the critical trigger of the rare cases of myocarditis due to components from SARS-CoV-2, potentially increasing sudden deaths among elite male athletes.

Caforio, A. L. P. (2021). "Receipt of mRNA Vaccine against Covid-19 and Myocarditis." N Engl J Med **385**(23): 2189-2190.

Calcaterra, G., et al. (2021). "COVID 19 Vaccine for Adolescents. Concern about Myocarditis and Pericarditis." Pediatr Rep **13**(3): 530-533.

The alarming onset of some cases of myocarditis and pericarditis following the administration of Pfizer-BioNTech and Moderna COVID-19 mRNA-based vaccines in adolescent males has recently been highlighted. All occurred after the second dose of the vaccine. Fortunately, none of patients were critically ill and each was discharged home. Owing to the possible link between these cases and vaccine administration, the US and European health regulators decided to continue to investigate the potential causal relationship between COVID-19 mRNA vaccines and myocarditis. In any case, none of the patients fulfilled the criteria for multi-system inflammatory syndrome or Kawasaki-like disease and there was no evidence of acute SARS-CoV-2 infection.

Camastra, G., et al. (2022). "Monitoring the evolution of myocarditis following COVID-19 mRNA vaccination with serial cardiac magnetic resonance imaging." Int J Cardiovasc Imaging **38**(9): 2077-2079.

Caredda, G. (2022). "Editorial Comment: Cardiac MRI as a Fundamental Tool in the Evaluation of Suspected Myocarditis After COVID-19 mRNA Vaccination in Young Patients." AJR Am J Roentgenol **218**(4): 658.

Carleton, B. C., et al. (2023). "Benefits v. risks of COVID-19 vaccination: an examination of vaccination policy impact on the occurrence of myocarditis and pericarditis." Lancet Reg Health West Pac: 100797.

Studies of myocarditis/pericarditis following mRNA COVID-19 vaccines in Hong Kong have been published. Data are consistent with data from other active surveillance or healthcare databases. The mRNA COVID-19 vaccines have been shown to rarely increase risk of myocarditis, with the highest risk among males aged 12-17 after the second dose. An increased risk of pericarditis has also been shown after the second dose, though less common than myocarditis and more evenly distributed among different sex and age groups. Because of the increased risk of post-vaccine myocarditis, Hong Kong implemented a single dose mRNA COVID-19 vaccine policy on September 15, 2021 for adolescents (age 12-17 years). Post-policy, there were no cases of carditis. 40,167 first dose patients did not receive a second dose. This policy was highly successful in the reduction of carditis, but the trade-off is the potential risk of disease and cost to

population-level immunity. This commentary brings forward some important global policy considerations.

Cavalcante, J. L., K. E. Shaw and M. Gossl (2022). "Cardiac Magnetic Resonance Imaging Midterm Follow Up of COVID-19 Vaccine-Associated Myocarditis." JACC Cardiovasc Imaging **15**(10): 1821-1824.

Ceylan, M. E., et al. (2022). "A case of myocarditis and isolated hypopotassemia after Biontech-Pfizer vaccine for Covid-19." Vaccine **40**(21): 2897-2898.

Chachar, T. S., et al. (2021). "First Report of Acute Myocarditis Post-Pfizer-BioNTech COVID-19 Vaccination in the Kingdom of Bahrain." Cureus **13**(12): e20313.

We present a case of a 24-year-old male patient who presented to our institution five days after receiving his first dose of Pfizer-BioNTech vaccine to rule out acute coronary syndrome due to chest pain along with troponin increase and ECG changes. Acute coronavirus disease 2019 (COVID-19) infection was excluded based on a negative real-time reverse transcription-polymerase chain reaction (RT-PCR) test of specimens acquired using nasopharyngeal swabs for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and all other viral serologies were found to be negative. Coronary angiogram showed normal coronaries, and the presence of late gadolinium enhancement, which is indicative of myocarditis, was identified using cardiac magnetic resonance imaging (MRI). Our case report raises concern that the COVID-19 vaccine may cause myocarditis as a rare side effect.

Chai, Q., et al. (2021). "Multisystem inflammatory syndrome in a male adolescent after his second Pfizer-BioNTech COVID-19 vaccine." Acta Paediatr.

Multisystem inflammatory syndrome (MIS) in children (MIS-C) is a complication of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, while myocarditis is a rare adverse effect to messenger ribonucleic acid (mRNA) SARS-CoV-2 vaccines, especially in males aged 12-17 years.

Chamling, B., et al. (2021). "Occurrence of acute infarct-like myocarditis following COVID-19 vaccination: just an accidental co-incidence or rather vaccination-associated autoimmune myocarditis?" Clin Res Cardiol **110**(11): 1850-1854.

Chelala, L., et al. (2022). "Cardiac MRI Findings of Myocarditis After COVID-19 mRNA Vaccination in Adolescents." AJR Am J Roentgenol **218**(4): 651-657.

BACKGROUND. A possible association has been reported between COVID-19 messenger RNA (mRNA) vaccination and myocarditis. OBJECTIVE. The purpose of our study was to describe cardiac MRI findings in patients with myocarditis after COVID-19 mRNA vaccination. METHODS. This retrospective study included patients without known prior SARS-CoV-2 infection who underwent cardiac MRI between May 14, 2021, and June 14, 2021, for suspected myocarditis within 2 weeks of COVID-19 mRNA vaccination. Information regarding clinical presentation, hospital course, and events after hospital

discharge were recorded. A cardiothoracic imaging fellow and cardiothoracic radiologist reviewed cardiac MRI examinations in consensus. Data were summarized descriptively. RESULTS. Of 52 patients without known prior SARS-CoV-2 infection who underwent cardiac MRI during the study period, five underwent MRI for suspected myocarditis after recent COVID-19 mRNA vaccination. All five patients were male patients ranging in age from 16 to 19 years (mean, 17.2 +/- 1.0 [SD] years) who presented within 4 days of receiving the second dose of a COVID-19 mRNA vaccine. Troponin levels were elevated in all patients (mean peak troponin I value, 6.82 +/- 4.13 ng/mL). Alternate possible causes of myocarditis were deemed clinically unlikely on the basis of medical history, physical examination findings, myocarditis viral panel, and toxicology screening. Cardiac MRI findings were consistent with myocarditis in all five patients on the basis of the Lake Louise criteria, including early gadolinium enhancement and late gadolinium enhancement (LGE) in all patients and corresponding myocardial edema in four patients. All five patients had a favorable hospital course and were discharged from the hospital in stable condition with improved or resolved symptoms after hospitalization (mean length of hospital stay, 4.8 days). Two patients underwent repeat cardiac MRI that showed persistent, although decreased, LGE. Three patients reported mild intermittent self-resolving chest pain after hospital discharge, and two patients had no recurrent symptoms after discharge. CONCLUSION. In this small case series, all patients with myocarditis after COVID-19 vaccination were male adolescents and had a favorable initial clinical course. All patients showed cardiac MRI findings typical of myocarditis from other causes. LGE persisted in two patients who underwent repeat MRI. These observations do not establish causality. CLINICAL IMPACT. Radiologists should be aware of a possible association of COVID-19 mRNA vaccination and myocarditis and recognize the role of cardiac MRI in the assessment of suspected myocarditis after COVID-19 vaccination.

Chellapandian, S. B., et al. (2022). "Myocarditis following COVID-19 mRNA (mRNA-1273) vaccination." Clin Case Rep **10**(4): e05741.

In this case report, we presented a case of myocarditis as a rare complication that developed after Covid mRNA-1273 vaccine. Cases of post-vaccine myocarditis usually progress with mild symptoms. However, it should be a situation that healthcare workers should keep in mind, that myocarditis may develop after vaccination.

Chen, J. H., et al. (2022). "COVID-19 Vaccine-Related Myocarditis: A Descriptive Study of 40 Case Reports." Cureus **14**(1): e21740.

After the surging rise in the Coronavirus disease 2019 (COVID-19) pandemic, the Food and Drug Administration (FDA) approved emergency approval of vaccinations to prevent life-threatening complications of COVID-19 infection. These vaccines are BNT162b2, mRNA-1273. Later, the FDA also approved JNJ-78436735. COVID-19 vaccination does not have major side effects, but there are some concerning adverse events reported right after vaccination. Myocarditis is one of them. Based on our analysis of 40 case reports, we are presenting the epidemiology and clinical picture of myocarditis related to the COVID-19 vaccine. Based on our analysis, we found that the majority of cases were seen

in males with 90% predominance, and these cases were seen in the age group of 29.13 years old (mean, SD of 14.39 years). In 65% of cases, patients took the BNT162b2 vaccine; 30% of cases were reported with the mRNA-1273 vaccine; and 5% of cases with JNJ-78436735. Of all the cases, 80% of them are reported after the second dose of the vaccine with either Moderna or Pfizer. The characteristics of COVID-19 vaccine-related myocarditis were analyzed in this study. We identified several findings, ranging from age, gender, type of vaccination, presentation of symptoms, and diagnosis modality. This depicts the picture of COVID-19 vaccine-related myocarditis and what physicians should expect when dealing with the disease. Our analysis showed that more cases were reported after receiving the BNT162b2 vaccine compared to mRNA-1273 and JNJ-78436735 vaccines. Further research needs to be conducted to analyze the underlying cause of this association.

Cheon, D. Y., et al. (2022). "Acute Myocarditis After COVID-19 Vaccination." Int J Heart Fail **4**(4): 205-208.

Cho, J. Y., et al. (2023). "COVID-19 vaccination-related myocarditis: a Korean nationwide study." Eur Heart J **44**(24): 2234-2243.

AIMS: A comprehensive nationwide study on the incidence and outcomes of COVID-19 vaccination-related myocarditis (VRM) is in need. METHODS AND RESULTS: Among 44 276 704 individuals with at least 1 dose of COVID-19 vaccination, the incidence and clinical courses of VRM cases confirmed by the Expert Adjudication Committee of the Korea Disease Control and Prevention Agency were analyzed. COVID-19 VRM was confirmed in 480 cases (1.08 cases per 100 000 persons). Vaccination-related myocarditis incidence was significantly higher in men than in women (1.35 vs. 0.82 per 100 000 persons, $P < 0.001$) and in mRNA vaccines than in other vaccines (1.46 vs. 0.14 per 100 000 persons, $P < 0.001$). Vaccination-related myocarditis incidence was highest in males between the ages of 12 and 17 years (5.29 cases per 100 000 persons) and lowest in females over 70 years (0.16 cases per 100 000 persons). Severe VRM was identified in 95 cases (19.8% of total VRM, 0.22 per 100 000 vaccinated persons), 85 intensive care unit admission (17.7%), 36 fulminant myocarditis (7.5%), 21 extracorporeal membrane oxygenation therapy (4.4%), 21 deaths (4.4%), and 1 heart transplantation (0.2%). Eight out of 21 deaths were sudden cardiac death (SCD) attributable to VRM proved by an autopsy, and all cases of SCD attributable to VRM were aged under 45 years and received mRNA vaccines. CONCLUSION: Although COVID-19 VRM was rare and showed relatively favorable clinical courses, severe VRM was found in 19.8% of all VRM cases. Moreover, SCD should be closely monitored as a potentially fatal complication of COVID-19 vaccination.

Choi, S., et al. (2021). "Myocarditis-induced Sudden Death after BNT162b2 mRNA COVID-19 Vaccination in Korea: Case Report Focusing on Histopathological Findings." J Korean Med Sci **36**(40): e286.

We present autopsy findings of a 22-year-old man who developed chest pain 5 days after the first dose of the BNT162b2 mRNA vaccine and died 7 hours later. Histological

examination of the heart revealed isolated atrial myocarditis, with neutrophil and histiocyte predominance. Immunohistochemical C4d staining revealed scattered single-cell necrosis of myocytes which was not accompanied by inflammatory infiltrates. Extensive contraction band necrosis was observed in the atria and ventricles. There was no evidence of microthrombosis or infection in the heart and other organs. The primary cause of death was determined to be myocarditis, causally-associated with the BNT162b2 vaccine.

Corrao, G., et al. (2022). "Increased risk of myocarditis and pericarditis and reduced likelihood of severe clinical outcomes associated with COVID-19 vaccination: a cohort study in Lombardy, Italy." BMC Infect Dis **22**(1): 844.

INTRODUCTION: We aimed to assess harms (post-vaccine myocarditis and pericarditis) and benefits (preventing severe disease) of COVID-19 vaccination. METHODS: We conducted a population-based retrospective cohort study. Using the integrated platform of the vaccination campaign of Lombardy Region (Italy), after the exclusion of 24,188 individuals not beneficiaries of the Regional Health Service, 9,184,146 citizens candidates to vaccine at December 27, 2020 were followed until November 30, 2021 (the loss to follow-up rate was 0.5%). From the date of administration of each vaccine dose to day 28 post-administration, three periods that covered exposure to the first, second, and third dose were defined. The benefit-risk profile of vaccines was performed by comparing the number needed to harm (NNH) and number needed to treat (NNT) by sex, age, and vaccine type. RESULTS: Incidence rates of myocarditis were 9.9 and 5.2 per million person-months during the exposure and no-exposure periods, respectively, and the incidence rates of pericarditis were 19.5 and 15.9 per million person-months, respectively. The risk of myocarditis was highest following exposure to the second dose of the Moderna vaccine (adjusted HR: 5.5, 95% CI: 3.7 to 8.1). Exposure to the Moderna vaccine was also associated with an increased risk of pericarditis (adjusted HR 2.2, 1.5 to 3.1). NNT was higher than NNH (9471 vs. 7213) for 16 to 19-year-old men who received the Moderna vaccine, while all other sex, age, and vaccine subgroups had a favourable harm-benefit profile. CONCLUSIONS: Men 16 to 19 years of age has the highest rates of myocarditis within a few days after receiving the Moderna vaccines. The balance between harms and benefits was almost always in favour of vaccination.

Correa, H., et al. (2022). "Acute Myopericarditis Post-Intravenous Injection of Coronavirus Disease 2019 (COVID-19) mRNA Vaccine Differs From Viral Myocarditis." Clin Infect Dis **75**(1): e926.

Cueva-Recalde, J. F., et al. (2023). "Acute myocarditis after administration of BNT162b2 vaccine against COVID-19." Arch Cardiol Mex **93**(2): 243-245.

Cui, G., et al. (2021). "Case Report: COVID-19 Vaccination Associated Fulminant Myocarditis." Front Cardiovasc Med **8**: 769616.

Herein, we describe a novel finding of fulminant myocarditis (FM) in two subjects the day after administration of the first dose of the currently available inactivated SARS-CoV-

2 vaccine (Vero cell). Cardiac magnetic resonance imaging revealed extensive myocardial edema and necrosis. A pathologic evaluation of the endocardial biopsy tissues revealed inflammatory cell (lymphocytes) infiltration and interstitial edema, myocyte necrosis, and focal areas of fibrosis. A life-support-based comprehensive treatment regimen comprising mechanical circulatory support using intra-aortic balloon pulsation and immunomodulatory therapy-glucocorticoids and intravenous immunoglobulin-was used to treat the patients with FM; eventually, the patients recovered and were discharged. To our knowledge, these are the first two reported cases of FM, with no other identified cause or associated illness, after receiving the inactivated SARS-CoV-2 vaccine (Vero cell). These findings suggest a novel pathogenesis of myocarditis which mentions to pay more attention to this rare, but lethal complication of COVID-19 vaccination.

Das, B. B., et al. (2021). "Myocarditis and Pericarditis Following mRNA COVID-19 Vaccination: What Do We Know So Far?" Children (Basel) **8**(7).

This is a cross-sectional study of 29 published cases of acute myopericarditis following COVID-19 mRNA vaccination. The most common presentation was chest pain within 1-5 days after the second dose of mRNA COVID-19 vaccination. All patients had an elevated troponin. Cardiac magnetic resonance imaging revealed late gadolinium enhancement consistent with myocarditis in 69% of cases. All patients recovered clinically rapidly within 1-3 weeks. Most patients were treated with non-steroidal anti-inflammatory drugs for symptomatic relief, and 4 received intravenous immune globulin and corticosteroids. We speculate a possible causal relationship between vaccine administration and myocarditis. The data from our analysis confirms that all myocarditis and pericarditis cases are mild and resolve within a few days to few weeks. The bottom line is that the risk of cardiac complications among children and adults due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection far exceeds the minimal and rare risks of vaccination-related transient myocardial or pericardial inflammation.

Dawson, J. L., et al. (2022). "Clozapine, mRNA COVID-19 vaccination and drug-induced myocarditis." Aust N Z J Psychiatry **56**(7): 879.

Dhaduk, K., et al. (2022). "COVID-19 vaccination and myocarditis: A review of current literature." World J Virol **11**(4): 170-175.

Vaccination for coronavirus disease 2019 (COVID-19) is a critical strategy in controlling the current pandemic of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). After widespread COVID-19 vaccine imple-mentation, isolated case reports about myocarditis as a potential adverse reaction started coming. As of November 12, 2021, Centers for Disease Control and Prevention (CDC) has reported 1793 cases of myocarditis or pericarditis among young people with age 12-29 years, most cases have been reported in the male adolescent age group after the second dose of mRNA COVID-19 vaccines. It is very important to monitor the safety standards and adverse reactions of vaccines to effectively implement the vaccination policies. The CDC and the United States Food and Drug Administration actively monitor vaccine-associated adverse

reactions a well-known platform such as Vaccine Adverse Event Reporting System. CDC continues to recommend COVID-19 vaccines and booster doses for eligible individuals (age limit according to the type of vaccine) after careful consideration from risk-benefit assessment and favorable outcomes from vaccination. Mechanisms behind COVID-19 vaccine-induced myocarditis are not clear yet but several possibilities such as molecular mimicry between the spike protein of SARS-CoV-2 and self-antigens, immune response to mRNA, and activation of host immunological system, trigger of the pre-existing dysregulated immunological system have been documented in the literature. Overall, data suggests a good prognosis, especially in young patients. In this review article, we cover currently available data on COVID-19 vaccine-related myocarditis incidence, concerns, possible mechanisms of myocarditis, current treatment, and outcome trends, risk vs benefit assessment of COVID-19 vaccination in this current pandemic.

Di Dedda, E. A., et al. (2022). "Cardiac magnetic resonance imaging of myocarditis and pericarditis following COVID-19 vaccination: a multicenter collection of 27 cases." Eur Radiol **32**(7): 4352-4360.

OBJECTIVES: To assess clinical and cardiac magnetic resonance (CMR) imaging features of patients with peri-myocarditis following Coronavirus Disease 2019 (COVID-19) vaccination. METHODS: We retrospectively collected a case series of 27 patients who underwent CMR in the clinical suspect of heart inflammation following COVID-19 vaccination, from 16 large tertiary centers. Our patient's cohort was relatively young (36.6 +/- 16.8 years), predominately included males (n = 25/27) with few comorbidities and covered a catchment area of approximately 8 million vaccinated patients. RESULTS: CMR revealed typical mid-subepicardial non-ischemic late gadolinium enhancement (LGE) in 23 cases and matched positively with CMR T2 criteria of myocarditis. In 7 cases, typical hallmarks of acute pericarditis were present. Short-term follow-up (median = 20 days) from presentation was uneventful for 25/27 patients and unavailable in two cases. CONCLUSIONS: While establishing a causal relationship between peri-myocardial inflammation and vaccine administration can be challenging, our clinical experience suggests that CMR should be performed for diagnosis confirmation and to drive clinical decision-making and follow-up. KEY POINTS: * Acute onset of dyspnea, palpitations, or acute and persisting chest pain after COVID-19 vaccination should raise the suspicion of possible myocarditis or pericarditis, and patients should seek immediate medical attention and treatment to help recovery and avoid complications. * In case of elevated troponin levels and/or relevant ECG changes, cardiac magnetic resonance should be considered as the best non-invasive diagnostic option to confirm the diagnosis of myocarditis or pericarditis and to drive clinical decision-making and follow-up.

Diaz, G. A., et al. (2021). "Myocarditis and Pericarditis After Vaccination for COVID-19." JAMA **326**(12): 1210-1212.

This study investigates the incidence of myocarditis and pericarditis emergency department or inpatient hospital encounters before COVID-19 vaccine availability (January 2019-January 2021) and during a COVID-19 vaccination period (February-May 2021) in a large US health care system.

Dionne, A., et al. (2021). "Association of Myocarditis With BNT162b2 Messenger RNA COVID-19 Vaccine in a Case Series of Children." JAMA Cardiol **6**(12): 1446-1450.

IMPORTANCE: The BNT162b2 (Pfizer-BioNTech) messenger RNA COVID-19 vaccine was authorized on May 10, 2021, for emergency use in children aged 12 years and older. Initial reports showed that the vaccine was well tolerated without serious adverse events; however, cases of myocarditis have been reported since approval. OBJECTIVE: To review results of comprehensive cardiac imaging in children with myocarditis after COVID-19 vaccine. DESIGN, SETTING, AND PARTICIPANTS: This study was a case series of children younger than 19 years hospitalized with myocarditis within 30 days of BNT162b2 messenger RNA COVID-19 vaccine. The setting was a single-center pediatric referral facility, and admissions occurred between May 1 and July 15, 2021. MAIN OUTCOMES AND MEASURES: All patients underwent cardiac evaluation including an electrocardiogram, echocardiogram, and cardiac magnetic resonance imaging. RESULTS: Fifteen patients (14 male patients [93%]; median age, 15 years [range, 12-18 years]) were hospitalized for management of myocarditis after receiving the BNT162b2 (Pfizer) vaccine. Symptoms started 1 to 6 days after receipt of the vaccine and included chest pain in 15 patients (100%), fever in 10 patients (67%), myalgia in 8 patients (53%), and headache in 6 patients (40%). Troponin levels were elevated in all patients at admission (median, 0.25 ng/mL [range, 0.08-3.15 ng/mL]) and peaked 0.1 to 2.3 days after admission. By echocardiographic examination, decreased left ventricular (LV) ejection fraction (EF) was present in 3 patients (20%), and abnormal global longitudinal or circumferential strain was present in 5 patients (33%). No patient had a pericardial effusion. Cardiac magnetic resonance imaging findings were consistent with myocarditis in 13 patients (87%) including late gadolinium enhancement in 12 patients (80%), regional hyperintensity on T2-weighted imaging in 2 patients (13%), elevated extracellular volume fraction in 3 patients (20%), and elevated LV global native T1 in 2 patients (20%). No patient required intensive care unit admission, and median hospital length of stay was 2 days (range 1-5). At follow-up 1 to 13 days after hospital discharge, 11 patients (73%) had resolution of symptoms. One patient (7%) had persistent borderline low LV systolic function on echocardiogram (EF 54%). Troponin levels remained mildly elevated in 3 patients (20%). One patient (7%) had nonsustained ventricular tachycardia on ambulatory monitor. CONCLUSIONS AND RELEVANCE: In this small case series study, myocarditis was diagnosed in children after COVID-19 vaccination, most commonly in boys after the second dose. In this case series, in short-term follow-up, patients were mildly affected. The long-term risks associated with postvaccination myocarditis remain unknown. Larger studies with longer follow-up are needed to inform recommendations for COVID-19 vaccination in this population.

Dlewati, M., et al. (2022). "COVID-19 mRNA Vaccine-Associated Myocarditis Presenting as STEMI in a 48-Year-Old Male." Case Rep Cardiol **2022**: 2284530.

Myocarditis has been recognized as a rare complication of coronavirus disease 2019 (COVID-19) mRNA vaccinations. Young adult and adolescent males < 30 years of age are the most commonly affected group, with decreased incidence with older age. This is a

case of a 48-year-old male who presented with chest pain and EKG findings of STEMI shortly after receiving the second dose of the Moderna COVID-19 mRNA vaccine. Emergent left heart catheterization revealed normal coronaries. Subsequently, the patient had rapid resolution of his symptoms and improvement in serum markers. The exact etiology factors to this new and rare phenomenon are yet to be fully understood. This patient did have a history of previous viral myocarditis 7 years ago; however, it remains unclear if this could be a predisposing factor to the development of mRNA vaccine-associated myocarditis.

Dobronyi, I., et al. (2022). "A Case of Recurrent Myocarditis After COVID-19 Vaccination, Due to Acute Myeloid Leukemia." CJC Open **4**(12): 1027-1030.

A 25-year-old man presented with chest pain and an elevated troponin level following COVID-19 vaccination. Despite initial response to nonsteroidal anti-inflammatory drugs, he developed a recurrent and relapsing course requiring multiple readmissions. Cardiac magnetic resonance imaging confirmed myocarditis. Due to progressing macrocytic anemia, he was eventually diagnosed with acute myeloid leukemia, thought to be the underlying driver of his recurrent and persistent myocarditis.

Dong, Y. M., et al. (2022). "Case report: Myocarditis following COVID-19 protein subunit vaccination." Front Cardiovasc Med **9**: 970045.

We report findings in a 34-year-old female patient who presented with fulminant myocarditis 8 days after receiving the first dose of the ZF2001 RBD-subunit vaccine against coronavirus disease 2019 (COVID-19). Autopsy showed severe interstitial myocarditis, including multiple patchy infiltrations of lymphocytes and monocytes in the myocardium of the left and right ventricular walls associated with myocyte degeneration and necrosis. This report highlights the details of clinical presentations and autopsy findings of myocarditis after ZF2001 (RBD-subunit vaccine) vaccination. The correlation between vaccination and death due to myocarditis is discussed.

Donzelli, A. (2023). "Letter by Donzelli Regarding Article, "Risk of Myocarditis After Sequential Doses of COVID-19 Vaccine and SARS-CoV-2 Infection by Age and Sex"." Circulation **147**(10): e653-e654.

Dove, M. L., et al. (2023). "Cardiac Magnetic Resonance Findings of Coronavirus Disease 2019 (COVID-19) Vaccine-Associated Myopericarditis at Intermediate Follow-Up: A Comparison with Classic Myocarditis." J Pediatr **260**: 113462.

OBJECTIVE: To report intermediate cardiac magnetic resonance (CMR) findings of coronavirus disease 2019 (COVID-19) vaccine-associated myopericarditis (C-VAM) and compare with classic myocarditis. STUDY DESIGN: Retrospective cohort study including children diagnosed with C-VAM from May 2021 through December 2021 with early and intermediate CMR. Patients with classic myocarditis from January 2015 through December 2021 and intermediate CMR were included for comparison. RESULTS: There were 8 patients with C-VAM and 20 with classic myocarditis. Among those with C-VAM, CMR performed at a median 3 days (IQR 3, 7) revealed 2 of 8 patients with left

ventricular ejection fraction <55%, 7 of 7 patients receiving contrast with late gadolinium enhancement (LGE), and 5 of 8 patients with elevated native T1 values. Borderline T2 values suggestive of myocardial edema were present in 6 of 8 patients. Follow-up CMRs performed at a median 107 days (IQR 97, 177) showed normal ventricular systolic function, T1, and T2 values; 3 of 7 patients had LGE. At intermediate follow-up, patients with C-VAM had fewer myocardial segments with LGE than patients with classic myocarditis (4/119 vs 42/340, P = .004). Patients with C-VAM also had a lower frequency of LGE (42.9 vs 75.0%) and lower percentage of left ventricular ejection fraction <55% compared with classic myocarditis (0.0 vs 30.0%), although these differences were not statistically significant. Five patients with classic myocarditis did not receive an early CMR, leading to some selection bias in study design. CONCLUSIONS: Patients with C-VAM had no evidence of active inflammation or ventricular dysfunction on intermediate CMR, although a minority had persistent LGE. Intermediate findings in C-VAM revealed less LGE burden compared with classic myocarditis.

Eggebrecht, H., et al. (2022). "Trends in ambulatory cardiology consultations for suspected myocarditis after COVID-19 vaccination." Clin Res Cardiol **111**(2): 237-239.

Ehrlich, P., et al. (2021). "Biopsy-proven lymphocytic myocarditis following first mRNA COVID-19 vaccination in a 40-year-old male: case report." Clin Res Cardiol **110**(11): 1855-1859.

Esposito, S., et al. (2022). "Myocarditis Following COVID-19 Vaccine Use: Can It Play a Role for Conditioning Immunization Schedules?" Front Immunol **13**: 915580.

Myocarditis (MYO) is a relatively uncommon inflammatory disease that involves the heart muscle. It can be a very severe disease as it can lead to the development of acute or chronic heart failure and, in a not marginal number of cases, to death. Most of the cases are diagnosed in healthy people younger than 30 years of age. Moreover, males are affected about twice as much as females. Viruses are among the most common causes of MYO, but how viral infection can lead to MYO development is not precisely defined. After COVID-19 pandemic declaration, incidence rate of MYO has significantly increased worldwide because of the SARS-CoV-2 infection. After the introduction of anti-COVID-19 vaccines, reports of post-immunization MYO have emerged, suggesting that a further cause of MYO together with the SARS-CoV-2 infection could increase the risk of heart damage during pandemic. Main aim of this study is to discuss present knowledge regarding etiopathogenesis and clinical findings of MYO associated with COVID-19 vaccine administration and whether the risk of this adverse events can modify the initially suggested recommendation for the use of COVID-19 vaccines in pediatric age. Literature analysis showed that MYO is an adverse event that can follow the COVID-19 immunization with mRNA vaccines in few persons, particularly young adults, adolescents, and older children. It is generally a mild disease that should not modify the present recommendations for immunization with the authorized COVID-19 mRNA vaccines. Despite this, further studies are needed to evaluate presently undefined aspects of MYO development after COVID-19 vaccine administration and reduce the risk of development of this kind of vaccine complication. Together with a better definition of

the true incidence of MYO and the exact role of the various factors in conditioning incidence variations, it is essential to establish long-term evolution of acute COVID-19 related MYO.

Etuk, A. S., I. N. Jackson and H. Panayiotou (2022). "A Rare Case of Myocarditis After the First Dose of Moderna Vaccine in a Patient With Two Previous COVID-19 Infections." Cureus **14**(5): e24802.

Myocarditis is the inflammation of the cardiac muscle caused by a variety of factors ranging from infections to autoimmune diseases. Most cases of vaccine-induced myocarditis occur after the second dose of vaccination; however, a few cases have been reported following the first dose of vaccination with or without previous coronavirus disease 2019 (COVID-19) infection. A case of myocarditis occurring about three weeks after the first dose of the Moderna vaccine has been reported in a patient with one previous COVID-19 infection. However, there have not been any documented cases of myocarditis after the first dose of the Moderna vaccine in a patient with two prior COVID-19 infections. Our index patient had already experienced two COVID-19 infections in the past and was diagnosed with myocarditis eight hours after receiving the first dose of the Moderna vaccine. The susceptibility to developing this likely stems from the possible production of antibodies to the viral antigen from previous COVID-19 infections. Furthermore, the fact that our patient developed symptoms eight hours after receiving the vaccine suggests a possible additive effect of antibodies produced from the two previous COVID-19 infections. This case report suggests that individuals repeatedly infected with COVID-19 may be at increased risk of myocarditis following the administration of the Moderna vaccine.

Evertz, R., et al. (2022). "Cardiovascular magnetic resonance imaging patterns of acute COVID-19 mRNA vaccine-associated myocarditis in young male patients: A first single-center experience." Front Cardiovasc Med **9**: 965512.

BACKGROUND: The risk of myocarditis after mRNA vaccination against COVID-19 has emerged recently. Current evidence suggests that young male patients are predominantly affected. In the majority of the cases, only mild symptoms were observed. However, little is known about cardiac magnetic resonance (CMR) imaging patterns in mRNA-related myocarditis and their differences when compared to classical viral myocarditis in the acute phase of inflammation. METHODS AND RESULTS: In total, 10 mRNA vaccination-associated patients with myocarditis were retrospectively enrolled in this study and compared to 10 patients suffering from viral myocarditis, who were matched for age, sex, comorbidities, and laboratory markers. All patients (n = 20) were hospitalized and underwent a standardized clinical examination, as well as an echocardiography and a CMR. Both, clinical and imaging findings and, in particular, functional and volumetric CMR assessments, as well as detailed tissue characterization using late gadolinium enhancement and T1 + T2-weighted sequences, were compared between both groups. The median age of the overall cohort was 26 years (group 1: 25.5; group 2: 27.5; p = 0.57). All patients described chest pain as the leading reason for their initial presentation. CMR volumetric and functional parameters did not differ

significantly between both groups. In all cases, the lateral left ventricular wall showed late gadolinium enhancement without significant differences in terms of the localization or in-depth tissue characterization (late gadolinium enhancement [LGE] enlargement: group 1: 5.4%; group 2: 6.5%; p = 0.14; T2 global/maximum value: group 1: 38.9/52 ms; group 2: 37.8/54.5 ms; p = 0.79 and p = 0.80). CONCLUSION: This study yielded the first evidence that COVID-19 mRNA vaccine-associated myocarditis does not show specific CMR patterns during the very acute stage in the most affected patient group of young male patients. The observed imaging markers were closely related to regular viral myocarditis in our cohort. Additionally, we could not find any markers implying adverse outcomes in this relatively little number of patients; however, this has to be confirmed by future studies that will include larger sample sizes.

Fatima, M., et al. (2023). "Development of myocarditis and pericarditis after COVID-19 vaccination: A deeper insight." Clin Cardiol **46**(4): 460-461.

Fatima, M., et al. (2022). "Development of myocarditis and pericarditis after COVID-19 vaccination in adult population: A systematic review." Ann Med Surg (Lond) **76**: 103486.
OBJECTIVES: A clear temporal relationship between myocarditis and pericarditis after COVID-19 vaccination has led to the belief that the vaccine may act as a trigger for these cardiologic complications. The aim of this systematic review is to explore the incidence, clinical presentation, management, and association between them. METHODS: We conducted a systematic literature search on Cochrane, MEDLINE, and EMBASE as per guidelines of PRISMA (Preferred Reporting Items for Systematic Reviews). A total of 41 case reports and case series describing 97 patients, and 5 original articles describing 15,585,309 participants were selected as part of this review. RESULTS: Of the 97 reported cases describing vaccine-associated myocarditis/pericarditis, 67 (69%) patients received Pfizer-BioNTech and 25 (25.7%) received Moderna. The mean onset of symptoms after vaccine administration was 3.8 +/- 4.5 days with three-quarters developing symptoms after the second dose. Chest pain (n = 88, 90%) and fever (n = 33, 34%) were the most common presenting complaints. Out of 97, 80 (82.5%) patients recovered while 4 (4.1%) patients expired. The pooled incidence of myocarditis and pericarditis extrapolated from original studies is 0.001% and 0.0004%, respectively. In the original studies, nearly all the cases of myocarditis and pericarditis were mild. Chest pain and fever were the most common presenting symptoms. CONCLUSION: Myocarditis and pericarditis after the COVID-19 vaccine have been reported more in young adult males and are most likely to occur after the second dose of mRNA vaccines. The presentation is mild and the majority of the patients recover either completely or partially.

Fatima, M., et al. (2023). "Development of myocarditis and pericarditis after COVID-19 vaccination in children and adolescents: A systematic review." Clin Cardiol **46**(3): 243-259.
Myocarditis and pericarditis have been reported after COVID-19 vaccine administration in children and adolescents, raising the concern about their possible association with these vaccines. The objective was to explore the incidence, clinical presentation, and

association of myocarditis and pericarditis with COVID-19 vaccines in children and adolescents. We conducted a systematic literature search on three databases, that is, Cochrane, MEDLINE/PubMed, and EMBASE from inception till March 2022. A total of three case reports, four case series, and six observational studies were included in the review. For case reports and case series, the mean age of the patients was 17.4 years, with 96.9% being male. Chest pain (n = 31, 93.9%), fever (n = 18, 54.5%), myalgias (n = 15, 45.4%) and headache (n = 9, 27.2%) were the most common presentations. Out of 33 patients, 32 (96.9%) of patients received Pfizer-BioNTech whereas only one (3.03%) received Moderna (mRNA 1273). Clinical investigations revealed ST elevation (n = 32, 97%), and elevated CRP (n = 9, 27.2%) and cardiac troponin (n = 29, 87.8%). The pooled incidence of myocarditis and pericarditis from observational studies was (0.00063%) and (0.000074%) %, respectively. Myocarditis and pericarditis in children and adolescents after the COVID-19 vaccines were more prevalent among males and more commonly observed after the second dose of Pfizer. Though the overall incidence was low, however, the clinicians should consider myocarditis and pericarditis as probable diagnosis when encountering young patients, with a history of vaccine administration, presenting with suggestive findings.

Fosch, X., et al. (2022). "Acute myocarditis after a third dose of the BNT162b2 COVID-19 vaccine." Rev Esp Cardiol (Engl Ed) **75**(7): 614-616.

Fronza, M., et al. (2022). "Myocardial Injury Pattern at MRI in COVID-19 Vaccine-Associated Myocarditis." Radiology **304**(3): 553-562.

Background There are limited data on the pattern and severity of myocardial injury in patients with COVID-19 vaccination-associated myocarditis. Purpose To describe myocardial injury following COVID-19 vaccination and to compare these findings to other causes of myocarditis. Materials and Methods In this retrospective cohort study, consecutive adult patients with myocarditis with at least one T1-based and at least one T2-based abnormality at cardiac MRI performed at a tertiary referral hospital from December 2019 to November 2021 were included. Patients were classified into one of three groups: myocarditis following COVID-19 vaccination, myocarditis following COVID-19 illness, and other myocarditis not associated with COVID-19 vaccination or illness. Results Of the 92 included patients, 21 (23%) had myocarditis following COVID-19 vaccination (mean age, 31 years +/- 14 [SD]; 17 men; messenger RNA-1273 in 12 [57%] and BNT162b2 in nine [43%]). Ten of 92 (11%) patients had myocarditis following COVID-19 illness (mean age, 51 years +/- 14; three men) and 61 of 92 (66%) patients had other myocarditis (mean age, 44 years +/- 18; 36 men). MRI findings in the 21 patients with vaccine-associated myocarditis included late gadolinium enhancement (LGE) in 17 patients (81%) and left ventricular dysfunction in six (29%). Compared with other causes of myocarditis, patients with vaccine-associated myocarditis had a higher left ventricular ejection fraction and less extensive LGE, even after controlling for age, sex, and time from symptom onset to MRI. The most frequent location of LGE in all groups was subepicardial at the basal inferolateral wall, although septal involvement was less common in vaccine-associated myocarditis. At short-term follow-up (median, 22 days

[IQR, 7-48 days]), all patients with vaccine-associated myocarditis were asymptomatic with no adverse events. Conclusion Cardiac MRI demonstrated a similar pattern of myocardial injury in vaccine-associated myocarditis compared with other causes, although abnormalities were less severe, with less frequent septal involvement and no adverse events over the short-term follow-up. (c) RSNA, 2022 Online supplemental material is available for this article. See also the editorial by Raman and Neubauer in this issue.

Fronza, M., et al. (2022). "Cardiac MRI and Clinical Follow-up in COVID-19 Vaccine-associated Myocarditis." Radiology **304**(3): E48-E49.

Frustaci, A., et al. (2022). "Hypersensitivity Myocarditis after COVID-19 mRNA Vaccination." J Clin Med **11**(6).

BACKGROUND: Myocarditis, even in a severe and lethal form, may occur after COVID-19 mRNA (BNT162b2) vaccination. However, its pathway, morphomolecular characterization and treatment are still unknown. METHODS: Routine hematochemical screening, ECG, Holter monitoring, 2D echocardiogram cardiac magnetic resonance (CMR) and invasive cardiac studies (cardiac catheterization, selective coronary angiography, left ventriculography and left ventricular endomyocardial biopsy) are reported from three patients (39F-pt1, 78M-pt2, 52M-pt3) with severe compromise of conduction tissue (junctional rhythm and syncope, pt1) or cardiac function compromise (LVEF </= 35%, pt2 and pt3) after COVID-19 mRNA (BNT162b2). RESULTS: Hematochemical data and coronary angiography were normal in the patients studied. Histology showed in all three patients extensive myocardial infiltration of degranulated eosinophils and elevation of serum cationic protein directly responsible for cardiomyocyte damage. These findings demonstrate myocarditis hypersensitivity to some component of the vaccine (spike protein?) acting as a hapten to some macromolecules of cardiomyocytes. Steroid administration (prednisone, 1 mg/kg die for 3 days, followed by 0.33 mg/kg for 4 weeks) was followed by complete recovery of cardiac contractility in pt2 and pt3. CONCLUSIONS: Eosinophilic myocarditis is a possible adverse reaction to the mRNA COVID-19 vaccine. Its pathway is mediated by release of cationic protein and responds to short courses of steroid administration.

Gargano, J. W., et al. (2021). "Use of mRNA COVID-19 Vaccine After Reports of Myocarditis Among Vaccine Recipients: Update from the Advisory Committee on Immunization Practices - United States, June 2021." MMWR Morb Mortal Wkly Rep **70**(27): 977-982.

In December 2020, the Food and Drug Administration (FDA) issued Emergency Use Authorizations (EUAs) for the Pfizer-BioNTech COVID-19 (BNT162b2) vaccine and the Moderna COVID-19 (mRNA-1273) vaccine,(dagger) and the Advisory Committee on Immunization Practices (ACIP) issued interim recommendations for their use in persons aged >/=16 years and >/=18 years, respectively.(section sign) In May 2021, FDA expanded the EUA for the Pfizer-BioNTech COVID-19 vaccine to include adolescents aged 12-15 years; ACIP recommends that all persons aged >/=12 years receive a COVID-19 vaccine. Both Pfizer-BioNTech and Moderna vaccines are mRNA vaccines encoding the

stabilized prefusion spike glycoprotein of SARS-CoV-2, the virus that causes COVID-19. Both mRNA vaccines were authorized and recommended as a 2-dose schedule, with second doses administered 21 days (Pfizer-BioNTech) or 28 days (Moderna) after the first dose. After reports of myocarditis and pericarditis in mRNA vaccine recipients,(paragraph sign) which predominantly occurred in young males after the second dose, an ACIP meeting was rapidly convened to review reported cases of myocarditis and pericarditis and discuss the benefits and risks of mRNA COVID-19 vaccination in the United States. Myocarditis is an inflammation of the heart muscle; if it is accompanied by pericarditis, an inflammation of the thin tissue surrounding the heart (the pericardium), it is referred to as myopericarditis. Hereafter, myocarditis is used to refer to myocarditis, pericarditis, or myopericarditis. On June 23, 2021, after reviewing available evidence including that for risks of myocarditis, ACIP determined that the benefits of using mRNA COVID-19 vaccines under the FDA's EUA clearly outweigh the risks in all populations, including adolescents and young adults. The EUA has been modified to include information on myocarditis after receipt of mRNA COVID-19 vaccines. The EUA fact sheets should be provided before vaccination; in addition, CDC has developed patient and provider education materials about the possibility of myocarditis and symptoms of concern, to ensure prompt recognition and management of myocarditis.

Gautam, N., et al. (2021). "A Late Presentation of COVID-19 Vaccine-Induced Myocarditis." Cureus **13**(9): e17890.

With the introduction of the coronavirus disease 2019 (COVID-19) mRNA vaccines, the incidence of severe infection has significantly decreased. While the vaccines have been shown to be effective and safe, there have been few case reports of acute myocarditis within 3-5 days following the second dose of the vaccine. We report a case of an elderly man who presented with acute-onset chest pain after three months of receiving the second dose of the mRNA vaccine. He was found to have acute myocarditis on cardiac magnetic resonance imaging (CMRI), which was attributed to exposure to the COVID-19 vaccine in the absence of any other risk factors. Our patient demonstrated quick resolution of symptoms and was discharged within 72 hours. We review the literature and summarize published case reports on COVID-19 vaccine-associated myocarditis. The present case report provides new evidence regarding the possible subacute presentation of myocarditis post-COVID-19 vaccine, and further highlights the favorable outcome in this newly described clinical entity.

Gellad, W. F. (2021). "Myocarditis after vaccination against covid-19." BMJ **375**: n3090.

Gill, J. R., R. Tashjian and E. Duncanson (2022). "Autopsy Histopathologic Cardiac Findings in 2 Adolescents Following the Second COVID-19 Vaccine Dose." Arch Pathol Lab Med **146**(8): 925-929.

CONTEXT.-: Myocarditis in adolescents has been diagnosed clinically following the administration of the second dose of an mRNA vaccine for coronavirus disease 2019 (COVID-19). OBJECTIVE.-: To examine the autopsy microscopic cardiac findings in

adolescent deaths that occurred shortly following administration of the second Pfizer-BioNTech COVID-19 dose to determine if the myocarditis described in these instances has the typical histopathology of myocarditis. DESIGN.-: Clinical and autopsy investigation of 2 teenage boys who died shortly following administration of the second Pfizer-BioNTech COVID-19 dose. RESULTS.-: The microscopic examination revealed features resembling a catecholamine-induced injury, not typical myocarditis pathology. CONCLUSIONS.-: The myocardial injury seen in these postvaccine hearts is different from typical myocarditis and has an appearance most closely resembling a catecholamine-mediated stress (toxic) cardiomyopathy. Understanding that these instances are different from typical myocarditis and that cytokine storm has a known feedback loop with catecholamines may help guide screening and therapy.

Giray, D. and S. Epcacan (2022). "Acute myocarditis following COVID-19 mRNA vaccination: a paediatric case." Cardiol Young **32**(7): 1178-1180.

Myocarditis is an inflammation of the heart muscle. In this case, a previously healthy, 17-year-old adolescent with myocarditis after BNT162b2 mRNA vaccination was reported. He was admitted to the hospital with severe chest pain, changes in electrocardiography, and elevation in serum troponin level after fourth day of receiving first dose of vaccine. There was no coronary arterial disease in coronary angiogram. A diagnosis of vaccine-induced myocarditis was made, and supportive treatment was initiated.

Goddard, K., et al. (2022). "Incidence of Myocarditis/Pericarditis Following mRNA COVID-19 Vaccination Among Children and Younger Adults in the United States." Ann Intern Med **175**(12): 1169-1771.

Goddard, K., et al. (2022). "Risk of myocarditis and pericarditis following BNT162b2 and mRNA-1273 COVID-19 vaccination." Vaccine **40**(35): 5153-5159.

BACKGROUND: Evidence indicates that mRNA COVID-19 vaccination is associated with risk of myocarditis and possibly pericarditis, especially in young males. It is not clear if risk differs between mRNA-1273 versus BNT162b2. We assessed if risk differs using comprehensive health records on a diverse population. METHODS: Members 18-39 years of age at eight integrated healthcare-delivery systems were monitored using data updated weekly and supplemented with medical record review of myocarditis and pericarditis cases. Incidence of myocarditis and pericarditis events that occurred among vaccine recipients 0 to 7 days after either dose 1 or 2 of a messenger RNA (mRNA) vaccine was compared with that of vaccinated concurrent comparators who, on the same calendar day, had received their most recent dose 22 to 42 days earlier. Rate ratios (RRs) were estimated by conditional Poisson regression, adjusted for age, sex, race and ethnicity, health plan, and calendar day. Head-to-head comparison directly assessed risk following mRNA-1273 versus BNT162b2 during 0-7 days post-vaccination. RESULTS: From December 14, 2020 - January 15, 2022 there were 41 cases after 2,891,498 doses of BNT162b2 and 38 cases after 1,803,267 doses of mRNA-1273. Cases had similar demographic and clinical characteristics. Most were hospitalized for </=1 day; none required intensive care. During days 0-7 after dose 2 of BNT162b2, the incidence was

14.3 (CI: 6.5-34.9) times higher than the comparison interval, amounting to 22.4 excess cases per million doses; after mRNA-1273 the incidence was 18.8 (CI: 6.7-64.9) times higher than the comparison interval, amounting to 31.2 excess cases per million doses. In head-to-head comparisons 0-7 days after either dose, risk was moderately higher after mRNA-1273 than after BNT162b2 (RR: 1.61, CI 1.02-2.54). CONCLUSIONS: Both vaccines were associated with increased risk of myocarditis and pericarditis in 18-39-year-olds. Risk estimates were modestly higher after mRNA-1273 than after BNT162b2.

Gomes, D. A., et al. (2022). "Acute Myocarditis Following mRNA COVID-19 Vaccine." Arq Bras Cardiol **118**(4): 783-786.

Guduguntla, V. and M. H. Katz (2021). "COVID-19 Messenger RNA Vaccination and Myocarditis-A Rare and Mostly Mild Adverse Effect." JAMA Intern Med **181**(12): 1560.

Guglin, M. E., et al. (2023). "Fulminant Myocarditis and Cardiogenic Shock Following COVID-19 Infection Versus COVID-19 Vaccination: A Systematic Literature Review." J Clin Med **12**(5).

BACKGROUND: Myocarditis, diagnosed by symptoms and troponin elevation, has been well-described with COVID-19 infection, as well as shortly after COVID-19 vaccination. The literature has characterized the outcomes of myocarditis following COVID-19 infection and vaccination, but clinicopathologic, hemodynamic, and pathologic features following fulminant myocarditis have not been well-characterized. We aimed to compare clinical and pathological features of fulminant myocarditis requiring hemodynamic support with vasopressors/inotropes and mechanical circulatory support (MCS), in these two conditions. METHODS: We analyzed the literature on fulminant myocarditis and cardiogenic shock associated with COVID-19 and COVID-19 vaccination and systematically reviewed all cases and case series where individual patient data were presented. We searched PubMed, EMBASE, and Google Scholar for "COVID", "COVID-19", and "coronavirus" in combination with "vaccine", "fulminant myocarditis", "acute heart failure", and "cardiogenic shock". The Student's t-test was used for continuous variables and the chi2 statistic was used for categorical variables. For non-normal data distributions, the Wilcoxon Rank Sum Test was used for statistical comparisons. RESULTS: We identified 73 cases and 27 cases of fulminant myocarditis associated with COVID-19 infection (COVID-19 FM) and COVID-19 vaccination (COVID-19 vaccine FM), respectively. Fever, shortness of breath, and chest pain were common presentations, but shortness of breath and pulmonary infiltrates were more often present in COVID-19 FM. Tachycardia, hypotension, leukocytosis, and lactic acidosis were seen in both cohorts, but patients with COVID-19 FM were more tachycardic and hypotensive. Histologically, lymphocytic myocarditis dominated both subsets, with some cases of eosinophilic myocarditis in both cohorts. Cellular necrosis was seen in 44.0% and 47.8% of COVID-19 FM and COVID-19 vaccine FM, respectively. Vasopressors and inotropes were used in 69.9% of COVID-19 FM and in 63.0% of the COVID-19 vaccine FM. Cardiac arrest was observed more in COVID-19 FM ($p = 0.008$). Venoarterial extracorporeal membrane oxygenation (VA-ECMO) support for cardiogenic shock was also used more commonly in the COVID-19 fulminant myocarditis group ($p = 0.0293$). Reported mortality was similar (27.7%) and

27.8%, respectively) but was likely worse for COVID-19 FM as the outcome was still unknown in 11% of cases. CONCLUSIONS: In the first series to retrospectively assess fulminant myocarditis associated with COVID-19 infection versus COVID-19 vaccination, we found that both conditions had a similarly high mortality rate, while COVID-19 FM had a more malignant course with more symptoms on presentation, more profound hemodynamic decompensation (higher heart rate, lower blood pressure), more cardiac arrests, and higher temporary MCS requirements including VA-ECMO. In terms of pathology, there was no difference in most biopsies/autopsies that demonstrated lymphocytic infiltrates and some eosinophilic or mixed infiltrates. There was no predominance of young males in COVID-19 vaccine FM cases, with male patients representing only 40.9% of the cohort.

Guo, W., et al. (2022). "Profiling COVID-19 Vaccine Adverse Events by Statistical and Ontological Analysis of VAERS Case Reports." Front Pharmacol **13**: 870599.

Since the beginning of the COVID-19 pandemic, vaccines have been developed to mitigate the spread of SARS-CoV-2, the virus that causes COVID-19. These vaccines have been effective in reducing the rate and severity of COVID-19 infection but also have been associated with various adverse events (AEs). In this study, data from the Vaccine Adverse Event Reporting System (VAERS) was queried and analyzed via the Cov19VaxKB vaccine safety statistical analysis tool to identify statistically significant (i.e., enriched) AEs for the three currently FDA-authorized or approved COVID-19 vaccines. An ontology-based classification and literature review were conducted for these enriched AEs. Using VAERS data as of 31 December 2021, 96 AEs were found to be statistically significantly associated with the Pfizer-BioNTech, Moderna, and/or Janssen COVID-19 vaccines. The Janssen COVID-19 vaccine had a higher crude reporting rate of AEs compared to the Moderna and Pfizer COVID-19 vaccines. Females appeared to have a higher case report frequency for top adverse events compared to males. Using the Ontology of Adverse Event (OAE), these 96 adverse events were classified to different categories such as behavioral and neurological AEs, cardiovascular AEs, female reproductive system AEs, and immune system AEs. Further statistical comparison between different ages, doses, and sexes was also performed for three notable AEs: myocarditis, GBS, and thrombosis. The Pfizer vaccine was found to have a closer association with myocarditis than the other two COVID-19 vaccines in VAERS, while the Janssen vaccine was more likely to be associated with thrombosis and GBS AEs. To support standard AE representation and study, we have also modeled and classified the newly identified thrombosis with thrombocytopenia syndrome (TTS) AE and its subclasses in the OAE by incorporating the Brighton Collaboration definition. Notably, severe COVID-19 vaccine AEs (including myocarditis, GBS, and TTS) rarely occur in comparison to the large number of COVID-19 vaccinations administered in the United States, affirming the overall safety of these COVID-19 vaccines.

Hajjo, R., et al. (2021). "Shedding the Light on Post-Vaccine Myocarditis and Pericarditis in COVID-19 and Non-COVID-19 Vaccine Recipients." Vaccines (Basel) **9**(10).

Myocarditis and pericarditis have been linked recently to COVID-19 vaccines without exploring the underlying mechanisms, or compared to cardiac adverse events post-non-COVID-19 vaccines. We introduce an informatics approach to study post-vaccine adverse events on the systems biology level to aid the prioritization of effective preventive measures and mechanism-based pharmacotherapy by integrating the analysis of adverse event reports from the Vaccine Adverse Event Reporting System (VAERS) with systems biology methods. Our results indicated that post-vaccine myocarditis and pericarditis were associated most frequently with mRNA COVID-19 vaccines followed by live or live-attenuated non-COVID-19 vaccines such as smallpox and anthrax vaccines. The frequencies of cardiac adverse events were affected by vaccine, vaccine type, vaccine dose, sex, and age of the vaccinated individuals. Systems biology results suggested a central role of interferon-gamma (INF-gamma) in the biological processes leading to cardiac adverse events, by impacting MAPK and JAK-STAT signaling pathways. We suggest that increasing the time interval between vaccine doses minimizes the risks of developing inflammatory adverse reactions. We also propose glucocorticoids as preferred treatments based on system biology evidence. Our informatics workflow provides an invaluable tool to study post-vaccine adverse events on the systems biology level to suggest effective mechanism-based pharmacotherapy and/or suitable preventive measures.

Han, J., et al. (2022). "Case report: Myocarditis with nonsustained ventricular tachycardia following COVID-19 mRNA vaccination in a female adolescent." Front Pediatr **10**: 995167.

Children with underlying medical conditions potentially develop severe illness from Coronavirus disease 2019 (COVID-19). The use of vaccines against COVID-19 is currently recommended for the pediatric population. The COVID-19 vaccine has a temporal association with the occurrence of myocarditis. Although most patients with COVID-19 vaccination-associated myocarditis (C-VAM) exhibit a mild clinical course and rapid recovery, C-VAM potentially causes electrical instability and sudden cardiac death. Herein, we report the case of a 17-year-old woman who presented with chest pain and syncope following the first dose of the messenger RNA COVID-19 vaccine. The patient's heart function was impaired, and nonsustained ventricular tachycardia was frequent. Cardiac magnetic resonance (CMR) imaging satisfied the criteria for myocarditis. Despite the administration of immunomodulatory drugs, the patient's heart function was not fully restored, and the concentration of cardiac enzymes remained above the normal range. Persistence of late gadolinium enhancement was observed on short-term follow-up CMR imaging. Although most patients with C-VAM exhibit mild symptoms, significant cardiac arrhythmias potentially occur. Furthermore, some patients with C-VAM demonstrate prolonged impaired heart function and sustained late gadolinium enhancement on follow-up CMR imaging. Therefore, monitoring of electrical and functional cardiac abnormalities in patients with C-VAM is crucial and the long-term outcomes and prognosis of patients with C-VAM require further investigation.

Hanneman, K. and P. Thavendiranathan (2023). "Editorial for "Cardiac Magnetic Resonance Imaging Findings in COVID-19 Vaccine-Related Myocarditis: A Pooled Analysis of 468 Patients"." J Magn Reson Imaging **57**(4): 1289-1290.

Harris, D. A., et al. (2023). "Comparative Risks of Potential Adverse Events Following COVID-19 mRNA Vaccination Among Older US Adults." JAMA Netw Open **6**(8): e2326852.

IMPORTANCE: Head-to-head safety comparisons of the mRNA vaccines for SARS-CoV-2 are needed for decision making; however, current evidence generalizes poorly to older adults, lacks sufficient adjustment, and inadequately captures events shortly after vaccination. Additionally, no studies to date have explored potential variation in comparative vaccine safety across subgroups with frailty or an increased risk of adverse events, information that would be useful for tailoring clinical decisions. OBJECTIVE: To compare the risk of adverse events between mRNA vaccines for COVID-19 (mRNA-1273 and BNT162b2) overall, by frailty level, and by prior history of the adverse events of interest. DESIGN, SETTING, AND PARTICIPANTS: This retrospective cohort study was conducted between December 11, 2020, and July 11, 2021, with 28 days of follow-up following the week of vaccination. A novel linked database of community pharmacy and Medicare claims data was used, representing more than 50% of the US Medicare population. Community-dwelling, fee-for-service beneficiaries aged 66 years or older who received mRNA-1273 vs BNT162b2 as their first COVID-19 vaccine were identified. Data analysis began on October 18, 2022. EXPOSURE: Dose 1 of mRNA-1273 vs BNT162b2 vaccine. MAIN OUTCOMES AND MEASURES: Twelve potential adverse events (eg, pulmonary embolism, thrombocytopenia purpura, and myocarditis) were assessed individually. Frailty was measured using a claims-based frailty index, with beneficiaries being categorized as nonfrail, prefrail, and frail. The risk of diagnosed COVID-19 was assessed as a secondary outcome. Generalized linear models estimated covariate-adjusted risk ratios (RRs) and risk differences (RDs) with 95% CIs. RESULTS: This study included 6 388 196 eligible individuals who received the mRNA-1273 or BNT162b2 vaccine. Their mean (SD) age was 76.3 (7.5) years, 59.4% were women, and 86.5% were White. A total of 38.1% of individuals were categorized as prefrail and 6.0% as frail. The risk of all outcomes was low in both vaccine groups. In adjusted models, the mRNA-1273 vaccine was associated with a lower risk of pulmonary embolism (RR, 0.96 [95% CI, 0.93-1.00]; RD, 9 [95% CI, 1-16] events per 100 000 persons) and other adverse events in subgroup analyses (eg, 11.0% lower risk of thrombocytopenia purpura among individuals categorized as nonfrail). The mRNA-1273 vaccine was also associated with a lower risk of diagnosed COVID-19 (RR, 0.86 [95% CI, 0.83-0.87]), a benefit that was attenuated by frailty level (frail: RR, 0.94 [95% CI, 0.89-0.99]). CONCLUSIONS AND RELEVANCE: In this cohort study of older US adults, the mRNA-1273 vaccine was associated with a slightly lower risk of several adverse events compared with BNT162b2, possibly due to greater protection against COVID-19. Future research should seek to formally disentangle differences in vaccine safety and effectiveness and consider the role of frailty in assessments of COVID-19 vaccine performance.

Holland, D. J., et al. (2022). "Myocarditis and Cardiac Complications Associated With COVID-19 and mRNA Vaccination: A Pragmatic Narrative Review to Guide Clinical Practice." Heart Lung Circ **31**(7): 924-933.

Coronavirus disease 2019 (COVID-19) caused by the SARS-CoV-2 virus is likely to remain endemic globally despite widespread vaccination. There is increasing concern for myocardial involvement and ensuing cardiac complications due to COVID-19, however, the available evidence suggests these risks are low. Pandemic publishing has resulted in rapid manuscript availability though pre-print servers. Subsequent article retractions, a lack of standardised definitions, over-reliance on isolated troponin elevation and the heterogeneity of studied patient groups (i.e. severe vs. symptomatic vs all infections) resulted in early concern for high rates of myocarditis in patients with and recovering from COVID-19. The estimated incidence of myocarditis in COVID-19 infection is 11 cases per 100,000 infections compared with an estimated 2.7 cases per 100,000 persons following mRNA vaccination. For substantiated cases, the clinical course of myocarditis related to COVID-19 or mRNA vaccination appears mild and self-limiting, with reports of severe/fulminant myocarditis being rare. There is limited data available on the management of myocarditis in these settings. Clinical guidance for appropriate use of cardiac investigations and monitoring in COVID-19 is needed for effective risk stratification and efficient use of cardiac resources in Australia. An amalgamation of national and international position statements and guidelines is helpful for guiding clinical practice. This paper reviews the current available evidence and guidelines and provides a summary of the risks and potential use of cardiac investigations and monitoring for patients with COVID-19.

Holland, D. J. and T. Stanton (2022). "Reply to Letter to the Editor Regarding: "Myocarditis and Cardiac Complications Associated With COVID-19 and mRNA Vaccination"." Heart Lung Circ **31**(10): e131.

Horiuchi, K., et al. (2022). "Fulminant myocarditis after the first dose of mRNA-1273 vaccination in a patient with previous COVID-19: a case report." Eur Heart J Case Rep **6**(7): ytac290.

BACKGROUND: COVID-19 vaccines have shown success in protecting people worldwide, although serious adverse effects have been reported in very rare cases. CASE SUMMARY: A 32-year-old male with a prior medical history of mild COVID-19 infection developed fulminant myocarditis five days after mRNA-1273 vaccination (first dose), which was confirmed using endomyocardial biopsy. He acutely developed respiratory failure and cardiogenic shock with ventricular tachycardia, but recovered completely with short-term high-dose steroid therapy and mechanical cardiac support, which is the recommended treatment for fulminant lymphocytic myocarditis. DISCUSSION: COVID-19 vaccine-induced myocarditis varies from mild to severe. In the present case, the patient was treated as for fulminant lymphocytic myocarditis and recovered relatively quickly. The mechanism of COVID-19 vaccine-associated myocarditis needs to be urgently investigated.

Hoshino, N., et al. (2022). "An autopsy case report of fulminant myocarditis: Following mRNA COVID-19 vaccination." J Cardiol Cases **26**(6): 391-394.

There have been few case reports on fatal outcomes in patients with acute myocarditis after mRNA coronavirus disease 2019 (COVID-19) vaccination. In most cases of myocarditis after mRNA COVID-19 vaccination, the myocarditis is mild, and the prognosis is good. Here we report an autopsy case of fulminant myocarditis following mRNA COVID-19 vaccination. LEARNING OBJECTIVE: The global distribution of the mRNA coronavirus disease 2019 vaccine requires consideration of appropriate treatment for postvaccination myocarditis. Eosinophil-mediated immunological injury to cardiomyocytes can be involved in the cause of fulminant inflammation from the pathological findings of postvaccination myocarditis.

Hudson, B., R. Mantooth and M. DeLaney (2021). "Myocarditis and pericarditis after vaccination for COVID-19." J Am Coll Emerg Physicians Open **2**(4): e12498.

Two previously healthy males presented to the emergency symptoms with signs of pericarditis/myocarditis after being vaccinated with an mRNA vaccine for COVID-19.

Husby, A. and L. Kober (2022). "COVID-19 mRNA vaccination and myocarditis or pericarditis." Lancet **399**(10342): 2168-2169.

Ilonze, O. J. and M. E. Guglin (2022). "Myocarditis following COVID-19 vaccination in adolescents and adults: a cumulative experience of 2021." Heart Fail Rev **27**(6): 2033-2043.

Clinical course and outcomes of myocarditis after COVID-19 vaccination remain variable. We retrospectively collected data on patients > 12 years old from 01/01/2021 to 12/30/2021 who received COVID-19 messenger RNA (mRNA) vaccination and were diagnosed with myocarditis within 60 days of vaccination. Myocarditis cases were based on case definitions by authors. We report on 238 patients of whom most were male (n = 208; 87.1%). The mean age was 27.4 +/- 16 (range 12-80) years. Females presented at older ages (41.3 +/- 21.5 years) than men 25.7 +/- 14 years (p = 0.001). In patients > 20 years of age, the mean duration from vaccination to symptoms was 4.8 days +/- 5.5 days, but in < 20, it was 3.0 +/- 3.3 days (p = 0.04). Myocarditis occurred most commonly after the Pfizer-BioNTech mRNA vaccine (n = 183; 76.45) and after the second dose (n = 182; 80%). Symptoms started 3.95 +/- 4.5 days after vaccination. The commonest symptom was chest pain (n = 221; 93%). Patients were treated with non-steroidal anti-inflammatory drugs (n = 105; 58.3%), colchicine (n = 38; 21.1%), or glucocorticoids (n = 23; 12.7%). About 30% of the patients had left ventricular ejection fraction but more than half recovered the on repeat imaging. Abnormal cardiac MRIs were common; 168 patients (96% of 175 patients that had MRI) had late gadolinium enhancement, while 120 patients (68.5%) had myocardial edema. Heart failure guideline-directed medical therapy use was common (n = 27; 15%). Eleven patients had cardiogenic shock; and 4 patients required mechanical circulatory support. Five patients (1.7%) died; of these, 3 patients had endomyocardial biopsy/autopsy-confirmed myocarditis. Most cases of COVID-19 vaccine myocarditis are mild. Females presented at older ages than men and duration from vaccination to symptoms was longer in patients

> 20 years. Cardiogenic shock requiring mechanical circulatory support was seen and mortality was low. Future studies are needed to better evaluate risk factors, and long-term outcomes of COVID-19 mRNA vaccine myocarditis.

Ioannou, A. (2021). "Myocarditis should be considered in those with a troponin rise and unobstructed coronary arteries following Pfizer-BioNTech COVID-19 vaccination." QJM.

Ioannou, A. (2022). "Myocarditis should be considered in those with a troponin rise and unobstructed coronary arteries following Pfizer-BioNTech COVID-19 vaccination." QJM **115**(7): 499.

Isaak, A., A. Feisst and J. A. Luetkens (2021). "Myocarditis Following COVID-19 Vaccination." Radiology **301**(1): E378-E379.

Istampoulouoglou, I., et al. (2021). "Myocarditis and pericarditis in association with COVID-19 mRNA-vaccination: cases from a regional pharmacovigilance centre." Glob Cardiol Sci Pract **2021**(3): e202118.

In this article we summarize suspected adverse events following immunization (AEFI) of pericarditis, myocarditis and perimyocarditis that were reported by our regional pharmacovigilance centre after COVID-19 mRNA-vaccination and discuss their association with these vaccines. Seventeen cases were reported between March and July 2021. Of these, nine had perimyocarditis, five myocarditis and three pericarditis. Twelve patients were male (71%). The median age was 38 years (range 17-88). The most commonly observed presenting symptom was acute chest pain (65%). While 47% of the patients were previously healthy, 53% had at least one pre-existing comorbidity, with hypertension being the most prevalent (24%). The European Society of Cardiology diagnostic criteria for the reported AEFIs were fulfilled in twelve cases (71%). The AEFIs occurred after the first vaccine dose in six cases (35%), after the second vaccine dose in ten cases (59%) and after both doses in one case (6%). The median latency of all AEFIs taken together was 14 days (range 1-28) after the first vaccination and 3 days (range 1-17) after the second one. All patients except one were hospitalized (94%) with a median length of stay of 7.5 days (range 3-13). The majority of patients (n = 11, 65%) did not experience any complications, and 13 (77%) of the patients had recovered or were recovering at the time of discharge. In 16 of the 17 cases (94%), the association between the AEFI and mRNA-vaccination was considered possible by the pharmacovigilance centre.

Jain, S. S., et al. (2021). "COVID-19 Vaccination-Associated Myocarditis in Adolescents." Pediatrics **148**(5).

OBJECTIVES: In this study, we aimed to characterize the clinical presentation, short-term prognosis, and myocardial tissue changes as noted on cardiovascular magnetic resonance (CMR) or cardiac MRI in pediatric patients with coronavirus disease 2019 vaccination-associated myocarditis (C-VAM). METHODS: In this retrospective multicenter study across 16 US hospitals, patients <21 years of age with a diagnosis of C-VAM were

included and compared with a cohort with multisystem inflammatory syndrome in children. Younger children with C-VAM were compared with older adolescents. RESULTS: Sixty-three patients with a mean age of 15.6 years were included; 92% were male. All had received a messenger RNA vaccine and, except for one, presented after the second dose. Four patients had significant dysrhythmia; 14% had mild left ventricular dysfunction on echocardiography, which resolved on discharge; 88% met the diagnostic CMR Lake Louise criteria for myocarditis. Myocardial injury as evidenced by late gadolinium enhancement on CMR was more prevalent in comparison with multisystem inflammatory syndrome in children. None of the patients required inotropic, mechanical, or circulatory support. There were no deaths. Follow-up data obtained in 86% of patients at a mean of 35 days revealed resolution of symptoms, arrhythmias, and ventricular dysfunction. CONCLUSIONS: Clinical characteristics and early outcomes are similar between the different pediatric age groups in C-VAM. The hospital course is mild, with quick clinical recovery and excellent short-term outcomes. Myocardial injury and edema are noted on CMR. Close follow-up and further studies are needed to understand the long-term implications and mechanism of these myocardial tissue changes.

Janga, C., et al. (2023). "Delayed presentation of biopsy-proven eosinophilic myocarditis following COVID-19 mRNA vaccine." Glob Cardiol Sci Pract **2023**(2): e202310.

Myopericarditis associated with COVID-19 mRNA vaccines has been recognized as an uncommon adverse reaction, especially among young, healthy adult males. Eosinophilic myocarditis is a rare form of inflammation reflecting a hypersensitivity reaction following an inciting event commonly caused by drugs including vaccines. Eosinophilic myocarditis, a subtype of myocarditis, is characterized by eosinophilic myocardial infiltrates. It is usually accompanied by systemic eosinophilia in the form of a drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome and is rarely associated with myocyte fibrosis and/or necrosis. In this report, we present a case of biopsy-proven eosinophilic myocarditis in a 24-year-old male patient, likely secondary to COVID-19 mRNA vaccination. To our knowledge, this is the first report to describe delayed eosinophilic myocarditis following the COVID-19 mRNA vaccine. Clinicians should be aware of possible delayed presentation to avoid associated morbidity.

Jani, C., et al. (2021). "COVID-19 Vaccine-Associated Takotsubo Cardiomyopathy." Am J Ther **28**(3): 361-364.

Kan, A. K. C., et al. (2023). "Adult-onset Still's disease after mRNA COVID-19 vaccination presenting with severe myocarditis with acute heart failure and cardiogenic shock: a case report." Hong Kong Med J **29**(2): 162-164.

Kaneta, K., et al. (2022). "Young Male With Myocarditis Following mRNA-1273 Vaccination Against Coronavirus Disease-2019 (COVID-19)." Circ J **86**(4): 721.

Kang, D. H., et al. (2022). "Fulminant Giant Cell Myocarditis following Heterologous Vaccination of ChAdOx1 nCoV-19 and Pfizer-BioNTech COVID-19." Medicina (Kaunas) **58**(3).

A 48-year-old female patient underwent a heart transplantation for acute fulminant myocarditis, following heterologous vaccination with the ChAdOx1 nCoV-19 and Pfizer-BioNTech COVID-19. She had no history of severe acute respiratory syndrome coronavirus-2 infection. She did not exhibit clinical signs or have laboratory findings of concomitant infection before or after vaccination. Heart transplantation was performed because her heart failed to recover with venoarterial extracorporeal oxygenation support. Organ autopsy revealed giant cell myocarditis, possibly related to the vaccines. Clinicians may have to consider the possibility of the development of giant cell myocarditis, especially in patients with rapidly deteriorating cardiac function and myocarditis symptoms after COVID-19 vaccination.

Karemingi, C., et al. (2023). "Anesthetic Management of Suspected COVID-19 Vaccination Pericarditis/Myocarditis Scheduled for a Pericardial Window: A Case Report and Literature Review." Cureus **15**(5): e39222.

The unique challenges posed by the COVID vaccination continue to affect multiple healthcare specialties. Although short-term studies have shown that COVID-19 vaccines are both safe and effective, reports of side effects continue to emerge. Cardiovascular side effects such as myo-pericardial inflammation are of particular interest to the fields of cardiology, anesthesiology, and surgery. Myocarditis and pericarditis necessitate diagnostic and therapeutic procedures such as transesophageal echocardiography (TEE) and pericardial window surgery. Intraoperative monitoring of clinical status and heart rhythm and careful adjustments to anesthetic management are required to ensure successful outcomes. This case report follows a 50-year-old male with a known history of pericardial effusion post-COVID vaccination who presented to the emergency department with shortness of breath and chest pain, necessitating further management. We examine the importance of TEE in preventing unnecessary pericardial window procedures and shed light on the importance of careful patient monitoring and management in promoting successful outcomes from an anesthesiology perspective.

Kato, S., N. Horita and D. Utsunomiya (2022). "Incidence of Myocarditis after Messenger RNA Vaccine for COVID-19 in Young Male Recipients." Am J Cardiol **172**: 159-161.

Kato, S., N. Horita and D. Utsunomiya (2023). "Imaging characteristics of myocarditis after mRNA-based COVID-19 vaccination: a meta-analysis." ESC Heart Fail **10**(1): 748-750.

Katoto, P., et al. (2023). "Systematic review and meta-analysis of myocarditis and pericarditis in adolescents following COVID-19 BNT162b2 vaccination." NPJ Vaccines **8**(1): 89.

Myocarditis and pericarditis are frequent complications of COVID-19, but have also been reported following vaccination against COVID-19 in adolescents. To build vaccine confidence and inform policy, we characterized the incidence of myocarditis/pericarditis in adolescents following BNT162b2 vaccination and explored the association with dose and sex. We searched national and international databases for studies reporting the incidence of myocarditis/pericarditis following BNT162b2 vaccination as the primary endpoint. The intra-study risk of bias was appraised, and random-effects meta-analyses

were performed to estimate the pooled incidence by dose stratified by sex. The pooled incidence of myocarditis/pericarditis was 4.5 (95%CI: 3.14-6.11) per 100,000 vaccinations across all doses. Compared to dose 1, the risk was significantly higher after dose 2 (RR: 8.62, 95%CI: 5.71-13.03). However, adolescents experienced a low risk after a booster dose than after dose 2 (RR: 0.06; 95%CI: 0.04-0.09). Males were approximately seven times (RR: 6.66, 95%CI: 4.77-4.29) more likely than females to present myocarditis/pericarditis. In conclusion, we found a low frequency of myocarditis/pericarditis after BNT162b2, which occurred predominantly after the second dose in male adolescents. The prognosis appears to be favorable, with full recovery in both males and females. National programs are recommended to adopt the causality framework to reduce overreporting, which undercuts the value of the COVID-19 vaccine on adolescent life, as well as to extend the inter-dose interval policy, which has been linked to a lower frequency of myocarditis/pericarditis.

Kaufmann, C. C., et al. (2023). "Cardiac inflammation associated with COVID-19 mRNA vaccination in patients with and without previous myocarditis." Minerva Cardiol Angiol **71**(3): 242-248.

BACKGROUND: mRNA COVID-19 vaccines have been associated with myocarditis in the general population. However, application of gold standard techniques is often missing, and data about patients with history of myocarditis have not been reported yet. METHODS: We evaluated 21 patients (median age 27, 86% males) for suspected myocarditis after receiving mRNA COVID-19 vaccine. We divided cases with previous diagnosis of myocarditis (PM, N.=7), from naive controls (NM, N.=14). All patients were investigated thoroughly by cardiac magnetic resonance (100%) with or without endomyocardial biopsy (14%). RESULTS: Overall, 57% of patients met updated Lake Louise criteria and none fulfilled Dallas criteria, with no remarkable differences between groups. Acute coronary syndrome-like presentation was more frequent in NM with earlier normalization of troponin than PM. NM and PM already healed from myocarditis were clinically comparable, whereas PM with active inflammation had subtle presentation and were evaluated for immunosuppressive therapy modulation. None had fulminant myocarditis and/or malignant ventricular arrhythmia at presentation. No major cardiac events occurred by 3 months. CONCLUSIONS: In this study, the suspicion of mRNA COVID-19 vaccine-associated myocarditis was inconstantly confirmed by gold standard diagnostics. Myocarditis was uncomplicated in both PM and NM patients. Larger studies with longer follow-up are needed to validate COVID-19 vaccination in this population.

Kaul, R., et al. (2021). "Myocarditis following COVID-19 vaccination." Int J Cardiol Heart Vasc **36**: 100872.

Kawahara, H., et al. (2022). "Myocarditis After the Third Dose of mRNA-1273 Coronavirus Disease 2019 (COVID-19) Vaccine." Circ Rep **4**(8): 388-389.

Kawano, H., et al. (2023). "Fulminant Myocarditis and Acute Appendicitis after COVID-19 Vaccination." Intern Med **62**(3): 411-417.

A 19-year-old Japanese man was hospitalized for cardiogenic shock 28 days after receiving a second dose of the coronavirus disease 2019 (COVID-19) mRNA-1273 vaccine. He had had a high fever for three days with vomiting and abdominal pain before arriving at our hospital. The patient visited a local hospital and was diagnosed with heart failure and acute appendicitis. An endomyocardial biopsy specimen showed myocarditis. Thereafter, Impella CP left ventricular assist device implantation and venoarterial peripheral extracorporeal membranous oxygenation were initiated immediately along with inotropic support and steroid pulse therapy. Given these findings, he was finally diagnosed with multiple inflammatory syndrome and fulminant myocarditis.

Kawauchi, H., et al. (2022). "Course of Cardiac Magnetic Resonance Imaging Findings in Acute Myocarditis after COVID-19 mRNA Vaccination." Intern Med **61**(17): 2625-2629.

Myocarditis is being increasingly reported as a rare complication of coronavirus disease 2019 (COVID-19) mRNA vaccines. We herein report a case of myocarditis following COVID-19 mRNA vaccination in a man. Cardiac magnetic resonance imaging (CMRI) revealed an area of high signal intensity on short T1 inversion recovery (STIR) and late gadolinium enhancement (LGE), which are characteristic of myocarditis. Follow-up CMRI performed six months later revealed improvement in the myocardial edema and LGE findings. CMRI is a useful non-invasive imaging modality for making an initial diagnosis as well as for follow-up in cases of myocarditis after COVID-19 mRNA vaccination.

Kazama, S., et al. (2022). "Biopsy-Proven Fulminant Myocarditis Requiring Mechanical Circulatory Support Following COVID-19 mRNA Vaccination." CJC Open **4**(5): 501-505.

A 48-year-old woman suffered from cardiogenic shock with fulminant myocarditis following the second dose of COVID-19 vaccine (mRNA-1273). Venoarterial extracorporeal membrane oxygenation and Impella support were essential in achieving hemodynamic stability. Endomyocardial biopsy revealed lymphocytic infiltration with predominant immunostaining for CD8- and CD68-positive cells. The left ventricular ejection fraction improved significantly after treatment with mechanical circulatory support. Myocarditis following COVID-19 mRNA vaccination may also occur in middle-aged women; it may be fulminant and require mechanical circulatory support. Although our results suggest the involvement of cytotoxic T lymphocytes and macrophages, further investigation is needed before these can be established as pathogenetic mechanisms.

Kerbl, R. (2021). "[Myocarditis after COVID-19 mRNA vaccination]." Monatsschr Kinderheilkd **169**(10): 893-894.

Keshavarz, P., et al. (2022). "Myocarditis Following COVID-19 Vaccination: Cardiac Imaging Findings in 118 Studies." Tomography **8**(4): 1959-1973.

We reviewed the reported imaging findings of myocarditis in the literature following COVID-19 vaccination on cardiac imaging by a literature search in online databases,

including Scopus, Medline (PubMed), Web of Science, Embase (Elsevier), and Google Scholar. In total, 532 cases of myocarditis after COVID-19 vaccination were reported (462, 86.8% men and 70, 13.2% women, age range 12 to 80) with the following distribution: Pfizer-BioNTech: 367 (69%), Moderna: 137 (25.8%), AstraZeneca: 12 (2.3%), Janssen/Johnson & Johnson: 6 (1.1%), COVAXIN: 1 (0.1%), and unknown mRNA vaccine: 9 (1.7%). The distribution of patients receiving vaccine dosage was investigated. On cardiac MR Imaging, late intravenous gadolinium enhancement (LGE) was observed mainly in the epicardial/subepicardial segments (90.8%, 318 of 350 enhancing segments), with the dominance of inferolateral segment and inferior walls. Pericardial effusion was reported in 13.1% of cases. The vast majority of patients (94%, 500 of 532) were discharged from the hospital except for 4 (0.7%) cases. Post-COVID-19 myocarditis was most commonly reported in symptomatic men after the second or third dose, with CMRI findings including LGE in 90.8% of inferior and inferolateral epicardial/subepicardial segments. Most cases were self-limited.

Khan, Z., et al. (2022). "COVID-19 Vaccine-Induced Myocarditis: A Systemic Review and Literature Search." Cureus **14**(7): e27408.

Myocarditis is one of the complications reported with COVID-19 vaccines, particularly both Pfizer-BioNTech and Moderna vaccines. Most of the published data about this association come from case reports and series. Integrating the geographical data, clinical manifestations, and outcomes is therefore important in patients with myocarditis to better understand the disease. A thorough literature search was conducted in Cochrane library, PubMed, ScienceDirect, and Google Scholar for published literature till 30 March 2022. We identified 26 patients eligible from 29 studies; the data were pooled from these qualifying case reports and case series. Around 94% of patients were male in this study, the median age for onset of myocarditis was 22 years and 85% developed symptoms after the second dose. The median time of admission for patients to hospitals post-vaccination was three days and chest pain was the most common presenting symptom in these patients. Most patients had elevated troponin on admission and about 90% of patients had cardiac magnetic resonance imaging (CMR) that showed late gadolinium enhancement. All patients admitted with myocarditis were discharged home after a median stay of four days. Results from this current analysis show that post-mRNA vaccination myocarditis is mainly seen in young males after the second dose of vaccination. The pathophysiology of vaccine-induced myocarditis is not entirely clear and late gadolinium enhancement is a common finding on CMR in these patients that may indicate myocardial fibrosis or necrosis. Prognosis remains good and all patients recovered from myocarditis, however further studies are advisable to assess long-term prognosis of myocarditis.

Kiblboeck, D., et al. (2022). "Myocarditis following mRNA COVID-19 vaccination: call for endomyocardial biopsy." ESC Heart Fail **9**(3): 1996-2002.

Acute myocarditis following mRNA COVID-19 vaccination was reported by the European Medicine Agency safety committee as a rare adverse event. We present a case series of three young male patients with suspected acute myocarditis following BNT162b2 mRNA

COVID-19 vaccination including results of endomyocardial biopsies (EMB). Additionally, we analysed EMB of another 21 patients with clinically suspected acute myocarditis following vaccination to determine the pathohistological pattern. Overall, EMB revealed acute lymphocytic myocarditis in 5 (20.8%), chronic lymphocytic myocarditis in 6 (25%), cardiac sarcoidosis in 1 (4.2%), healed myocarditis in 6 (25%), and other diagnoses with cardiac damage of unclear aetiology in 6 (25%) cases. Our findings support the necessity of EMB in patients with suspected acute myocarditis following mRNA COVID-19 vaccination presenting with reduced EF to establish a correct and definite diagnosis. Concerns of these rare severe adverse events after COVID-19 immunization should not undermine its value for the global community.

Kim, H. W., et al. (2021). "Patients With Acute Myocarditis Following mRNA COVID-19 Vaccination." JAMA Cardiol **6**(10): 1196-1201.

Importance: Vaccine-associated myocarditis is an unusual entity that has been described for the smallpox vaccine, but only anecdotal case reports have been described for other vaccines. Whether COVID-19 vaccination may be linked to the occurrence of myocarditis is unknown. Objective: To describe a group of 7 patients with acute myocarditis over 3 months, 4 of whom had recent messenger RNA (mRNA) COVID-19 vaccination. Design, Setting, and Participants: All patients referred for cardiovascular magnetic resonance imaging at Duke University Medical Center were asked to participate in a prospective outcomes registry. Two searches of the registry database were performed: first, to identify patients with acute myocarditis for the 3-month period between February 1 and April 30 for 2017 through 2021, and second, to identify all patients with possible vaccine-associated myocarditis for the past 20 years. Once patients with possible vaccine-associated myocarditis were identified, data available in the registry were supplemented by additional data collection from the electronic health record and a telephone interview. Exposures: mRNA COVID-19 vaccine. Main Outcomes and Measures: Occurrence of acute myocarditis by cardiovascular magnetic resonance imaging. Results: In the 3-month period between February 1 and April 30, 2021, 7 patients with acute myocarditis were identified, of which 4 occurred within 5 days of COVID-19 vaccination. Three were younger male individuals (age, 23-36 years) and 1 was a 70-year-old female individual. All 4 had received the second dose of an mRNA vaccine (2 received mRNA-1273 [Moderna], and 2 received BNT162b2 [Pfizer]). All presented with severe chest pain, had biomarker evidence of myocardial injury, and were hospitalized. Coincident testing for COVID-19 and respiratory viruses provided no alternative explanation. Cardiac magnetic resonance imaging findings were typical for myocarditis, including regional dysfunction, late gadolinium enhancement, and elevated native T1 and T2. Conclusions and Relevance: In this study, magnetic resonance imaging findings were found to be consistent with acute myocarditis in 7 patients; 4 of whom had preceding COVID-19 vaccination. Further investigation is needed to determine associations of COVID-19 vaccination and myocarditis.

Kim, I. C., et al. (2021). "Cardiac Imaging of Acute Myocarditis Following COVID-19 mRNA Vaccination." J Korean Med Sci **36**(32): e229.

Increasing rates of coronavirus disease 2019 (COVID-19) vaccination coverage will result in more vaccine-related side effects, including acute myocarditis. In Korea, we present a 24-year-old male with acute myocarditis following COVID-19 vaccination (BNT162b2). His chest pain developed the day after vaccination and cardiac biomarkers were elevated. Echocardiography showed minimal pericardial effusion but normal myocardial contractility. Electrocardiography revealed diffuse ST elevation in lead II, and V2-5. Cardiac magnetic resonance images showed the high signal intensity of T2- short tau inversion recovery image, the high value of T2 mapping sequence, and late gadolinium enhancement in basal inferior and inferolateral wall. It was presumed that COVID-19 mRNA vaccination was probably responsible for acute myocarditis. Clinical course of the patient was favorable and he was discharged without any adverse event.

Kimura, M., et al. (2022). "Fulminant necrotizing eosinophilic myocarditis after COVID-19 vaccination survived with mechanical circulatory support." ESC Heart Fail **9**(4): 2732-2737.

A 69-year-old man was hospitalized for heart failure 7 days after coronavirus disease 2019 (COVID-19) mRNA vaccination. Electrocardiography showed ST-segment elevation and echocardiography demonstrated severe left ventricular dysfunction. Venoarterial extracorporeal membrane oxygenation and Impella 5.0 were instituted because of cardiogenic shock and ventricular fibrillation. Endomyocardial biopsy demonstrated necrotizing eosinophilic myocarditis (NEM). Severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) PCR test was negative. He had no infection or history of new drug exposure. NEM was likely related to COVID-19 vaccination. He was administered 10 mg/kg of prednisolone following methylprednisolone pulse treatment (1000 mg/day for 3 days). Left ventricular function recovered and he was weaned from mechanical circulatory support (MCS). Follow-up endomyocardial biopsy showed no inflammatory cell infiltration. This is the first report of biopsy-proven NEM after COVID-19 vaccination survived with MCS and immunosuppression therapy. It is a rare condition but early, accurate diagnosis and early aggressive intervention can rescue patients.

Kittichokechai, P., P. Seripanu and T. Laksomya (2023). "Long-term follow-up of cardiac magnetic resonance imaging in myocarditis following messenger ribonucleic acid COVID-19 vaccination: a case report." Eur Heart J Case Rep **7**(5): ytad245.

BACKGROUND: Presently, the association between myocarditis and messenger ribonucleic acid (mRNA) COVID-19 vaccination is well established. From the most current data, cases of myocarditis following COVID-19 vaccination seem to be mild with fast clinical recovery. Nevertheless, the complete resolution of the inflammatory process is still unclear. CASE SUMMARY: We report the case of a 13-year-old boy who developed chest pain following the second dose of the Pfizer-BioNTech COVID-19 vaccine with long-term follow-up of cardiac magnetic resonance (CMR) imaging. An electrocardiogram (ECG) revealed progressively ST-segment elevation on the 2nd day of admission with a rapid improvement within 3 hours where only mild ST-segment elevation remained. The peak level of high-sensitivity cardiac troponin T was 1546 ng/L with rapid reduction. Echocardiogram revealed depressed left ventricular septal wall motion. CMR mapping techniques showed myocardial oedema with an increase in native T1 and extracellular

volume (ECV). On the other hand, T1-weighted and T2-weighted images and late gadolinium enhancement (LGE) did not detect inflammation. The patient's symptoms were relieved by oral ibuprofen. After 2 weeks, ECG and echocardiogram were unremarkable. However, the inflammation process was still present based on the CMR by mapping technique. During the 6-month follow-up, CMR returned to normal. DISCUSSION: In our case, the subtle myocardial inflammation was diagnosed by mapping technique with only a T1-based marker according to the updated Lake Louise Criteria and the inflammation of the myocardium returned to normal within 6 months after the onset of the disease. Further follow-up and larger studies are needed to determine the complete resolution of the disease.

Klamer, T. A., M. Linschoten and F. W. Asselbergs (2022). "The benefit of vaccination against COVID-19 outweighs the potential risk of myocarditis and pericarditis." Neth Heart J **30**(4): 190-197.

Vaccines against coronavirus 2019 disease (COVID-19) have shown to be greatly effective in preventing viral spread, serious illness and death from this infectious disease and are therefore critical for the management of the COVID-19 pandemic. However, the listing of myocarditis and pericarditis as possible rare side effects of the messenger RNA (mRNA) vaccines against COVID-19 by regulatory agencies has sparked discussion on the vaccines' safety. The most important published cohort studies to date demonstrat that myocarditis is a very rare side effect after COVID-19 mRNA vaccination, with an incidence of approximately 1-4 cases per 100,000 vaccinated persons. Young males (16-29 years) appear to be at highest risk, predominantly after receiving the second dose. The disease course is self-limiting in a vast majority of cases: 95% of patients show a rapid resolution of symptoms and normalisation of cardiac biomarkers, electro- and echocardiographic findings within days. Importantly, the available data suggest that the incidence rate of myocarditis in the context of COVID-19 is much greater than the risk of this side effect following vaccination. We conclude that the benefit of vaccination against COVID-19 outweighs the potential risk of myocarditis and pericarditis in both adolescents and adults. Prospective follow-up of patients who have developed these complications after vaccination is required to assess long-term outcomes.

Kleebayoon, A. and V. Wiwanitkit (2023). "Acute myocarditis after administration of COVID-19 vaccine: comment." Arch Cardiol Mex **93**(3): 382-383.

Kleebayoon, A. and V. Wiwanitkit (2023). "Development of myocarditis and pericarditis after COVID-19 vaccination: Comment." Clin Cardiol **46**(4): 459.

Kleebayoon, A. and V. Wiwanitkit (2023). "Gadolinium changes detected on cardiovascular magnetic resonance imaging following COVID-19 vaccine-related myocarditis in adolescents." Pediatr Radiol **53**(5): 1041.

Kleebayoon, A. and V. Wiwanitkit (2023). "Systemic lupus erythematosus myocarditis and COVID-19 vaccination: Comment." Reumatol Clin (Engl Ed) **19**(6): 349.

Kleebayoon, A. and V. Wiwanitkit (2023). "Vasospastic angina following COVID-19 vaccine-related myocarditis: comment." Cardiol Young **33**(4): 672.

Knudsen, B. and V. Prasad (2023). "COVID-19 vaccine induced myocarditis in young males: A systematic review." Eur J Clin Invest **53**(4): e13947.

BACKGROUND: Myocarditis is a rare but significant adverse event associated with COVID-19 vaccination, especially for men under 40. If the risk of myocarditis is not stratified by pertinent risk factors, it may be diluted for high-risk and inflated for low-risk groups. We sought to assess how the risk of myocarditis is reported in the literature. METHODS: In accordance with PRISMA standards, we reviewed primary publications in PubMed, Embase, Google Scholar and MedRxiv (through 3/2022) and included studies that estimated the incidence of myocarditis/pericarditis after receiving either the BNT162b2 (Pfizer), mRNA-1273 (Moderna) or Ad26COVS1 (Janssen) vaccine. The main outcome was the percentage of studies using 4, 3, 2, 1 or 0 stratifiers (i.e. sex, age, dose number and manufacturer) when reporting the highest risk of myocarditis. Secondary outcomes included the incidence of myocarditis in males after dose 1 and 2 of the BNT162b2 (Pfizer) or mRNA-1273 (Moderna) vaccine. RESULTS: The 29 included studies originated in North America, Europe, Asia, or were Worldwide. Of them, 28% (8/29) used all four stratifiers, and 45% (13/29) used 1 or 0 stratifiers. The highest incidence of myocarditis ranged from 8.1-39 cases per 100,000 persons (or doses) in studies using four stratifiers. Six studies reported an incidence greater than 15 cases per 100,000 persons (or doses) in males aged 12-24 after dose 2 of an mRNA-based vaccine. CONCLUSIONS: Only one in four articles reporting myocarditis used four stratifiers, and men younger than 40 receiving a second dose of an mRNA vaccine are at greatest risk.

Kobayashi, K., et al. (2023). "Multisystem inflammatory syndrome and lymphohistiocytic myocarditis after Covid-19 vaccine in a middle-aged woman." ESC Heart Fail **10**(2): 1435-1439.

We describe a 51-year-old otherwise healthy woman hospitalized for hypotension, fever, and weakness 4 days after the second-dose Covid-19 mRNA vaccine. Elevated inflammatory markers, natriuretic peptide levels and troponin levels, and slightly reduced left ventricular ejection fraction of 50% were noted. We also found the multiple organ damage, including mucocutaneous, gastrointestinal, and neurologic systems. In addition, we revealed the positive results for anti-nucleocapsid SARS-CoV-2 IgG, albeit negative for SARS-CoV-2 polymerase chain reaction testing, suggesting the prior asymptomatic Covid-19 infection. We finally diagnosed her as multisystem inflammatory syndrome after vaccination. Of note, we obtained myocardial specimen from the patients and demonstrated the lymphohistiocytic myocarditis, which is a rare form of myocarditis.

Koiwaya, H., et al. (2022). "Serial histopathologic assessment of fulminant myocarditis after the first mRNA COVID-19 vaccine dose." Eur Heart J **43**(20): 1995.

Kojima, N., et al. (2022). "Case Report: Myocarditis Associated With COVID-19 mRNA Vaccination Following Myocarditis Associated With Campylobacter Jejuni." Front Cardiovasc Med **9**: 837759.

We herein present our experience with a case involving a 17-year-old Japanese boy suffering from acute myocarditis after his second coronavirus disease-2019 (COVID-19) messenger RNA (mRNA) vaccine shot. The patients had a history of myocarditis associated with Campylobacter jejuni 3 years prior. This has been the first-ever documented case of myocarditis associated with COVID-19 mRNA vaccination in a patient with a history of myocarditis. We present a series of images and blood biomarkers for different types of myocarditis that developed in this single patient.

Kounis, N. G., et al. (2023). "Rare acute hypersensitivity myocardial infarction (Kounis syndrome) and hypersensitivity myocarditis following COVID-19 vaccination." QJM **116**(1): 81-82.

Kounis, N. G., et al. (2022). "Rare Hypersensitivity Myocardial Reactions Following COVID-19 Vaccination: Hypersensitivity Myocardial Infarction (Kounis Syndrome) and Hypersensitivity Myocarditis." Anatol J Cardiol **26**(3): 245-246.

Kounis, N. G., et al. (2022). "First Identified Case of Fatal Fulminant Eosinophilic Myocarditis Following the Initial Dose of the Pfizer-BioNTech mRNA COVID-19 Vaccine (BNT162b2, Comirnaty): an Extremely Rare Idiosyncratic Necrotizing Hypersensitivity Reaction Different to Hypersensitivity or Drug-Induced Myocarditis." J Clin Immunol **42**(4): 736-737.

Kounis, N. G., et al. (2022). "Hypersensitivity Myocarditis and the Pathogenetic Conundrum of COVID-19 Vaccine-Related Myocarditis." Cardiology **147**(4): 413-415.

Kounis, N. G., et al. (2022). "Letter by Kounis et al Regarding Article, "Biopsy-Proven Giant Cell Myocarditis Following the COVID-19 Vaccine"." Circ Heart Fail **15**(10): e009826.

Kounis, N. G., et al. (2022). "The pathogenesis of potential myocarditis induced by COVID-19 vaccine." Am J Emerg Med **56**: 382-383.

Kounis, N. G., et al. (2022). "Encephalitis, myocarditis, and thrombocytopenia after COVID-19 mRNA vaccination: Clinical and pathophysiological considerations." J Neuroimmunol **373**: 577988.

Kounis, N. G., et al. (2022). "[Rare cases of myocarditis after COVID-19 vaccination: searching for diagnosis, type, treatment and prevention]." Rev Esp Cardiol **75**(3): 278-279.

Kracalik, I., et al. (2022). "Outcomes at least 90 days since onset of myocarditis after mRNA COVID-19 vaccination in adolescents and young adults in the USA: a follow-up surveillance study." Lancet Child Adolesc Health **6**(11): 788-798.

BACKGROUND: Data on medium-term outcomes in indivduals with myocarditis after mRNA COVID-19 vaccination are scarce. We aimed to assess clinical outcomes and

quality of life at least 90 days since onset of myocarditis after mRNA COVID-19 vaccination in adolescents and young adults. METHODS: In this follow-up surveillance study, we conducted surveys in US individuals aged 12-29 years with myocarditis after mRNA COVID-19 vaccination, for whom a report had been filed to the Vaccine Adverse Event Reporting System between Jan 12 and Nov 5, 2021. A two-component survey was administered, one component to patients (or parents or guardians) and one component to health-care providers, to assess patient outcomes at least 90 days since myocarditis onset. Data collected were recovery status, cardiac testing, and functional status, and EuroQol health-related quality-of-life measures (dichotomised as no problems or any problems), and a weighted quality-of-life measure, ranging from 0 to 1 (full health). The EuroQol results were compared with published results in US populations (aged 18-24 years) from before and early on in the COVID-19 pandemic. FINDINGS: Between Aug 24, 2021, and Jan 12, 2022, we collected data for 519 (62%) of 836 eligible patients who were at least 90 days post-myocarditis onset: 126 patients via patient survey only, 162 patients via health-care provider survey only, and 231 patients via both surveys. Median patient age was 17 years (IQR 15-22); 457 (88%) patients were male and 61 (12%) were female. 320 (81%) of 393 patients with a health-care provider assessment were considered recovered from myocarditis by their health-care provider, although at the last health-care provider follow-up, 104 (26%) of 393 patients were prescribed daily medication related to myocarditis. Of 249 individuals who completed the quality-of-life portion of the patient survey, four (2%) reported problems with self-care, 13 (5%) with mobility, 49 (20%) with performing usual activities, 74 (30%) with pain, and 114 (46%) with depression. Mean weighted quality-of-life measure (0.91 [SD 0.13]) was similar to a pre-pandemic US population value (0.92 [0.13]) and significantly higher than an early pandemic US population value (0.75 [0.28]; $p<0.0001$). Most patients had improvements in cardiac diagnostic marker and testing data at follow-up, including normal or back-to-baseline troponin concentrations (181 [91%] of 200 patients with available data), echocardiograms (262 [94%] of 279 patients), electrocardiograms (240 [77%] of 311 patients), exercise stress testing (94 [90%] of 104 patients), and ambulatory rhythm monitoring (86 [90%] of 96 patients). An abnormality was noted among 81 (54%) of 151 patients with follow-up cardiac MRI; however, evidence of myocarditis suggested by the presence of both late gadolinium enhancement and oedema on cardiac MRI was uncommon (20 [13%] of 151 patients). At follow-up, most patients were cleared for all physical activity (268 [68%] of 393 patients). INTERPRETATION: After at least 90 days since onset of myocarditis after mRNA COVID-19 vaccination, most individuals in our cohort were considered recovered by health-care providers, and quality of life measures were comparable to those in pre-pandemic and early pandemic populations of a similar age. These findings might not be generalisable given the small sample size and further follow-up is needed for the subset of patients with atypical test results or not considered recovered. FUNDING: US Centers for Disease Control and Prevention.

Kravchenko, D., et al. (2022). "Cardiac magnetic resonance follow-up of COVID-19 vaccine associated acute myocarditis." Front Cardiovasc Med **9**: 1049256.

BACKGROUND: Mass COVID-19 vaccination campaigns have helped impede the COVID-19 pandemic. In rare cases, some vaccines have led to vaccine associated myocarditis in a specific subset of the population, usually young males. Cardiac magnetic resonance (CMR) can reliably diagnose vaccine associated myocarditis, but follow-up data of CMR proven acute myocarditis is scarce. MATERIALS AND METHODS: Nine patients with acute vaccine associated myocarditis underwent baseline and follow-up CMR examinations and were compared to baseline parameters at initial presentation and to a group of 20 healthy controls. CMR protocol included functional assessment, T1 and T2 mapping, T2 signal intensity ratio, strain feature tracking, and late gadolinium enhancement (LGE). RESULTS: Myocarditis patients (n = 9, aged 24 +/- 6 years, 8 males) underwent CMR follow-up after an average of 5.8 +/- 4.3 months. All patients showed a complete resolution of visual myocardial edema while also demonstrating a reduction in overall LGE extent from baseline to follow-up (4.2 +/- 2.1 vs. 0.9 +/- 0.8%, $p < 0.001$), although visual LGE was still noted in all patients. Left ventricular ejection fraction was normal at baseline and at follow-up (58 +/- 6 vs. 62 +/- 4%, $p = 0.10$) as well as compared to a healthy control group (60 +/- 4%, $p = 0.24$). T1 (1024 +/- 77 vs. 971 +/- 34 ms, $p = 0.05$) and T2 relaxations times (57 +/- 6 vs. 51 +/- 3 ms, $p = 0.03$) normalized at follow-up. Most patients reported a resolution of clinical symptoms, while two (22%) reported new onset of exertional dyspnea. CONCLUSION: Patients with COVID-19 vaccine associated acute myocarditis showed a complete, uncomplicated resolution of myocardial inflammation on follow-up CMR, which was associated with a near complete resolution of symptoms. Minor, residual myocardial scarring was present on follow-up LGE imaging. The long-term implications of the remaining myocardial scar-tissue after vaccine associated myocarditis remain unknown warranting further studies.

Kravchenko, D., et al. (2022). "Cardiac MRI in Suspected Acute Myocarditis After COVID-19 mRNA Vaccination." Rofo **194**(9): 1003-1011.

PURPOSE: To evaluate cardiac MRI characteristics in patients with suspected hypersensitivity myocarditis following mRNA COVID-19 vaccination. MATERIALS AND METHODS: Patients clinically suspected of acute myocarditis after COVID-19 vaccination were retrospectively analyzed and compared against a healthy control group. Cardiac MRI protocol included parameters such as T1 and T2 relaxation times, extracellular volume (ECV), T2 signal intensity ratio, and late gadolinium enhancement (LGE). Lymph node size was assessed in the patient group on the injection side. Student t-test, analyses of variance (ANOVA) with Tukey post-hoc test, and chi(2) test were used for statistical analysis. RESULTS: 20 patients with clinically suspected post-vaccine myocarditis (28 +/- 12 years; 12 men) and 40 controls (31 +/- 11 years; 25 men) were evaluated. According to the 2018 Lake Louise criteria (LLC), patients with clinically suspected myocarditis were further subdivided into an LLC-positive group (n = 9) and an LLC-negative group (n = 11). The mean time of symptom onset after vaccination was 1.1 +/- 1.2 days (LLC-positive) and 6.5 +/- 9.2 days (LLC-negative). Group differences in inflammatory variables between myocarditis patients and control subjects were more pronounced in the LLC-positive group (e. g., T1 relaxation time: 1041 +/- 61 ms [LLC positive] vs. 1008 +/- 79 ms [LLC-negative] vs. 970 +/- 25 ms [control]; $p < .001$; or T2

signal intensity ratio 2.0 +/- 0.3 vs. 1.6 +/- 0.3 [LLC-negative] and vs. 1.6 +/- 0.3 [control], p = .012). LLC-positive patients were significantly faster in receiving an MRI after initial symptom onset (8.8 +/- 6.1 days vs. 52.7 +/- 33.4 days; p = .001) and had higher troponin T levels (3938 +/- 5850 ng/l vs. 9 +/- 11 ng/l; p <.001). LGE lesions were predominantly located at the subepicardium of the lateral wall. Axillary lymphadenopathy was more frequent in the LLC-positive group compared to the LLC-negative group (8/9 [89 %] vs. 0/11 [0 %], p < 0.001). CONCLUSION: Vaccine-induced myocarditis should be considered in patients with acute symptom onset after mRNA vaccination, especially if elevated serum troponin T is observed. Imaging findings of vaccine-induced myocarditis are similar to virus-induced myocarditis, allowing for the use of the Lake Louise Criteria for diagnostic purposes. KEY POINTS: . Vaccine-induced hypersensitivity myocarditis can be confirmed with cardiac MRI. . Especially patients with sudden onset of symptoms and elevated serum troponin T had positive cardiac MRI findings. . Cardiac MRI characteristics of vaccine-induced myocarditis are similar to those in virus-induced myocarditis. CITATION FORMAT: . Kravchenko D, Isaak A, Mesropyan N et al. Cardiac MRI in Suspected Acute Myocarditis After COVID-19 mRNA Vaccination. Fortschr Rontgenstr 2022; 194: 1003 - 1011.

Krug, A., J. Stevenson and T. B. Hoeg (2022). "BNT162b2 Vaccine-Associated Myo/Pericarditis in Adolescents: A Stratified Risk-Benefit Analysis." Eur J Clin Invest **52**(5): e13759.

BACKGROUND: Male patients ages 12-17 years have an elevated risk of mRNA vaccination-associated myo/pericarditis. A risk-benefit analysis of first and second doses of mRNA vaccination in adolescent boys by health status and history of SARS-CoV-2 infection has not been performed. METHODS: Using the Vaccine Adverse Event Reporting System (VAERS), we identified BNT162b2 [Pfizer-BioNTech] myo/pericarditis occurrence according to CDC criteria. Main outcomes were as follows: 1) post-vaccination myo/pericarditis crude incidence in adolescents aged 12-15 and 16-17; and 2) two risk-benefit analyses by age, sex, comorbidity, variant and history of infection. RESULTS: Cases of myo/pericarditis (n = 253) included 129 after dose 1 and 124 after dose 2; 86.9% were hospitalized. Incidence per million after dose two in male patients aged 12-15 and 16-17 was 162.2 and 93.0, respectively. Weighing post-vaccination myo/pericarditis against COVID-19 hospitalization during delta, our risk-benefit analysis suggests that among 12-17-year-olds, two-dose vaccination was uniformly favourable only in nonimmune girls with a comorbidity. In boys with prior infection and no comorbidities, even one dose carried more risk than benefit according to international estimates. In the setting of omicron, one dose may be protective in nonimmune children, but dose two does not appear to confer additional benefit at a population level. CONCLUSIONS: Our findings strongly support individualized paediatric COVID-19 vaccination strategies which weigh protection against severe disease vs. risks of vaccine-associated myo/pericarditis. Research is needed into the nature and implications of this adverse effect as well as immunization strategies which reduce harms in this overall low-risk cohort.

Krychtiuk, K. A. and L. K. Newby (2022). "Moderna COVID-19 vaccine was linked to myocarditis or myopericarditis at 28 d (4.2 events/100 000 persons)." Ann Intern Med **175**(5): JC58.

Husby A, Hansen JV, Fosbol E, et al. SARS-CoV-2 vaccination and myocarditis or myopericarditis: population based cohort study. BMJ. 2021;375:e068665. 34916207.

Kuehn, B. M. (2021). "Adolescent Myocarditis After COVID-19 Vaccination Is Rare." JAMA **326**(10): 902.

Kuehn, B. M. (2022). "Myocarditis Adverse Event Less Common After COVID-19 Vaccine Booster." JAMA **327**(14): 1324.

Kyaw, H., et al. (2022). "COVID-19 mRNA Vaccine-Associated Myocarditis." Cureus **14**(1): e21009.

Coronavirus disease 2019 (COVID-19) has been reported to cause cardiovascular complications including myocarditis, pericardial effusion, pericarditis, and arrhythmias. With the introduction of the vaccine, there have been reports of myocarditis possibly associated with the mRNA COVID-19 vaccine. We report a case of cardiac involvement following the second dose of Pfizer-BioNTech COVID-19 vaccine in a young male. A healthy 24-year-old male presented to the emergency department with complaints of non-radiating mid-sternal chest pain and pressure. He noticed his symptoms started six hours after he received the second dose of Pfizer COVID vaccine. Laboratory tests revealed elevated cardiac troponin I-CtNI levels. Computed tomography angiography of the chest did not show evidence of pulmonary embolism. Given his presentation of acute chest pain associated with elevated troponin levels, a coronary angiogram was performed which revealed normal coronary arteries. He was subsequently treated for acute peri-myocarditis with colchicine, non-steroidal anti-inflammatory drugs (NSAIDs), and beta-blockers for tachycardia and the prevention of arrhythmia. Although rare, clinicians should be aware of the risk for myocarditis and pericarditis, which should be considered in individuals presenting with chest pain within a week after vaccination, especially in the younger population. Although the long-term risk in these patients is uncertain, early diagnosis and treatment are key to minimizing complications.

Lagousi, T., et al. (2022). "Paving the Way Towards Precision Vaccinology: The Paradigm of Myocarditis After Coronavirus Disease 2019 (COVID-19) Vaccination." Clin Infect Dis **75**(Suppl 1): S18-S23.

Systems vaccinology approaches have introduced novel tools for the evaluation of the safety profile of novel vaccine antigens by developing biomarkers of vaccine reactogenicity associated with potential adverse events. The use of such approaches may prove extremely advantageous in the context of a global pandemic where accelerated approval of new vaccine formulations for all ages is essential for the containment of the epidemic. The spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has had devastating effects on global health, but the emergency authorization of mRNA vaccines significantly reduced SARS-CoV-2-associated morbidity and mortality. Despite their favorable safety profile in adult populations,

recent reports have raised concerns about an association of the mRNA-based vaccines with acute myocarditis, predominantly among male adolescents and young adults following the second vaccine dose. Here, we review data on myocarditis epidemiology following SARS-CoV-2 mRNA vaccination and describe potential mechanisms involved that may explain the sex- and age-related differences, focusing on mRNA immune reactivity. The case of vaccine-associated myocarditis highlights the need to incorporate precision vaccinology approaches for the development of safe and effective vaccines for everyone.

Lai, F. T. T., et al. (2022). "Prognosis of Myocarditis Developing After mRNA COVID-19 Vaccination Compared With Viral Myocarditis." J Am Coll Cardiol **80**(24): 2255-2265.

BACKGROUND: Association between messenger RNA (mRNA) COVID-19 vaccines and myocarditis has aroused public concern over vaccine safety. OBJECTIVES: The goal of this study was to compare the prognosis of this condition with viral infection-related myocarditis over 180 days. METHODS: A territory-wide electronic public health care database in Hong Kong linked with population-based vaccination records was used to conduct a retrospective cohort study. Since the roll-out of BNT162b2 (Pfizer-BioNTech), patients aged >/=12 years hospitalized with myocarditis within 28 days after BNT162b2 vaccination were compared against viral infection-related myocarditis recorded before the pandemic (2000-2019), over a 180-day follow-up period (starting from diagnosis of myocarditis). All-cause mortality, heart failure, dilated cardiomyopathy, heart transplant, and postdischarge health care utilization were examined with Cox proportional hazards models. RESULTS: A total of 866 patients were included for analysis. Over the follow-up period, 1 death (1.0%) of 104 patients with postvaccination myocarditis and 84 deaths (11.0%) of 762 patients with viral infection-related myocarditis were identified. One case (1.0%) of dilated cardiomyopathy and 2 cases (1.9%) of heart failure were identified in the postvaccination group, compared with 28 (3.7%) and 93 (12.2%) in the viral infection-related myocarditis group, respectively. Adjusted analysis showed that the postvaccination myocarditis group had a 92% lower mortality risk (adjusted HR: 0.08; 95% CI: 0.01-0.57). No significant differences in other prognostic outcomes were seen. CONCLUSIONS: This study found a significantly lower rate of mortality among individuals with myocarditis after mRNA vaccination compared with those with viral infection-related myocarditis. Prognosis of this iatrogenic condition may be less severe than naturally acquired viral infection-related myocarditis.

Lai, Y. W., et al. (2022). "Autoimmune Rheumatic Disease Flares with Myocarditis Following COVID-19 mRNA Vaccination: A Case-Based Review." Vaccines (Basel) **10**(10).

Since the introduction of coronavirus disease 2019 (COVID-19) messenger ribonucleic acid (mRNA) vaccines, there have been multiple reports of post-vaccination myocarditis (mainly affecting young healthy males). We report on four patients with active autoimmune rheumatic diseases (ARDs) and probable or confirmed myocarditis following COVID-19 mRNA vaccination managed at a tertiary hospital in Singapore; we reviewed the literature on post-COVID-19 mRNA vaccination-related myocarditis and ARD flares. Three patients had existing ARD flares (two had systemic lupus

erythematosus (SLE), one had eosinophilic granulomatosis polyangiitis (EGPA)), and one had new-onset EGPA. All patients recovered well after receiving immunosuppressants comprising high-dose glucocorticoids, cyclophosphamide, and rituximab. Thus far, only one case of active SLE with myocarditis has been reported post-COVID-19 mRNA vaccination in the literature. In contrast to isolated post-COVID-19 mRNA vaccination myocarditis, our older-aged patients had myocarditis associated with ARD flares post-COVID-19 vaccination (that occurred after one dose of an mRNA vaccine), associated with other features of ARD flares, and required increased immunosuppression to achieve myocarditis resolution. This case series serves to highlight the differences in clinical and therapeutic aspects in ARD patients, heighten the vigilance of rheumatologists for this development, and encourage the adoption of risk reduction strategies in this vulnerable population.

Lane, S., A. Yeomans and S. Shakir (2022). "Reports of myocarditis and pericarditis following mRNA COVID-19 vaccination: a systematic review of spontaneously reported data from the UK, Europe and the USA and of the scientific literature." BMJ Open **12**(5): e059223.

OBJECTIVES: To combine spontaneously reported data from multiple countries to estimate reporting rate, and better understand risk factors for myocarditis and pericarditis following COVID-19 messenger RNA (mRNA) vaccines. DESIGN: Systematic review of spontaneously reported data from UK, USA and European Union/European Economic Area (EU/EEA) and of the scientific literature. DATA SOURCES: UK Yellow Card scheme, Vaccine Adverse Event Reporting System (VAERS), EudraVigilance were searched from date of vaccine launch to 14 March 2022-16 March 2022. PubMed/MEDLINE and Embase were searched to 15 March 2022. ELIGIBILITY CRITERIA: We included publicly available spontaneous reporting data for 'Myocarditis' and 'Pericarditis' from UK, USA and EU/EEA following COVID-19 mRNA vaccines. Pharmacoepidemiological observational studies investigating myocarditis/pericarditis following mRNA COVID-19 vaccines were included (no restrictions on language or date). Critical Appraisal Skills Programme tools assessed study quality. DATA EXTRACTION AND SYNTHESIS: Two researchers extracted data. Events of myocarditis and pericarditis were presented for each data source, stratified by vaccine, age, sex and dose (where available). Reporting rates were calculated for myocarditis and pericarditis for each population. For published pharmacoepidemiological studies, design, participant characteristics, and study results were tabulated. RESULTS: Overall, 18 204 myocarditis and pericarditis events were submitted to the UK, USA and EU/EEA regulators during the study period. Males represented 62.24% (n=11 331) of myocarditis and pericarditis reports. In the UK and USA, most reports concerned vaccinees aged <40 years (59.7% and 47.3% of reported events, respectively); trends in age were less clear for EU/EEA. Reports were more frequent following a second dose (47.1% of reports, where data available). Reporting rates were consistent between the data sources. Thirty-two pharmacoepidemiological studies were included; results were consistent with our spontaneous report analyses. CONCLUSIONS: Younger vaccinees more frequently report myocarditis and pericarditis following mRNA COVID-19 vaccines than older vaccinees. Results from published literature supported the results of our analyses.

Lane, S., A. Yeomans and S. Shakir (2022). "Systematic review of spontaneous reports of myocarditis and pericarditis in transplant recipients and immunocompromised patients following COVID-19 mRNA vaccination." BMJ Open **12**(7): e060425.

OBJECTIVES: To determine whether spontaneous reporting rates of myocarditis and pericarditis differed in immunocompromised patients compared with the whole population overall, and in terms of demographics, vaccine dose and time-to-onset. DESIGN: Systematic review of spontaneously reported data from the European Union/European Economic Area (EU/EEA), the USA and the UK. DATA SOURCES: EudraVigilance (EU/EEA), Vaccine Adverse Event Reporting System (VAERS; USA) and the Medicines and Healthcare products Regulatory Agency (UK) spontaneous reporting databases were searched from date of vaccine launch to 1 December 2021. ELIGIBILITY CRITERIA: Publicly available spontaneous reporting data for 'myocarditis' and 'pericarditis' from EU/EEA and USA following COVID-19 messenger RNA vaccines. Reports with comorbidities or concurrent medication indicative of transplantation, HIV infection or cancer ('immunocompromised' population) were compared with each overall database population. DATA EXTRACTION AND SYNTHESIS: Two researchers extracted data. Spontaneously reported events of myocarditis and pericarditis were presented for immunocompromised populations for each data source, stratified by age, sex, dose and time-to-onset (where available). Seriousness of each event was determined according to the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guideline E2A definition. Proportional reporting ratio (PRR) was calculated. RESULTS: There were 178 reports of myocarditis and pericarditis among immunocompromised individuals overall. Seriousness was comparable between the immunocompromised and overall populations in both databases. No trends in age or sex were observed among immunocompromised individuals. Most reports followed a second vaccine dose and occurred within 14 days. The frequency of reporting was similar to the wider population (PRR=1.36 (95% CI=0.89 to 1.82) for VAERS population). CONCLUSIONS: Myocarditis and pericarditis following COVID-19 vaccination are very rare, and benefits of COVID-19 vaccination continue to outweigh any perceived risks. Reporting rates of myocarditis and pericarditis were similar in immunocompromised individuals, however defining characteristics differed compared with the whole population; therefore, continued monitoring of adverse events following vaccination remains vital to understand differences between population subgroups.

Lazniak-Pfajfer, A., et al. (2022). "Myocarditis associated with COVID-19 vaccination in three male teenagers." Pol Arch Intern Med **132**(2).

Lee, A. S. Y., et al. (2022). "Myocarditis Following COVID-19 Vaccination: A Systematic Review (October 2020-October 2021)." Heart Lung Circ **31**(6): 757-765.

INTRODUCTION: Reports of SARS-CoV-2 coronavirus (COVID-19) vaccine-related myocarditis, particularly after mRNA vaccines, have raised concerns amongst the general public. This review examined the literature regarding myocarditis post COVID-19

vaccination, drawing from vaccine safety surveillance databases and case reports. METHODS: Combinations of search terms were used in PubMed and COVID-19-specific repositories - LitCovid and the Cochrane COVID-19 Study Register - between 1 October 2020 and 31 October 2021. Manual searches of GoogleScholar and screening of article bibliographies were also performed. RESULTS: Information was obtained from five vaccine safety surveillance databases. Fifty-two (52) case reports totalling 200 cases of possible COVID-19 vaccine-related myocarditis were summarised. Vaccine surveillance databases differed in reporting formats and vaccination rates; however, gross estimates suggested low overall incidence rates of 2-5 per million mRNA vaccines. The incidence appeared to be higher in younger male populations, with onset of symptoms within a few days, usually after the second dose. Some with prior COVID-19 infections had onset after the first dose. Cases with prior unrelated myocarditis were also noted. Almost all presented with chest pain (98.0%). Troponin elevation was universally described and cardiac magnetic resonance imaging was commonly reported based on the updated Lake Louise criteria. Clinical course was mild in the majority, with response to anti-inflammatory treatment. CONCLUSION: COVID-19 vaccine-related myocarditis is an important but rare adverse event. More research is needed into its pathogenesis and reasons for its predominance in young males, while gaps in data exist in those aged <16 years, as well as those with prior COVID-19 infections and prior myocarditis.

Lee, C. H. and E. J. Kong (2022). "FDG PET/MRI of Acute Myocarditis After mRNA COVID-19 Vaccination." Clin Nucl Med **47**(5): e421-e422.

A 22-year-old man visited the emergency department with chest pain. He had received a second dose of the coronavirus disease 2019 (COVID-19) mRNA (Moderna) vaccine 5 days prior. 18F-FDG PET/MR revealed a focal FDG uptake and late gadolinium enhancement on the basal posterolateral wall of the left ventricle. Myocarditis after a COVID-19 vaccination has been reported predominantly after the second dose of mRNA vaccines in young men. This was a case of acute focal myocarditis after a COVID-19 mRNA vaccination, which was well-visualized by FDG PET/MRI.

Lee, E., et al. (2021). "Reply to "Letter to the editor: Myocarditis should be considered in those with a troponin rise and unobstructed coronary arteries following PfizerBioNTech COVID-19 vaccination"." QJM.

Lee, E., et al. (2022). "Reply to 'Letter to the editor: Myocarditis should be considered in those with a troponin rise and unobstructed coronary arteries following PfizerBioNTech COVID-19 vaccination'." QJM **115**(7): 500-501.

Levin, D., et al. (2021). "Myocarditis following COVID-19 vaccination - A case series." Vaccine **39**(42): 6195-6200.

There have been reports of myocarditis following COVID-19 vaccination. We surveyed all hospitalized military personnel in the Isareli Defense Forces during the period of the COVID-19 vaccination operation (12/28/2021-3/7/2021) for diagnosed myocarditis. We identified 7 cases of myocarditis with symptoms starting in the first week after the

second dose of COVID-19 Pfizer-BioNTech vaccine. One case of myocarditis diagnosed 10 days after the second dose of the vaccine was not included. These 8 cases comprise of all events of myocarditis diagnosed in military personnel during this time period. All patients were young and generally healthy. All had mild disease with no sequalae. The incidence of myocarditis in the week following a second dose of the vaccine was 5.07/100,000 people vaccinated. Due to the nature of this report no causality could be established. Clinicians should be aware of the possibility of myocarditis following Pfizer-BioNTech vaccination. True incidence rates should be further investigated.

Li, M., et al. (2022). "Myocarditis or Pericarditis Following the COVID-19 Vaccination in Adolescents: A Systematic Review." Vaccines (Basel) **10**(8).

Background: By 16 May 2022, 12,186,798,032 people had been vaccinated with COVID-19 vaccines. Our study found that myocarditis/pericarditis may occur in adolescents after COVID-19 vaccination. Methods: In this regard, we conducted a meta-analysis of seven groups of adolescents aged 12-19 years to compare the incidence of myocarditis/pericarditis after vaccination and compare the relative risk incidence after the first and second doses of a COVID-19 vaccine, and between males and females for risk incidence. Results: We analyzed 22,020,997 subjects from seven studies, including 130 cases of confirmed myocarditis/pericarditis. The overall mean incidence rate was 1.69 cases per 100,000 person-years. Of these, 19 of the 12,122,244 people who received a first dose of a COVID-19 vaccine had myocarditis/pericarditis, an incidence rate of 0.0022% (95% CI 0.0001-0.0034), and 111 of the 1,008,753 people who received a second dose had myocarditis/pericarditis, an incidence rate of 0.0107% (95% CI 0.0059-0.0155). The prevalence relative ratio (RR) after the first and second doses was RR = 5.53 (95% CI: 3.01-10.16), with a higher prevalence after the second dose than after the first dose of a COVID-19 vaccine. After a second dose of a COVID-19 vaccine, the RR for males relative to females was RR = 13.91 (95% CI: 4.30-44.95), with a more pronounced risk of disease in males than in females. Conclusions: Our study showed that myocarditis/pericarditis occurred after vaccination with the BNT162b2 or Comirnaty vaccine, especially after the second vaccination in male adolescents, but the incidence of myocarditis/pericarditis after vaccination with the above vaccines was very rare (0.0022%). Therefore, it is recommended that adolescents should be vaccinated with the COVID-19 universal vaccine as soon as possible and closely monitored for subsequent adverse reactions, which can be treated promptly.

Li, M., et al. (2021). "Myocarditis and Pericarditis following COVID-19 Vaccination: Inequalities in Age and Vaccine Types." J Pers Med **11**(11).

An increasing number of myocarditis/pericarditis incidences has been reported after coronavirus disease-19 (COVID-19) vaccination in adolescents and young adults. This study was designed to investigate the incidence rate of-and risk for-myocarditis and pericarditis following COVID-19 vaccination in the United States according to age and vaccine type. This study used the Vaccine Adverse Events Reporting System (VAERS) from 11 December 2020 to 13 August 2021. A population-based data mining approach was performed based on the reporting odds ratio (ROR). Adverse events of myocarditis and

pericarditis following COVID-19 vaccination were rare, with an incidence rate of 5.98 (95% CI = 5.73-6.24) cases per million doses administered. The incidence rate was higher in adolescents and after the administration of the second dose of messenger RNA (mRNA) vaccines. Overall, two mRNA vaccines were significantly associated with increased risks for myocarditis/pericarditis (mRNA-1273 (Moderna): ROR = 2.91, 95% CI = 2.21-3.83; BNT162b2 (Pfizer-BioNTech): ROR = 5.37, 95% CI = 4.10-7.04) compared to all other vaccines from VAERS. The viral vector vaccine of Ad26.COV2.S (Janssen) was not associated with signals of myocarditis/pericarditis (ROR = 1.39; 95% CI = 0.99-1.97). This study found increased risks for myocarditis/pericarditis following mRNA COVID-19 vaccines. For patients at high risk for myocarditis/pericarditis or with myocardial injuries, the viral vector vaccine may be an alternative for consideration.

Li, X., et al. (2022). "Myocarditis Following COVID-19 BNT162b2 Vaccination Among Adolescents in Hong Kong." JAMA Pediatr **176**(6): 612-614.

This cohort study assesses the association between the single-dose COVID-19 BNT162b2 vaccination regimen and myocarditis risk among vaccinated adolescents in Hong Kong before and after the single-dose policy.

Licata, T. and A. Clements (2022). "Case Report of COVID-19 mRNA Vaccine-Associated Myocarditis." WMJ **121**(3): E50-E52.

INTRODUCTION: We present a case report highlighting a single patient out of 3 who developed myocarditis within days after receiving Pfizer and Moderna COVID-19 mRNA vaccines. CASE PRESENTATION: A 19-year-old male was admitted to our hospitalist service with substernal chest pain that was sharp, constant, and varied with position. He had received his second dose of the Pfizer-BioNTech COVID-19 vaccine (Pfizer vaccine) 2 days prior. Electrocardiogram was consistent with pericarditis. He had persistently elevated troponins and globally reduced systolic function by echocardiogram, which was consistent with myocarditis. He received colchicine, ibuprofen, and proton pump inhibitors with a resolution of symptoms. After 32 days, follow-up echocardiogram had returned to normal, and his symptoms had resolved completely. DISCUSSION: Given the onset of symptoms after the second dose of vaccine and our review of similar cases in the literature, it seems likely the patient's myopericarditis was caused by the vaccine. Rare complications of new vaccines given to millions of people are rapidly identified by the Vaccine Adverse Event Reporting System. CONCLUSIONS: The identification of myopericarditis as a complication of mRNA vaccines will need further study to understand the pathophysiology, incidence, and prevalence in specific age groups and biological sexes.

Lin, W., et al. (2022). "Ventricular tachycardia from myocarditis following COVID-19 vaccination with tozinameran (BNT162b2, Pfizer-BioNTech)." Pacing Clin Electrophysiol **45**(9): 1097-1100.

To combat the coronavirus disease 2019 (COVID-19) pandemic, many countries have started population vaccination programs using messenger ribonucleic acid (mRNA) vaccines. With the widespread use of such vaccines, reports are emerging worldwide, of the vaccine's association with the development of myocarditis. Younger men are more

likely to develop postvaccine myocarditis, which usually presents as self-limiting chest pain within a week after the second dose. We present a case of myocarditis following vaccination with tozinameran (BNT162b2, Pfizer-BioNTech), which presented late, with ventricular tachycardia (VT) reduced left ventricular ejection fraction (LVEF).

Lu, J., et al. (2022). "Inspiration to mRNA-based COVID-19 vaccination: Serious adverse case reports with hepatitis B vaccine in real-world." Front Pediatr **10**: 888686.

OBJECTIVES: The hepatitis B vaccine comprises hepatitis B surface antigen (HBsAg) produced by transgenic yeast cells. There are few serious adverse events (SAE) reports after Hepatitis B vaccination. METHODS: The authors searched the Chinese legal documents database for all SAE with Hepatitis B vaccination from January 2010 to January 2022. RESULTS: All seven patients received yeast-derived recombinant hepatitis B vaccine. Three cases of myocarditis (death), 2 cases of interstitial pneumonia (death), and 2 cases of encephalitis. The mean time of onset of SAE was 8.3 +/- 4.3 h after vaccination. CONCLUSION: The mechanism of vaccine-induced myocarditis may come from immune protein reactions. Based on the experience of Hepatitis B vaccine adverse events, we present new insights into the mechanism of myocarditis caused by the COVID-19 vaccine.

Luk, A., et al. (2021). "Myocarditis and Pericarditis After COVID-19 mRNA Vaccination: Practical Considerations for Care Providers." Can J Cardiol **37**(10): 1629-1634.

The mRNA vaccines against COVID-19 infection have been effective in reducing the number of symptomatic cases worldwide. With widespread uptake, case series of vaccine-related myocarditis/pericarditis have been reported, particularly in adolescents and young adults. Men tend to be affected with greater frequency, and symptom onset is usually within 1 week after vaccination. Clinical course appears to be mild in most cases. On the basis of the available evidence, we highlight a clinical framework to guide providers on how to assess, investigate, diagnose, and report suspected and confirmed cases. In any patient with highly suggestive symptoms temporally related to COVID-19 mRNA vaccination, standardized workup includes serum troponin measurement and polymerase chain reaction testing for COVID-19 infection, routine additional lab work, and a 12-lead electrocardiogram. Echocardiography is recommended as the imaging modality of choice for patients with unexplained troponin elevation and/or pathologic electrocardiogram changes. Cardiovascular specialist consultation and hospitalization should be considered on the basis of the results of standard investigations. Treatment is largely supportive, and myocarditis/pericarditis that is diagnosed according to defined clinical criteria should be reported to public health authorities in every jurisdiction. Finally, we recommend COVID-19 vaccination in all individuals in accordance with the Health Canada and National Advisory Committee on Immunization guidelines. In patients with suspected myocarditis/pericarditis after the first dose of an mRNA vaccine, deferral of a second dose is recommended until additional reports become available.

Luo, J., et al. (2023). "Incidence Rates and Clinical Characteristics of Patients With Confirmed Myocarditis or Pericarditis Following COVID-19 mRNA Vaccination: Experience of the Veterans Health Administration Through 9 October 2022." Open Forum Infect Dis **10**(7): ofad268.

BACKGROUND: Although the benefits outweigh the risks, COVID-19 vaccines have been associated with an increased risk of myocarditis and pericarditis. This report is based on a national US veteran population with confirmed myocarditis/pericarditis following mRNA COVID-19 vaccines according to the near real-time active surveillance program of Veterans Affairs. METHODS: This study is based on a cohort evaluation of all adults administered >/=1 mRNA COVID-19 vaccine, including boosters, in the Veterans Health Administration between 14 December 2020 and 9 October 2022. ICD-10-CM diagnosis codes were used to identify potential safety signals in near real time through a database analysis. All potential cases of myocarditis/pericarditis identified in the database analysis underwent in-depth chart review and case validation by a team of pharmacists and expert clinicians. Our main outcome was the incidence rate of confirmed myocarditis/pericarditis among vaccine recipients (overall and those aged 18-39 years) within 21 days of a first, second, or booster dose of a mRNA COVID-19 vaccine. We calculated the ratio of observed events among COVID-19 vaccine recipients over expected events from historical vaccine recipient controls (2015-2020) in the Veterans Health Administration. We used confirmed cases to calculate incidence rates and 95% CIs. RESULTS: Through 9 October 2022, 3 877 453 doses of BNT162b2 (Pfizer-BioNTech) and 4 221 397 doses of mRNA-1273 (Moderna) were administered as first or second dose across Veterans Affairs, and 1 012 561 BNT162b2 and 1 156 160 mRNA-1273 booster doses were administered. Among all doses, the rapid cycle analysis identified 178 potential cases of myocarditis/pericarditis among vaccinees of any age and 22 potential cases among those aged 18-39 years. Of these, 33 cases, including 6 among those 18-39 years old, were confirmed after in-depth chart review and validation, corresponding with an overall incidence rate per million ranging from 0.46 (95% CI, .01-2.55) for Moderna dose 1 to 6.91 (95% CI, 2.78-14.24) for Pfizer booster. Among those aged 18-39, incidence rates ranged from 7.1 (95% CI, .18-39.56) for Moderna dose 2 to 19.76 (95% CI, 5.38-50.58) for Pfizer dose 2. Patients with confirmed cases were hospitalized for a mean 4.1 days (range, 1-15). The final disposition for 32 (97%) of 33 cases was discharge to home. CONCLUSIONS: This report is a real-world demonstration of the Veterans Affairs' active surveillance system for vaccines. Although the rapid cycle analysis initially identified 178 potential cases of myocarditis/pericarditis, only 1 of 5 cases was confirmed to be related to a COVID-19 vaccine after chart review. These findings highlight the paramount importance of active surveillance and chart validation for rare but serious adverse events related to COVID-19 vaccines.

Mahasing, C., et al. (2023). "Myocarditis and Pericarditis following COVID-19 Vaccination in Thailand." Vaccines (Basel) **11**(4).

BACKGROUND: Myocarditis and pericarditis cases following Coronavirus 2019 (COVID-19) vaccination were reported worldwide. In Thailand, COVID-19 vaccines were approved for emergency use. Adverse event following immunization (AEFI) surveillance has been strengthened to ensure the safety of the vaccines. This study aimed to describe

the characteristics of myocarditis and pericarditis, and identify the factors associated with myocarditis and pericarditis following COVID-19 vaccination in Thailand. METHOD: We carried out a descriptive study of reports of myocarditis and pericarditis to Thailand's National AEFI Program (AEFI-DDC) between 1 March and 31 December 2021. An unpaired case-control study was conducted to determine the factors associated with myocarditis and pericarditis after the CoronaVac, ChAdOx1-nCoV, BBIBP-CorV, BNT162b2, and mRNA-1273 vaccines. The cases consisted of COVID-19 vaccine recipients who met the definition of confirmed, probable, or suspected cases of myocarditis or pericarditis within 30 days of vaccination. The controls were people who underwent COVID-19 vaccination between 1 March and 31 December 2021, with no adverse reactions documented after vaccination. RESULTS: Among the 31,125 events recorded in the AEFI-DDC after 104.63 million vaccinations, 204 cases of myocarditis and pericarditis were identified. The majority of them were male (69%). The median age was 15 years (interquartile range (IQR): 13-17). The incidence was highest following the BNT162b2 vaccination (0.97 cases per 100,000 doses administered). Ten deaths were reported in this study; no deaths were reported among children who received the mRNA vaccine. Compared with the age-specific incidence of myocarditis and pericarditis in Thailand before the introduction of the COVID-19 vaccination, the incidence of myocarditis and pericarditis after the BNT162b2 vaccine was greater in the 12-17 and 18-20 age groups in both males and females. It was higher after the second dose in 12- to 17-year-olds (2.68 cases per 100,000 doses administered) and highest after the second dose in male 12- to 17-year-olds (4.43 cases per 100,000 doses administered). Young age and a mRNA-based vaccination were associated with myocarditis and pericarditis following administration of the COVID-19 vaccine after multivariate analysis. CONCLUSIONS: Myocarditis and pericarditis following vaccination against COVID-19 were uncommon and mild, and were most likely to affect male adolescents. The COVID-19 vaccine offers the recipients enormous benefits. The balance between the risks and advantages of the vaccine and consistent monitoring of AEFI are essential for management of the disease and identification of AEFI.

Maisch, B. (2023). "SARS-CoV-2, vaccination or autoimmunity as causes of cardiac inflammation. Which form prevails?" Herz **48**(3): 195-205.

The causes of cardiac inflammation during the COVID-19 pandemic are manifold and complex, and may have changed with different virus variants and vaccinations. The underlying viral etiology is self-evident, but its role in the pathogenic process is diverse. The view of many pathologists that myocyte necrosis and cellular infiltrates are indispensable for myocarditis does not suffice and contradicts the clinical criteria of myocarditis, i.e., a combination of serological evidence of necrosis based on troponins or MRI features of necrosis, edema, and inflammation based on prolonged T1 and T2 times and late gadolinium enhancement. The definition of myocarditis is still debated by pathologists and clinicians. We have learned that myocarditis and pericarditis can be induced by the virus via different pathways of action such as direct viral damage to the myocardium through the ACE2 receptor. Indirect damage occurs via immunological effector organs such as the innate immune system by macrophages and cytokines, and

then later the acquired immune system via T cells, overactive proinflammatory cytokines, and cardiac autoantibodies. Cardiovascular diseases lead to more severe courses of SARS-CoV-2 disease. Thus, heart failure patients have a double risk for complicated courses and lethal outcome. So do patients with diabetes, hypertension, and renal insufficiency. Independent of the definition, myocarditis patients benefitted from intensive hospital care, ventilation, if needed, and cortisone treatment. Postvaccination myocarditis and pericarditis affect primarily young male patients after the second RNA vaccine. Both are rare events but severe enough to deserve our full attention, because treatment according to current guidelines is available and necessary.

Mancini, N., et al. (2022). "[A rare case of myocarditis and pulmonary embolism after BNT162b2 mRNA vaccine]." G Ital Cardiol (Rome) **23**(4): 244-246.

In the clinical research arsenal, the COVID-19 vaccines are the strongest weapons against the most important worldwide sanitary crisis of the last centuries. Even if vaccine adverse events have mild clinical relevance, several thromboembolic events occurring after adenoviral recombinant vaccine administration have been reported. Cases of myocarditis and pericarditis after administration of mRNA vaccines have also recently been described. We report the case of a patient who suffered from two rare adverse events after BNT162b2 mRNA vaccine administration (Pfizer-BioNTech): acute myocarditis and pulmonary embolism. Although the temporal consequentiality does not demonstrate a causal link, the strong analogies emerging in the latest clinical reports suggest a possible relation. Further studies are needed to understand the potential mechanisms of myocardial damage and atypical thrombosis. Despite the favorable and self-limiting clinical course of post-vaccinal myocarditis, in these cases a tight follow-up is advisable and vaccine adverse event reporting remains mandatory, especially if not described during pivotal clinical trials.

Manfredi, R., et al. (2022). "Clinical Profiles and CMR Findings of Young Adults and Pediatrics with Acute Myocarditis Following mRNA COVID-19 Vaccination: A Case Series." Vaccines (Basel) **10**(2).

Messenger RNA (mRNA) coronavirus disease of 2019 (COVID-19) vaccines have been recently associated with acute myocarditis, predominantly in healthy young males. Out of 231,989 vaccines administrated in our region (Marche, Italy), we report a case series of six healthy patients (four males and two females, 16.5 years old (Q1, Q3: 15, 18)) that experienced mRNA-COVID-19-vaccines side effects. All patients were hospitalized due to fever and troponins elevation following the second dose of an mRNA-based COVID-19 vaccine. Cardiovascular magnetic resonance (CMR) was performed 72-96 h after vaccination. All patients were treated with colchicine and ibuprofen. Myocarditis was prevalent in males. It was characterized by myocardial edema and late gadolinium enhancement (LGE) in the lateral wall of the left ventricle (LV). One patient showed sole right ventricular involvement, while the females presented with myopericarditis (myocarditis + pericardial effusion). All patients in our series had preserved LV ejection fraction and remained clinically stable during a relatively short inpatient hospital stay. One case presented with atrial tachycardia. At the follow-up, no significant CMR findings

were documented after a three-month medical treatment. According to other recently published case series, our report suggests a possible association between acute myocarditis and myopericarditis with mRNA COVID-19 vaccination in healthy young adults and pediatric patients. Not only males are involved, while some arrhythmic manifestations are possible, such as atrial tachycardia. Conversely, we here highlight the benign nature of such complications and the absence of CMR findings after a three-month medical treatment with colchicine and ibuprofen.

Mannan, V., et al. (2022). "COVID-19 Vaccination-Associated Myocarditis: A Literature Review." Cureus **14**(11): e32022.

Myocarditis is defined as a non-ischemic inflammation of the middle layer of the heart. It ensues changes that can lead to acute heart failure, dilated cardiomyopathy, and sudden death. Myocarditis is caused by several infectious and non-infectious agents. Vaccines are also known to cause myocarditis. The use of the coronavirus disease (COVID-19) vaccination was started to combat the severity of the COVID-19 infection and reduce the mortality and morbidity associated with it. The vaccination, however, caused side effects like myocarditis, among others. In order to investigate the association between the COVID-19 vaccination and myocarditis in adults and adolescents, we conducted a literature review by searching three databases: Google Scholar, PubMed, and ScienceDirect. From the published literature, we found that, though it is rare, the various vaccinations available can cause symptoms of myocarditis as a side effect more commonly in patients who have received both doses of a particular vaccine and that there are significant changes in cardiac magnetic resonance imaging (CMRI) and other biochemical markers, with young males being more commonly affected. Further prospective trial-based studies are required to establish a concrete relationship between myocarditis and the COVID-19 vaccine.

Manno, E. C., et al. (2023). "Higher Troponin Levels on Admission are associated With Persistent Cardiac Magnetic Resonance Lesions in Children Developing Myocarditis After mRNA-Based COVID-19 Vaccination." Pediatr Infect Dis J **42**(2): 166-171.

BACKGROUND: Acute pericarditis/myocarditis is a rare complication of the mRNA-based vaccines and although mostly self-limiting, long-term sequelae remain unclear. METHODS: We enrolled all patients admitted to the emergency department between September 2021 and February 2022 meeting the CDC work case definition, with symptoms onset after mRNA-based COVID-19 vaccine. Alternative virologic causes were excluded. Clinical data, laboratory values, cardiologic evaluation, electrocardiogram (ECG), and echocardiogram (ECHO) were collected on admission, at discharge, and during follow-up in all patients. Cardiac Magnetic Resonance (CMR) was performed only in those with signs consistent with myocarditis. RESULTS: We observed 13 patients (11M and 2F), median age 15 years, affected by acute pericarditis/myocarditis after COVID-19 mRNA vaccination (11 after Comirnaty(R) and 2 after Spikevax(R)). Symptoms'onset occurred at a median of 5 days (range, 1 to 41 days) after receiving mRNA vaccine (13 Prizer 2 Moderna): 4 patients (31%) after the 1st dose, 6 (46%) after the 2nd, and 3 (23%) after 3rd dose. Increased levels of high-sensitive troponin T (hsTnT) (median 519,5

ng/mL) and N-terminal-pro hormone BNP (NT-proBNP) (median 268 pg/mL) and pathognomonic ECG and ECHO abnormalities were detected. On admission, 7 of 13 (54%) presented with myopericarditis, 3 (23%) with myocarditis, and 3 (23%) with pericarditis; CMR was performed in 5 patients upon pediatric cardiologist prescription and findings were consistent with myocarditis. At 12 weeks of follow-up, all but one patient (92%), still presenting mild pericardial effusion at ECHO, were asymptomatic with normal hsTnT and NT-proBNP levels and ECG. On CMR 6 of 9 patients showed persistent, although decreased, myocardial injury. Higher hsTnT levels on admission significantly correlated with persistent CMR lesions. CONCLUSION: Evidence of persistent CMR lesions highlights the need for a close and standardized follow-up for those patients who present high hsTnT levels on admission.

Mansour, J., et al. (2021). "Acute myocarditis after a second dose of the mRNA COVID-19 vaccine: a report of two cases." Clin Imaging **78**: 247-249.

We report two cases of myocarditis, in two young and previously healthy individuals, temporally related to the second dose of the mRNA-COVID-19 vaccine. Both patients developed acute chest pain, changes on electrocardiogram (ECG), and elevated serum troponin within two days of receiving their second dose. Cardiac magnetic resonance (CMR) findings were consistent with acute myocarditis.

Manu, P. (2023). "Fatal Myocarditis After COVID-19 Vaccination: Fourteen Autopsy-Confirmed Cases." Am J Ther **30**(3): e259-e260.

Maria Perez Lopez, E., D. Rangel Sousa and J. Navarro Roldan (2023). "Myocarditis and Pericarditis related to mRNA COVID-19 Vaccination: A Case Report." Curr Drug Saf.

INTRODUCTION: Reported cases after the post-commercialization phase of mRNA vaccines against COVID-19 have revealed that myocarditis and pericarditis may occur predominantly in male adolescents after the second dose of the vaccine. CASE PRESENTATION: We report two cases of cardiac disorders associated with mRNA COVID-19 vaccination, both of them in 15 year-old males. One of the patients presented acute pericarditis and the second one presented acute myocarditis with left ventricular dysfunction at hospital discharge. DISCUSSION AND CONCLUSION: Physicians should be aware with the typical manifestations of these cardiovascular events after the vaccination and report suspicious cases to pharmacovigilance agencies as soon as possible. The population should rely on the pharmacovigilance system that continues to recommend vaccination as the most effective strategy to reduce the negative consequences of the pandemic.

Mariani, M., et al. (2022). "Protection against MIS-C outweighs the risk of myocarditis after Covid-19 vaccination in children." Ital J Pediatr **48**(1): 142.

From March 2020 to July 2022, in Liguria region (North-West Italy) incidence of MIS-C among pediatric patients infected by SARS-CoV-2 was 38.7/100.000, which is higher than that of myocarditis after COVID-19 vaccination. In our opinion severity of MIS-C-related cardiac disease outweigh the risk of myocarditis after COVID-19 vaccine.

Marschner, C. A., et al. (2022). "Myocarditis Following COVID-19 Vaccination." Cardiol Clin **40**(3): 375-388.

Myocarditis is an established but rare adverse event following administration of messenger RNA-based coronavirus disease 2019 (COVID-19) vaccines and is most common in male adolescents and young adults. Symptoms typically develop within a few days of vaccine administration. Most patients have mild abnormalities on cardiac imaging with rapid clinical improvement with standard treatment. However, longer term follow-up is needed to determine whether imaging abnormalities persist, to evaluate for adverse outcomes, and to understand the risk associated with subsequent vaccination. The purpose of the review is to evaluate the current literature related to myocarditis following COVID-19 vaccination, including the incidence, risk factors, clinical course, imaging findings, and proposed pathophysiologic mechanisms.

Marschner, C. A., et al. (2023). "Myocarditis Following COVID-19 Vaccination." Heart Fail Clin **19**(2): 251-264.

Myocarditis is an established but rare adverse event following administration of messenger RNA-based coronavirus disease 2019 (COVID-19) vaccines and is most common in male adolescents and young adults. Symptoms typically develop within a few days of vaccine administration. Most patients have mild abnormalities on cardiac imaging with rapid clinical improvement with standard treatment. However, longer term follow-up is needed to determine whether imaging abnormalities persist, to evaluate for adverse outcomes, and to understand the risk associated with subsequent vaccination. The purpose of the review is to evaluate the current literature related to myocarditis following COVID-19 vaccination, including the incidence, risk factors, clinical course, imaging findings, and proposed pathophysiologic mechanisms.

Marshall, M., et al. (2021). "Symptomatic Acute Myocarditis in 7 Adolescents After Pfizer-BioNTech COVID-19 Vaccination." Pediatrics **148**(3).

Trials of coronavirus disease 2019 (COVID-19) vaccination included limited numbers of children, so they may not have detected rare but important adverse events in this population. We report 7 cases of acute myocarditis or myopericarditis in healthy male adolescents who presented with chest pain all within 4 days after the second dose of Pfizer-BioNTech COVID-19 vaccination. Five patients had fever around the time of presentation. Acute COVID-19 was ruled out in all 7 cases on the basis of negative severe acute respiratory syndrome coronavirus 2 real-time reverse transcription polymerase chain reaction test results of specimens obtained by using nasopharyngeal swabs. None of the patients met criteria for multisystem inflammatory syndrome in children. Six of the 7 patients had negative severe acute respiratory syndrome coronavirus 2 nucleocapsid antibody assay results, suggesting no previous infection. All patients had an elevated troponin. Cardiac MRI revealed late gadolinium enhancement characteristic of myocarditis. All 7 patients resolved their symptoms rapidly. Three patients were treated with nonsteroidal antiinflammatory drugs only, and 4 received intravenous immunoglobulin and corticosteroids. In this report, we provide a summary of each

adolescent's clinical course and evaluation. No causal relationship between vaccine administration and myocarditis has been established. Continued monitoring and reporting to the US Food and Drug Administration Vaccine Adverse Event Reporting System is strongly recommended.

Massari, M., et al. (2022). "Postmarketing active surveillance of myocarditis and pericarditis following vaccination with COVID-19 mRNA vaccines in persons aged 12 to 39 years in Italy: A multi-database, self-controlled case series study." PLoS Med **19**(7): e1004056.

BACKGROUND: Myocarditis and pericarditis following the Coronavirus Disease 2019 (COVID-19) mRNA vaccines administration have been reported, but their frequency is still uncertain in the younger population. This study investigated the association between Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) mRNA vaccines, BNT162b2, and mRNA-1273 and myocarditis/pericarditis in the population of vaccinated persons aged 12 to 39 years in Italy. METHODS AND FINDINGS: We conducted a self-controlled case series study (SCCS) using national data on COVID-19 vaccination linked to emergency care/hospital discharge databases. The outcome was the first diagnosis of myocarditis/pericarditis between 27 December 2020 and 30 September 2021. Exposure risk period (0 to 21 days from the vaccination day, subdivided in 3 equal intervals) for first and second dose was compared with baseline period. The SCCS model, adapted to event-dependent exposures, was fitted using unbiased estimating equations to estimate relative incidences (RIs) and excess of cases (EC) per 100,000 vaccinated by dose, age, sex, and vaccine product. Calendar period was included as time-varying confounder in the model. During the study period 2,861,809 persons aged 12 to 39 years received mRNA vaccines (2,405,759 BNT162b2; 456,050 mRNA-1273); 441 participants developed myocarditis/pericarditis (346 BNT162b2; 95 mRNA-1273). Within the 21-day risk interval, 114 myocarditis/pericarditis events occurred, the RI was 1.99 (1.30 to 3.05) after second dose of BNT162b2 and 2.22 (1.00 to 4.91) and 2.63 (1.21 to 5.71) after first and second dose of mRNA-1273. During the [0 to 7) days risk period, an increased risk of myocarditis/pericarditis was observed after first dose of mRNA-1273, with RI of 6.55 (2.73 to 15.72), and after second dose of BNT162b2 and mRNA-1273, with RIs of 3.39 (2.02 to 5.68) and 7.59 (3.26 to 17.65). The number of EC for second dose of mRNA-1273 was 5.5 per 100,000 vaccinated (3.0 to 7.9). The highest risk was observed in males, at [0 to 7) days after first and second dose of mRNA-1273 with RI of 12.28 (4.09 to 36.83) and RI of 11.91 (3.88 to 36.53); the number of EC after the second dose of mRNA-1273 was 8.8 (4.9 to 12.9). Among those aged 12 to 17 years, the RI was of 5.74 (1.52 to 21.72) after second dose of BNT162b2; for this age group, the number of events was insufficient for estimating RIs after mRNA-1273. Among those aged 18 to 29 years, the RIs were 7.58 (2.62 to 21.94) after first dose of mRNA-1273 and 4.02 (1.81 to 8.91) and 9.58 (3.32 to 27.58) after second dose of BNT162b2 and mRNA-1273; the numbers of EC were 3.4 (1.1 to 6.0) and 8.6 (4.4 to 12.6) after first and second dose of mRNA-1273. The main study limitations were that the outcome was not validated through review of clinical records, and there was an absence of information on the length of hospitalization and, thus, the severity of the outcome. CONCLUSIONS: This population-based study of about 3 millions of residents in Italy

suggested that mRNA vaccines were associated with myocarditis/pericarditis in the population younger than 40 years. According to our results, increased risk of myocarditis/pericarditis was associated with the second dose of BNT162b2 and both doses of mRNA-1273. The highest risks were observed in males of 12 to 39 years and in males and females 18 to 29 years vaccinated with mRNA-1273. The public health implication of these findings should be considered in the light of the proven mRNA vaccine effectiveness in preventing serious COVID-19 disease and death.

Matar, R. H., et al. (2022). "Clinical Characteristics of Patients with Myocarditis following COVID-19 mRNA Vaccination: A Systematic Review and Meta-Analysis." J Clin Med **11**(15).

COVID-19 mRNA vaccinations have recently been implicated in causing myocarditis. Therefore, the primary aim of this systematic review and meta-analysis was to investigate the clinical characteristics of patients with myocarditis following mRNA vaccination. The secondary aims were to report common imaging and laboratory findings, as well as treatment regimes, in these patients. A literature search was performed from December 2019 to June 2022. Eligible studies reported patients older than 18 years vaccinated with mRNA, a diagnosis of myocarditis, and subsequent outcomes. Pooled mean or proportion were analyzed using a random-effects model. Seventy-five unique studies (patient n = 188, 89.4% male, mean age 18-67 years) were included. Eighty-six patients had Moderna vaccines while one hundred and two patients had Pfizer-BioNTech vaccines. The most common presenting symptoms were chest pain (34.5%), fever (17.1%), myalgia (12.4%), and chills (12.1%). The most common radiologic findings were ST-related changes on an electrocardiogram (58.7%) and hypokinesia on cardiac magnetic resonance imaging or echocardiography (50.7%). Laboratory findings included elevated Troponin I levels (81.7%) and elevated C-reactive protein (71.5%). Seven patients were admitted to the intensive care unit. The most common treatment modality was non-steroid anti-inflammatory drugs (36.6%) followed by colchicine (28.5%). This meta-analysis presents novel evidence to suggest possible myocarditis post mRNA vaccination in certain individuals, especially young male patients. Clinical practice must therefore take appropriate pre-cautionary measures when administrating COVID-19 mRNA vaccinations.

Matta, A., et al. (2021). "Post-mRNA COVID-19 Vaccination Myocarditis." Eur J Case Rep Intern Med **8**(8): 002769.

A new trend of myocarditis among young adults who received mRNA vaccines for COVID-19 is emerging. We present the case of a young adult who presented with chest pain 3 days after the second dose of Pfizer-BioNTech COVID-19 vaccine. He had elevated troponin I and C-reactive protein levels at the time of admission. Electrocardiogram (ECG) and echocardiogram findings were unremarkable. The patient improved with conservative management and was discharged home the next day. LEARNING POINTS: Myocarditis is rare but is increasingly being reported in young adults post vaccination for COVID-19.Patients usually present with chest pain, elevated troponin and/or inflammatory markers.The condition carries a good prognosis and patients usually recover with supportive care.

Mengesha, B., et al. (2022). "Severe Acute Myocarditis after the Third (Booster) Dose of mRNA COVID-19 Vaccination." Vaccines (Basel) **10**(4).

Vaccination with mRNA vaccines against coronavirus disease 2019 (COVID-19) has been associated with a risk of developing myocarditis and pericarditis, with an estimated standardized incidence ratio of myocarditis being 5.34 (95% CI, 4.48 to 6.40) as compared to the expected incidence based on historical data according to a large national study in Israel. Most cases of myocarditis in vaccine recipients occur in young males, particularly following the second dose, and the presentation is usually mild. Recently, the third (booster) dose has been shown to reduce confirmed infections and severe illness even against common variants of the virus. In Israel, over 4.4 million citizens (more than 45% of the population) have been vaccinated with the third dose of Pfizer-BioNTech vaccine BNT162b2. Herein, we report the first case of a histologically confirmed severe myocarditis following the third dose of BNT162b2 COVID-19 vaccine.

Mevorach, D., et al. (2021). "Myocarditis after BNT162b2 mRNA Vaccine against Covid-19 in Israel." N Engl J Med.

BACKGROUND: Approximately 5.1 million Israelis had been fully immunized against coronavirus disease 2019 (Covid-19) after receiving two doses of the BNT162b2 messenger RNA vaccine (Pfizer-BioNTech) by May 31, 2021. After early reports of myocarditis during adverse events monitoring, the Israeli Ministry of Health initiated active surveillance. METHODS: We retrospectively reviewed data obtained from December 20, 2020, to May 31, 2021, regarding all cases of myocarditis and categorized the information using the Brighton Collaboration definition. We analyzed the occurrence of myocarditis by computing the risk difference for the comparison of the incidence after the first and second vaccine doses (21 days apart); by calculating the standardized incidence ratio of the observed-to-expected incidence within 21 days after the first dose and 30 days after the second dose, independent of certainty of diagnosis; and by calculating the rate ratio 30 days after the second dose as compared with unvaccinated persons. RESULTS: Among 304 persons with symptoms of myocarditis, 21 had received an alternative diagnosis. Of the remaining 283 cases, 142 occurred after receipt of the BNT162b2 vaccine; of these cases, 136 diagnoses were definitive or probable. The clinical presentation was judged to be mild in 129 recipients (95%); one fulminant case was fatal. The overall risk difference between the first and second doses was 1.76 per 100,000 persons (95% confidence interval [CI], 1.33 to 2.19), with the largest difference among male recipients between the ages of 16 and 19 years (difference, 13.73 per 100,000 persons; 95% CI, 8.11 to 19.46). As compared with the expected incidence based on historical data, the standardized incidence ratio was 5.34 (95% CI, 4.48 to 6.40) and was highest after the second dose in male recipients between the ages of 16 and 19 years (13.60; 95% CI, 9.30 to 19.20). The rate ratio 30 days after the second vaccine dose in fully vaccinated recipients, as compared with unvaccinated persons, was 2.35 (95% CI, 1.10 to 5.02); the rate ratio was again highest in male recipients between the ages of 16 and 19 years (8.96; 95% CI, 4.50 to 17.83), with a ratio of 1 in 6637. CONCLUSIONS: The incidence of myocarditis, although low, increased after the receipt of the BNT162b2

vaccine, particularly after the second dose among young male recipients. The clinical presentation of myocarditis after vaccination was usually mild.

Mevorach, D., et al. (2022). "Myocarditis After BNT162b2 COVID-19 Third Booster Vaccine in Israel." Circulation **146**(10): 802-804.

Mimouni, H., et al. (2022). "Cardiogenic shock revealing myocarditis after mRNA vaccination against covid-19: Case report and brief review for the first case in Morocco." Ann Med Surg (Lond) **74**: 103210.

INTRODUCTION: and importance: After its unexpected effectiveness in the clinical trials, the anti-COVID-19 vaccine type mRNA was launched on December 11, 2020, but a few months later, several reports of post-mRNA vaccination myocarditis were published, but without any proven causal link. CASE PRESENTATION: We report the case of a 14-year-old teenager admitted to the emergency department for a cardiogenic shock, the patient mentioned that he had an anti-COVID 19 vaccination 10 days before his admission. First, the vasoactive drugs had stabilized the patient; the troponins came back highly favorable but later confirmed myocarditis by magnetic resonance imaging. In this sense an etiological analysis was made and it came back without any particularities, leaving us relating the myocarditis to the vaccination. CLINICAL DISCUSSION: Post-vaccination myocarditis is a rare event, with very few reports in the literature. After the introduction of COVID vaccination, several reports were published, mostly after the mRNA vaccine. Until now, no causal link has been proven, so we need to have more reports in this sense to have a better knowledge of this phenomenon. CONCLUSION: Until we obtain a more precise explanation of the mechanism of myocarditis after vaccination with the anti-COVID-19 vaccine, all symptoms suggesting myocarditis should be systematically monitored during the first 7 days after vaccination.

Minocha, P. K., et al. (2021). "Recurrence of Acute Myocarditis Temporally Associated with Receipt of the mRNA Coronavirus Disease 2019 (COVID-19) Vaccine in a Male Adolescent." J Pediatr **238**: 321-323.

Miqdad, M. A., et al. (2021). "Acute Myocarditis Following the Administration of the Second BNT162b2 COVID-19 Vaccine Dose." Cureus **13**(10): e18880.

COVID-19 disease has infected millions of people worldwide during the pandemic; hence, the need for an effective and safe vaccine was urgently required. A two-dose of the BNT162b2 mRNA COVID-19 vaccine was reported to have 95% efficacy in preventing COVID-19. The short-term safety profile recorded mild to moderate pain at the injection site, fatigue, and headache. The critical adverse effects were low and similar in the placebo group. However, we report the case of an 18-year-old male who developed acute central crushing chest pain four days following administration of the second dose of the BNT162b2 COVID-19 vaccine. After extensive cardiac workup, including coronary arteries diagnostic angiography, myocarditis was suspected and confirmed by a cardiac MRI. Fortunately, the patient's clinical condition gradually improved in the form of

clinical symptoms and laboratory findings. He was discharged after one week of stay in hospital with regular follow-up in the cardiac clinic.

Mohammed, L. M., et al. (2022). "Myocarditis Secondary to COVID-19 mRNA Vaccine: A Case Report." Cureus **14**(2): e22345.

Vaccine-induced myocarditis has been acknowledged in the past as a rare complication after vaccine administration including influenza and smallpox. Over the past year, there has been an increased number of myopericarditis cases reported by The Center for Disease Control and Prevention (CDC) following the administration of the BNT162b2 and mRNA-1273 vaccines. Most of these cases were among healthy young male adolescents. We report a case of myocarditis in a young male adolescent who presented with chest pain 2 weeks following the first dose of the mRNA COVID-19 vaccine. In the context of the COVID-19 pandemic, we believe it's crucial for healthcare providers to recognize and consider myocarditis as a differential diagnosis in young otherwise healthy individuals who present with chest pain and cardiac symptoms.

Molina-Ramos, A. I., et al. (2022). "Myocarditis Related to COVID-19 and SARS-CoV-2 Vaccination." J Clin Med **11**(23).

The coronavirus disease of 2019 (COVID-19) has been a cause of significant morbidity and mortality worldwide. Among the short- and long-term consequences of COVID-19, myocarditis is a disease to be taken into consideration. Myocarditis, in general, is related to a poor prognosis. However, the epidemiology and prognosis of myocarditis related to COVID-19 are currently unknown. While vaccination against COVID-19 is of great benefit at a public health level, the risk of myocarditis should be considered in the context of the global benefits of vaccination. In this narrative review, we will summarize the etiopathogenic bases, the epidemiology, the clinical manifestations, the course, diagnosis, prognosis, and the treatment of myocarditis related to SARS-CoV-2, as well as myocarditis secondary to mRNA vaccines.

Montag, K. and G. Kampf (2022). "Hospitalised Myocarditis and Pericarditis Cases in Germany Indicate a Higher Post-Vaccination Risk for Young People Mainly after COVID-19 Vaccination." J Clin Med **11**(20).

It was recently described that the overall risk of myopericarditis after receiving a COVID-19 vaccine is low, except for younger males receiving mRNA vaccines [...].

Montgomery, J., et al. (2021). "Myocarditis Following Immunization With mRNA COVID-19 Vaccines in Members of the US Military." JAMA Cardiol **6**(10): 1202-1206.

IMPORTANCE: Myocarditis has been reported with COVID-19 but is not clearly recognized as a possible adverse event following COVID-19 vaccination. OBJECTIVE: To describe myocarditis presenting after COVID-19 vaccination within the Military Health System. DESIGN, SETTING, AND PARTICIPANTS: This retrospective case series studied patients within the US Military Health System who experienced myocarditis after COVID-19 vaccination between January and April 2021. Patients who sought care for chest pain following COVID-19 vaccination and were subsequently diagnosed with clinical

myocarditis were included. EXPOSURE: Receipt of a messenger RNA (mRNA) COVID-19 vaccine between January 1 and April 30, 2021. MAIN OUTCOMES AND MEASURES: Clinical diagnosis of myocarditis after COVID-19 vaccination in the absence of other identified causes. RESULTS: A total of 23 male patients (22 currently serving in the military and 1 retiree; median [range] age, 25 [20-51] years) presented with acute onset of marked chest pain within 4 days after receipt of an mRNA COVID-19 vaccine. All military members were previously healthy with a high level of fitness. Seven received the BNT162b2-mRNA vaccine and 16 received the mRNA-1273 vaccine. A total of 20 patients had symptom onset following the second dose of an appropriately spaced 2-dose series. All patients had significantly elevated cardiac troponin levels. Among 8 patients who underwent cardiac magnetic resonance imaging within the acute phase of illness, all had findings consistent with the clinical diagnosis of myocarditis. Additional testing did not identify other etiologies for myocarditis, including acute COVID-19 and other infections, ischemic injury, or underlying autoimmune conditions. All patients received brief supportive care and were recovered or recovering at the time of this report. The military administered more than 2.8 million doses of mRNA COVID-19 vaccine in this period. While the observed number of myocarditis cases was small, the number was higher than expected among male military members after a second vaccine dose. CONCLUSIONS AND RELEVANCE: In this case series, myocarditis occurred in previously healthy military patients with similar clinical presentations following receipt of an mRNA COVID-19 vaccine. Further surveillance and evaluation of this adverse event following immunization is warranted. Potential for rare vaccine-related adverse events must be considered in the context of the well-established risk of morbidity, including cardiac injury, following COVID-19 infection.

Montgomery, J. R., et al. (2023). "Cardiac Adverse Events Following COVID-19 Vaccination in Patients With Prior Vaccine-Associated Myocarditis." Fed Pract **40**(1): 6-10.

BACKGROUND: Limited information exists to guide shared clinical decision making on COVID-19 vaccination in persons with a prior history of vaccine-associated myocarditis, pericarditis, or myopericarditis (VAMP). The objective of this retrospective observational case series was to characterize cardiac outcomes within 30 days following receipt of 1 or more COVID-19 vaccinations during 2021 in US service members diagnosed with prior non-COVID-19 VAMP between 1998 and 2019. METHODS: As part of the collaborative public health mission with the Centers for Disease Control and Prevention for enhanced vaccine adverse events surveillance, the Defense Health Agency Immunization Healthcare Division maintains a clinical database of service members and beneficiaries referred for suspected adverse events following immunizations. Cases in this database recorded between January 1, 2003, and February 28, 2022, were reviewed to identify individuals with prior VAMP who received a COVID-19 vaccine in 2021 and developed signs or symptoms suggestive of VAMP within 30 days following COVID-19 vaccination. RESULTS: Before the COVID-19 pandemic, 431 service members had verified VAMP. Among these 431 patients, 179 had records that confirmed receipt of a COVID-19 vaccine in 2021. Of these 179 patients, 171 (95.5%) were male. Their median age was 39 years (range, 21-67) at the time of COVID-19 vaccination. Most (n = 172; 96.1%)

experienced their original VAMP episode after receipt of the live replicating smallpox vaccine. Eleven patients experienced cardiac-suggestive symptoms (chest pain, palpitations, or dyspnea) within 30 days of COVID-19 vaccination. Four patients met the criteria for recurrent VAMP. Three men aged 49, 50, and 55 years developed myocarditis within 3 days of an mRNA COVID-19 vaccine. One 25-year-old man developed pericarditis within 4 days of receiving an mRNA vaccine. All 4 COVID-19 recurrent VAMP cases fully recovered with minimal supportive care within weeks (myocarditis) to months (pericarditis). CONCLUSIONS: As demonstrated by this case series, albeit rare, VAMP may reoccur after COVID-19 vaccination among patients who experienced cardiac injury after smallpox vaccination. The clinical characteristics and course of the 4 recurring cases were mild, appearing similar to the post-COVID-19 VAMP described in individuals without a history of VAMP. More research is warranted on factors that may predispose patients to vaccine-associated cardiac injury and which vaccine platforms or schedules may reduce the risk of recurrence among patients who have experienced these events.

Morgan, M. C., et al. (2022). "COVID-19 vaccine-associated myocarditis." World J Cardiol **14**(7): 382-391.

Myocarditis is now recognized as a rare complication of coronavirus disease 2019 (COVID-19) mRNA vaccination, particularly in adolescent and young adult males. Since the authorization of the Pfizer-BioNTech and Moderna mRNA vaccines targeting the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) spike protein, the Centers for Disease Control and Prevention (CDC) has reported 1175 confirmed cases of myocarditis after COVID-19 vaccination in individuals ages 30 years and younger as of January 2022. According to CDC data in June 2021, the incidence of vaccine-mediated myocarditis in males ages 12-29 years old was estimated to be 40.6 cases per million second doses of COVID-19 mRNA vaccination administered. Individuals with cases of COVID-19 vaccine-mediated myocarditis typically present with acute chest pain and elevated serum troponin levels, often within one week of receiving the second dose of mRNA COVID-19 vaccination. Most cases follow a benign clinical course with prompt resolution of symptoms. Proposed mechanisms of COVID-19 vaccine myocarditis include molecular mimicry between SARS-CoV-2 spike protein and self-antigens and the triggering of preexisting dysregulated immune pathways in predisposed individuals. The higher incidence of COVID-19 vaccine myocarditis in young males may be explained by testosterone and its role in modulating the immune response in myocarditis. There is limited data on long-term outcomes in these cases given the recency of their occurrence. The CDC continues to recommend COVID-19 vaccination for everyone 5 years of age and older given the greater risk of serious complications related to natural COVID-19 infection including hospitalization, multisystem organ dysfunction, and death. Further study is needed to better understand the immunopathology and long-term outcomes behind COVID-19 mRNA vaccine-mediated myocarditis.

Mormile, R. (2022). "Myocarditis and pericarditis following mRNA COVID-19 vaccination in younger patients: is there a shared thread?" Expert Rev Cardiovasc Ther **20**(2): 87-90.

Rare cases of myocarditis and pericarditis after COVID-19 mRNA vaccination have been recently reported in male adolescents and young adults. Acute myocarditis and pericarditis following COVID-19 mRNA vaccination in male adolescents and young adults may be connected with age-related lower levels of T-bet and PD-1 in predisposed individulas with T-bet polymorphisms by the release od autoreactive CD8+CTL. Upregulatiomn of T-Bet and PD-1 by estrogen might explai the higher incidence of men developing myocarditis or pericarditis in comparison to women.

Morz, M. (2022). "A Case Report: Multifocal Necrotizing Encephalitis and Myocarditis after BNT162b2 mRNA Vaccination against COVID-19." Vaccines (Basel) **10**(10).

The current report presents the case of a 76-year-old man with Parkinson's disease (PD) who died three weeks after receiving his third COVID-19 vaccination. The patient was first vaccinated in May 2021 with the ChAdOx1 nCov-19 vector vaccine, followed by two doses of the BNT162b2 mRNA vaccine in July and December 2021. The family of the deceased requested an autopsy due to ambiguous clinical signs before death. PD was confirmed by post-mortem examinations. Furthermore, signs of aspiration pneumonia and systemic arteriosclerosis were evident. However, histopathological analyses of the brain uncovered previously unsuspected findings, including acute vasculitis (predominantly lymphocytic) as well as multifocal necrotizing encephalitis of unknown etiology with pronounced inflammation including glial and lymphocytic reaction. In the heart, signs of chronic cardiomyopathy as well as mild acute lympho-histiocytic myocarditis and vasculitis were present. Although there was no history of COVID-19 for this patient, immunohistochemistry for SARS-CoV-2 antigens (spike and nucleocapsid proteins) was performed. Surprisingly, only spike protein but no nucleocapsid protein could be detected within the foci of inflammation in both the brain and the heart, particularly in the endothelial cells of small blood vessels. Since no nucleocapsid protein could be detected, the presence of spike protein must be ascribed to vaccination rather than to viral infection. The findings corroborate previous reports of encephalitis and myocarditis caused by gene-based COVID-19 vaccines.

Munro, C. (2021). "Covid-19: Boys are more at risk of myocarditis after vaccination than of hospital admission for covid." BMJ **374**: n2251.

Murakami, Y., et al. (2022). "Myocarditis Following a COVID-19 Messenger RNA Vaccination: A Japanese Case Series." Intern Med **61**(4): 501-505.

COVID-19 vaccine-related myocarditis has been reported worldwide. We herein report two Japanese cases with suspected vaccine-related myocarditis. A 27-year-old man was admitted with chest pain 4 days after the second vaccination. An electrocardiogram (ECG) did not reveal any significant abnormalities. The second patient, a 37-year-old man, was admitted with chest pain 9 days after the first vaccination. His ECG exhibited ST-elevation in multiple leads. In both cases, cardiac magnetic resonance imaging findings were consistent with myocarditis. They recovered with symptomatic relief within a few days. These cases suggest that the benefit of COVID-19 vaccination exceeds the risk of vaccine-related myocarditis.

Murase, H., et al. (2022). "Case report: Five patients with myocarditis after mRNA COVID-19 vaccination." Front Pediatr **10**: 977476.

OBJECTIVES: To describe clinical features and laboratory data of myocarditis after the mRNA COVID-19 vaccine in children. METHODS: We reviewed patients younger than 18 years of age, who visited our hospital because of myocarditis within 1 week after BNT162b2 from June 2021 to January 2022. RESULTS: We identified five male patients aged 12-16 years who presented to our hospital with myocarditis within 2-3 days after the second dose of BNT162b2 COVID-19 vaccination between June 2021 and January 2022. All patients experienced chest pain, and fever, pain other than chest pain, and shortness of breath were present in two, three, and two patients, respectively. The serum troponin I level was increased in all patients except one, and electrocardiogram (ECG) showed ST elevation in all patients. Echocardiography revealed pericardial effusion and decreased ejection fraction in three and one patients, respectively. In accordance with the Japanese guidelines for myocarditis, the patients were treated with colchicine and aspirin. Chest pain improved within a few days with no hemodynamic instability. The patients were discharged with no sequelae. CONCLUSIONS: ST changes on ECG and elevated troponin I levels may aid the diagnosis of myocarditis after mRNA COVID-19 vaccination.

Mustafa Alhussein, M., et al. (2022). "Natural History of Myocardial Injury After COVID-19 Vaccine-Associated Myocarditis." Can J Cardiol **38**(11): 1676-1683.

BACKGROUND: Acute myocarditis is a rare complication of mRNA-based COVID-19 vaccination. Little is known about the natural history of this complication. METHODS: Baseline and convalescent (>/= 90 days) cardiac magnetic resonance (CMR) imaging assessments were performed in 20 consecutive patients meeting Updated Lake Louise Criteria for acute myocarditis within 10 days of mRNA-based vaccination. CMR-based changes in left ventricular volumes, mass, ejection fraction (LVEF), markers of tissue inflammation (native T1 and T2 mapping), and fibrosis (late gadolinium enhancement [LGE] and extracellular volume [ECV]) were assessed between baseline and convalescence. Cardiac symptoms and clinical outcomes were captured. RESULTS: Median age was 23.1 years (range 18-39 years), and 17 (85%) were male. Convalescent evaluations were performed at a median (IQR) 3.7 (3.3-6.2) months. The LVEF showed a mean 3% absolute improvement, accompanied by a 7% reduction in LV end-diastolic volume and 5% reduction in LV mass (all $P < 0.015$). Global LGE burden was reduced by 66% ($P < 0.001$). Absolute reductions in global T2, native T1, and ECV of 2.1 ms, 58 ms, and 2.9%, repectively, were documented (all P </= 0.001). Of 5 patients demonstrating LVEF </= 50% at baseline, all recovered to above this threshold in convalescence. A total of 18 (90%) patients showed persistence of abnormal LGE although mean fibrosis burden was < 5% of LV mass in 85% of cases. No patient experienced major clinical outcomes. CONCLUSIONS: COVID-19 mRNA vaccine-associated myocarditis showed rapid improvements in CMR-based markers of edema, contractile function, and global LGE burden beyond 3 months of recovery in this young patient cohort. However,

regional fibrosis following edema resolution was commonly observed, justifying need for ongoing surveillance.

Muthukumar, A., et al. (2021). "In-Depth Evaluation of a Case of Presumed Myocarditis After the Second Dose of COVID-19 mRNA Vaccine." Circulation **144**(6): 487-498.
Supplemental Digital Content is available in the text.

Nagasaka, T., et al. (2022). "Acute myocarditis associated with COVID-19 vaccination: A case report." J Cardiol Cases **25**(5): 285-288.
Recently, new vaccine platforms-including mRNA vaccines for coronavirus disease 2019 (COVID-19) have been given emergency use authorization in Japan. Here, we present a rare case of myocarditis following a COVID-19 vaccine. In this case, myocarditis was confirmed by cardiac magnetic resonance imaging, endomyocardial biopsy, and troponin levels. The degree of myocardial inflammation in the endomyocardial biopsy samples was mild and the patient's clinical course was not severe. Although the pathology of myocarditis in this case was mild, further investigation would be needed. <Learning objective: Vaccination for coronavirus disease 2019 is advancing worldwide, but post-vaccination myocarditis is getting attention as a rare side effect. Although the myocarditis in this case was mild, the pathogenesis of the disease is unclear and needs to be thoroughly investigated in the vaccination.>.

Naghashzadeh, F., et al. (2022). "Myocarditis following rAd26 and rAd5 vector-based COVID-19 vaccine: case report." ESC Heart Fail **9**(2): 1483-1486.
SARS-CoV-2 vaccines provide a safe solution with a major impact on reducing the spread of the virus and mild side effects. Research has shown rare cases of myocarditis after mRNA vaccines. This study presents a 29-year-old male with chest pain after 48 h of receiving rAd26 and rAd5 vector-based COVID-19 vaccine (Sputnik V vaccine). The electrocardiogram revealed ST-segment elevation. Also, the laboratory screening was remarkable for elevated cardiac Troponin-I level, and leukocytosis; and echocardiography depicted severe left ventricular systolic dysfunction. Overall, endomyocardial biopsy proved lymphocytic myocarditis such that the patient was successfully treated with immunosuppressive and guideline-directed medical treatment.

Nassar, M., et al. (2021). "Corrigendum to "COVID-19 vaccine-induced myocarditis case report with literature review" [Diabetes & Metabolic Syndrome: Clinical Research & Reviews Volume 15, Issue 5, September-October 2021, 102205]." Diabetes Metab Syndr **15**(5): 102277.

Nassar, M., et al. (2021). "COVID-19 vaccine-induced myocarditis: Case report with literature review." Diabetes Metab Syndr **15**(5): 102205.

Navar, A. M., et al. (2021). "Temporal Associations Between Immunization With the COVID-19 mRNA Vaccines and Myocarditis: The Vaccine Safety Surveillance System Is Working." JAMA Cardiol **6**(10): 1117-1118.

Naveed, Z., et al. (2023). "A population-based assessment of myocarditis after messenger RNA COVID-19 booster vaccination among adult recipients." Int J Infect Dis **131**: 75-78.

OBJECTIVES: We aimed to estimate the rate of myocarditis after the messenger RNA (mRNA) COVID-19 booster vaccination by vaccine type, age, and sex. METHODS: We used data from the British Columbia COVID-19 Cohort, a population-based cohort surveillance platform. The exposure was a booster dose of an mRNA vaccine. The outcome was diagnosis of myocarditis during hospitalization or an emergency department visit within 7-21 days of booster vaccination. RESULTS: The overall rate of myocarditis was lower for the booster dose (6.41, 95% confidence interval [CI]: 3.50-10.75) than the second dose (17.97, 95% CI: 13.78-23.04); (Rate ratio(booster vs dose-2) = 0.34, 95% CI: 0.17-0.61). This difference was more apparent for the mRNA-1273 vaccine type. After the second dose, the myocarditis rate in males was significantly lower for BNT162b2 than mRNA-1273 overall and among those aged 18-39 years. In contrast, after the booster dose, no significant differences between myocarditis and vaccine type was observed overall or within the specific age groups among males or females. CONCLUSION: Myocarditis after mRNA COVID-19 vaccines is a rare event. A lower absolute risk of myocarditis was observed after a booster dose of mRNA vaccine than the primary series second dose.

Nevet, A. (2021). "Acute myocarditis associated with anti-COVID-19 vaccination." Clin Exp Vaccine Res **10**(2): 196-197.

Novel anti-coronavirus disease 2019 mRNA vaccines are rapidly implemented worldwide. Therefore, attention should be given to potentially life-threatening adverse reactions. We report on three young male patients, who developed acute myocarditis 2 days after receiving the second dose of the BNT162b2 vaccine. Primary acute myocarditis was not previously reported in association with vaccines that do not include adjuvants. A high index of suspicion should be maintained in order to diagnose and treat patients who develop auto-inflammatory vaccine-related complications in a timely manner. Further research is required in order to explore the significance of this phenomenon and its underlying molecular mechanism.

Nguyen, T. D., et al. (2021). "Acute myocarditis after COVID-19 vaccination with mRNA-1273 in a patient with former SARS-CoV-2 infection." ESC Heart Fail **8**(6): 4710-4714.

We describe a case of a 20-year-old healthy man developing chest pain and classical symptoms of vaccine reactogenicity 12 h after receiving the first dose of mRNA-1273 (Moderna). Cardiac troponin T was increased, and subepicardial inflammation and focal contractile dysfunction were detected by cardiac magnetic resonance imaging and echocardiography. We confirmed the diagnosis of acute myocarditis by endomyocardial biopsy demonstrating significant infiltration of monocytes and T lymphocytes. Although we detected IgG against nucleocapsid protein of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) indicating prior infection, the patient repeatedly tested negative for SARS-CoV-2 and had been asymptomatic for several months. Furthermore, viral genome analysis of endomyocardial biopsy samples was negative for SARS-CoV-2 and other potential cardiotropic viruses. These findings and the strong temporal relation

between the vaccination and the symptom onset imply a potential side effect of mRNA-1273.

Nishibayashi, H., et al. (2022). "Myocarditis in 13-Year-Old Monochorionic Diamniotic Twins After COVID-19 Vaccination." J Clin Immunol **42**(7): 1351-1353.

Nunn, S., et al. (2022). "Case Report: Myocarditis After COVID-19 Vaccination - Case Series and Literature Review." Front Med (Lausanne) **9**: 836620.

BACKGROUND: The ongoing COVID-19 pandemic demands a series of measures and, above all, the vaccination of a substantial proportion of the population. Acute myocarditis is a rare complication of the widely used mRNA-based vaccines. CASE PRESENTATION: We present a case series of four patients (three men and one woman, 16 to 47 years old) with acute pericarditis/myocarditis 3 to 17 days after mRNA vaccination. They presented with chest pain, fever, and flu-like symptoms. Diagnosis was made based on the synopsis of clinical presentation, elevated levels of troponin T and NT-proBNP, impaired systolic function on echocardiography, and findings in non-invasive tissue characterization by cardiovascular magnetic resonance imaging. Two patients also underwent endomyocardial biopsies. As none of the patients showed signs of cardiogenic shock, they were discharged from ward care only a few days after their initial presentations. CONCLUSIONS: Our data are consistent with other case reports of myocarditis early after mRNA vaccination and demonstrate the need for multimodal diagnostics. In view of its rarity and mild course, the risk-benefit ratio of vaccination remains positive compared to potential SARS-CoV-2 infection.

Ohtani, K., et al. (2022). "Acute necrotizing eosinophilic myocarditis after COVID-19 vaccination." Eur Heart J **43**(27): 2640.

Ojha, V., et al. (2022). "Advanced cardiac MRI to detect myocarditis after COVID-19 vaccination in a 22-year-old man." Acta Cardiol **77**(9): 855-856.

Ojo, A., et al. (2023). "Recurrent ventricular tachycardia in a patient with COVID-19 vaccine-associated myocarditis: a case report." Ann Transl Med **11**(6): 267.

BACKGROUND: The development of coronavirus disease 2019 (COVID-19) vaccine-associated myocarditis has been reported. Most of the reported cases are mild, with quick clinical recovery and excellent short-term outcomes. Cases of COVID-19 vaccine-associated myocarditis presenting with sustained ventricular tachycardia (VT) are rare. CASE DESCRIPTION: A 46-year-old male patient with no prior cardiac history presented following two episodes of syncope. Two days earlier, he had received his second dose of COVID-19 mRNA vaccine (Pfizer)-first dose was administered three weeks earlier. He had an episode of VT while in the emergency room. His cardiac magnetic resonance imaging (MRI) findings were consistent with myocarditis. He was eventually diagnosed with COVID-19 vaccine-associated myocarditis after all other work up were unremarkable [echocardiogram, coronary angiogram, diagnostic electrophysiology study and later (18)F-fluorodeoxyglucose (FDG) metabolism cardiac sarcoid positron emission

tomography (PET) study]. An implantable cardiac monitor was implanted to monitor for recurrence of VT. Seven months after initial presentation, he had recurrent VT and he underwent implantation of an implantable cardioverter defibrillator (ICD). He has received appropriate ICD therapies on account of recurrent VT and he is currently maintained on an antiarrhythmic medication. CONCLUSIONS: Excellent short-term outcomes have been reported in patients with COVID-19 vaccine associated myocarditis. Our case shows that long-term outcomes may not be benign in everyone, particularly in those who develop myocardial scar.

Oka, A., et al. (2022). "Fulminant myocarditis after the second dose of COVID-19 mRNA vaccination." Clin Case Rep **10**(2): e05378.

Myocarditis is an adverse event associated with coronavirus disease 2019 (COVID-19) mRNA vaccination. A 50-year-old man presented with dyspnea and resting chest pain after receiving the second dose of the COVID-19 mRNA vaccine and developed cardiogenic shock. Fulminant myocarditis was diagnosed by endomyocardial biopsy and treated with intravenous corticosteroids.

Onderko, L., et al. (2021). "Myocarditis in the Setting of Recent COVID-19 Vaccination." Case Rep Cardiol **2021**: 6806500.

We report three patients who presented with chest pain after receiving either the BNT162b2 Pfizer/BioNTech or mRNA-1273 Moderna/NIH vaccine. Clinical presentation, biomarker, and cardiac MRI supported myocarditis. It is imperative that potential side effects of COVID-19 vaccine are reported to improve our knowledge about COVID-19 and mRNA vaccines.

Onishi, N., et al. (2023). "Fulminant myocarditis with complete atrioventricular block after mRNA COVID-19 vaccination: A case report." J Cardiol Cases **27**(5): 229-232.

A 71-year-old man was transferred urgently to our hospital after collapsing near his home post the first shot of the BNT162b2 coronavirus disease 2019 vaccine (Pfizer-BioNTech, Comirnaty(R)). Immediately after arrival at our hospital, cardiac arrest due to complete atrioventricular block with no ventricular escaped beats was observed on electrocardiogram. Echocardiography showed preserved left ventricular ejection fraction, however, diffuse severe hypokinesia was revealed after 3 weeks, and he died 3 months after admission because of worsening heart failure. An autopsy examination revealed eosinophilic myocarditis or hypersensitivity myocarditis with extensive fibrosis and widespread myocardial dropout throughout the heart. LEARNING OBJECTIVE: 1. Severe myocarditis occurs extremely rarely after mRNA coronavirus disease 2019 (COVID-19) vaccination. 2. Myocarditis after mRNA COVID-19 vaccination might cause complete atrioventricular block, followed by a course of decreased left ventricular ejection fraction. 3. Histologically, severe myocarditis after mRNA COVID-19 vaccination seems to present as fulminant necrotizing eosinophilic myocarditis or hypersensitivity myocarditis.

Oster, M. E., D. K. Shay and T. T. Shimabukuro (2022). "Myocarditis Cases After mRNA-Based COVID-19 Vaccination in the US-Reply." JAMA **327**(20): 2020-2021.

Oster, M. E., et al. (2022). "Myocarditis Cases Reported After mRNA-Based COVID-19 Vaccination in the US From December 2020 to August 2021." JAMA **327**(4): 331-340.

IMPORTANCE: Vaccination against COVID-19 provides clear public health benefits, but vaccination also carries potential risks. The risks and outcomes of myocarditis after COVID-19 vaccination are unclear. OBJECTIVE: To describe reports of myocarditis and the reporting rates after mRNA-based COVID-19 vaccination in the US. DESIGN, SETTING, AND PARTICIPANTS: Descriptive study of reports of myocarditis to the Vaccine Adverse Event Reporting System (VAERS) that occurred after mRNA-based COVID-19 vaccine administration between December 2020 and August 2021 in 192 405 448 individuals older than 12 years of age in the US; data were processed by VAERS as of September 30, 2021. EXPOSURES: Vaccination with BNT162b2 (Pfizer-BioNTech) or mRNA-1273 (Moderna). MAIN OUTCOMES AND MEASURES: Reports of myocarditis to VAERS were adjudicated and summarized for all age groups. Crude reporting rates were calculated across age and sex strata. Expected rates of myocarditis by age and sex were calculated using 2017-2019 claims data. For persons younger than 30 years of age, medical record reviews and clinician interviews were conducted to describe clinical presentation, diagnostic test results, treatment, and early outcomes. RESULTS: Among 192 405 448 persons receiving a total of 354 100 845 mRNA-based COVID-19 vaccines during the study period, there were 1991 reports of myocarditis to VAERS and 1626 of these reports met the case definition of myocarditis. Of those with myocarditis, the median age was 21 years (IQR, 16-31 years) and the median time to symptom onset was 2 days (IQR, 1-3 days). Males comprised 82% of the myocarditis cases for whom sex was reported. The crude reporting rates for cases of myocarditis within 7 days after COVID-19 vaccination exceeded the expected rates of myocarditis across multiple age and sex strata. The rates of myocarditis were highest after the second vaccination dose in adolescent males aged 12 to 15 years (70.7 per million doses of the BNT162b2 vaccine), in adolescent males aged 16 to 17 years (105.9 per million doses of the BNT162b2 vaccine), and in young men aged 18 to 24 years (52.4 and 56.3 per million doses of the BNT162b2 vaccine and the mRNA-1273 vaccine, respectively). There were 826 cases of myocarditis among those younger than 30 years of age who had detailed clinical information available; of these cases, 792 of 809 (98%) had elevated troponin levels, 569 of 794 (72%) had abnormal electrocardiogram results, and 223 of 312 (72%) had abnormal cardiac magnetic resonance imaging results. Approximately 96% of persons (784/813) were hospitalized and 87% (577/661) of these had resolution of presenting symptoms by hospital discharge. The most common treatment was nonsteroidal anti-inflammatory drugs (589/676; 87%). CONCLUSIONS AND RELEVANCE: Based on passive surveillance reporting in the US, the risk of myocarditis after receiving mRNA-based COVID-19 vaccines was increased across multiple age and sex strata and was highest after the second vaccination dose in adolescent males and young men. This risk should be considered in the context of the benefits of COVID-19 vaccination.

Otsuka, K., et al. (2022). "A case of BNT162b2 COVID-19 vaccine-associated fulminant myocarditis in a very elderly woman." Clin Case Rep **10**(9): e6161.

Coronavirus disease 2019 (COVID-19) vaccination is reportedly safe and effective. The histologic features of post-COVID-19 vaccination myocarditis are unknown. We present a case of a 77-year-old Japanese woman diagnosed with eosinophilic myocarditis using endomyocardial biopsy, 7 days after the second dose of BNT162b2 COVID-19 vaccine. Steroid pulse therapy was effective.

Ozdemir, O., et al. (2023). "Myocarditis development after COVID-19 vaccination in an immunodeficient case." Immunol Lett **260**: 22-23.

Paredes-Vazquez, J. G., et al. (2023). "Soluble factors in COVID-19 mRNA vaccine-induced myocarditis causes cardiomyoblast hypertrophy and cell injury: a case report." Virol J **20**(1): 203.

BACKGROUND: Inflammation affecting the heart and surrounding tissues is a clinical condition recently reported following COVID-19 mRNA vaccination. Assessing trends of these events related to immunization will improve vaccine safety surveillance and best practices for forthcoming vaccine campaigns. However, the causality is unknown, and the mechanisms associated with cardiac myocarditis are not understood. CASE PRESENTATION: After the first dose, we reported an mRNA vaccine-induced perimyocarditis in a young patient with a history of recurrent myocardial inflammation episodes and progressive loss of cardiac performance. We tested this possible inflammatory cytokine-mediated cardiotoxicity after vaccination in the acute phase (ten days), and we found a significant elevation of MCP-1, IL-18, and IL-8 inflammatory mediators. Still, these cytokines decreased considerably at the recovery phase (42 days later). We used the cardiomyoblasts cell line to test the effect of serum on cell viability, observing that serum from the acute phase reduced the cell viability to 75%. We did not detect this toxicity in cells when we tested serum from the patient in the recovery phase. We also tested serum-induced hypertrophy, a phenomenon in myocarditis and heart failure. We found that acute phase-serum has hypertrophy effects, increasing 25% of the treated cardiac cells' surface and significantly increasing B-type natriuretic peptide. However, we did not observe the hypertrophic effect in the recovery phase or sera from healthy controls. CONCLUSION: Our results opened the possibility of the inflammatory cytokines or serum soluble mediators as key factors for vaccine-associated myocarditis. In this regard, identifying anti-inflammatory molecules that reduce inflammatory cytokines could help avoid vaccine-induced myocardial inflammation.

Park, D. Y., et al. (2022). "Myocarditis after COVID-19 mRNA vaccination: A systematic review of case reports and case series." Clin Cardiol **45**(7): 691-700.

BACKGROUND: The coronavirus disease of 2019 (COVID-19) is a global pandemic with over 266 million cases and 5 million deaths worldwide. Anti-COVID-19 vaccinations have had exceptional success in subduing the incidence, prevalence, and disease severity of COVID-19, but rare cases of myocarditis have been reported after COVID-19 vaccinations. HYPOTHESIS: Myocarditis occurring after COVID-19 mRNA vaccinations have distinguishable clinical characteristics. They usually have a favorable prognosis.

METHODS: We performed a systematic literature search on PUBMED and MEDLINE database from inception to December 5, 2021. Studies were analyzed based on predetermined eligibility criteria. RESULTS: A total of 57 studies containing 275 cases of COVID-19 vaccine-associated myocarditis were catalogued. Mean age was 26.7 years and male to female ratio was 14:1. For 86.9% of patients, myocarditis occurred after the second dose. Average time to onset and length of hospitalization were 3.7 and 3.9 days, respectively. Prognosis was largely benign, but there was a 1.1% reported mortality. Chest pain (95.2%), elevation of troponin (100%), and ST elevation on electrocardiography (68.5%) were common. Nonsteroidal anti-inflammatory drugs (81.4%) were the most used medication, followed by colchicine (33.1%). CONCLUSIONS: Patients with COVID-19 vaccine-associated myocarditis are usually younger males presenting with chest pain 3-4 days after receiving their second dose of COVID vaccine. Diagnosis is made by exclusion of all other etiologies. Given significant population benefit from COVID-19 vaccination, physicians should continue to encourage vaccination while remaining vigilant of the very rare occurrence of myocarditis following COVID-19 vaccination.

Park, H., et al. (2021). "Epidemiology and Clinical Features of Myocarditis/Pericarditis before the Introduction of mRNA COVID-19 Vaccine in Korean Children: a Multicenter Study." J Korean Med Sci **36**(32): e232.

BACKGROUND: Korean health authority plans to vaccinate adolescents against coronavirus disease 2019 (COVID-19) starting high school seniors during the summer vacation of 2021. However, the myocarditis/pericarditis following COVID-19 vaccine has been reported recently in adolescents and young adults. This study was performed to answer the urgent questions about the basic epidemiology and clinical course of myocarditis/pericarditis in hospitalized patients prior to the introduction of COVID-19 vaccines in pediatric population. METHODS: A retrospective medical record analysis including frequency, clinical characteristics, etiology and outcome of myocarditis/pericarditis was conducted in 17 years and younger patients who were hospitalized in two referral hospitals in Korea between 2010 and 2019. RESULTS: Total 142 patients with myocarditis (n = 119) and/or pericarditis (n = 23) were identified. Median age was 5.4 years (interquartile range, 0.6-12.9 years; range, 11 days-17.8 years), and male was 61%. In adolescents aged 12-17 years, the male to female ratio was 3.2. Myocarditis/pericarditis occurred 0.70 per 1,000 in-patients during the study period: 0.96 (< 1 year), 0.50 (1-5 years), 0.67 (6-11 years) and 1.22 (12-17 years) per 1,000 in-patients, respectively. There was an increasing tendency for the annual frequency from 0.34 in 2010 to 1.25 per 1,000 in-patients in 2019 (P = 0.021). Among the 56 (40%) proven pathogens at admission, Mycoplasma pneumoniae (n = 11, 8%) and enterovirus (n = 10, 7%) were most common. Of the 142 patients, 99 (70%) required pediatric intensive care unit care and 10 (7%) received heart transplantation. In addition, 61 patients (61/131, 47%) without heart medication at admission needed heart medication when they were discharged. Eleven (7.7%) patients died, of which five patients were previously healthy. The median age of deceased patients was lower than the survival group (0.8 vs. 6.3 years, P = 0.014). CONCLUSION: The frequency of

myocarditis/pericarditis was highest among male adolescent in-patients; however, the outcome was favorable in this group without any mortality.

Park, S. and J. You (2022). "A Case of Myocarditis Presenting With a Hyperechoic Nodule After the First Dose of COVID-19 mRNA Vaccine." J Korean Med Sci **37**(16): e131.

Myocarditis and/or pericarditis have been reported as adverse events following coronavirus disease 2019 (COVID-19) messenger RNA vaccination, with most cases occurring within 1 week after the second dose. We report a rare case of myocarditis after the first dose of the BNT162b2 (Pfizer-BioNTech) COVID-19 vaccine in a 17-year-old boy. Here, we describe the laboratory, electrocardiographic, and imaging findings of myocarditis.

Parmar, K., et al. (2022). "Myocarditis following COVID-19 mRNA vaccination." Proc (Bayl Univ Med Cent) **35**(2): 209-213.

Messenger RNA vaccines are the main COVID-19 vaccines authorized for use in the United States. Side effects are typically minor and transient. We report a case series of four subjects with an acute myocarditis-like illness following mRNA COVID-19 vaccination who were hospitalized at our hospital in Lubbock, Texas. Three patients were young men who presented with acute chest pain after the second dose of the mRNA-1273 vaccine. Another patient was a 53-year-old white woman who presented with acute left arm pain 3 days after the first dose of the mRNA-1273 vaccine. She was later found to have acute decompensated heart failure, and endomyocardial biopsy revealed eosinophilic injury-mediated myocarditis.

Pasha, M. A., S. Isaac and Z. Khan (2022). "Recurrent Myocarditis Following COVID-19 Infection and the mRNA Vaccine." Cureus **14**(7): e26650.

COVID-19 infection has cardiovascular manifestations such as acute myocarditis, arrhythmia, ischemic cardiomyopathy, heart failure, pericardial effusion, cardiac tamponade, and thromboembolism. The COVID-19 mRNA vaccines BNT162b2 (Pfizer-BioNTech), mRNA-1273 (Moderna), and viral vector vaccine Ad26.COV2.S (Johnson & Johnson - Janssen) were initially approved for emergency authorized use by the US-FDA. Cases of myocarditis were reported primarily in adolescents and young adults after administration of COVID-19 mRNA vaccines, with the subsequent emergence of cases of myocarditis after administration of viral vector vaccine Ad26.COV2.S. A majority of these cases were observed after the second dose of the mRNA vaccine. This case report demonstrates the occurrence of symptomatic myocarditis in a patient during acute COVID-19 infection, followed by recurrence of symptoms after the first dose of mRNA COVID-19 vaccine and subsequent recurrence of cardiac MRI-proven myocarditis after the second dose of mRNA COVID-19 vaccine. This case stands out due to the occurrence of symptoms with COVID-19 infection and after vaccination, suggesting possible incomplete interval resolution of infection-related myocarditis.

Patel, H., et al. (2023). "Evaluation of Autoantibody Binding to Cardiac Tissue in Multisystem Inflammatory Syndrome in Children and COVID-19 Vaccination-Induced Myocarditis." JAMA Netw Open **6**(5): e2314291.

IMPORTANCE: Cardiac dysfunction and myocarditis have emerged as serious complications of multisystem inflammatory syndrome in children (MIS-C) and vaccines against SARS-CoV-2. Understanding the role of autoantibodies in these conditions is essential for guiding MIS-C management and vaccination strategies in children. OBJECTIVE: To investigate the presence of anticardiac autoantibodies in MIS-C or COVID-19 vaccine-induced myocarditis. DESIGN, SETTING, AND PARTICIPANTS: This diagnostic study included children with acute MIS-C or acute vaccine myocarditis, adults with myocarditis or inflammatory cardiomyopathy, healthy children prior to the COVID-19 pandemic, and healthy COVID-19 vaccinated adults. Participants were recruited into research studies in the US, United Kingdom, and Austria starting January 2021. Immunoglobulin G (IgG), IgM, and IgA anticardiac autoantibodies were identified with immunofluorescence staining of left ventricular myocardial tissue from 2 human donors treated with sera from patients and controls. Secondary antibodies were fluorescein isothiocyanate-conjugated antihuman IgG, IgM, and IgA. Images were taken for detection of specific IgG, IgM, and IgA deposits and measurement of fluorescein isothiocyanate fluorescence intensity. Data were analyzed through March 10, 2023. MAIN OUTCOMES AND MEASURES: IgG, IgM and IgA antibody binding to cardiac tissue. RESULTS: By cohort, there were a total of 10 children with MIS-C (median [IQR] age, 10 [13-14] years; 6 male), 10 with vaccine myocarditis (median age, 15 [14-16] years; 10 male), 8 adults with myocarditis or inflammatory cardiomyopathy (median age, 55 [46-63] years; 6 male), 10 healthy pediatric controls (median age, 8 [13-14] years; 5 male), and 10 healthy vaccinated adults (all older than 21 years, 5 male). No antibody binding above background was observed in human cardiac tissue treated with sera from pediatric patients with MIS-C or vaccine myocarditis. One of the 8 adult patients with myocarditis or cardiomyopathy had positive IgG staining with raised fluorescence intensity (median [IQR] intensity, 11 060 [10 223-11 858] AU). There were no significant differences in median fluorescence intensity in all other patient cohorts compared with controls for IgG (MIS-C, 6033 [5834-6756] AU; vaccine myocarditis, 6392 [5710-6836] AU; adult myocarditis or inflammatory cardiomyopathy, 5688 [5277-5990] AU; healthy pediatric controls, 6235 [5924-6708] AU; healthy vaccinated adults, 7000 [6423-7739] AU), IgM (MIS-C, 3354 [3110-4043] AU; vaccine myocarditis, 3843 [3288-4748] AU; healthy pediatric controls, 3436 [3313-4237] AU; healthy vaccinated adults, 3543 [2997-4607] AU) and IgA (MIS-C, 3559 [2788-4466] AU; vaccine myocarditis, 4389 [2393-4780] AU; healthy pediatric controls, 3436 [2425-4077] AU; healthy vaccinated adults, 4561 [3164-6309] AU). CONCLUSIONS AND RELEVANCE: This etiological diagnostic study found no evidence of antibodies from MIS-C and COVID-19 vaccine myocarditis serum binding cardiac tissue, suggesting that the cardiac pathology in both conditions is unlikely to be driven by direct anticardiac antibody-mediated mechanisms.

Patel, P., et al. (2022). "Symptomatic Myocarditis Post COVID-19 Vaccination." Cureus **14**(4): e24052.

There are few major adverse events after the coronavirus disease 2019 (COVID-19) vaccination. However, increasing cases of myocarditis and pericarditis are being reported to the Vaccine Adverse Event Reporting System (VAERS) in young people, primarily after the second dose of messenger RNA (mRNA) COVID-19 vaccines. We present a case series of myopericarditis post mRNA (Moderna) and myocarditis post vector-based (Johnson & Johnson) COVID-19 vaccines. We intend to highlight the importance of early diagnosis and treatment of vaccine-related myocarditis to reduce mortality and morbidity.

Patel, T., et al. (2022). "Comparison of Multisystem Inflammatory Syndrome in Children-Related Myocarditis, Classic Viral Myocarditis, and COVID-19 Vaccine-Related Myocarditis in Children." J Am Heart Assoc **11**(9): e024393.

Background Although rare, classic viral myocarditis in the pediatric population is a disease that carries significant morbidity and mortality. Since 2020, myocarditis has been a common component of multisystem inflammatory syndrome in children (MIS-C) following SARS-CoV-2 infection. In 2021, myocarditis related to mRNA COVID-19 vaccines was recognized as a rare adverse event. This study aims to compare classic, MIS-C, and COVID-19 vaccine-related myocarditis with regard to clinical presentation, course, and outcomes. Methods and Results In this retrospective cohort study, we compared patients aged <21 years hospitalized at our institution with classic viral myocarditis from 2015 to 2019, MIS-C myocarditis from March 2020 to February 2021, and vaccine-related myocarditis from May 2021 to June 2021. Of 201 total participants, 43 patients had classic myocarditis, 149 had MIS-C myocarditis, and 9 had vaccine-related myocarditis. At presentation, ejection fraction was lowest for those with classic myocarditis, with ejection fraction <55% present in 58% of patients. Nearly all patients with MIS-C myocarditis (n=139, 93%) and all patients with vaccine-related myocarditis (n=9, 100%) had normal left ventricular ejection fraction at the time of discharge compared with 70% (n=30) of the classic myocarditis group (P<0.001). At 3 months after discharge, of the 21 children discharged with depressed ejection fraction, none of the 10 children with MIS-C myocarditis had residual dysfunction compared with 3 of the 11 (27%) patients in the classic myocarditis group. Conclusions Compared with classic myocarditis, those with MIS-C myocarditis had better clinical outcomes, including rapid recovery of cardiac function. Patients with vaccine-related myocarditis had prompt resolution of symptoms and improvement of cardiac function.

Patel, Y. R., et al. (2021). "Cardiovascular magnetic resonance findings in young adult patients with acute myocarditis following mRNA COVID-19 vaccination: a case series." J Cardiovasc Magn Reson **23**(1): 101.

BACKGROUND: Messenger RNA (mRNA) coronavirus disease of 2019 (COVID-19) vaccine are known to cause minor side effects at the injection site and mild global systemic symptoms in first 24-48 h. Recently published case series have reported a possible association between acute myocarditis and COVID-19 vaccination, predominantly in young males. METHODS: We report a case series of 5 young male patients with cardiovascular magnetic resonance (CMR)-confirmed acute myocarditis within 72 h after receiving a dose of an mRNA-based COVID-19 vaccine. RESULTS: Our case series suggests

that myocarditis in this setting is characterized by myocardial edema and late gadolinium enhancement in the lateral wall of the left ventricular (LV) myocardium, reduced global LV longitudinal strain, and preserved LV ejection fraction. All patients in our series remained clinically stable during a relatively short inpatient hospital stay. CONCLUSIONS: In conjunction with other recently published case series and national vaccine safety surveillance data, this case series suggests a possible association between acute myocarditis and COVID-19 vaccination in young males and highlights a potential pattern in accompanying CMR abnormalities.

Patel, Y. R., et al. (2022). "Cardiac MRI Findings in Male Patients with Acute Myocarditis in the Presence or Absence of COVID-19 Vaccination." Radiol Cardiothorac Imaging **4**(3): e220008.
By comparing phenotypic clinical characteristics and cardiovascular magnetic resonance (CMR) findings in 14 patients with COVID-19 mRNA vaccine-associated myocarditis to 14 patients with acute myocarditis from other causes, we found that patients with COVID-19 vaccination- associated acute myocarditis have higher left ventricular ejection fraction, higher left ventricular global circumferential and radial strain, and less involvement of late gadolinium enhancement in the septal segments with less involvement of midmyocardial pattern of late gadolinium enhancement, compared to patients with acute myocarditis from other causes.

Patel, Y. R., et al. (2022). "Follow-Up Cardiovascular Magnetic Resonance Findings in Patients With COVID-19 Vaccination-Associated Acute Myocarditis." JACC Cardiovasc Imaging **15**(11): 2007-2010.

Patone, M., et al. (2022). "Risk of Myocarditis After Sequential Doses of COVID-19 Vaccine and SARS-CoV-2 Infection by Age and Sex." Circulation **146**(10): 743-754.
BACKGROUND: Myocarditis is more common after severe acute respiratory syndrome coronavirus 2 infection than after COVID-19 vaccination, but the risks in younger people and after sequential vaccine doses are less certain. METHODS: A self-controlled case series study of people ages 13 years or older vaccinated for COVID-19 in England between December 1, 2020, and December 15, 2021, evaluated the association between vaccination and myocarditis, stratified by age and sex. The incidence rate ratio and excess number of hospital admissions or deaths from myocarditis per million people were estimated for the 1 to 28 days after sequential doses of adenovirus (ChAdOx1) or mRNA-based (BNT162b2, mRNA-1273) vaccines, or after a positive SARS-CoV-2 test. RESULTS: In 42 842 345 people receiving at least 1 dose of vaccine, 21 242 629 received 3 doses, and 5 934 153 had SARS-CoV-2 infection before or after vaccination. Myocarditis occurred in 2861 (0.007%) people, with 617 events 1 to 28 days after vaccination. Risk of myocarditis was increased in the 1 to 28 days after a first dose of ChAdOx1 (incidence rate ratio, 1.33 [95% CI, 1.09-1.62]) and a first, second, and booster dose of BNT162b2 (1.52 [95% CI, 1.24-1.85]; 1.57 [95% CI, 1.28-1.92], and 1.72 [95% CI, 1.33-2.22], respectively) but was lower than the risks after a positive SARS-CoV-2 test before or after vaccination (11.14 [95% CI, 8.64-14.36] and 5.97 [95% CI, 4.54-7.87], respectively). The risk of myocarditis was higher 1 to 28 days after a second dose of mRNA-1273 (11.76

[95% CI, 7.25-19.08]) and persisted after a booster dose (2.64 [95% CI, 1.25-5.58]). Associations were stronger in men younger than 40 years for all vaccines. In men younger than 40 years old, the number of excess myocarditis events per million people was higher after a second dose of mRNA-1273 than after a positive SARS-CoV-2 test (97 [95% CI, 91-99] versus 16 [95% CI, 12-18]). In women younger than 40 years, the number of excess events per million was similar after a second dose of mRNA-1273 and a positive test (7 [95% CI, 1-9] versus 8 [95% CI, 6-8]). CONCLUSIONS: Overall, the risk of myocarditis is greater after SARS-CoV-2 infection than after COVID-19 vaccination and remains modest after sequential doses including a booster dose of BNT162b2 mRNA vaccine. However, the risk of myocarditis after vaccination is higher in younger men, particularly after a second dose of the mRNA-1273 vaccine.

Patone, M., et al. (2022). "Risks of myocarditis, pericarditis, and cardiac arrhythmias associated with COVID-19 vaccination or SARS-CoV-2 infection." Nat Med **28**(2): 410-422.

Although myocarditis and pericarditis were not observed as adverse events in coronavirus disease 2019 (COVID-19) vaccine trials, there have been numerous reports of suspected cases following vaccination in the general population. We undertook a self-controlled case series study of people aged 16 or older vaccinated for COVID-19 in England between 1 December 2020 and 24 August 2021 to investigate hospital admission or death from myocarditis, pericarditis and cardiac arrhythmias in the 1-28 days following adenovirus (ChAdOx1, n = 20,615,911) or messenger RNA-based (BNT162b2, n = 16,993,389; mRNA-1273, n = 1,006,191) vaccines or a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) positive test (n = 3,028,867). We found increased risks of myocarditis associated with the first dose of ChAdOx1 and BNT162b2 vaccines and the first and second doses of the mRNA-1273 vaccine over the 1-28 days postvaccination period, and after a SARS-CoV-2 positive test. We estimated an extra two (95% confidence interval (CI) 0, 3), one (95% CI 0, 2) and six (95% CI 2, 8) myocarditis events per 1 million people vaccinated with ChAdOx1, BNT162b2 and mRNA-1273, respectively, in the 28 days following a first dose and an extra ten (95% CI 7, 11) myocarditis events per 1 million vaccinated in the 28 days after a second dose of mRNA-1273. This compares with an extra 40 (95% CI 38, 41) myocarditis events per 1 million patients in the 28 days following a SARS-CoV-2 positive test. We also observed increased risks of pericarditis and cardiac arrhythmias following a positive SARS-CoV-2 test. Similar associations were not observed with any of the COVID-19 vaccines, apart from an increased risk of arrhythmia following a second dose of mRNA-1273. Subgroup analyses by age showed the increased risk of myocarditis associated with the two mRNA vaccines was present only in those younger than 40.

Pepe, S., A. T. Gregory and A. R. Denniss (2021). "Myocarditis, Pericarditis and Cardiomyopathy After COVID-19 Vaccination." Heart Lung Circ **30**(10): 1425-1429.

Piche-Renaud, P. P., S. K. Morris and K. A. Top (2023). "A narrative review of vaccine pharmacovigilance during mass vaccination campaigns: Focus on myocarditis and pericarditis after COVID-19 mRNA vaccination." Br J Clin Pharmacol **89**(3): 967-981.

Vaccines have had a tremendous impact on reducing the burden of infectious diseases; however, they have the potential to cause adverse events following immunization (AEFIs). Prelicensure clinical trials are limited in their ability to detect rare AEFIs that may occur in less than one per thousand individuals. While postmarketing surveillance systems have shown COVID-19 mRNA vaccines to be safe, they led to the identification of rare cases of myocarditis and pericarditis after COVID-19 vaccination that were not initially detected in clinical trials. In this narrative review, we highlight concepts of vaccine pharmacovigilance during mass vaccination campaigns and compare the approaches used in the context of myocarditis and pericarditis following COVID-19 vaccination to historical examples. We describe mechanisms of passive and active surveillance, their strengths and limitations, and how they interacted to identify and characterize the safety signal of myocarditis and pericarditis after COVID-19 mRNA vaccination. Articles were synthesized from a PubMed search using relevant keywords for articles published on vaccine surveillance systems and myocarditis and pericarditis after COVID-19 vaccination, as well as the authors' collections of relevant publications and grey literature reports. The global experience around the identification and monitoring of myocarditis and pericarditis after COVID-19 mRNA vaccination has provided important lessons for vaccine safety surveillance and highlighted its importance in maintaining public trust in mass vaccination programmes in a pandemic context.

Pieroni, M., et al. (2022). "COVID-19 mRNA vaccination in patients with previous myocarditis." Eur J Intern Med **104**: 116-117.

Pillay, J., et al. (2022). "Incidence, risk factors, natural history, and hypothesised mechanisms of myocarditis and pericarditis following covid-19 vaccination: living evidence syntheses and review." BMJ **378**: e069445.

OBJECTIVES: To synthesise evidence on incidence rates and risk factors for myocarditis and pericarditis after use of mRNA vaccination against covid-19, clinical presentation, short term and longer term outcomes of cases, and proposed mechanisms. DESIGN: Living evidence syntheses and review. DATA SOURCES: Medline, Embase, and the Cochrane Library were searched from 6 October 2020 to 10 January 2022; reference lists and grey literature (to 13 January 2021). One reviewer completed screening and another verified 50% of exclusions, using a machine learning program to prioritise records. A second reviewer verified all exclusions at full text, extracted data, and (for incidence and risk factors) risk of bias assessments using modified Joanna Briggs Institute tools. Team consensus determined certainty of evidence ratings for incidence and risk factors using GRADE (Grading of Recommendations, Assessment, Development and Evaluation). ELIGIBILITY CRITERIA FOR SELECTING STUDIES: Large (>10 000 participants) or population based or multisite observational studies and surveillance data (incidence and risk factors) reporting on confirmed myocarditis or pericarditis after covid-19 mRNA vaccination; case series (n>/=5, presentation, short term clinical course and longer term outcomes); opinions, letters, reviews, and primary studies focused on describing or supporting hypothesised mechanisms. RESULTS: 46 studies were included (14 on

incidence, seven on risk factors, 11 on characteristics and short term course, three on longer term outcomes, and 21 on mechanisms). Incidence of myocarditis after mRNA vaccines was highest in male adolescents and male young adults (age 12-17 years, range 50-139 cases per million (low certainty); 18-29 years, 28-147 per million (moderate certainty)). For girls and boys aged 5-11 years and women aged 18-29 years, incidence of myocarditis after vaccination with BNT162b2 (Pfizer/BioNTech) could be fewer than 20 cases per million (low certainty). Incidence after a third dose of an mRNA vaccine had very low certainty evidence. For individuals of 18-29 years, incidence of myocarditis is probably higher after vaccination with mRNA-1273 (Moderna) compared with Pfizer (moderate certainty). Among individuals aged 12-17, 18-29, or 18-39 years, incidence of myocarditis or pericarditis after dose two of an mRNA vaccine for covid-19 might be lower when administered >/=31 days compared with </=30 days after dose one (low certainty). Data specific to men aged 18-29 years indicated that the dosing interval might need to increase to >/=56 days to substantially drop myocarditis or pericarditis incidence. For clinical course and short term outcomes, only one small case series (n=8) was found for 5-11 year olds. In adolescents and adults, most (>90%) myocarditis cases involved men of a median 20-30 years of age and with symptom onset two to four days after a second dose (71-100%). Most people were admitted to hospital (>/=84%) for a short duration (two to four days). For pericarditis, data were limited but more variation than myocarditis has been reported in patient age, sex, onset timing, and rate of admission to hospital. Three case series with longer term (3 months; n=38) follow-up suggested persistent echocardiogram abnormalities, as well as ongoing symptoms or a need for drug treatments or restriction from activities in >50% of patients. Sixteen hypothesised mechanisms were described, with little direct supporting or refuting evidence. CONCLUSIONS: These findings indicate that adolescent and young adult men are at the highest risk of myocarditis after mRNA vaccination. Use of a Pfizer vaccine over a Moderna vaccine and waiting for more than 30 days between doses might be preferred for this population. Incidence of myocarditis in children aged 5-11 years is very rare but certainty was low. Data for clinical risk factors were very limited. A clinical course of mRNA related myocarditis appeared to be benign, although longer term follow-up data were limited. Prospective studies with appropriate testing (eg, biopsy and tissue morphology) will enhance understanding of mechanism.

Power, J. R., L. K. Keyt and E. D. Adler (2022). "Myocarditis following COVID-19 vaccination: incidence, mechanisms, and clinical considerations." Expert Rev Cardiovasc Ther **20**(4): 241-251.

INTRODUCTION: Vaccines have demonstrated protection against the morbidity and mortality of COVID-19, but concerns regarding the rare side effect of acute myocarditis have stymied immunization efforts. This review aims to describe the incidence and theorized mechanisms of COVID vaccine-associated myocarditis and review relevant principles for management of vaccine-associated myocarditis. AREAS COVERED: Epidemiologic studies of myocarditis after COVID vaccination are reviewed, which show an incidence of approximately 20-30 per million patients. The vast majority of these cases are seen with mRNA vaccines especially in male patients under 30 years of age. Mechanisms are largely theoretical, but molecular mimicry and dysregulated innate

immune reactions have been proposed. While studies suggest that this subtype of myocarditis is mild and self-limited, long-term evidence is lacking. Principles of myocarditis treatment and surveillance are outlined as they apply to COVID vaccine-associated myocarditis. EXPERT OPINION: COVID vaccine-associated myocarditis is rare but well described in certain at-risk groups. Better understanding of its pathogenesis is key to mitigating this complication and advancing vaccination efforts. Risk-benefit analyses demonstrate that individual- and population-level benefits of vaccination exceed the risks of this rare and mild form of myocarditis.

Puchalski, M., et al. (2022). "COVID-19-Vaccination-Induced Myocarditis in Teenagers: Case Series with Further Follow-Up." Int J Environ Res Public Health **19**(6).

Presently, the whole globe is struggling the tough challenge of the COVID-19 pandemic. Vaccination remains the most effective and safe COVID-19 weapon for adults and in the paediatric population. Aside from possible mild and moderate post-vaccination side effects, more severe side effects may occur. We retrospectively analysed a group of 5 teenagers aged from 15 to 17 years with obesity/overweight (BMI ranging from 24.8 to 30) who presented typical myocarditis symptoms following the first or second dose (3 and 2 patients, respectively) of the COVID-19 vaccine. In the whole study group, a significant increase in troponin serum concentration was observed (1674-37,279.6 ng/L) with a further quick reduction within 3-4 days. In all patients, ST segments elevation or depression with repolarisation time abnormalities in electrocardiography were noticed. Chest X-ray results were within normal limits. Echocardiography showed normal left ventricular diameter (47-56.2 mm) with ejection fraction between 61-72%. All patients were diagnosed with myocarditis based on cardiac magnetic resonance (CMR) imaging. During further hospitalisation, swift clinical improvement was notable. Follow-up in the whole study group was obtained after 106-134 days from initial CMR, revealing no myocarditis symptoms, proper troponin level, and no ECG or echocardiographic abnormalities. At the same time, persistent myocardium injury features were detected in the whole study group, including ongoing myocarditis. COVID-19-vaccine-induced myocarditis seems to be a mild disease with fast clinical recovery, but the complete resolution of the inflammatory process may last over 3 months. Further follow-up and investigation for assessing subsequent implications and long-term COVID-19-vaccine-induced myocarditis is required.

Reza, R. R., et al. (2023). "Takotsubo Cardiomyopathy Following COVID-19 Vaccine Booster Dose: A Case Report." Cureus **15**(8): e43295.

Although the efficacy and safety of the coronavirus disease 2019 (COVID-19) vaccine have been established, side effects and adverse events related to the COVID-19 vaccine are still coming out. COVID-19 vaccine also has the potential to cause acute and long-term cardiovascular effects, which include myocarditis, pericarditis, myopericarditis, myocardial infarction, pulmonary embolism, thrombotic thrombocytopenia, and pulmonary hemorrhage. Although uncommon, takotsubo cardiomyopathy (TCM) has also been reported following COVID-19 vaccination. We report a case of TCM following the COVID-19 vaccine in a 59-year-old female who presented with intermittent chest

pain and dyspnea following the COVID-19 vaccine booster dose. She had no identifiable triggers for TCM, no risk factors for cardiovascular disease, and normal cardiac enzyme levels, ruling out other causes of cardiac dysfunction. The diagnosis of TCM was supported by imaging findings and the absence of obstructive or thrombotic lesions on angiography.

Roh, D. E., et al. (2022). "Chest Pain and Suspected Myocarditis Related to COVID-19 Vaccination in Adolescents-A Case Series." Children (Basel) **9**(5).

As adolescents started to be vaccinated against coronavirus disease 2019 (COVID-19), suspected myocarditis and pericarditis related to the vaccine were reported in adolescents. According to the Korea Disease Control and Prevention Agency (KDCA), 2,796,270 persons aged 12-18 years were fully vaccinated by December 8. Among these, 9223 adverse events were reported (0.33%). We aimed to elucidate the clinical courses and short-term outcomes for adolescents aged 12-18 with cardiac symptoms and suspected myo- or peri-carditis related to COVID-19 vaccination in South Korea. Methods: We retrospectively collected data on patients </= 18 years of age who had suspected myocarditis or pericarditis within 30 days of COVID-19 vaccination, from July 2021 to January 2022. Results: We reported on 40 adolescents in different South Korean provinces at two centers. Twenty-six cases (65%) were male, and the median age was 16 years (range, 13-18; IQR 14.5-17). Twenty-five cases (62.5%) occurred at the first dose, and fifteen (37.5%) occurred after the second dose. Symptoms started at a median of 2 days (range 0-29 days; IQR 1-5 days) after vaccination. The patients were treated with nonsteroidal anti-inflammatory drugs (77.5%), intravenous immunoglobulin (2.5%), glucocorticoids (20%), colchicine (5%), or no therapy (15%). Five patients (12.5%) required intensive care unit admission; one patient needed inotropic/vasoactive support. No patients required extracorporeal membrane oxygenation or died. The median hospital stay was one day (range 0-8 days; IQR 0-2 days). Twenty-one patients (52.5%) had an abnormal electrocardiogram; among these, seven patients had an elevated ST segment, six patients (15%) had decreased ejection fraction (<55%), and LV function was completely recovered in all of them. Conclusions: Most cases of suspected myocarditis after COVID-19 vaccination in adolescents </= 18 years had mild symptoms and clinical courses, as well as a complete recovery. Further studies are needed to evaluate long-term outcomes.

Rose, J. and P. A. McCullough (2021). "A Report on Myocarditis Adverse Events in the U.S. Vaccine Adverse Events Reporting System (VAERS) in Association with COVID-19 Injectable Biological Products." Curr Probl Cardiol: 101011.

Following the global rollout and administration of the Pfizer Inc./BioNTech BNT162b2 and Moderna mRNA-1273 vaccines on December 17, 2020, in the United States, and of the Janssen Ad26.COV2.S product on April 1(st), 2021, in an unprecedented manner, hundreds of thousands of individuals have reported adverse events (AEs) using the Vaccine Adverse Events Reports System (VAERS). We used VAERS data to examine cardiac AEs, primarily myocarditis, reported following injection of the first or second dose of the COVID-19 injectable products. Myocarditis rates reported in VAERS were

significantly higher in youths between the ages of 13 to 23 (p<0.0001) with approximately 80% occurring in males. Within 8 weeks of the public offering of COVID-19 products to the 12-15-year-old age group, we found 19 times the expected number of myocarditis cases in the vaccination volunteers over background myocarditis rates for this age group. In addition, a 5-fold increase in myocarditis rate was observed subsequent to dose 2 as opposed to dose 1 in 15-year-old males. A total of 67% of all cases occurred with BNT162b2. Of the total myocarditis AE reports, 6 individuals died (1.1%) and of these, 2 were under 20 years of age - 1 was 13. These findings suggest a markedly higher risk for myocarditis subsequent to COVID-19 injectable product use than for other known vaccines, and this is well above known background rates for myocarditis. COVID-19 injectable products are novel and have a genetic, pathogenic mechanism of action causing uncontrolled expression of SARS-CoV-2 spike protein within human cells. When you combine this fact with the temporal relationship of AE occurrence and reporting, biological plausibility of cause and effect, and the fact that these data are internally and externally consistent with emerging sources of clinical data, it supports a conclusion that the COVID-19 biological products are deterministic for the myocarditis cases observed after injection.

Rosner, C. M., et al. (2022). "Patients With Myocarditis Associated With COVID-19 Vaccination." J Am Coll Cardiol **79**(13): 1317-1319.

Rosner, C. M., et al. (2021). "Myocarditis Temporally Associated With COVID-19 Vaccination." Circulation **144**(6): 502-505.

Supplemental Digital Content is available in the text.

Saadi, S. M., A. A. Bossei and L. K. Alsulimani (2022). "Acute myocarditis after COVID-19 vaccination." Saudi Med J **43**(11): 1270-1275.

Heart muscle inflammations were reported following SARS-CoV-2 messenger ribonucleic acid (RNA) vaccination by the Disease Control Centers in America, and cases of these inflammations reported as adverse effects of this COVID-19 vaccine application increased 1000 times since April 2021. A male individual, 18-year-old received vaccination with mRNA-1273 vaccine, and after a while attended the Emergency Department at King Abdulaziz University Hospital, Jeddah, Saudi Arabia. Upon presentation, the patient complained of a history of chest pain, and he had a high troponin level along with new-onset electrocardiogram changes. During his stay in hospital the patient's blood circulation status remained stable, and no evidence of another infectious or immune cases was found. Although these vaccines are a must and very advantageous in fighting COVID-19 and their benefits are far beyond their risks, although it seems that there is a risk of myopericarditis cases. Under such conditions it is essential to rely on early diagnosis for control and deal with the possible cases of morbidity and mortality associated with these conditions.

Salah, H. M. and J. L. Mehta (2021). "COVID-19 Vaccine and Myocarditis." Am J Cardiol **157**: 146-148.

Samimisedeh, P., et al. (2022). "Cardiac MRI Findings in COVID-19 Vaccine-Related Myocarditis: A Pooled Analysis of 468 Patients." J Magn Reson Imaging **56**(4): 971-982.

Understanding the pattern and severity of myocarditis caused by the coronavirus disease 2019 (COVID-19) vaccine is imperative for improving the care of the patients, and cardiac evaluation by MRI plays a key role in this regard. Our systematic review and meta-analysis aimed to summarize cardiac MRI findings in COVID-19 vaccine-related myocarditis. We performed a comprehensive systematic review of literature in PubMed, Scopus, and Google Scholar databases using key terms covering COVID-19 vaccine, myocarditis, and cardiac MRI. Individual-level patient data (IPD) and aggregated-level data (AD) studies were pooled through a two-stage analysis method. For this purpose, all IPD were first gathered into a single data set and reduced to AD, and then this AD (from IPD studies) was pooled with existing AD (from the AD studies) using fixed/random effect models. I(2) was used to assess the degree of heterogeneity, and the prespecified level of statistical significance (P value for heterogeneity) was <0.1. Based on meta-analysis of 102 studies (n = 468 patients), 79% (95% confidence interval [CI]: 54%-97%) of patients fulfilled Lake Louise criteria (LLC) for diagnosis of myocarditis. Cardiac MRI abnormalities included elevated T2 in 72% (95% CI: 50%-90%), myocardial late gadolinium enhancement (LGE) in 93% (95% CI: 83%-99%; nearly all with a subepicardial and/or midwall pattern), impaired left ventricular ejection fraction (LVEF) (<50%) in 4% (95% CI: 1.0%-9.0%). Moreover, elevated T1 and extracellular volume fraction (ECV) (>30), reported only by some IPD studies, were detected in 74.5% (76/102) and 32% (16/50) of patients, respectively. In conclusion, our findings may suggest that over two-thirds of patients with clinically suspected myocarditis following COVID-19 vaccination meet the LLC. COVID-19 vaccine-associated myocarditis may show a similar pattern compared to other acute myocarditis entities. Notably, preserved LVEF is probably a common finding in these patients. EVIDENCE LEVEL: 4 TECHNICAL EFFICACY: Stage 3.

Sanada, Y., et al. (2022). "Overlapping Myocarditis and Postural Orthostatic Tachycardia Syndrome After COVID-19 Messenger RNA Vaccination: A Case Report." Cureus **14**(11): e31006.

The worldwide spread of the coronavirus disease 2019 (COVID-19) pandemic and the significant morbidity and mortality rate associated with it led to the rapid development of several COVID-19 vaccines. While serious side effects related to the vaccines are rare, various adverse events have been reported to occur after COVID-19 messenger RNA (mRNA) vaccination, including myocarditis, Guillain-Barre syndrome, and thrombosis. Postural orthostatic tachycardia syndrome (POTS) is a chronic cardiovascular dysautonomia among young and middle-aged individuals. Although the pathophysiology of POTS is thought to be heterogeneous, vaccine-induced immune-mediated autonomic dysfunction is hypothesized to be one cause of the syndrome. In this report, we present a case of myocarditis and POTS occurring in a 13-year-old male following COVID-19 mRNA vaccination. He presented with persistent severe fatigue and headache. The patient's symptoms improved after intravenous immunoglobulin for myocarditis, non-pharmacologic interventions, and multiple medications for POTS.

Sanchez Tijmes, F., et al. (2021). "Cardiac MRI Assessment of Nonischemic Myocardial Inflammation: State of the Art Review and Update on Myocarditis Associated with COVID-19 Vaccination." Radiol Cardiothorac Imaging **3**(6): e210252.

Myocarditis is a nonischemic inflammatory disease of the myocardium that can be triggered by a multitude of events, including viral infection and toxins. Recently, there has been heightened interest in myocarditis given its association with COVID-19 vaccination. Timely identification of myocarditis can affect patient management and prognosis. Therefore, it is crucial for radiologists and cardiac imagers to understand the role of cardiac imaging to establish a diagnosis and inform treatment decisions. Cardiac MRI is the most important noninvasive imaging modality for evaluation of myocarditis, with typical findings of focal or diffuse myocardial edema and myocardial damage, including presence of late gadolinium enhancement. There are currently limited data available to indicate that the pattern of myocardial injury following COVID-19 vaccination is similar to other causes of myocarditis, although the severity of disease may be relatively mild. A description of the role of imaging and typical imaging features will be reviewed here, with a focus on emerging data in the setting of myocarditis after COVID-19 vaccination. Keywords: MRI, Heart, Inflammation (c) RSNA, 2021.

Sanchez Tijmes, F., et al. (2022). "Imaging of Myocarditis Following mRNA COVID-19 Booster Vaccination." Radiol Cardiothorac Imaging **4**(2): e220019.

Keywords: Echocardiography, MR-Functional Imaging, MRI, Cardiac Supplemental material is available for this article.

Sandeep, N., M. P. Fairchok and K. Hasbani (2022). "Myocarditis After COVID-19 Vaccination in Pediatrics: A Proposed Pathway for Triage and Treatment." J Am Heart Assoc **11**(21): e026097.

Sano, M., et al. (2022). "Cardiac magnetic resonance findings in acute myocarditis after mRNA COVID-19 vaccination." J Cardiol Cases **26**(1): 17-20.

There is increasing evidence for myocarditis as a complication of the mRNA coronavirus disease 2019 (COVID-19) vaccination. We report the case of a 20-year-old previously healthy man who presented with fever and chest pain 2 days after the second dose of mRNA-1273 vaccine. Electrocardiogram and laboratory studies showed extensive ST-segment elevation accompanied by elevated cardiac biomarkers. Cardiac magnetic resonance (CMR) revealed late gadolinium enhancement (LGE) characteristics of myocarditis. The patient rapidly improved with conservative management and was discharged on hospital day 6. As an advantage over previous reports, we performed a 1-month follow-up CMR. It showed improvement in myocardial edema but persistence of LGE which may indicate irreversible fibrosis. CMR may be useful not only for diagnosis but also for prognostic evaluation of myocarditis after COVID-19 mRNA vaccination. <Learning objective: With the expansion of coronavirus disease 2019 (COVID-19) vaccine administration, the number of cases of myocarditis as a complication has been increasing. Cardiac magnetic resonance imaging can be useful for the diagnosis and follow-up of patients with myocarditis after mRNA COVID-19 vaccination. Persistent late gadolinium enhancement may indicate irreversible myocardial fibrosis, and it is also

associated with poor prognosis, similar to previously reported cases of other acute myocarditis.>.

Schirmacher, P., T. Longerich and C. Schwab (2023). "Letter to the Editors: "Autopsy-based histopathological characterization of myocarditis after anti-SARS-CoV-2-vaccination" by C. Schwab et al." Clin Res Cardiol: 1-2.

Schmitt, P., et al. (2021). "Acute Myocarditis after COVID-19 vaccination: A case report." Rev Med Interne **42**(11): 797-800.

INTRODUCTION: The etiology of myocarditis often remains undetermined. A large variety of infectious agents, systemic diseases, drugs, and toxins can cause the disease. We report the case of a 19-year-old man who developed myocarditis three days after Pfizer-BioNTech COVID-19 booster vaccination. CASE REPORT: A 19-year-old man, presenting with troponin-positive acute chest pain, was referred to our department. He had received the Pfizer-BioNTech COVID-19 vaccine three days prior to his admission. The diagnosis of acute myocarditis was confirmed by cardiovascular magnetic resonance imaging. Patient hemodynamic status remained stable during hospitalization. The left ventricular ejection fraction was preserved during hospital stay and at one-month follow-up. We found no evidence for another infectious or autoimmune etiology. CONCLUSION: Although imputability of the vaccine cannot be formally established on the basis of this case report, the findings raise the possibility of an association between mRNA COVID-19 vaccination and acute myocarditis.

Schwab, C., et al. (2023). "Autopsy-based histopathological characterization of myocarditis after anti-SARS-CoV-2-vaccination." Clin Res Cardiol **112**(3): 431-440.

Cases of myocarditis, diagnosed clinically by laboratory tests and imaging have been described in the context of mRNA-based anti-SARS-CoV-2 vaccination. Autopsy-based description of detailed histological features of vaccine-induced myocarditis is lacking. We describe the autopsy findings and common characteristics of myocarditis in untreated persons who received anti-SARS-CoV-2 vaccination. Standardized autopsies were performed on 25 persons who had died unexpectedly and within 20 days after anti-SARS-CoV-2 vaccination. In four patients who received a mRNA vaccination, we identified acute (epi-)myocarditis without detection of another significant disease or health constellation that may have caused an unexpected death. Histology showed patchy interstitial myocardial T-lymphocytic infiltration, predominantly of the CD4 positive subset, associated with mild myocyte damage. Overall, autopsy findings indicated death due to acute arrhythmogenic cardiac failure. Thus, myocarditis can be a potentially lethal complication following mRNA-based anti-SARS-CoV-2 vaccination. Our findings may aid in adequately diagnosing unclear cases after vaccination and in establishing a timely diagnosis in vivo, thus, providing the framework for adequate monitoring and early treatment of severe clinical cases.

Seneff, S., et al. (2022). "Innate immune suppression by SARS-CoV-2 mRNA vaccinations: The role of G-quadruplexes, exosomes, and MicroRNAs." Food Chem Toxicol **164**: 113008.

The mRNA SARS-CoV-2 vaccines were brought to market in response to the public health crises of Covid-19. The utilization of mRNA vaccines in the context of infectious disease has no precedent. The many alterations in the vaccine mRNA hide the mRNA from cellular defenses and promote a longer biological half-life and high production of spike protein. However, the immune response to the vaccine is very different from that to a SARS-CoV-2 infection. In this paper, we present evidence that vaccination induces a profound impairment in type I interferon signaling, which has diverse adverse consequences to human health. Immune cells that have taken up the vaccine nanoparticles release into circulation large numbers of exosomes containing spike protein along with critical microRNAs that induce a signaling response in recipient cells at distant sites. We also identify potential profound disturbances in regulatory control of protein synthesis and cancer surveillance. These disturbances potentially have a causal link to neurodegenerative disease, myocarditis, immune thrombocytopenia, Bell's palsy, liver disease, impaired adaptive immunity, impaired DNA damage response and tumorigenesis. We show evidence from the VAERS database supporting our hypothesis. We believe a comprehensive risk/benefit assessment of the mRNA vaccines questions them as positive contributors to public health.

Sessa, F., et al. (2021). "Autopsy Findings and Causality Relationship between Death and COVID-19 Vaccination: A Systematic Review." J Clin Med **10**(24).

The current challenge worldwide is the administration of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine. Considering that the COVID-19 vaccination represents the best possibility to resolve this pandemic, this systematic review aims to clarify the major aspects of fatal adverse effects related to COVID-19 vaccines, with the goal of advancing our knowledge, supporting decisions, or suggesting changes in policies at local, regional, and global levels. Moreover, this review aims to provide key recommendations to improve awareness of vaccine safety. All studies published up to 2 December 2021 were searched using the following keywords: "COVID-19 Vaccine", "SARS-CoV-2 Vaccine", "COVID-19 Vaccination", "SARS-CoV-2 Vaccination", and "Autopsy" or "Post-mortem". We included 17 papers published with fatal cases with post-mortem investigations. A total of 38 cases were analyzed: 22 cases were related to ChAdOx1 nCoV-19 administration, 10 cases to BNT162b2, 4 cases to mRNA-1273, and 2 cases to Ad26.COV2.S. Based on these data, autopsy is very useful to define the main characteristics of the so-called vaccine-induced immune thrombotic thrombocytopenia (VITT) after ChAdOx1 nCoV-19 vaccination: recurrent findings were intracranial hemorrhage and diffused microthrombi located in multiple areas. Moreover, it is fundamental to provide evidence about myocarditis related to the BNT162B2 vaccine. Finally, based on the discussed data, we suggest several key recommendations to improve awareness of vaccine safety.

Shaheen, N., et al. (2023). "Myocarditis Following COVID-19 Vaccination: A Systematic Review." Cureus **15**(4): e37999.

COVID-19 vaccination has significantly reduced both the morbidity and mortality rates associated with SARS-CoV-2 infection. Vaccines, especially mRNA vaccines, have been

proposed in several studies to complicate viral myocarditis. Thus, our systematic and meta-analysis review aims to further investigate the possibility of an association between COVID-19 vaccines and myocarditis. We systematically searched PubMed, Web of Science, Scopus, Ovid, and Google Scholar and did a gray search of other databases using the following keywords and terms: "Myocarditis ("Myocarditis" Mesh) OR "Chagas Cardiomyopathy" Mesh) AND "COVID-19 Vaccines" Mesh. The studies were limited to only English articles that reported myocardial inflammation or myocarditis associated with COVID-19 vaccines. Pooled risk ratio with its 95% confidence interval was analyzed by RevMan software (5.4) to perform the meta-analysis. Our study included 671 patients from 44 studies with a mean age of 14-40 years. Nevertheless, myocarditis was noted in a mean of (3.227) days, and 4.19 per million vaccination recipients experienced myocarditis. Most cases were clinically presented with manifestations of cough, chest pain, and fever. Laboratory tests revealed increased C-reactive protein, and troponin with all other cardiac markers in most patients. Cardiac magnetic resonance imaging (MRI) revealed late gadolinium enhancement with myocardial edema and cardiomegaly. Also, electrocardiograms revealed ST-segment elevation in most patients. Furthermore, the incidence of myocarditis was statistically significantly lower in the COVID-19 vaccine group as compared with the control group (RR = 0.15, 95% CI = 0.10-0.23, p-value < 0.00001). No significant association was found between COVID-19 vaccines and the incidence of myocarditis. The study's findings highlight the importance of implementing evidence-based COVID-19 prevention strategies, such as vaccination, to reduce the public health impact of COVID-19 and its associated complications.

Shahid, R., et al. (2023). "Is the mRNA COVID-19 Vaccine Safe in Patients With a Prior History of Myocarditis?" J Card Fail **29**(1): 108-111.

BACKGROUND: Numerous studies have reported myocarditis resulting from messenger RNA (mRNA) coronavirus disease 2019 (COVID-19) vaccination. However, to date, there have been no reports highlighting the safety of mRNA COVID-19 vaccines in children and adults with a prior history of myocarditis, which was the intent of this study. METHODS AND RESULTS: Children and adults cared for at the Cleveland Clinic were identified through the electronic health records, who had a history of myocarditis before the COVID-19 pandemic and had subsequently received at least 2 doses of the mRNA COVID-19 vaccines (n = 34). Only 1 patient in this series had recurrence of myocarditis confirmed by cardiac magnetic resonance imaging after receiving the second dose. He was a White man who had his first episode of myocarditis at age 20 and was 27 years of age at the time of recurrence. He was hospitalized for 2 days with no need for cardiac support or reported arrhythmias and was stable at outpatient follow-up. CONCLUSIONS: In patients with an old history of non-COVID-19 myocarditis, the risk of recurrent myocarditis after receipt of mRNA COVID-19 vaccination is low, and when it occurs it seems to be self-limiting. Our study will be valuable to clinicians while discussing the risk-benefit ratio of vaccinations in patients with a prior history of myocarditis.

Shaikh, O. A., et al. (2021). "Coronavirus disease 2019 (COVID-19) mRNA vaccine and the risk of myocarditis: An increasing concern." Antimicrob Steward Healthc Epidemiol **1**(1): e56.

Sharma, K., et al. (2022). "A Comprehensive Analysis of Myocarditis in Formerly Healthy Individuals Following SARS-CoV-2 Vaccination (COVID-19 Immunization)." Cureus **14**(7): e26851.

Due to the rapid development of the coronavirus disease 2019 (COVID-19) pandemic, the Food and Drug Administration (FDA) expedited the authorization of immunizations to counteract life-threatening COVID-19 effects. COVID-19 immunization was seen as an essential component of surviving endemically with COVID-19. Although there were no major adverse event reports that mandated an early authorization of the mass vaccination approval in initial studies, a few significant adverse events were reported after real-world usage. The most prevalent adverse events are regional reactions, such as discomfort at the injection site. Anaphylactic shock and acute responses were quite infrequent. Current evidence strongly convince the community that the advantages of immunization outweigh the risks. The review investigates the potential adverse reaction in the form of myocarditis caused by the COVID-19 vaccine. Age, sexuality, vaccination type, clinical manifestations, and diagnostic modalities were among the confounding factors associated with vaccine-induced myocarditis. This picture depicts COVID-19 immunization-induced myocarditis and the treatment options available to practitioners. Further evaluation is needed to establish the underlying cause of this association. We compiled the most recent data on SARS-CoV-2 vaccine-induced myocarditis after reviewing available research. Information sources including PubMed and Google Scholar were evaluated retrospectively.

Shaw, K. E., et al. (2021). "Possible Association Between COVID-19 Vaccine and Myocarditis: Clinical and CMR Findings." JACC Cardiovasc Imaging **14**(9): 1856-1861.

Sheth, S. P. and R. Gandhi (2023). "Ventricular Arrhythmia and COVID-19 Vaccine-associated Myocarditis." Pediatr Infect Dis J **42**(4): e112-e113.

17-year-old male presented with COVID-19 vaccine-associated myocarditis. Six months later, due to chest discomfort with exercise, the patient underwent an exercise stress test that revealed a 3-beat run of nonsustained ventricular tachycardia at 230 bpm at peak exercise. The long-term outcomes of COVID-19 vaccine-associated myocarditis are unclear. This patient had nonsustained ventricular tachycardia over 6 months after diagnosis.

Shiyovich, A., et al. (2022). "Myocarditis Following COVID-19 Vaccination: A Follow-up Magnetic Resonance Imaging Study." JACC Cardiovasc Imaging **15**(11): 2006-2007.

Shiyovich, A., et al. (2022). "Myocarditis following COVID-19 vaccination in adolescents: Cardiac magnetic resonance imaging study." Front Cardiovasc Med **9**: 978592.

INTRODUCTION: Vaccination-associated myocarditis was reported following COVID-19 vaccine initially among persons aged 16 or older and recently among adolescents aged 12-15. OBJECTIVES: To describe the clinical and cardiac magnetic resonance (CMR) characteristics of adolescents aged 12-15 with myocarditis following the administration of the BNT162b2 mRNA COVID-19 vaccine. METHODS: CMR of adolescents (age 12-15)

with a clinical diagnosis of myocarditis within 42 days following the first COVID-19 vaccine were analyzed. RESULTS: A total of 182,605 adolescent were vaccinated, out of which 9 were diagnosed with clinically adjudicated myocarditis while CMR was performed in 5/9 patients (56%). Median age was 15 years (range 13-15), 4/5 (80%) males. All the patients we previously healthy. The ECG upon presentation was abnormal in 3/5 (60%) of patients. All cases were classified as clinically mild and no patient required inotropes or mechanical circulatory support treatment. The median follow-up time, for the 5-included patients, was 206 (IQR 192-229, range 179-233) days. During the follow-up, no re-admissions, deaths, or any other cardiac events have occurred.The median time between the diagnosis to the CMR was 104 days (range 27-149). The median left ventricular ejection fraction was within normal range 65% (range 62-69). Native T1 was available in four patients, the local T1 value was increased in three of them. T2 values were available in two patients and were all within normal range. The median late gadolinium enhancement (LGE) was 2% (range 0-6%) with inferolateral wall being the most common location (3/5). The patterns of the LGE were as following: (i) mid-wall in 3 patients; (ii) epicardial in 1-patient. LGE in the pericardium was present in 2/5 patients with pericardial effusion present in 4/5 patients with a median diameter of 4 mm (range 3-5 mm) at end-systole. CONCLUSIONS: CMR findings and clinical course of adolescents with COVID-19 vaccination associated myocarditis, are similar to those of older patients, being relatively mild and potentially implying favorable outcomes.

Shiyovich, A., et al. (2022). "Myocarditis following COVID-19 vaccination: magnetic resonance imaging study." Eur Heart J Cardiovasc Imaging **23**(8): 1075-1082.

AIMS: To describe the cardiac magnetic resonance (CMR) imaging findings of patients who developed myocarditis following messenger RNA (mRNA) coronavirus disease 2019 (COVID-19) vaccination. METHODS AND RESULTS: The present study retrospectively evaluated patients with clinically adjudicated myocarditis within 42 days of the first Pfizer-BNT162b2 mRNA COVID-19 vaccination, between 20 December 2020 and 24 May 2021 who underwent CMR. A total of 15 out 54 patients (28%) with myocarditis underwent a CMR and were included, 100% males, median age of 32 years (interquartile range = 22.5-40). Most patients presented with chest pain (87%) and had an abnormal electrocardiogram (79%). The severity of the disease was mild in 67% and intermediate in 33%. All patients survived and one patient was readmitted during the study period. CMR was performed at a median of 65 days (range 3-130 days) following diagnosis. Median ejection fraction was 58% (range 51-74%) global- and regional wall motion abnormalities were present in one and three patients, respectively. Native T1 was available in 13/15 patients (2/3 in 3 T and 11/12 in the 1.5 T), with increased values among 6/13. Late gadolinium enhancement (LGE) was found among 13/15 patients with a median of 2% (range 0-15%) with inferolateral wall being the most common location (8/13). The patterns of the LGE were: mid-wall in six patients; epicardial in five patients; and mid-wall and epicardial in two patients. CONCLUSIONS: Among patients who were diagnosed with post-vaccination clinical myocarditis, CMR imaging findings are mild and consistent with 'classical myocarditis'. The short-term clinical course and outcomes were favourable.

Shiyovich, A., et al. (2022). "A Case Series of Myocarditis Following Third (Booster) Dose of COVID-19 Vaccination: Magnetic Resonance Imaging Study." Front Cardiovasc Med **9**: 839090.

BACKGROUND: Myocarditis has been reported following the first two doses of Pfizer-BNT162b2 messenger RNA (mRNA) COVID-19 vaccination. Administration of a third dose (booster) of the vaccine was initiated recently in Israel. OBJECTIVE: The aim of this study was to describe the characteristics of patients referred for cardiac magnetic resonance (CMR) imaging with myocarditis following the booster. METHODS: Patients referred for CMR imaging with a clinical diagnosis of myocarditis within 21 days following the booster, between July 13 and November 11, 2021, were analyzed. RESULTS: Overall, 4 patients were included, 3/4 (75%) were men, and the mean age was 27 +/- 10 years. The time from booster administration to the onset of symptoms was 5.75 +/- 4.8 days (range 2-14). Obstructive coronary artery disease was excluded in 3 of the patients (75%). CMR was performed 34 +/- 15 days (range 8-47 days) following the 3rd vaccination. The mean left ventricular ejection fraction was 61 +/- 7% (range 53-71%), and regional wall motion abnormalities were present in one of the patients. Global T1 was increased in one of the patients, while focal T1 values were increased in 3 of the patients. Global T2 was increased in one of the patients, while focal T2 values were increased in all the patients. Global ECV was increased in 3 of the patients, while focal ECV was increased in all the patients. Median late gadolinium enhancement (LGE) was 4 +/- 3% (range 1-9%), with the inferolateral segment as the most common location (3 of the 4 patients). All the patients met the Updated Lake Louise Criteria. CONCLUSIONS: Patient characteristics and CMR imaging findings of myocarditis following the administration of the booster vaccine are relatively mild and consistent with those observed with the first two doses. Although larger-scale prospective studies are necessary, these initial findings are somewhat reassuring.

Sim, J. Y., S. Y. Kim and E. K. Kim (2023). "The incidence and clinical characteristics of myocarditis and pericarditis following mRNA-based COVID-19 vaccination in Republic of Korea adolescents from July 2021 to September 2022." Osong Public Health Res Perspect **14**(2): 76-88.

OBJECTIVES: Age-specific information regarding myocarditis/pericarditis in adolescents following mRNA-based coronavirus disease 2019 (COVID-19) vaccination in Asia remains insufficient. This study investigated the incidence and clinical characteristics of myocarditis/pericarditis in Republic of Korea adolescents after mRNA-based COVID-19 vaccination. METHODS: This retrospective descriptive study utilized patient data from the Korea Immunization Management System. Incidence rates were calculated according to age and sex. Clinical characteristics (symptoms/signs, laboratory values, and imaging results) were compared between mild and severe cases. RESULTS: Between July 19, 2021 and September 30, 2022, 3,728,224 individuals aged 12 to 19 years received 6,484,165 mRNA-based COVID-19 vaccines, and 173 cases met the case definition for myocarditis/pericarditis: 151 mild (87.3%) and 22 severe (12.7%). The incidence was 3.8-fold higher in males than in females. Troponin I/ troponin T was elevated in 96% of myocarditis cases, demonstrating higher sensitivity than creatine kinase-myocardial band (67.6%) or C-reactive protein (75.2%). ST-segment or Twave on electrography

abnormalities were found in 60.3% (85/141). Paroxysmal/sustained atrial/ventricular arrhythmias were more common in severe than in mild cases (45.5% vs. 16.8%, p=0.008). Edema on T2-weighted magnetic imaging occurred in 21.6% (8/37) and 62.5% (5/8) of mild and severe cases, respectively (p=0.03). Abnormal pericardial fluid collection or pericardial inflammation was found in 75.4% of pericarditis cases (49/65). CONCLUSION: Myocarditis/pericarditis occurred in rare cases following mRNA-based COVID-19 vaccination. Most cases were mild, but the incidence was higher in adolescent males and after the second dose. As bivalent severe acute respiratory syndrome coronavirus 2 mRNA vaccination started in Republic of Korea in October 2022, the post-vaccination incidence of myocarditis/pericarditis should be closely monitored, considering clinical characteristics.

Simone, A., et al. (2021). "Acute Myocarditis Following COVID-19 mRNA Vaccination in Adults Aged 18 Years or Older." JAMA Intern Med.

Simone, A., et al. (2022). "Acute myocarditis following a third dose of COVID-19 mRNA vaccination in adults." Int J Cardiol **365**: 41-43.

INTRODUCTION: Myocarditis has been reported following the second dose of COVID-19 mRNA vaccination. Whether administration of additional doses of COVID-19 vaccines further increases the risk of myocarditis is unknown. METHODS: We included individuals who received one to three doses of BNT162b2 or mRNA-1273 mRNA vaccine between 12/14/2020 and 2/18/2022. Myocarditis within 21 days of vaccine administration was identified using electronic medical records. Incidence rate ratios were calculated by comparing the observed incidence with the expected incidence from the same population during a 365-day baseline period. RESULTS: Of 3,076,660 KPSC members who received at least one dose of COVID-19 mRNA vaccines, 2,916,739 (94.5%) received at least two doses, and 1,146,254 (47.0%) received three doses. The incidence rate ratio for myocarditis was 0.86 (95% CI 0.31-1.93) for the first dose, 4.22 (95% CI 2.63-6.53) for the second dose, and 2.61 (1.13-5.29) for the third dose. Most myocarditis cases following the second and third dose occurred within seven days of vaccination. CONCLUSION: Myocarditis was a rare event observed after the second or third dose of vaccination. Most cases presented within seven days of vaccination. The incidence of myocarditis following the third dose was not significantly higher than that observed after the second dose.

Sinagra, G., et al. (2021). "[Myocarditis and pericarditis following mRNA COVID-19 vaccination. Expert opinion of the Italian Society of Cardiology]." G Ital Cardiol (Rome) **22**(11): 894-899.

The coronavirus disease (COVID-19) pandemic has caused 2.69 million deaths and 122 million infections. Great efforts have been made worldwide to promptly develop effective vaccines and reduce morbidity and mortality rates from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Available vaccines have proven highly effective at preventing symptomatic disease in clinical trials and real-world reports and are playing an essential role in flattening the epidemiology curve and, mostly, in reducing COVID-19 hospitalizations. Some concerns have been raised after

very rare cases of myocarditis and pericarditis recently reported by the Centers for Disease Control and Prevention (CDC) as potentially associated with COVID-19 mRNA vaccinations, namely the Pfizer-BioNTech mRNA vaccine (BNT162b2) and the Moderna mRNA vaccine (mRNA-1273). Therefore, the aim of this document is to explore the possible link between COVID-19 mRNA vaccination and the development of myocarditis and/or pericarditis by performing a critical analysis of available data and to provide indications for specific subgroups of individuals.

Sinagra, G., et al. (2022). "[2022 Update on myocarditis and pericarditis following COVID-19 vaccination. Expert Opinion of the Italian Society of Cardiology]." G Ital Cardiol (Rome) **23**(6): 408-413.

Vaccine-associated myocarditis and pericarditis usually develop within 14 days of COVID-19 vaccination, are exceptionally rare, manifest with mild clinical pictures and are commonly characterized by a favorable evolution. Young men inoculated with two doses of an mRNA vaccine are the subgroup at higher risk. Recent epidemiological studies evaluated the incidence and risk of vaccine-associated myocarditis and pericarditis among men and women, in different ranges of age and specific types of vaccines. Long-term population analyses demonstrated that the cardiovascular risk conferred by COVID-19 extends beyond the acute phase, representing the rationale for implementing prevention strategies for SARS-CoV-2 infection, monitoring specific populations at higher risk and pursuing the completion of the vaccination campaign. This document provides an update on the most recent scientific evidence and critical interpretation of available data in constant evolution towards personalized strategies of immunization.

Singh, B., et al. (2021). "COVID-19 mRNA Vaccine and Myocarditis." Eur J Case Rep Intern Med **8**(7): 002681.

Coronavirus disease 2019 (COVID-19) is believed to have originated in the Hua nan South China Seafood Market in Wuhan and can present with a spectrum of clinical manifestations. We report the case of 24-year-old male patient who developed chest pain after administration of the second dose of the Pfizer-BioNTech mRNA COVID-19 vaccine and who was diagnosed with myocarditis on work-up. LEARNING POINTS: Localized injection site reactions and systemic adverse effects can occur after administration of the various COVID-19 vaccines.Healthcare providers should maintain a high index of suspicion regarding myocarditis after mRNA COVID-19 vaccination in the appropriate clinical scenario.

Snapiri, O., et al. (2021). "Transient Cardiac Injury in Adolescents Receiving the BNT162b2 mRNA COVID-19 Vaccine." Pediatr Infect Dis J **40**(10): e360-e363.

BACKGROUND: Vaccines are paramount in the effort to end the coronavirus disease 2019 global epidemic. BNT162b2 is approved for the vaccination of adolescents over 16 years of age. Systemic adverse events were scarce though the pretested cohort of this age group was relatively small. The aim of the current study is to raise awareness for potential adverse reactions. METHODS: This is a case series of patients diagnosed with perimyocarditis following vaccination. Patients were compiled from 3 pediatric medical

centers in Israel through a network of pediatricians and data regarding those cases was collected. In addition, incidence of perimyocarditis during the vaccination period was compared with previous years. RESULTS: All patients were males 16-18 years old, of Jewish descent, who presented with chest pain that began 1-3 days following vaccination (mean, 2.1 days). In 6 of the 7 patients, symptoms began following the 2nd dose and in 1 patient following the 1st dose. All cases were mild and none required cardiovascular or respiratory support. The incidence of perimyocarditis during the vaccination period was elevated in comparison to previous years. CONCLUSIONS: This case series describes a time association between coronavirus disease 2019 vaccine and perimyocarditis in adolescents. All cases were mild, although only long-term follow-up can reveal the true impact of this cardiac injury. While it seems that the incidence of perimyocarditis during the vaccination campaign period is increased, a more comprehensive data collection on a wider scale should be done. We hope this report will serve as a reminder to report events and allow for analysis of potential adverse reactions.

Sogbe, M., et al. (2023). "Systemic lupus erythematosus myocarditis after COVID-19 vaccination." Reumatol Clin (Engl Ed) **19**(2): 114-116.

INTRODUCTION: Cases of acute myocarditis have been after administration of the BNT162b2 and Ad26.COV2.S vaccine. OBJECTIVE: Describe another possible mechanism of myocarditis after COVID-19 vaccination. CASE PRESENTATION: We describe the clinical case of a 72-year-old female with pleuritic chest pain one week after the third of the BNT162b2 mRNA vaccine. Serological tests for cardiotropic pathogens were negative, and autoimmunity screening was positive with anti-nuclear antibody (ANA) in 1:160 dilution, Anti-double-stranded DNA (anti-dsDNA), and anti-histone antibodies. (18)F-fluoro-deoxy-glucose (FDG) positron emission tomography/computed tomography (PET/CT) showed a focal myocardial and pericardial inflammatory process in the cardiac apex. RESULTS AND DISCUSSION: Systemic lupus erythematosus (SLE) diagnosis was made with myocardial affection. As far as we know, this is the first report of a case of lupus myocarditis after the COVID-19 vaccine. CONCLUSION: Given the pathogenic rationales, the association between SLE and myocarditis should be considered.

Sokolska, J. M., J. Kurcz and W. Kosmala (2021). "Every rose has its thorns - acute myocarditis following COVID-19 vaccination." Kardiol Pol.

Sookaromdee, P. and V. Wiwanitkit (2022). "Myocarditis after COVID-19 mRNA vaccination: Correspondence." Pathol Int **72**(9): 464.

Sookaromdee, P. and V. Wiwanitkit (2022). "Myocarditis, pericarditis, and COVID-19 mRNA-vaccination." Glob Cardiol Sci Pract **2022**(1-2): e202207.

Sovova, E. (2022). "Myocarditis as a manifestation of the disease COVID-19 and after vaccination against this disease." Cas Lek Cesk **161**(3-4): 135-138.

Although the involvement of the heart muscle in the coronavirus disease 2019 (COVID-19) is relatively common (5-10%), myocarditis is a complication with a much lower incidence, depending, however, on the diagnostic methods used. The pathophysiological mechanisms have been described, but there are significant gaps in current knowledge. Myocarditis in connection with vaccination against the disease COVID-19 is a separate nosological unit. Even here, the pathophysiological processes are not explored in detail. The incidence of this complication is estimated in the low tens per million vaccinated.

Starekova, J., et al. (2021). "Myocarditis Associated with mRNA COVID-19 Vaccination." Radiology **301**(2): E409-E411.

Stervbo, U., et al. (2023). "Case report: SARS-CoV-2 specific T-cells are associated with myocarditis after COVID-19 vaccination with mRNA-1273." Front Med (Lausanne) **10**: 1088764.
Vaccination of SARS-CoV-2 with BNT162b2 or mRNA-1273 both have a low incidence of induction of myocarditis. Here we report on utilizing adaptive immune receptor repertoire sequencing (AIRR-Seq) as a way to assess the specificity of tissue infiltrating immune cells.

Stowe, J., et al. (2023). "Risk of myocarditis and pericarditis after a COVID-19 mRNA vaccine booster and after COVID-19 in those with and without prior SARS-CoV-2 infection: A self-controlled case series analysis in England." PLoS Med **20**(6): e1004245.
BACKGROUND: An increased risk of myocarditis or pericarditis after priming with mRNA Coronavirus Disease 2019 (COVID-19) vaccines has been shown but information on the risk post-booster is limited. With the now high prevalence of prior Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection, we assessed the effect of prior infection on the vaccine risk and the risk from COVID-19 reinfection. METHODS AND FINDINGS: We conducted a self-controlled case series analysis of hospital admissions for myocarditis or pericarditis in England between 22 February 2021 and 6 February 2022 in the 50 million individuals eligible to receive the adenovirus-vectored vaccine (ChAdOx1-S) for priming or an mRNA vaccine (BNT162b2 or mRNA-1273) for priming or boosting. Myocarditis and pericarditis admissions were extracted from the Secondary Uses Service (SUS) database in England and vaccination histories from the National Immunisation Management System (NIMS); prior infections were obtained from the UK Health Security Agency's Second-Generation Surveillance Systems. The relative incidence (RI) of admission within 0 to 6 and 7 to 14 days of vaccination compared with periods outside these risk windows stratified by age, dose, and prior SARS-CoV-2 infection for individuals aged 12 to 101 years was estimated. The RI within 27 days of an infection was assessed in the same model. There were 2,284 admissions for myocarditis and 1,651 for pericarditis in the study period. Elevated RIs were only observed in 16- to 39-year-olds 0 to 6 days postvaccination, mainly in males for myocarditis. Both mRNA vaccines showed elevated RIs after first, second, and third doses with the highest RIs after a second dose 5.34 (95% confidence interval (CI) [3.81, 7.48]; $p < 0.001$) for BNT162b2 and 56.48 (95% CI [33.95, 93.97]; $p < 0.001$) for mRNA-1273 compared with 4.38 (95% CI [2.59, 7.38]; $p < 0.001$) and 7.88 (95% CI [4.02, 15.44];

p < 0.001), respectively, after a third dose. For ChAdOx1-S, an elevated RI was only observed after a first dose, RI 5.23 (95% CI [2.48, 11.01]; p < 0.001). An elevated risk of admission for pericarditis was only observed 0 to 6 days after a second dose of mRNA-1273 vaccine in 16 to 39 year olds, RI 4.84 (95% CI [1.62, 14.01]; p = 0.004). RIs were lower in those with a prior SARS-CoV-2 infection than in those without, 2.47 (95% CI [1.32,4.63]; p = 0.005) versus 4.45 (95% [3.12, 6.34]; p = 0.001) after a second BNT162b2 dose, and 19.07 (95% CI [8.62, 42.19]; p < 0.001) versus 37.2 (95% CI [22.18, 62.38]; p < 0.001) for mRNA-1273 (myocarditis and pericarditis outcomes combined). RIs 1 to 27 days postinfection were elevated in all ages and were marginally lower for breakthrough infections, 2.33 (95% CI [1.96, 2.76]; p < 0.001) compared with 3.32 (95% CI [2.54, 4.33]; p < 0.001) in vaccine-naive individuals respectively. CONCLUSIONS: We observed an increased risk of myocarditis within the first week after priming and booster doses of mRNA vaccines, predominantly in males under 40 years with the highest risks after a second dose. The risk difference between the second and the third doses was particularly marked for the mRNA-1273 vaccine that contains half the amount of mRNA when used for boosting than priming. The lower risk in those with prior SARS-CoV-2 infection, and lack of an enhanced effect post-booster, does not suggest a spike-directed immune mechanism. Research to understand the mechanism of vaccine-associated myocarditis and to document the risk with bivalent mRNA vaccines is warranted.

Suan, V. G. Y., R. Hawkins and M. S. Yew (2022). "Erroneous diagnosis of COVID-19 mRNA vaccine-associated acute myocarditis due to false-positive high-sensitive troponin I assay: a case report." Eur Heart J Case Rep **6**(12): ytac448.

BACKGROUND: Coronavirus disease 2019 (COVID-19) mRNA vaccine-associated acute myocarditis has been well described, and the demonstration of elevated high-sensitivity cardiac troponin (hs-cTn) is crucial for its diagnosis. However, falsely elevated hs-cTn can occasionally occur, leading to incorrect diagnosis. Here, we report the case of a patient who was given an erroneous diagnosis of COVID-19 mRNA vaccine-associated acute myocarditis due to falsely elevated hs-cTn, likely from assay interference. CASE SUMMARY: A 29-year-old Chinese male presented with 3 months of chest pain, dyspnoea, and palpitations starting a few days after his second dose of mRNA-1273 (Moderna) vaccine. High-sensitivity cardiac troponin I was elevated at presentation, which rose further 4 h later. The provisional diagnosis was acute myocarditis after a computed tomography coronary angiogram showed normal coronaries. Cardiac magnetic resonance was also negative for myocardial inflammation. The hs-cTn I levels fluctuated but remained elevated on outpatient serial testing, despite no new symptoms or clinical events. A paired serum sample showed elevated hs-cTn I but normal hs-cTn T, confirming a diagnosis of false-positive hs-cTn I. Further investigations, including blood tests before and after a subsequent uneventful mRNA-1273 booster vaccination, were performed to investigate for assay interference. DISCUSSION: Widespread COVID-19 mRNA vaccination has resulted in an awareness of vaccine-related acute myocarditis and a more thorough evaluation of post-vaccination cardiac symptoms. Although false-positive hs-cTn rarely occurs, extensive testing will inevitably result in a significant number of patients with falsely elevated hs-cTn. Clinicians should exclude this possibility

and consider using alternative hs-cTn assay when investigation results and clinical presentation appear discordant.

Sulemankhil, I., M. Abdelrahman and S. I. Negi (2022). "Temporal Association Between the COVID-19 Ad26.COV2.S Vaccine and Acute Myocarditis: A Case Report and Literature Review." Cardiovasc Revasc Med **38**: 117-123.

With the recent approval and widespread administration of the Pfizer-BioNTech, Moderna, and Janssen vaccines worldwide, incidence of severe Coronavirus Disease 2019 (COVID-19) infection has significantly decreased. In spite of their undisputed role in reducing the severity of the disease and reduction of the disease burden in the community, there have been case reports of serious side effects with these vaccines. We aim to describe a case report of myocarditis following administration of the Janssen vaccine in a healthy, young male and review the available literature on COVID-19 vaccine related myocarditis and its possible pathogenesis. This case and literature review notes a temporal association between COVID-19 vaccination and myocarditis. Despite these observations, the benefits of the vaccines far outweigh the risks of possible myocarditis.

Sung, K., et al. (2022). "Biopsy-Proven Giant Cell Myocarditis Following the COVID-19 Vaccine." Circ Heart Fail **15**(4): e009321.

Sutcu, M., et al. (2022). "Rhabdomyolysis after BNT162b2 mRNA Covid-19 vaccine in an adolescent male." Malawi Med J **34**(2): 154-156.

Pfizer-BioNTech COVID-19 (BNT162b2) conferred a high level of protection against Covid-19 with a proven short-term safety profile. Although cases of vaccine-associated myopericarditis have been reported, the existence of rhabdomyolysis without myocarditis has not yet been published. A 16-year-old, healthy male patient, who did not use any herbal or illegal drugs before, was admitted with muscle pain that developed after the second dose of BNT162b2 vaccine. Cardiac examination and heart enzymes were normal and the patient had significantly higher creatinine kinase levels. The patient, whose enzymes returned to normal with only force hydration therapy, recovered without complications. Reporting the side effects of the vaccine, which has a short history of application to large populations, is of vital importance in the conduct of vaccine development studies and in identifying the risky group in terms of side effects.

Suzuki, H., et al. (2022). "Autopsy findings of post-COVID-19 vaccination deaths in Tokyo Metropolis, Japan, 2021." Leg Med (Tokyo) **59**: 102134.

BACKGROUND: COVID-19 vaccines have been used across Japan since 17 February 2021, and as of 17 April 2022, 1690 deaths potentially caused by vaccine-related adverse effects have been reported to the Ministry of Health, Labour and Welfare. However, the causal relationship between vaccination and death could not be fully evaluated because of a lack of sufficient information. METHODS: Autopsy cases in which deaths occurred within seven days after COVID-19 vaccination in Tokyo Metropolis and were handled by medical examiners were selected (n = 54). Age, sex, vaccine-related information, cause of death, and possible causal relationship between vaccination and death were

examined. RESULTS: The mean age of the deceased individuals was 68.1 years, and the study sample consisted of 34 males (63.9%) and 20 females (37.0%). Thirty-seven and six individuals received Comirnaty and Spikevax, respectively (68.5% and 11.1% respectively). The manner of death included natural (n = 43), non-natural (n = 8), and undetermined (n = 3). The most frequent cause of death was ischemic heart disease (n = 16). Regarding causal relationships, 46 cases (85.2%) did not show a causal relationship to vaccination, except for myocarditis (n = 3), thrombosis-related death (n = 4), and others (n = 1). CONCLUSION: Although many cases of deaths after COVID-19 vaccination in this study showed no definite causal relationship between the vaccination and deaths, some cases showed possible adverse events such as myocarditis. Autopsies are essential for detecting vaccine-related deaths, and the Japanese death investigation system needs to be reinforced from this viewpoint.

Takahashi, M., et al. (2022). "An autopsy case report of aortic dissection complicated with histiolymphocytic pericarditis and aortic inflammation after mRNA COVID-19 vaccination." Leg Med (Tokyo) **59**: 102154.

A male in his 90 s consulted a doctor because he experienced several days of general fatigue and dyspnea. He was diagnosed with heart failure, and diuretic medications taken for 3 days relieved his symptoms. However, he was found dead on the morning of the fourth day after consultation. He had received a third dose of coronavirus disease 2019 (COVID-19) vaccine approximately 2 weeks before death. An autopsy revealed dissection of the ascending aorta and pericardial hemotamponade. The heart showed a white villous surface, and the pericardium was fibrously thick. Microscopic examination revealed pericarditis with predominantly macrophage and lymphocyte infiltration. These histological findings were compatible with those of post-vaccination myocarditis. To the best of our knowledge, histopathologically proven pericarditis after COVID-19 vaccination has not been reported. In the present case, extended inflammation of the aortic adventitia was a possible cause of aortic wall fragility followed by dissection.

Takeda, M., et al. (2022). "Eosinophilic Myocarditis Following Coronavirus Disease 2019 (COVID-19) Vaccination." Circ J **86**(6): 1020.

Tan, L. J., et al. (2022). "A systemic review and recommendation for an autopsy approach to death followed the COVID 19 vaccination." Forensic Sci Int **340**: 111469.

The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) started in December 2019. An immediate prevention approach for the outbreak is the development of a vaccination program. Despite a growing number of publications showing the effectiveness of vaccination in preventing SARS-CoV-2 outbreak and reducing the mortality rate, substantial fatal adverse effects were reported after vaccination. Confirmation of the causal relationship of death is required to reimburse under the national vaccination program and could provide a reference for the selection of vaccination. However, a lack of guidelines in the laboratory study and autopsy approach hampered the investigation of post-vaccination death. In this paper, we performed a systematic electronic search on scientific articles related to severe Covid-19

vaccination adverse effects and approaches in identifying the severe side effects using PubMed and Cochrane libraries. A summary on the onset, biochemistry changes and histopathological analyzes of major lethally side effects post-vaccination were discussed. Ultimately, a checklist is suggested to improve the quality of investigation.

Tanaka, A., S. Fukuoka and H. Nagata (2023). "Vasospastic angina following COVID-19 vaccine-related myocarditis: an underlying cause of chest pain." Cardiol Young: 1-3.

We present a 13-year-old boy who had recurrent chest pain with elevated cardiac enzymes and abnormal ST segments in electrocardiogram 36 hours after the second dose of BNT162b2 vaccination. Cardiac MRI and coronary angiography with acetylcholine provocation confirmed myocarditis and vasospastic angina, respectively. Coronary vasospasm may play a pivotal role in the chest pain in COVID-19 vaccine-related myocarditis.

Teran Brage, E., et al. (2022). "Fulminant myocarditis in a patient with a lung adenocarcinoma after the third dose of modern COVID-19 vaccine. A case report and literature review." Curr Probl Cancer Case Rep **6**: 100153.

Introduction COVID-19 disease has caused a global health and economic crisis. The introduction of the different COVID-19 vaccines has resulted in a significant decrease in the morbidity and mortality associated with this disease. Adverse effects have been reported, including cardiological ones such as myocarditis or pericarditis after administration. Likewise, tyrosine kinase inhibitor drugs such as osimertinib used in lung cancer patients with epidermal growth factor receptor (EGFR) mutation are associated with heart failure or prolongation of the QT interval. Case report 62-year-old woman diagnosed in September 2019 of lung adenocarcinoma stage IV with bilateral lung and lymph node involvement, carrier of an EGFR mutation (Ex19Del) on treatment with osimertinib. She attended emergency department for fever and hypotension 24 h after administration of the third dose of Moderna(R) COVID-19 vaccine in the context of acute myocarditis with evidence of severe left ventricular (LV) dysfunction in cardiogenic shock. She required vasoactive support, non-invasive mechanical ventilation, corticotherapy, immunoglobulins and subsequent ventricular support with Impella, with improvement of the clinical picture after 3 days. Cardiac magnetic resonance imaging (MRI) showed evidence of global myocardial oedema compatible with acute myocarditis. Coronary CT showed a lesion in the anterior descending coronary artery requiring revascularization. A few days later, she presented febrile symptoms with isolation of Staphylococcus aureus in the central line catheter and antibiotherapy with cloxacillin was started, with subsequent resolution of the infectious symptoms. Conclusion This is an exceptional and controversial case of fulminant myocarditis probably related to the Modern COVID-19 vaccine in a patient diagnosed with metastatic lung adenocarcinoma on treatment with osimertinib. An increasing number of cases of myocarditis and pericarditis have been reported following vaccination with COVID-19 mRNA vaccines. In addition, retrospective data have shown an increased risk of QT prolongation and heart failure in patients treated with tyrosine kinase inhibitors. Hence, the need for close monitoring of cardiac function during treatment of these patients. Future studies will be

necessary to evaluate unknown adverse reactions of these vaccines and their possible interaction with other antineoplastic drugs.

Tome, J., L. T. Cowan and I. C. Fung (2023). "A Pharmacoepidemiological Study of Myocarditis and Pericarditis Following the First Dose of mRNA COVID-19 Vaccine in Europe." Microorganisms **11**(5).

This study assessed the myocarditis and pericarditis reporting rate of the first dose of mRNA COVID-19 vaccines in Europe. Myocarditis and pericarditis data pertinent to mRNA COVID-19 vaccines (1 January 2021-11 February 2022) from EudraVigilance database were combined with European Centre for Disease Prevention and Control (ECDC)'s vaccination tracker data. The reporting rate was expressed as events (occurring within 28 days of the first dose) per 1 million individuals vaccinated. An observed-to-expected (OE) analysis quantified excess risk for myocarditis or pericarditis following the first mRNA COVID-19 vaccination. The reporting rate of myocarditis per 1 million individuals vaccinated was 17.27 (95% CI, 16.34-18.26) for CX-024414 and 8.44 (95% CI, 8.18-8.70) for TOZINAMERAN; and of pericarditis, 9.76 (95% CI, 9.06-10.51) for CX-024414 and 5.79 (95% CI, 5.56-6.01) for TOZINAMERAN. Both vaccines produced a myocarditis standardized morbidity ratio (SMR) > 1, with the CX-024414 vaccine having a greater SMR than TOZINAMERAN. Regarding TOZINAMERAN, SMR for pericarditis was >1 when considering the lowest background incidence, but <1 when considering the highest background incidence. Our results suggest an excess risk of myocarditis following the first dose of the mRNA COVID-19 vaccine, but the relationship between pericarditis and the mRNA COVID-19 vaccine remains unclear.

Truong, D. T., et al. (2022). "Clinically Suspected Myocarditis Temporally Related to COVID-19 Vaccination in Adolescents and Young Adults: Suspected Myocarditis After COVID-19 Vaccination." Circulation **145**(5): 345-356.

BACKGROUND: Understanding the clinical course and short-term outcomes of suspected myocarditis after the coronavirus disease 2019 (COVID-19) vaccination has important public health implications in the decision to vaccinate youth. METHODS: We retrospectively collected data on patients <21 years old presenting before July 4, 2021, with suspected myocarditis within 30 days of COVID-19 vaccination. Lake Louise criteria were used for cardiac MRI findings. Myocarditis cases were classified as confirmed or probable on the basis of the Centers for Disease Control and Prevention definitions. RESULTS: We report on 139 adolescents and young adults with 140 episodes of suspected myocarditis (49 confirmed, 91 probable) at 26 centers. Most patients were male (n=126, 90.6%) and White (n=92, 66.2%); 29 (20.9%) were Hispanic; and the median age was 15.8 years (range, 12.1-20.3; interquartile range [IQR], 14.5-17.0). Suspected myocarditis occurred in 136 patients (97.8%) after the mRNA vaccine, with 131 (94.2%) after the Pfizer-BioNTech vaccine; 128 (91.4%) occurred after the second dose. Symptoms started at a median of 2 days (range, 0-22; IQR, 1-3) after vaccination. The most common symptom was chest pain (99.3%). Patients were treated with nonsteroidal anti-inflammatory drugs (81.3%), intravenous immunoglobulin (21.6%), glucocorticoids (21.6%), colchicine (7.9%), or no anti-inflammatory therapies (8.6%).

Twenty-six patients (18.7%) were in the intensive care unit, 2 were treated with inotropic/vasoactive support, and none required extracorporeal membrane oxygenation or died. Median hospital stay was 2 days (range, 0-10; IQR, 2-3). All patients had elevated troponin I (n=111, 8.12 ng/mL; IQR, 3.50-15.90) or T (n=28, 0.61 ng/mL; IQR, 0.25-1.30); 69.8% had abnormal ECGs and arrhythmias (7 with nonsustained ventricular tachycardia); and 18.7% had left ventricular ejection fraction <55% on echocardiogram. Of 97 patients who underwent cardiac MRI at a median 5 days (range, 0-88; IQR, 3-17) from symptom onset, 75 (77.3%) had abnormal findings: 74 (76.3%) had late gadolinium enhancement, 54 (55.7%) had myocardial edema, and 49 (50.5%) met Lake Louise criteria. Among 26 patients with left ventricular ejection fraction <55% on echocardiogram, all with follow-up had normalized function (n=25). CONCLUSIONS: Most cases of suspected COVID-19 vaccine myocarditis occurring in persons <21 years have a mild clinical course with rapid resolution of symptoms. Abnormal findings on cardiac MRI were frequent. Future studies should evaluate risk factors, mechanisms, and long-term outcomes.

Uesako, H., et al. (2022). "Prominent J Waves and Ventricular Fibrillation Caused by Myocarditis and Pericarditis After BNT162b2 mRNA COVID-19 Vaccination." Can J Cardiol **38**(6): 844-847.

Unger, K., C. D. Ponte and D. Anderson (2022). "A Possible Case of COVID-19 Booster Vaccine-Associated Rhabdomyolysis and Acute Kidney Injury." J Pharm Technol **38**(4): 247-250.

Background: Nearly 10 billion doses of the various messenger ribonucleic acid (mRNA) and viral vector vaccines against Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) have been administered worldwide. Adverse drug reactions (ADRs) have been overwhelmingly mild to moderate in nature. Rare side effects have included myocarditis/pericarditis, thrombosis with thrombocytopenia syndrome (TTS), Guillain-Barre Syndrome (GBS), and death. However, vaccine-related ADR data are still being collected using a variety of reporting systems. Purpose: We will describe a case of suspected mRNA coronavirus disease 2019 (COVID-19) booster-related rhabdomyolysis in a woman who developed signs and symptoms 10 days after administration of the vaccine dose. With a Naranjo ADR probability score of 4, the vaccine was deemed to be a possible cause of our patient's rhabdomyolysis. Methods: A search of the VAERS (Vaccine Adverse Event Reporting System) mined in November 2021 revealed 386 reported cases of COVID-19 vaccine-related rhabdomyolysis. However, system limitations make the utility of the information problematic. Conclusions: It is vitally important that clinicians, scientists, and patients are aware of rhabdomyolysis as a potential side effect of vaccination. Suspected vaccine-related ADRs should be promptly and accurately reported via VAERS or other surveillance systems to support the ongoing effort to ensure vaccine safety.

Vago, H., et al. (2022). "Immunological response and temporal associations in myocarditis after COVID-19 vaccination using cardiac magnetic resonance imaging: An amplified T-cell response at the heart of it?" Front Cardiovasc Med **9**: 961031.

INTRODUCTION: Although myocarditis after anti-SARS-CoV-2 vaccination is increasingly recognized, we have little data regarding the course of the disease and, consequently, the imaging findings, including the tissue-specific features. The purpose of this study is to describe the clinical, immunological, and cardiac magnetic resonance (CMR) features of myocarditis after COVID-19 immunization in the acute phase and during follow-up. We aimed to compare the trajectory of the disease to myocarditis cases unrelated to COVID-19. METHODS: We assembled a CMR-based registry of potentially COVID-19 vaccination-related myocarditis cases. All patients who experienced new-onset chest pain and troponin elevation after COVID-19 vaccination and imaging confirming the clinical suspicion of acute myocarditis were enrolled in our study. Participants underwent routine laboratory testing and testing of their humoral and cellular immune response to COVID-19 vaccination. Clinical and CMR follow-up was performed after 3-6 months. We included two separate, sex- and age-matched control groups: (1) individuals with myocarditis unrelated to COVID-19 infection or vaccination confirmed by CMR and (2) volunteers with similar immunological exposure to SARS-CoV-2 compared to our group of interest (no difference in the number of doses, types and the time since anti-SARS-CoV-2 vaccination and no difference in anti-nucleocapsid levels). RESULTS: We report 16 CMR-confirmed cases of myocarditis presenting (mean +/- SD) 4 +/- 2 days after administration of the anti-SARS-CoV-2 vaccine (male patients, 22 +/- 7 years), frequently with predisposing factors such as immune-mediated disease and previous myocarditis. We found that 75% received mRNA vaccines, and 25% received vector vaccines. During follow-up, CMR metrics depicting myocardial injury, including oedema and necrosis, decreased or completely disappeared. There was no difference regarding the CMR metrics between myocarditis after immunization and myocarditis unrelated to COVID-19. We found an increased T-cell response among myocarditis patients compared to matched controls ($p < 0.01$), while there was no difference in the humoral immune response. CONCLUSION: In our cohort, myocarditis occurred after both mRNA and vector anti-SARS-CoV-2 vaccination, frequently in individuals with predisposing factors. Upon follow-up, the myocardial injury had healed. Notably, an amplified cellular immune response was found in acute myocarditis cases occurring 4 days after COVID-19 vaccination.

Vaiyani, D., et al. (2023). "Patients with Post-COVID-19 Vaccination Myocarditis Have More Favorable Strain in Cardiac Magnetic Resonance Than Those With Viral Myocarditis." Pediatr Cardiol **44**(5): 1108-1117.

There have been reports of myocarditis following vaccination against COVID-19. We sought to describe cardiac magnetic resonance (CMR) findings among pediatric patients. Retrospective review at a large academic center of patients clinically diagnosed with post-vaccine myocarditis (PVM) undergoing CMR. Data collected included parametric mapping, ventricular function, and degree of late gadolinium enhancement (LGE). Post-processing strain analysis was performed using feature tracking. Strain values, T1/T2 values, and ventricular function were compared to age- and gender-matched controls with viral myocarditis using a Wilcoxon Signed Rank test. Among 12 patients with presumed PVM, 11 were male and 11 presented after the second vaccination dose,

typically within 4 days. All presented with chest pain and elevated troponin. 10 met MRI criteria for acute myocarditis. All had LGE typically seen in the lateral and inferior walls; only five had prolonged T1 values. 10 met criteria for edema based on skeletal muscle to myocardium signal intensity ratio and only 5 had prolonged T2 mapping values. Patients with PVM had greater short-axis global circumferential and radial strain, right ventricle function, and cardiac output when compared to those with viral myocarditis. Patients with PVM have greater short-axis global circumferential and radial strains compared to those with viral myocarditis. LGE was universal in our cohort. Signal intensity ratios between skeletal muscle and myocardium may be more sensitive in identifying edema than T2 mapping. Overall, the impact on myocardial strain by CMR is less significant in PVM compared to more classic viral myocarditis.

Valore, L., et al. (2023). "Case report: mRNA-1273 COVID-19 vaccine-associated myopericarditis: Successful treatment and re-exposure with colchicine." Front Cardiovasc Med **10**: 1135848.
INTRODUCTION: Vaccine-induced myocarditis is a rare complication of messenger RNA (mRNA) COVID-19 vaccines. CASE PRESENTATION: We report a case of acute myopericarditis in a recipient of allogeneic hematopoietic cells following the first dose of the mRNA-1273 vaccine and the successful administration of a second and third dose while on prophylactic treatment with colchicine to successfully complete the vaccination. CONCLUSION: Treatment and prevention of mRNA-vaccine-induced myopericarditis represent a clinical challenge. The use of colchicine is feasible and safe to potentially reduce the risk of this rare but severe complication and allows re-exposure to an mRNA vaccine.

Varma, S. K., et al. (2022). "Myocarditis after COVID-19 mRNA vaccination in Australia." Med J Aust **217**(5): 260-261.

Verma, A. K., K. J. Lavine and C. Y. Lin (2021). "Myocarditis after Covid-19 mRNA Vaccination." N Engl J Med **385**(14): 1332-1334.

Visclosky, T., et al. (2021). "Myocarditis Following mRNA COVID-19 Vaccine." Pediatr Emerg Care **37**(11): 583-584.
A growing number of adolescents are being diagnosed with acute myocarditis following mRNA COVID-19 vaccinations. This case describes an adolescent who presented to the emergency department with chest pain and tachycardia following the Pfizer-BioNTech COVID-19 vaccination. Point-of-care ultrasound was performed prior to the return of laboratory studies and revealed depressed left ventricular systolic function. Point-of-care ultrasound may be a tool used to rapidly diagnose or risk stratify patients with potential post-COVID-19 vaccine myocarditis.

Viskin, D., et al. (2021). "Myocarditis Associated With COVID-19 Vaccination: Echocardiography, Cardiac Tomography, and Magnetic Resonance Imaging Findings." Circ Cardiovasc Imaging **14**(9): e013236.

Voleti, N., S. P. Reddy and P. Ssentongo (2022). "Myocarditis in SARS-CoV-2 infection vs. COVID-19 vaccination: A systematic review and meta-analysis." Front Cardiovasc Med **9**: 951314.

BACKGROUND: This study aimed to compare the incidence of myocarditis in COVID-19 vaccines and in severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) infection groups. METHODS: Electronic databases (MEDLINE, Scopus, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and the WHO Global Literature on Coronavirus Disease) and trial registries were searched up to May 2022, for randomized controlled trials and observational cohort studies reporting the risk of myocarditis associated with the COVID-19 vaccines and the risk associated with SARS-CoV-2 infection. We estimated the effect of COVID-19 infection and vaccines on rates of myocarditis by random-effects meta-analyses using the generic inverse variance method. Meta-regression analyses were conducted to assess the effect of sex and age on the incidence of myocarditis. RESULTS: We identified 22 eligible studies consisting of 55.5 million vaccinated cohorts and 2.5 million in the infection cohort. The median age was 49 years (interquartile range (IQR): 38-56), and 49% (IQR: 43 to 52%) were men. Of patients diagnosed with myocarditis (in both vaccination and COVID-19 cohort) 1.07% were hospitalized and 0.015% died. The relative risk (RR) for myocarditis was more than seven times higher in the infection group than in the vaccination group [RR: 15 (95% CI: 11.09-19.81, infection group] and RR: 2 (95% CI: 1.44-2.65, vaccine group). Of patients who developed myocarditis after receiving the vaccine or having the infection, 61% (IQR: 39-87%) were men. Meta-regression analysis indicated that men and younger populations had a higher risk of myocarditis. A slow decline in the rates of myocarditis was observed as a function of time from vaccination. The risk of bias was low. CONCLUSION: In this systematic review and meta-analysis, we found that the risk of myocarditis is more than seven fold higher in persons who were infected with the SARS-CoV-2 than in those who received the vaccine. These findings support the continued use of mRNA COVID-19 vaccines among all eligible persons per CDC and WHO recommendations.

Voltarelli, C. L., et al. (2022). "COVID-19-Induced Myocarditis and mRNA Vaccine-Related Pericarditis: A Case Report." Cureus **14**(8): e28440.

Acute inflammatory cardiac disease is an increasing cause of COVID-19 vaccine-induced complications. We report a case of acute pericarditis following the second dose of the COVID-19 vaccine (BNT162b2) in a 49-year-old woman with previous COVID-19-induced myocarditis and heart failure. A clinical presentation compatible with acute decompensated heart failure elevated troponin levels and a cardiac-MRI showing myocardial fibrosis and inflammatory pericardial effusion led to the diagnosis of perimyocarditis. She was treated with non-steroidal anti-inflammatory drugs (NSAIDs) and colchicine. Her condition improved in eight days. Physicians should be aware of the possible diagnosis of pericarditis and/or a myocardial injury after COVID-19 infection and vaccination.

Walker, P., et al. (2023). "Myocarditis in Australian children following SARS-CoV-2 infection or COVID-19 vaccination: a retrospective case series." Med J Aust **218**(10): 482-483.

Wang, M., et al. (2022). "Meta-Analysis of Risk of Myocarditis After Messenger RNA COVID-19 Vaccine." Am J Cardiol **167**: 155-157.

Watanabe, K., et al. (2022). "Case Report: Importance of MRI Examination in the Diagnosis and Evaluation of COVID-19 mRNA Vaccination Induced Myocarditis: Our Experience and Literature Review." Front Cardiovasc Med **9**: 844626.

Acute myocarditis is a rare but serious complication associated with mRNA-based coronavirus disease 2019 (COVID-19) vaccination. In this article, four COVID-19 mRNA vaccination induced myocarditis cases managed at our tertiary Medical Center have been discussed. Three patients had typical myocarditis. One patient suffered from atrioventricular block and heart failure, which required more intensive treatment, but eventually improved. Additionally, a review of cardiac magnetic resonance imaging (MRI) features related to the diagnosis of myocarditis showed that COVID-19 mRNA vaccine-associated myocarditis tend to have more late-gadolinium enhancement (LGE) accumulation in the inferior lateral wall direction. According to a report by the U.S. Centers for Disease Control and Prevention (CDC), the diagnosis of COVID-19 mRNA vaccine-associated myocarditis is based on clinical symptoms, altered myocardial enzymes, cardiac MRI finding, or histopathology. Cardiac MRI is relatively less invasive than myocardial biopsy and plays an important role in the diagnosis of myocarditis. This review may aid in the diagnosis of COVID-19 mRNA vaccine-associated myocarditis.

Weerts, V., et al. (2023). "[Facing COVID-19 : myocarditis following vaccination with mRNA SARS-CoV-2]." Rev Med Liege **78**(3): 141-146.

Myocarditis is a relatively uncommon and underdiagnosed heart disease. Its clinical presentation is variable, from pauci-symptomatic to a symptomatology of sudden chest pain. The latter mimics cardiological emergencies and must therefore be quickly discerned to guide the rest of the treatment. The treatment is mainly supportive and rarely directly etiological. This is a pathology that resurfaced with the onset of the COVID-19 pandemic but also with vaccination. We present here the case of a mRNA SARS-CoV-2 vaccine-induced myocarditis whose clinical manifestations impose a rapid decision concerning the differential diagnosis with an acute coronary syndrome.

Weintraub, E. S., M. E. Oster and N. P. Klein (2022). "Myocarditis or Pericarditis Following mRNA COVID-19 Vaccination." JAMA Netw Open **5**(6): e2218512.

Weiss, S. R. (2022). "Myocarditis Cases After mRNA-Based COVID-19 Vaccination in the US." JAMA **327**(20): 2019-2020.

Witberg, G., et al. (2021). "Myocarditis after Covid-19 Vaccination in a Large Health Care Organization." N Engl J Med **385**(23): 2132-2139.

BACKGROUND: Reports have suggested an association between the development of myocarditis and the receipt of messenger RNA (mRNA) vaccines against coronavirus disease 2019 (Covid-19), but the frequency and severity of myocarditis after vaccination

have not been extensively explored. METHODS: We searched the database of Clalit Health Services, the largest health care organization (HCO) in Israel, for diagnoses of myocarditis in patients who had received at least one dose of the BNT162b2 mRNA vaccine (Pfizer-BioNTech). The diagnosis of myocarditis was adjudicated by cardiologists using the case definition used by the Centers for Disease Control and Prevention. We abstracted the presentation, clinical course, and outcome from the patient's electronic health record. We performed a Kaplan-Meier analysis of the incidence of myocarditis up to 42 days after the first vaccine dose. RESULTS: Among more than 2.5 million vaccinated HCO members who were 16 years of age or older, 54 cases met the criteria for myocarditis. The estimated incidence per 100,000 persons who had received at least one dose of vaccine was 2.13 cases (95% confidence interval [CI], 1.56 to 2.70). The highest incidence of myocarditis (10.69 cases per 100,000 persons; 95% CI, 6.93 to 14.46) was reported in male patients between the ages of 16 and 29 years. A total of 76% of cases of myocarditis were described as mild and 22% as intermediate; 1 case was associated with cardiogenic shock. After a median follow-up of 83 days after the onset of myocarditis, 1 patient had been readmitted to the hospital, and 1 had died of an unknown cause after discharge. Of 14 patients who had left ventricular dysfunction on echocardiography during admission, 10 still had such dysfunction at the time of hospital discharge. Of these patients, 5 underwent subsequent testing that revealed normal heart function. CONCLUSIONS: Among patients in a large Israeli health care system who had received at least one dose of the BNT162b2 mRNA vaccine, the estimated incidence of myocarditis was 2.13 cases per 100,000 persons; the highest incidence was among male patients between the ages of 16 and 29 years. Most cases of myocarditis were mild or moderate in severity. (Funded by the Ivan and Francesca Berkowitz Family Living Laboratory Collaboration at Harvard Medical School and Clalit Research Institute.).

Wong, H. L., et al. (2022). "Risk of myocarditis and pericarditis after the COVID-19 mRNA vaccination in the USA: a cohort study in claims databases." Lancet **399**(10342): 2191-2199.

BACKGROUND: Several passive surveillance systems reported increased risks of myocarditis or pericarditis, or both, after COVID-19 mRNA vaccination, especially in young men. We used active surveillance from large health-care databases to quantify and enable the direct comparison of the risk of myocarditis or pericarditis, or both, after mRNA-1273 (Moderna) and BNT162b2 (Pfizer-BioNTech) vaccinations. METHODS: We conducted a retrospective cohort study, examining the primary outcome of myocarditis or pericarditis, or both, identified using the International Classification of Diseases diagnosis codes, occurring 1-7 days post-vaccination, evaluated in COVID-19 mRNA vaccinees aged 18-64 years using health plan claims databases in the USA. Observed (O) incidence rates were compared with expected (E) incidence rates estimated from historical cohorts by each database. We used multivariate Poisson regression to estimate the adjusted incidence rates, specific to each brand of vaccine, and incidence rate ratios (IRRs) comparing mRNA-1273 and BNT162b2. We used meta-analyses to pool the adjusted incidence rates and IRRs across databases. FINDINGS: A total of 411 myocarditis or pericarditis, or both, events were observed among 15 148 369 people aged 18-64 years who received 16 912 716 doses of BNT162b2 and 10 631 554 doses of mRNA-

1273. Among men aged 18-25 years, the pooled incidence rate was highest after the second dose, at 1.71 (95% CI 1.31 to 2.23) per 100 000 person-days for BNT162b2 and 2.17 (1.55 to 3.04) per 100 000 person-days for mRNA-1273. The pooled IRR in the head-to-head comparison of the two mRNA vaccines was 1.43 (95% CI 0.88 to 2.34), with an excess risk of 27.80 per million doses (-21.88 to 77.48) in mRNA-1273 recipients compared with BNT162b2. INTERPRETATION: An increased risk of myocarditis or pericarditis was observed after COVID-19 mRNA vaccination and was highest in men aged 18-25 years after a second dose of the vaccine. However, the incidence was rare. These results do not indicate a statistically significant risk difference between mRNA-1273 and BNT162b2, but it should not be ruled out that a difference might exist. Our study results, along with the benefit-risk profile, continue to support vaccination using either of the two mRNA vaccines. FUNDING: US Food and Drug Administration.

Wong, J., et al. (2022). "COVID-19 mRNA vaccine (Comirnaty)-induced myocarditis." Med J Aust **216**(3): 122-123.

Woo, W., et al. (2022). "Clinical characteristics and prognostic factors of myocarditis associated with the mRNA COVID-19 vaccine." J Med Virol **94**(4): 1566-1580.

To analyze the clinical presentation and outcomes of myocarditis after administration of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) messenger RNA (mRNA) vaccine. Nine case series and 15 case reports (74 patients) of myocarditis after administration of the BNT162b2 or mRNA-1273 vaccine were reviewed from PubMed, Scopus, Embase, and Web of Science. We analyzed clinical manifestations, diagnostic findings, and outcomes. In addition, we performed a pooled analysis and investigated risk factors leading to admission to the intensive care unit and recovery with conservative care. Most patients were male (94.6%), and the median age (range) was 17.6 (14-70) years. Patients who received the BNT162b2 (n = 58, 78.4%) vaccine presented fewer systemic symptoms and left ventricular dysfunction than mRNA-1273 recipients. Although patients under 20 years experienced more fever and myalgia, they had better ejection fraction and less prominent myocardial inflammation in magnetic resonance imaging than older patients. The clinical course of all patients was favorable without mortality, and one-third of patients resolved with conservative care alone. Risk factor analyses revealed that patients with gastrointestinal symptoms required intensive care (odds ratio: 20.3, 95% confidence interval 1.90-217, p = 0.013). The risk of fatality in myocarditis subjected to mRNA vaccination seems to be low. However, patients with gastrointestinal symptoms received more intensive care, and a significant proportion of patients recovered with conservative management.

Wu, Y. C., et al. (2023). "Bivalent mRNA COVID-19 Vaccine-Related Pericarditis on 18 F-FDG PET/CT." Clin Nucl Med **48**(8): e396-e397.

A 13-year-old boy was suspected with pericarditis after a second booster dose of bivalent mRNA COVID-19 vaccine. After specific preparation for cardiac inflammation with carbohydrate-free, high-fat diet, the 18 F-FDG PET/CT successfully demonstrated

simultaneous presentation of vaccination-related axillary lymphadenopathy and pericarditis without the interference of physiological myocardial uptake.

Yamada, T. (2023). "Acute myocarditis after the third dose of COVID-19 mRNA-1273 vaccine." J Gen Fam Med **24**(3): 188-189.

Myocarditis caused by the mRNA-1273 coronavirus disease 2019 vaccine must be considered for patients complaining of acute constant general fatigue postvaccination.

Yamamoto, J., et al. (2023). "Myocarditis with ventricular tachycardia following bivalent COVID-19 mRNA vaccination." CJC Open.

Yamamoto, M., et al. (2022). "Pathological findings of clinically suspected myocarditis temporally associated with COVID-19 vaccination." Eur J Heart Fail **24**(6): 1132-1138.

Reports on the pathological findings of patients with myocarditis after coronavirus disease 2019 (COVID-19) vaccination are limited. We present a case series of four patients with clinically suspected myocarditis temporally associated with COVID-19 vaccination who underwent endomyocardial biopsy with no evidence of viral genomes in tissue specimens. Two patients had fulminant myocarditis with marked inflammatory cell infiltration comprised mostly of CD8+ T-cells and macrophages, and the other two had suspected myocarditis based on the biochemical evidence of myocardial injury and ST changes on an electrocardiogram. However, they did not meet the histological criteria of myocarditis. Immunosuppressive therapy effectively reduced myocardial damage, and all four patients had improved clinical courses. Temporal association does not prove causation, and it cannot be excluded that the two biopsy-proven cases reported are simply a random association of a naturally occurring virus-negative immune-mediated lymphocytic myocarditis occurring after vaccination.

Yamamoto, S., Y. Arita and N. Ogasawara (2022). "Myocarditis Following the Second Dose of COVID-19 Vaccination in a Japanese Adolescent." Cureus **14**(3): e23474.

As COVID-19 vaccines continue to be deployed worldwide, countries are now planning to vaccinate their pediatric populations as well. However, several vaccine-related adverse events, including myocarditis, have been reported. Although the incidence of myocarditis after BNT162b2 vaccination is low, it is higher, particularly after receiving the second dose, among young male recipients. A 13-year-old male adolescent presented with chest pain after the second dose of the BNT162b2 vaccination. Electrocardiography, echocardiography, cardiac magnetic resonance imaging, and blood examinations were consistent with myocarditis. He was treated conservatively because his symptoms were relatively mild. In Japan, it is expected that the chances of diagnosing vaccine-related myocarditis will increase as more children are getting vaccinated. Our case report raises concerns to physicians that the COVID-19 vaccination may cause rare cases of myocarditis, which must always be considered as a differential diagnosis.

Yap, J., et al. (2022). "Pericarditis and myocarditis after COVID-19 mRNA vaccination in a nationwide setting." Ann Acad Med Singap **51**(2): 96-100.

INTRODUCTION: Despite reports suggesting an association between COVID-19 mRNA vaccination and pericarditis and myocarditis, detailed nationwide population-based data are sparsely available. We describe the incidence of pericarditis and myocarditis by age categories and sex after COVID-19 mRNA vaccination from a nationwide mass vaccination programme in Singapore. METHODS: The incidence of adjudicated cases of pericarditis and myocarditis following COVID-19 mRNA vaccination that were reported to the vaccine safety committee between January to July 2021 was compared with the background incidence of myocarditis in Singapore. RESULTS: As of end July 2021, a total of 34 cases were reported (9 pericarditis only, 14 myocarditis only, and 11 concomitant pericarditis and myocarditis) with 7,183,889 doses of COVID-19 mRNA vaccine administered. Of the 9 cases of pericarditis only, all were male except one. The highest incidence of pericarditis was in males aged 12-19 years with an incidence of 1.11 cases per 100,000 doses. Of the 25 cases of myocarditis, 80% (20 cases) were male and the median age was 23 years (range 12-55 years) with 16 cases after the second dose. A higher-than-expected number of cases were seen in males aged 12-19 and 20-29 years, with incidence rates of 3.72 and 0.98 case per 100,000 doses, respectively. CONCLUSION: Data from the national registry in Singapore indicate an increased incidence of pericarditis and myocarditis in younger men after COVID-19 mRNA vaccination.

Yasmin, F., et al. (2023). "Adverse events following COVID-19 mRNA vaccines: A systematic review of cardiovascular complication, thrombosis, and thrombocytopenia." Immun Inflamm Dis **11**(3): e807.

BACKGROUND AND OBJECTIVES: Since publishing successful clinical trial results of mRNA coronavirus disease 2019 (COVID-19) vaccines in December 2020, multiple reports have arisen about cardiovascular complications following the mRNA vaccination. This study provides an in-depth account of various cardiovascular adverse events reported after the mRNA vaccines' first or second dose including pericarditis/myopericarditis, myocarditis, hypotension, hypertension, arrhythmia, cardiogenic shock, stroke, myocardial infarction/STEMI, intracranial hemorrhage, thrombosis (deep vein thrombosis, cerebral venous thrombosis, arterial or venous thrombotic events, portal vein thrombosis, coronary thrombosis, microvascular small bowel thrombosis), and pulmonary embolism. METHODS: A systematic review of original studies reporting confirmed cardiovascular manifestations post-mRNA COVID-19 vaccination was performed. Following the PRISMA guidelines, electronic databases (PubMed, PMC NCBI, and Cochrane Library) were searched until January 2022. Baseline characteristics of patients and disease outcomes were extracted from relevant studies. RESULTS: A total of 81 articles analyzed confirmed cardiovascular complications post-COVID-19 mRNA vaccines in 17,636 individuals and reported 284 deaths with any mRNA vaccine. Of 17,636 cardiovascular events with any mRNA vaccine, 17,192 were observed with the BNT162b2 (Pfizer-BioNTech) vaccine, 444 events with mRNA-1273 (Moderna). Thrombosis was frequently reported with any mRNA vaccine (n = 13,936), followed by stroke (n = 758), myocarditis (n = 511), myocardial infarction (n = 377), pulmonary embolism (n = 301), and arrhythmia (n = 254). Stratifying the results by vaccine type showed that thrombosis (80.8%) was

common in the BNT162b2 cohort, while stroke (39.9%) was common with mRNA-1273 for any dose. The time between the vaccination dosage and the first symptom onset averaged 5.6 and 4.8 days with the mRNA-1273 vaccine and BNT162b2, respectively. The mRNA-1273 cohort reported 56 deaths compared to the 228 with BNT162b2, while the rest were discharged or transferred to the ICU. CONCLUSION: Available literature includes more studies with the BNT162b2 vaccine than mRNA-1273. Future studies must report mortality and adverse cardiovascular events by vaccine types.

Yeni, M. (2023). "COVID-19 BNT162b2 mRNA vaccine induced myocarditis with left ventricular thrombus in a young male." Acta Cardiol **78**(4): 483-485.

Yih, W. K., et al. (2023). "A broad assessment of covid-19 vaccine safety using tree-based data-mining in the vaccine safety datalink." Vaccine **41**(3): 826-835.
BACKGROUND: Except for spontaneous reporting systems, vaccine safety monitoring generally involves pre-specifying health outcomes and post-vaccination risk windows of concern. Instead, we used tree-based data-mining to look more broadly for possible adverse events after Pfizer-BioNTech, Moderna, and Janssen COVID-19 vaccination. METHODS: Vaccine Safety Datalink enrollees receiving >/=1 dose of COVID-19 vaccine in 2020-2021 were followed for 70 days after Pfizer-BioNTech or Moderna and 56 days after Janssen vaccination. Incident diagnoses in inpatient or emergency department settings were analyzed for clustering within both the hierarchical ICD-10-CM code structure and the post-vaccination follow-up period. We used the self-controlled tree-temporal scan statistic and TreeScan software. Monte Carlo simulation was used to estimate p-values; p = 0.01 was the pre-specified cut-off for statistical significance of a cluster. RESULTS: There were 4.1, 2.6, and 0.4 million Pfizer-BioNTech, Moderna, and Janssen vaccinees, respectively. Clusters after Pfizer-BioNTech vaccination included: (1) unspecified adverse effects, (2) common vaccine reactions, such as fever, myalgia, and headache, (3) myocarditis/pericarditis, and (4) less specific cardiac or respiratory symptoms, all with the strongest clusters generally after Dose 2; and (5) COVID-19/viral pneumonia/sepsis/respiratory failure in the first 3 weeks after Dose 1. Moderna results were similar but without a significant myocarditis/pericarditis cluster. Further investigation suggested the fifth signal group was a manifestation of mRNA vaccine effectiveness after the first 3 weeks. Janssen vaccinees had clusters of unspecified or common vaccine reactions, gait/mobility abnormalities, and muscle weakness. The latter two were deemed to have arisen from confounding related to practices at one site. CONCLUSIONS: We detected post-vaccination clusters of unspecified adverse effects, common vaccine reactions, and, for the mRNA vaccines, chest pain and palpitations, as well as myocarditis/pericarditis after Pfizer-BioNTech Dose 2. Unique advantages of this data mining are its untargeted nature and its inherent adjustment for the multiplicity of diagnoses and risk intervals scanned.

Yonker, L. M., et al. (2023). "Circulating Spike Protein Detected in Post-COVID-19 mRNA Vaccine Myocarditis." Circulation **147**(11): 867-876.

BACKGROUND: Cases of adolescents and young adults developing myocarditis after vaccination with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-targeted mRNA vaccines have been reported globally, but the underlying immunoprofiles of these individuals have not been described in detail. METHODS: From January 2021 through February 2022, we prospectively collected blood from 16 patients who were hospitalized at Massachusetts General for Children or Boston Children's Hospital for myocarditis, presenting with chest pain with elevated cardiac troponin T after SARS-CoV-2 vaccination. We performed extensive antibody profiling, including tests for SARS-CoV-2-specific humoral responses and assessment for autoantibodies or antibodies against the human-relevant virome, SARS-CoV-2-specific T-cell analysis, and cytokine and SARS-CoV-2 antigen profiling. Results were compared with those from 45 healthy, asymptomatic, age-matched vaccinated control subjects. RESULTS: Extensive antibody profiling and T-cell responses in the individuals who developed postvaccine myocarditis were essentially indistinguishable from those of vaccinated control subjects, despite a modest increase in cytokine production. A notable finding was that markedly elevated levels of full-length spike protein (33.9+/-22.4 pg/mL), unbound by antibodies, were detected in the plasma of individuals with postvaccine myocarditis, whereas no free spike was detected in asymptomatic vaccinated control subjects (unpaired t test; P<0.0001). CONCLUSIONS: Immunoprofiling of vaccinated adolescents and young adults revealed that the mRNA vaccine-induced immune responses did not differ between individuals who developed myocarditis and individuals who did not. However, free spike antigen was detected in the blood of adolescents and young adults who developed post-mRNA vaccine myocarditis, advancing insight into its potential underlying cause.

Yu, C. K., et al. (2023). "Cardiovascular Assessment up to One Year After COVID-19 Vaccine-Associated Myocarditis." Circulation **148**(5): 436-439.

Yu, X. (2022). "Note the distinction between myocarditis, novel coronavirus myocarditis and COVID-19 vaccine-associated myocarditis." QJM **115**(10): 695.

Zhou, M., et al. (2023). "Case report: Coronavirus Disease 2019 (COVID-19) modified RNA vaccination-induced Adult-Onset Still's Disease with fulminant myocarditis as initial presentation." Front Cardiovasc Med **10**: 1066699.

Myocarditis is a rare complication of Coronavirus Disease 2019 (COVID-19) vaccination. We report a case of an elderly female who presented initially with acute myocarditis, fulminant heart failure, and atrial fibrillation after receiving a modified ribonucleic acid (mRNA) vaccine (BNT162b2). Unlike other patients with vaccine-induced myocarditis, she developed persistent fever, sore throat, polyarthralgia, diffuse macular rash, and lymphadenopathy. After extensive investigation, she was diagnosed with post-vaccination Adult-Onset Still's Disease. The systemic inflammation gradually subsided after the use of non-steroidal anti-inflammatory drugs and systemic steroids. She was discharged from hospital with stable hemodynamics. Methotrexate was subsequently given to maintain long-term remission.

Zornitzki, L., et al. (2022). "Immune Checkpoint Inhibitor-Induced Myocarditis vs. COVID-19 Vaccine-Induced Myocarditis-Same or Different?" Life (Basel) **12**(9).

Immune checkpoint inhibitor (ICI) and coronavirus disease 2019 (COVID-19) vaccine-induced myocarditis possibly share common mechanisms secondary to overactivation of the immune system. We aimed to compare the presenting characteristics of ICIs and COVID-19 vaccine-induced myocarditis. We performed a retrospective analysis of characteristics of patients diagnosed with either ICIs or COVID-19 vaccine-induced myocarditis and compared the results to a control group of patients diagnosed with acute viral myocarditis. Eighteen patients diagnosed with ICIs (ICI group) or COVID-19 vaccine (COVID-19 vaccine group)-induced myocarditis, and 20 patients with acute viral myocarditis (Viral group) were included. The ICI group presented mainly with dyspnea vs. chest pain and fever among the COVID-19 vaccine and Viral groups. Peak median high sensitivity Troponin I was markedly lower in the ICI group (median 619 vs. 15,527 and 7388 ng/L, $p = 0.004$). While the median left ventricular (LV) ejection fraction was 60% among all groups, the ICI group had a lower absolute mean LV global longitudinal strain (13%) and left atrial conduit strain (17%), compared to the COVID-19 vaccine (17% and 30%) and Viral groups (18% and 37%), $p = 0.016$ and $p = 0.001$, respectively. Despite a probable similar mechanism, ICI-induced myocarditis's presenting characteristics differed from COVID-19 vaccine-induced myocarditis.

Neurologic, non-stroke

Ballout, A. A., et al. (2022). "A Single-Health System Case Series of New-Onset CNS Inflammatory Disorders Temporally Associated With mRNA-Based SARS-CoV-2 Vaccines." Front Neurol **13**: 796882.

BACKGROUND: Since 2020, over 250 million doses of mRNA-based SARS-CoV-2 vaccines have been administered in the United States and hundreds of millions worldwide between the Pfizer-BioNTech and Moderna SARS-CoV-2 vaccines. To date, there have been rare reports associating mRNA-based SARS-CoV-2 vaccines with episodes of inflammatory and autoimmune CNS disorders. We report a case series of five patients with new-onset neurological disorders of inflammatory or immunological origin temporally associated with these vaccines. METHODS: A case-series of five patients within a single 23-hospital health system who developed new-onset CNS inflammatory disease within 2 weeks of receiving a dose of an mRNA-based SARS-CoV-2 vaccine. RESULTS: Five cases of post-vaccination CNS disorders of immune origin (fatal ADEM; n = 1, new-onset NMOSD; n = 2, new-clinical onset MS-like syndrome but with preexisting clinically silent mild demyelination; n = 1, meningoencephalitis; n = 1) observed within 2 weeks of inoculation with either the first or second dose of mRNA-based SARS-CoV-2 vaccines (Moderna = 3, Pfizer = 2). DISCUSSION: To our knowledge, these are among the emerging cases of CNS adverse events of immunological or inflammatory origin. These findings should be interpreted with great caution as they neither prove a mechanistic link nor imply a potential long-term increased risk in post-vaccination CNS autoimmunity. Larger prospective studies assessing the potential association between mRNA-based vaccination and the development of neurological adverse events of suspected immune origin, particularly among those with underlying CNS or systemic autoimmune disorders, are needed. The use of mRNA-based SARS-CoV-2 vaccines should continue to be strongly encouraged given their high efficacy in overcoming this pandemic.

Bellucci, M., et al. (2022). "Case Report: Post-COVID-19 Vaccine Recurrence of Guillain-Barre Syndrome Following an Antecedent Parainfectious COVID-19-Related GBS." Front Immunol **13**: 894872.

Guillain-Barre syndrome (GBS) is an autoimmune neurological disorder often preceded by viral illnesses or, more rarely, vaccinations. We report on a unique combination of postcoronavirus disease 2019 (COVID-19) vaccine GBS that occurred months after a parainfectious COVID-19-related GBS. Shortly after manifesting COVID-19 symptoms, a 57-year-old man developed diplopia, right-side facial weakness, and gait instability that, together with electrophysiology and cerebrospinal fluid examinations, led to a diagnosis of post-COVID-19 GBS. The involvement of cranial nerves and IgM seropositivity for ganglioside GD1b were noteworthy. COVID-19 pneumonia, flaccid tetraparesis, and autonomic dysfunction prompted his admission to ICU. He recovered after therapy with intravenous immunoglobulins (IVIg). Six months later, GBS recurred shortly after the first dose of the Pfizer/BioNTech vaccine. Again, the GBS diagnosis was confirmed by

cerebrospinal fluid and electrophysiology studies. IgM seropositivity extended to multiple gangliosides, namely for GM3/4, GD1a/b, and GT1b IgM. An IVIg course prompted complete recovery. This case adds to other previously reported observations suggesting a possible causal link between SARS-CoV-2 and GBS. Molecular mimicry and anti-idiotype antibodies might be the underlying mechanisms. Future COVID-19 vaccinations/revaccinations in patients with previous para-/post-COVID-19 GBS deserve a reappraisal, especially if they are seropositive for ganglioside antibodies.

Bonifacio, G. B., et al. (2022). "Bilateral facial weakness with paraesthesia variant of Guillain-Barre syndrome following Vaxzevria COVID-19 vaccine." J Neurol Neurosurg Psychiatry **93**(3): 341-342.

Cho, S. Y., et al. (2023). "Transverse myelitis caused by herpes zoster following COVID-19 vaccination: A case report." World J Clin Cases **11**(6): 1419-1425.

BACKGROUND: Transverse myelitis (TM) is characterized by sudden lower extremity progressive weakness and sensory impairment, and most patients have a history of advanced viral infection symptoms. A variety of disorders can cause TM in association with viral or nonviral infection, vascular, neoplasia, collagen vascular, and iatrogenic, such as vaccination. Vaccination has become common through the global implementation against coronavirus disease 2019 (COVID-19) and reported complications like herpes zoster (HZ) activation has increased. CASE SUMMARY: This is a 68-year-old woman who developed multiple pustules and scabs at the T6-T9 dermatome site 1 wk after vaccination with the COVID-19 vaccine (Oxford/AstraZeneca ([ChAdOx1Srecombinant]). The patient had a paraplegia aggravation 3 wk after HZ symptoms started. Spinal magnetic resonance imaging (MRI) showed transverse myelitis at the T6-T9 Level. Treatment was acyclovir with steroids combined with physical therapy. Her neurological function was slowly restored by Day 17. CONCLUSION: HZ developed after COVID-19 vaccination, which may lead to more severe complications. Therefore, HZ treatment itself should not be delayed. If neurological complications worsen after appropriate management, an immediate diagnostic procedure, such as magnetic resonance imaging and laboratory tests, will start and should treat the neurological complications.

da Gama, P. D., et al. (2022). "Extensive Longitudinal Transverse Myelitis Temporally Related to the Use of AZD1222, AstraZeneca COVID-19 Vaccine: Cerebrospinal Fluid Analysis and Recent Data Review." Case Rep Neurol Med **2022**: 8999853.

While mass immunization against coronavirus disease 2019 (COVID-19) rolls out around the globe, safety concerns and adverse events that need prompt evaluation are also emerging. Neurological complications such as transverse myelitis raise concerns as cases were observed in clinical trials. Cerebrospinal fluid analysis is routine in these cases and the characteristics of the abnormalities found are of great help not only in establishing the diagnosis but also in understanding this rare condition. We present a case of extensive longitudinal transverse myelitis after vaccination with AZD1222, AstraZeneca COVID-19 vaccine, which was the first case reported in Brazil. The abnormalities found in

the study of the cerebrospinal fluid in our case are reported and discussed using data from recent publications.

Doi, K., et al. (2022). "Cervical Transverse Myelitis Following COVID-19 Vaccination." NMC Case Rep J **9**: 145-149.

Various COVID-19 vaccines are associated with numerous adverse side effects. Associations between vaccinations and neurological disorders, such as transverse myelitis, stroke, Bell's palsy, acute disseminated encephalomyelitis, and Guillain-Barre syndrome, have been reported. A 27-year-old Japanese woman presented with paresthesia four days after receiving a second dose of the COVID-19 vaccine. One month after vaccination, she started to feel left lower limb weakness, and her symptoms almost improved after two steroid pulse therapies. Spinal cord tumor biopsy could potentially help make a definitive diagnosis in clinical situations. However, it is very important to review the patient's medical history, including vaccinations received, before performing a direct spinal cord biopsy, which is invasive and does not guarantee a definitive diagnosis.

Einstein, E. H., et al. (2021). "New-Onset Neurologic Symptoms and Related Neuro-Oncologic Lesions Discovered After COVID-19 Vaccination: Two Neurosurgical Cases and Review of Post-Vaccine Inflammatory Responses." Cureus **13**(6): e15664.

A global effort is underway to distribute coronavirus disease 2019 (COVID-19) vaccines to limit the crisis. Although adverse events related to vaccination are rare, there have been cases of new-onset neurologic symptoms following vaccination. We present two cases of new-onset neurologic symptoms post-vaccination that, upon further workup, revealed two different neuro-oncologic processes requiring neurosurgical intervention and further treatment. We hypothesize that despite these processes being unrelated to vaccination, the COVID-19 vaccines may induce an inflammatory cascade with the ability to uncover underlying sinister pathology. Our report therefore emphasizes the need for careful evaluation in the setting of new-onset neurologic symptoms after COVID-19 vaccination.

Erdem, N. S., et al. (2021). "Acute transverse myelitis after inactivated COVID-19 vaccine." Ideggyogy Sz **74**(7-08): 273-276.

Vaccines against the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been rapidly developed to prevent coronavirus disease 2019 (COVID-19) pandemic. There is increasing safety concerns regarding COVID-19 vaccines. We report a 78-year old woman who was presented with tetraparesis, paresthesias of bilateral upper extremities, and urinary retention of one-day duration. Three weeks before these symptoms, she was vaccinated with CoronaVAC vaccine (Sinovac Life Sciences, China). Spine magnetic resonance imaging showed longitudinally extensive transverse myelitis (TM) from the C1 to the T3 spinal cord segment. An extensive diagnostic workup was performed to exclude other possible causes of TM. We suggest that longitudinally extensive TM may be associated with COVID-19 vaccination in this case. To the best of our knowledge, this is the first report of longitudinally extensive TM developing after

CoronaVac vaccination. Clinicians should be aware of neurological symptoms after vaccination of COVID-19.

Esechie, A., et al. (2022). "A case report of longitudinal extensive transverse myelitis: immunotherapy related adverse effect vs. COVID-19 related immunization complications." Int J Neurosci: 1-4.

Background: Transverse myelitis (TM) is a rare, acquired neuro-immunological spinal cord disorder that occurs with rapid onset of motor weakness, sensory deficits with bowel and bladder dysfunction. Patients being treated with immune checkpoint inhibitors (ICIs) for advanced malignancy have a known higher propensity of developing neuro immune complications. With the advent of COVID-19 pandemic there have been reported cases of TM with COVID-19 immunization. The reported infrequency of TM with both of the aforementioned causes makes delineation of the etiology challenging.Methods: We present a patient with metastatic small cell lung cancer (SCLC) on maintenance Atezolizumab immunotherapy who developed longitudinal extensive transverse myelitis (LETM) after administration of second dose of COVID-19 mRNA vaccine one day prior to presenting symptoms of acute paralysis of the lower extremity, sensory loss from chest down with overflow incontinence. A clinical diagnosis of myelopathy was supported by MRI of the spine illustrating enhancing lesions from C7-T7 concerning for LETM.Results: A 5-day course of pulsed methylprednisolone followed by therapeutic plasma exchange for 3 days resulted in only minimal improvement in the neurologic exam with increased strength in his lower extremities while the sensory level remained unchanged.Conclusions: This case demonstrates the complication and symptomatology of TM in the setting of anti-PD-L1 monoclonal antibody with coincidental COVID-19 mRNA vaccine administration. The causal relationship between the vaccine and LETM is difficult to establish. However, the presence of a known inciting factor hints at a possible exaggeration of the existing neuro-inflammatory process.

Filfilan, N. N., et al. (2023). "Effects of Different Types of COVID-19 Vaccines on Menstrual Cycles of Females of Reproductive Age Group (15-49): A Multinational Cross-Sectional Study." Cureus **15**(5): e39640.

Background Globally, there are more than 474 million cases and around 6 million deaths due to COVID-19. The case fatality rate was 0.5-2.8% while for 80-89 years old, it was 3.7-14.8%. Given the seriousness of this infection, prevention becomes critical. Hence, the introduction of vaccines led to a significant reduction (> 75% protection) in COVID-19 cases. On the other hand, patients seeking help for serious pulmonary, cardiovascular, neurological, and gynecological complaints have also been recorded. Clinical studies on the effects of vaccination focused mostly on life-or-death results rather than reproductive outcomes such as menstruation, fertility, or even pregnancy outcomes. This survey was conducted to get more evidence on the association between menstrual cycle irregularities and some globally most prevalent COVID-19 vaccines. Methods An online cross-sectional survey was conducted by a team from Taif University, Kingdom of Saudi Arabia, from January to June 2022 on females within the reproductive age group (15-49 years) using a semi-structured questionnaire. Data were analyzed using SPSS Statistics

version 22.0 and presented as frequency and percentage. The chi-square test was applied for the association and a p-value of <0.05 was considered significant. Results A total of 2381 responses were included. The mean age of respondents was 25+/-7.7 years. Around 1604 (67%) participants observed post-vaccination menstrual changes, and the findings were significant (p< 0.001). A strong association (p=.008) was found between the type of vaccine and changes in the menstrual cycle in participants (AstraZeneca 11 (36%)) after one dose. A strong association (p=.004) was also seen between the type of vaccine (Pfizer 543 (83%)) and menstrual changes after the booster dose. Cycles became irregular 180 (36%) or prolonged 144 (29%) in females inoculated with Pfizer after two doses of vaccination (p=0.012). Conclusion Post-vaccination menstrual irregularities were reported by females of reproductive age, especially the new vaccines. Prospective studies for similar insights are needed. Finding the co-occurring impacts of vaccination and COVID-19 infections in the wake of the emerging new long-haul COVID-19 phenomena is crucial for reproductive health.

Finsterer, J. (2023). "Symmetric DWI hyperintensities in CMT1X patients after SARS-CoV-2 vaccination should not be classified as stroke-like lesions." World J Clin Cases **11**(16): 3929-3931.

The interesting case report by Zhang et al on a 39 years-old male with Charcot-Marie-Tooth disease type 1X has several limitations. The causal relation between the two episodes of asyndesis, dysphagia, and dyspnea 37 d after the second dose of the inactivated severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) vaccine (Beijing Institute of Biological Products Co., Ltd., Beijing, China) remains unproven. SARS-CoV-2 vaccination cannot trigger a genetic disorder. It also remains unsupported that the patient had a stroke-like episode (SLE). SLEs occur in mitochondrial disorders but not in hereditary neuropathies. Because of the episodic nature of the neurological symptoms, it is critical to rule out seizures. Overall, the causal relation between vaccination and the neurological complications remains unsupported and the interpretation of symmetric diffusion-weighted imaging lesions on cerebral magnetic resonance imaging should be carefully revised.

Guo, W., et al. (2022). "Profiling COVID-19 Vaccine Adverse Events by Statistical and Ontological Analysis of VAERS Case Reports." Front Pharmacol **13**: 870599.

Since the beginning of the COVID-19 pandemic, vaccines have been developed to mitigate the spread of SARS-CoV-2, the virus that causes COVID-19. These vaccines have been effective in reducing the rate and severity of COVID-19 infection but also have been associated with various adverse events (AEs). In this study, data from the Vaccine Adverse Event Reporting System (VAERS) was queried and analyzed via the Cov19VaxKB vaccine safety statistical analysis tool to identify statistically significant (i.e., enriched) AEs for the three currently FDA-authorized or approved COVID-19 vaccines. An ontology-based classification and literature review were conducted for these enriched AEs. Using VAERS data as of 31 December 2021, 96 AEs were found to be statistically significantly associated with the Pfizer-BioNTech, Moderna, and/or Janssen COVID-19 vaccines. The Janssen COVID-19 vaccine had a higher crude reporting rate of AEs compared to the Moderna and Pfizer COVID-19 vaccines. Females appeared to have a higher case report

frequency for top adverse events compared to males. Using the Ontology of Adverse Event (OAE), these 96 adverse events were classified to different categories such as behavioral and neurological AEs, cardiovascular AEs, female reproductive system AEs, and immune system AEs. Further statistical comparison between different ages, doses, and sexes was also performed for three notable AEs: myocarditis, GBS, and thrombosis. The Pfizer vaccine was found to have a closer association with myocarditis than the other two COVID-19 vaccines in VAERS, while the Janssen vaccine was more likely to be associated with thrombosis and GBS AEs. To support standard AE representation and study, we have also modeled and classified the newly identified thrombosis with thrombocytopenia syndrome (TTS) AE and its subclasses in the OAE by incorporating the Brighton Collaboration definition. Notably, severe COVID-19 vaccine AEs (including myocarditis, GBS, and TTS) rarely occur in comparison to the large number of COVID-19 vaccinations administered in the United States, affirming the overall safety of these COVID-19 vaccines.

Hsiao, Y. T., et al. (2021). "Acute Transverse Myelitis after COVID-19 Vaccination." Medicina (Kaunas) **57**(10).

The adverse effects of the COVID-19 vaccine have been discovered as the rapid application of the vaccines continues. Neurological complications such as transverse myelitis raise concerns as cases were observed in clinical trials. Transverse myelitis is a rare immune-mediated disease with spinal cord neural injury, resulting in neurological deficits in the motor, sensory, and autonomic system. Vaccine-related transverse myelitis is even rarer. We present a case of acute transverse myelitis after vaccination against COVID-19 with the ChAdOx1 nCOV-19 vaccine (AZD1222), which was the first case reported in Taiwan. Although it rarely occurs, post-vaccination neurological complications should not be ignored. As the pandemic of SARS-CoV-2 continues to spread and concern about vaccination efficacy and safety rises, heterologous vaccination were implemented in health public policy in several countries. A literature review of several clinical trials shows promising effects of mix-and-match vaccination. Further study on different combinations of vaccines can be expected.

Khan, E., et al. (2022). "Acute transverse myelitis following SARS-CoV-2 vaccination: a case report and review of literature." J Neurol **269**(3): 1121-1132.

OBJECTIVE: To report a unique case and literature review of post COVID-19 vaccination associated transverse myelitis and with abnormal MRI findings. BACKGROUND: Coronavirus disease have been reported to be associated with several neurological manifestations such as stroke, Guillain-Barre syndrome, meningoencephalitis amongst others. There are only a few reported cases of transverse myelitis with the novel coronavirus (n-CoV-2). Here, we identify a post COVID-19 vaccination patient diagnosed with acute transverse myelitis. METHOD: A retrospective chart review of a patient diagnosed with post SARS-CoV-2 vaccination acute transverse myelitis, and a review of literature of all the reported cases of other post vaccination and transverse myelitis, from December 1st, 2010 till July 15th, 2021, was performed. CONCLUSION: To our knowledge, this is the one of early reported case of transverse myelitis and with post

SARS-CoV-2 vaccination, who responded well to plasmapheresis. Further studies would be recommended to identify the underlying correlation between COVID-19 vaccination and transverse myelitis.

Khan, Z., et al. (2022). "Interstitial Lung Disease and Transverse Myelitis: A Possible Complication of COVID-19 Vaccine." Cureus **14**(2): e21875.

The clinical impact of the severe acute respiratory syndrome 2 (SARS-CoV-2) pandemic is growing, and vaccine-associated complications are becoming more evident. Although global vaccination against coronavirus disease 19 (COVID-19) is an outstanding accomplishment, safety concerns and adverse outcomes are also emerging that need to be addressed promptly. The most reported side effects of the COVID-19 vaccine include fever, myalgia, headache, and injection site reactions. Acute transverse myelitis (ATM) and interstitial lung disease (ILD) following the CoronaVac vaccine are rarely reported. We report a case of ILD followed by acute myelopathy in a female who presented with dyspnea, cough, and fever after the second dose of the COVID-19 vaccine. On the third day of admission, she developed paresthesia and bilateral upper and lower limb weakness. She was diagnosed with ILD and ATM due to the COVID-19 vaccine based on imaging and detailed investigations after ruling out all possible causes. Her neurological and respiratory manifestations improved gradually after starting intravenous methylprednisolone.

Kobayashi, K., et al. (2023). "Multisystem inflammatory syndrome and lymphohistiocytic myocarditis after Covid-19 vaccine in a middle-aged woman." ESC Heart Fail **10**(2): 1435-1439.

We describe a 51-year-old otherwise healthy woman hospitalized for hypotension, fever, and weakness 4 days after the second-dose Covid-19 mRNA vaccine. Elevated inflammatory markers, natriuretic peptide levels and troponin levels, and slightly reduced left ventricular ejection fraction of 50% were noted. We also found the multiple organ damage, including mucocutaneous, gastrointestinal, and neurologic systems. In addition, we revealed the positive results for anti-nucleocapsid SARS-CoV-2 IgG, albeit negative for SARS-CoV-2 polymerase chain reaction testing, suggesting the prior asymptomatic Covid-19 infection. We finally diagnosed her as multisystem inflammatory syndrome after vaccination. Of note, we obtained myocardial specimen from the patients and demonstrated the lymphohistiocytic myocarditis, which is a rare form of myocarditis.

Kolahchi, Z., M. Khanmirzaei and A. Mowla (2022). "Acute ischemic stroke and vaccine-induced immune thrombotic thrombocytopenia post COVID-19 vaccination; a systematic review." J Neurol Sci **439**: 120327.

INTRODUCTION: One of the rare but potentially serious side effects of COVID-19 vaccination is arterial and venous thrombosis. Acute ischemic stroke (AIS) cases have been reported post COVID-19 vaccination. Herein, we systematically reviewed the reported cases of AIS after COVID-19 vaccination. METHOD: This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline. We searched PubMed and Scopus until April 14, 2022 to

find studies that reported AIS post COVID-19 vaccination. RESULTS: We found 447 articles. From those, 140 duplicates were removed. After screening and excluding irrelevant articles, 29 studies (43 patients) were identified to be included. From all cases, 22 patients (51.1%) were diagnosed with AIS associated with Vaccine-induced immune thrombotic thrombocytopenia (VITT). Among AIS associated with VITT group, all received viral vector vaccines except one. The majority of cases with AIS and VITT were female (17 cases, 77.2%) and aged below 60 years (15 cases, 68%). Fourteen patients (32.5%) had additional thrombosis in other sites. Four of them (0.09%) showed concurrent CVST and ischemic stroke. Hemorrhagic transformation following AIS occurred in 7 patients (16.27%). Among 43 patients with AIS, at least 6 patients (14%) died during hospital admission. CONCLUSION: AIS has been reported as a rare complication within 4 weeks post COVID-19 vaccination, particularly with viral vector vaccines. Health care providers should be familiar with this rare consequence of COVID-19 vaccination in particular in the context of VITT to make a timely diagnosis and appropriate treatment plan.

Kubota, T., et al. (2021). "Case Report: Isolated, unilateral oculomotor palsy with anti-GQ1b antibody following COVID-19 vaccination." F1000Res **10**: 1142.

Neurological complications following vaccinations are extremely rare, but cannot be eliminated. Here, we report the first case of unilateral oculomotor nerve palsy (ONP) with anti-GQ1b antibody after receiving the Pfizer-BioNTech COVID-19 (BNT162b2) mRNA vaccine. A 65-year-old man developed diplopia and ptosis in the right eye 17 days after vaccination, without preceding infection. Neurological examination revealed mild blepharoptosis, limitation of adduction, and vertical gaze on the right side. Increased levels of anti-GQ1b ganglioside antibody in the serum and albuminocytologic dissociation in the cerebrospinal fluid were detected. Cranial magnetic resonance imaging showed swelling and enhancement of the right oculomotor nerve. The patient was diagnosed with right ONP accompanied with anti-GQ1b antibody, and intravenous immunoglobulin (IVIG) therapy for 5 days was administered. The limitation of adduction and vertical gaze improved, and ptosis markedly resolved after IVIG treatment. Given the temporal sequence of disease progression, laboratory findings, and a favorable response to IVIG, a causal relationship cannot be ruled out between the occurrence of ONP and COVID-19 immunization. Since immunomodulatory treatments significantly hasten the recovery and minimize the residual symptoms in anti-GQ1b antibody syndrome, clinicians should be aware of this clinical condition following COVID-19 vaccination.

Lopez-Mena, D., et al. (2022). "Stroke Among SARS-CoV-2 Vaccine Recipients in Mexico: A Nationwide Descriptive Study." Neurology **98**(19): e1933-e1941.

BACKGROUND AND OBJECTIVES: Information on stroke among severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccines remains scarce. We report stroke incidence as an adverse event following immunization (AEFI) among recipients of 79,399,446 doses of 6 different SARS-CoV-2 vaccines (BNT162b2, ChAdOx1 nCov-19, Gam-COVID-Vac, CoronaVac, Ad5-nCoV, and Ad26.COV2-S) between December 24, 2020, and August 31, 2021, in Mexico. METHODS: This retrospective descriptive study analyzed

stroke incidence per million doses among hospitalized adult patients (>/=18 years) during an 8-month interval. According to the World Health Organization, AEFIs were defined as clinical events occurring within 30 days after immunization and categorized as either nonserious or serious, depending on severity, treatment, and hospital admission requirements. Acute ischemic stroke (AIS), intracerebral hemorrhage (ICH), subarachnoid hemorrhage (SAH), and cerebral venous thrombosis (CVT) cases were collected through a passive epidemiologic surveillance system in which local health providers report potential AEFI to the Mexican General Board of Epidemiology. Data were captured with standardized case report formats by an ad hoc committee appointed by the Mexican Ministry of Health to evaluate potential neurologic AEFI against SARS-COV-2. RESULTS: We included 56 patients (31 female patients [55.5%]) for an overall incidence of 0.71 cases per 1,000,000 administered doses (95% CI 0.54-0.92). Median age was 65 years (interquartile range [IQR] 55-76 years); median time from vaccination to stroke (of any subtype) was 2 days (IQR 1-5 days). In 27 (48.2%) patients, the event was diagnosed within the first 24 hours after immunization. The most frequent subtype was AIS in 43 patients (75%; 0.54 per 1,000,000 doses, 95% CI 0.40-0.73), followed by ICH in 9 (16.1%; 0.11 per 1,000,000 doses, 95% CI 0.06-0.22) and SAH and CVT, each with 2 cases (3.6%; 0.03 per 1,000,000 doses, 95% CI 0.01-0.09). Overall, the most common risk factors were hypertension in 33 (58.9%) patients and diabetes in 22 (39.3%). Median hospital length of stay was 6 days (IQR 4-13 days). At discharge, functional outcome was good (modified Rankin Scale score 0-2) in 41.1% of patients; in-hospital mortality rate was 21.4%. DISCUSSION: Stroke is an exceedingly rare AEFI against SARS-CoV-2. Preexisting stroke risk factors were identified in most patients. Further research is needed to evaluate causal associations between SARS-COV-2 vaccines and stroke.

Lotan, I., et al. (2022). "Early safety and tolerability profile of the BNT162b2 COVID-19 vaccine in myasthenia gravis." Neuromuscul Disord **32**(3): 230-235.

Although the COVID-19 vaccines are currently recommended for people with myasthenia gravis (MG), there is no data regarding the safety of the vaccines in this population. In order to investigate the real-life safety data of the BNT162b2 COVID-19 vaccine in people with MG, an anonymous survey was distributed to 142 MG patients. Fifty-six MG patients completed the questionnaire. The median age was 53 years (range 23-83 years); 35 (62.5%) were males, and 25 (44.6%) had associated comorbidities. Thirty-seven participants (66.1%) were treated with immunotherapies. Fifty-five participants (98.2% of the responders) received the BNT162b2 COVID-19 vaccine. Of these, 32 (58.2%) were < 55 years old, and 23 (41.8%) were > 55 years old. Adverse events were more common in patients younger than 55 years old (46.9% Vs. 17.4%; p = 0.0428). Eight participants (14.5%) reported worsening neurological symptoms following the vaccination. Three of those who reported worsening of neurological symptoms (37.5%) required additional treatment. Most events occurred within the first few days after vaccination and resolved within a few weeks. This survey indicates an overall favorable safety and tolerability profile of the BNT162b2 vaccine in people with MG. Additional prospective, large-scale studies are warranted to confirm these findings.

Mathew, E., et al. (2022). "Transverse myelitis after Johnson & Johnson COVID-19 vaccine: illustrative case." J Neurosurg Case Lessons **4**(24).

> BACKGROUND: Transverse myelitis is a rare neurological occurrence with varied presentation. Imaging is necessary to properly diagnose this condition; however, identifying the cause of this condition may often be difficult. OBSERVATIONS: An otherwise healthy patient presented to the clinic with peculiar neurological symptoms without an obvious underlying cause. Imaging evidenced no significant structural defects but did lead to discovery of cord enhancement compatible with a diagnosis of transverse myelitis. Corticosteroid treatment was initiated rapidly to address this pathology, and the patient recovered without deficits. To identify the underlying cause, patient medical history was reviewed thoroughly and compared with existing literature. Previous tuberculosis infection could be a less likely cause of the neurological symptoms. However, recent vaccination with the Johnson & Johnson coronavirus disease 2019 (COVID-19) vaccine could be a more likely cause of the transverse myelitis, which has been rarely reported. LESSONS: Transverse myelitis after COVID-19 infection has been an escalating phenomenon. However, transverse myelitis after COVID-19 vaccination is a rare occurrence that is also on the rise. Given the increased rates of vaccination, transverse myelitis should not be overlooked as a potential pathology, due to the severity of neurological impairment if this condition is not treated rapidly.

McCullough, J., et al. (2022). "Posterior Reversible Encephalopathy Syndrome Onset Within 24 Hours Following Moderna mRNA Booster COVID-19 Vaccination: Vaccine Adverse Event Vs. Hypertension?" Cureus **14**(5): e24919.

> We present a case of a female who presented with the acute onset of neurological changes within 24 hours of receiving her third, or booster, dose of the mRNA Moderna (Cambridge, Massachusetts) coronavirus disease 2019 (COVID-19) vaccination. Her clinicoradiological findings were most consistent with posterior reversible encephalopathy syndrome (PRES). Although PRES has been reported with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, this raised suspicion of a possible vaccine-induced PRES with her only confounder being hypertension managed with a beta-blocker. Extensive workup for other entities associated with PRES, including infection, autoimmune, paraneoplastic syndrome, and alcohol were unrevealing. Thus far, there have not been any reports of PRES post mRNA vaccination. We encourage providers to report similar cases with neurological manifestations post mRNA vaccination to the vaccine adverse event reporting system (VAERS). Timely diagnosis and treatment of PRES may help minimize any irreversible neurological sequelae.

Nanatsue, K., et al. (2022). "A case of Miller Fisher syndrome with delayed onset peripheral facial nerve palsy after COVID-19 vaccination: a case report." BMC Neurol **22**(1): 309.

> BACKGROUND: To prevent the spread of the novel coronavirus disease 2019 (COVID-19) infection, various vaccines have been developed and used in a large number of people worldwide. One of the most commonly used vaccines is the mRNA vaccine developed by Moderna. Although several studies have shown this vaccine to be safe, the full extent of its side effects has not yet been known. Miller-Fisher syndrome (MFS) is a rare condition

that manifests ophthalmoplegia, ataxia, and loss of tendon reflexes. It is a subtype of Guillain-Barre syndrome and an immune-mediated disease related to serum IgG anti-GQ1b antibodies. Several vaccines including those for COVID-19 have been reported to induce MFS. However, there have been no reports of MFS following Moderna COVID-19 vaccine administration. CASE PRESENTATION: A 70-year-old man was referred to our hospital due to diplopia that manifested 1 week after receiving the second Moderna vaccine dose. The patient presented with restricted abduction of both eyes, mild ataxia, and loss of tendon reflexes. He was diagnosed with MFS based on his neurological findings and detection of serum anti-GQ1b antibodies. The patient was administered intravenous immunoglobulin, and his symptoms gradually improved. Five days after admission, the patient showed peripheral facial paralysis on the right side. This symptom was suggested to be a delayed onset of peripheral facial nerve palsy following MFS that gradually improved by administration of steroids and antiviral drugs. CONCLUSION: There have been no previous reports of MFS after Moderna COVID-19 vaccination. This case may provide new information about the possible neurological side effects of COVID-19 vaccines.

Notghi, A. A., J. Atley and M. Silva (2021). "Lessons of the month 1: Longitudinal extensive transverse myelitis following AstraZeneca COVID-19 vaccination." Clin Med (Lond) **21**(5): e535-e538.

Longitudinal extensive transverse myelitis (LETM) is a rare but recognised complication of vaccination. We report the case of a 58-year-old man admitted to hospital 10 days after his first AstraZeneca COVID-19 vaccination with progressive neurological symptoms and signs, and investigations and imaging consistent with LETM.This case reviews the literature and the investigative process behind excluding other diagnoses given the patient's background of pulmonary sarcoidosis. It is unique in being the first UK report of a case of LETM with a strong temporal link to COVID-19 vaccination.

Nunez, I., et al. (2022). "Seizures following COVID-19 vaccination in Mexico: A nationwide observational study." Epilepsia **63**(10): e144-e149.

The COVID-19 pandemic led to the development and emergency approval of an array of effective vaccines against SARS-CoV-2. Given the relatively small number of patients included in vaccine trials, postapproval epidemiological surveillance is crucial to detect infrequent vaccine-related adverse events. We conducted a nationwide retrospective descriptive study evaluating the incidence of seizures among recipients of SARS-CoV-2 vaccines in Mexico from December 24, 2020 (date of administration of first doses nationwide) to October 29, 2021. Among 81 916 351 doses of any vaccine that were administered, we documented seizures in 53 patients, of which 31 (60%) were new onset seizures. The incidence rate of seizures per million doses was highest for mRNA-1273 (Moderna) with 2.73 per million, followed by BNT162b2 (Pfizer-BioNTech) with 1.02 per million, and Ad5-nCoV (CanSino) with 1.01 per million. Thus, we found that seizures following SARS-CoV-2 vaccination are exceedingly rare events.

Ostovan, V. R., et al. (2022). "Clinical characteristics, radiological features and prognostic factors of transverse myelitis following COVID-19 vaccination: A systematic review." Mult Scler Relat Disord **66**: 104032.

BACKGROUND: Since introducing COVID-19 vaccines, many neurological complications such as acute transverse myelitis have been reported in the literature. This study aims to identify the clinical characteristics, radiological findings, and prognostic factors in patients with COVID-19 vaccine-associated transverse myelitis (TM). METHODS: We systematically reviewed Scopus, Pubmed, Cochrane library, Google Scholar, and preprint databases using appropriate keywords from inception till 8th April 2022. Besides, we manually searched the reference lists of the included studies and relevant previous reviews. RESULTS: We included 28 studies identifying 31 post-COVID-19 vaccination myelitis patients (17 female and 14 male). The mean age of the included patients was 52+/-19 years. ChAdOx1 nCoV-19 vaccine (Oxford-AstraZeneca) was the most common type of vaccine in association with myelitis (12 out of 31), followed by Pfizer (8 out of 31), Moderna (7 out of 31), Sinopharm (3 out of 31), and Janssen vaccine (1 out of 31). The myelitis occurred in 24 and 7 patients after administering the first and second dose of the vaccine, respectively. 21 and 10 patients had good recovery (Modified Rankin Score (MRS) <3 at the follow-up) and poor recovery (MRS>/=3 at the follow-up) from myelitis, respectively. Age (OR 1.09, 95%CI 1.01-1.18, p(value) 0.02), and MRS at admission (OR 17.67, 95%CI 1.46-213.76, p(value) 0.024) were two independent risk factors for poor recovery from myelitis. CONCLUSION: The patients with higher age and MRS at admission had a worse prognosis and needed timely and more aggressive therapeutic strategies.

Parry, P. I., et al. (2023). "'Spikeopathy': COVID-19 Spike Protein Is Pathogenic, from Both Virus and Vaccine mRNA." Biomedicines **11**(8).

The COVID-19 pandemic caused much illness, many deaths, and profound disruption to society. The production of 'safe and effective' vaccines was a key public health target. Sadly, unprecedented high rates of adverse events have overshadowed the benefits. This two-part narrative review presents evidence for the widespread harms of novel product COVID-19 mRNA and adenovectorDNA vaccines and is novel in attempting to provide a thorough overview of harms arising from the new technology in vaccines that relied on human cells producing a foreign antigen that has evidence of pathogenicity. This first paper explores peer-reviewed data counter to the 'safe and effective' narrative attached to these new technologies. Spike protein pathogenicity, termed 'spikeopathy', whether from the SARS-CoV-2 virus or produced by vaccine gene codes, akin to a 'synthetic virus', is increasingly understood in terms of molecular biology and pathophysiology. Pharmacokinetic transfection through body tissues distant from the injection site by lipid-nanoparticles or viral-vector carriers means that 'spikeopathy' can affect many organs. The inflammatory properties of the nanoparticles used to ferry mRNA; N1-methylpseudouridine employed to prolong synthetic mRNA function; the widespread biodistribution of the mRNA and DNA codes and translated spike proteins, and autoimmunity via human production of foreign proteins, contribute to harmful effects. This paper reviews autoimmune, cardiovascular, neurological, potential oncological

effects, and autopsy evidence for spikeopathy. With many gene-based therapeutic technologies planned, a re-evaluation is necessary and timely.

Rattanawong, W., et al. (2021). "Acute prolonged motor aura resembling ischemic stroke after COVID - 19 vaccination (CoronaVac): the first case report." J Headache Pain **22**(1): 93.

BACKGROUND: We report the first case of a patient who suffered transient focal neurological deficit mimicking stroke following CoronaVac vaccination. However, instead of an ischemic stroke, motor aura was suspected. CASE PRESENTATIONS: A 24 year-old Thai female presented with left hemiparesis fifteen minutes after receiving CoronaVac. She also had numbness of her left arm and legs, flashing lights, and headaches. On physical examination, her BMI was 32.8. Her vital signs were normal. She had moderate left hemiparesis (MRC grade III), numbness on her left face, arms, and legs. Her weakness continued for 5 days. A brain CT scan was done showing no evidence of acute infarction. Acute treatment with aspirin was given. MRI in conjunction with MRA was performed in which no restricted diffusion was seen. A SPECT was performed to evaluate the function of the brain showing significant hypoperfusion of the right hemisphere. The patient gradually improved and was discharged. DISCUSSIONS: In this study, we present the first case of stroke mimic after CoronaVac vaccination. After negative imaging studies had been performed repeatedly, we reach a conclusion that stroke is unlikely to be the cause. Presumably, this phenomenon could possibly have abnormal functional imaging study. Therefore, we believed that it might be due to cortical spreading depression, like migraine aura, which we had conducted a literature review.

Roman, G. C., et al. (2021). "Acute Transverse Myelitis (ATM):Clinical Review of 43 Patients With COVID-19-Associated ATM and 3 Post-Vaccination ATM Serious Adverse Events With the ChAdOx1 nCoV-19 Vaccine (AZD1222)." Front Immunol **12**: 653786.

INTRODUCTION: Although acute transverse myelitis (ATM) is a rare neurological condition (1.34-4.6 cases per million/year) COVID-19-associated ATM cases have occurred during the pandemic. CASE-FINDING METHODS: We report a patient from Panama with SARS-CoV-2 infection complicated by ATM and present a comprehensive clinical review of 43 patients with COVID-19-associated ATM from 21 countries published from March 2020 to January 2021. In addition, 3 cases of ATM were reported as serious adverse events during the clinical trials of the COVID-19 vaccine ChAdOx1 nCoV-19 (AZD1222). RESULTS: All patients had typical features of ATM with acute onset of paralysis, sensory level and sphincter deficits due to spinal cord lesions demonstrated by imaging. There were 23 males (53%) and 20 females (47%) ranging from ages 21- to 73-years-old (mean age, 49 years), with two peaks at 29 and 58 years, excluding 3 pediatric cases. The main clinical manifestations were quadriplegia (58%) and paraplegia (42%). MRI reports were available in 40 patients; localized ATM lesions affected </=3 cord segments (12 cases, 30%) at cervical (5 cases) and thoracic cord levels (7 cases); 28 cases (70%) had longitudinally-extensive ATM (LEATM) involving >/=4 spinal cord segments (cervicothoracic in 18 cases and thoracolumbar-sacral in 10 patients). Acute disseminated encephalomyelitis (ADEM) occurred in 8 patients, mainly women (67%) ranging from 27- to 64-years-old. Three ATM patients also had blindness from

myeloneuritis optica (MNO) and two more also had acute motor axonal neuropathy (AMAN). CONCLUSIONS: We found ATM to be an unexpectedly frequent neurological complication of COVID-19. Most cases (68%) had a latency of 10 days to 6 weeks that may indicate post-infectious neurological complications mediated by the host's response to the virus. In 32% a brief latency (15 hours to 5 days) suggested a direct neurotropic effect of SARS-CoV-2. The occurrence of 3 reported ATM adverse effects among 11,636 participants in the AZD1222 vaccine trials is extremely high considering a worldwide incidence of 0.5/million COVID-19-associated ATM cases found in this report. The pathogenesis of ATM remains unknown, but it is conceivable that SARS-CoV-2 antigens - perhaps also present in the AZD1222 COVID-19 vaccine or its chimpanzee adenovirus adjuvant- may induce immune mechanisms leading to the myelitis.

Roongpiboonsopit, D., et al. (2022). "Inactivated COVID-19 vaccine induced acute stroke-like focal neurologic symptoms: a case series." BMC Neurol **22**(1): 210.

BACKGROUND: A subgroup of individuals experienced stroke-like symptoms after receiving an inactivated COVID-19 vaccine. We present clinical characteristics, neuroimaging, and outcome of these patients. METHODS: Medical personals who had neurological symptoms after receiving inactivated COVID-19 vaccine were enrolled. Clinical, laboratory investigation and neuroimaging were collected. Subjects were prospectively followed-up on clinical and neuroimaging to detect brain parenchymal or cerebrovascular abnormality. RESULTS: Nineteen out of 385 subjects (4.9%) developed neurological symptoms after vaccination. There was a female predominance (89.5%) with mean age of 34 +/- 7.5 years. Majority of patients (52.6%) had symptoms within 60 min after vaccination. The most common neurological symptoms were numbness (94.7%) followed by headache (52.6%) and weakness (47.4%). The most common neurological signs were sensory deficit (79%) followed by motor weakness (52.6%) and tongue deviation (26.3%). Recurrent headache was observed in most patients (89.5%) during followed up. Serial brain imaging was done in all patients with median follow-up interval of 18 days. There was no evidence of acute brain infarction in any of the patients, 84.2% had no vascular abnormality, 15.8% had transient focal narrowing of cerebral vessels. Outcome was favorable, modified ranking scale 0-1 for all patients at 4 weeks after vaccination. CONCLUSIONS: Transient focal neurological symptoms and deficits can be found after COVID-19 vaccination. However, benefit to stop COVID-19 pandemic by vaccination is outweighed by these seemingly reversible side effects. The pathophysiology underlined these phenomena should be further investigated.

Salunkhe, M., et al. (2023). "Spectrum of various CNS inflammatory demyelination diseases following COVID-19 vaccinations." Acta Neurol Belg.

BACKGROUND AND PURPOSE: Although rare, neurological adverse events have been reported post-COVID-19 vaccination. This study reports 16 patients diagnosed with CNS inflammatory demyelinating diseases (CNS-IDD) within 6 weeks of COVID-19 vaccine administration. METHODOLOGY: A prospective observational study was conducted from June 2021 to May 2022. All patients were diagnosed according to the latest international guidelines with CNS-IDD within 6 weeks of COVID-19 vaccine exposure. Data regarding

the demographic profile, clinical features, type of COVID-19 vaccination, radiological findings and occurrence of symptoms were noted and further analysed using descriptive statistics. RESULTS: We reported 16 cases (median age 40 years) of CNS demyelination: fourteen occurred in temporal association with ChAdOx1-S vaccine and two in association with BBV152 vaccine. Median time duration of presenting symptoms after vaccination was 19 days (3-40 days). The most common presentation was myelitis (7/16 patients), followed by optic neuritis (6/16 patients). Demyelination events were reported after first and second dose in thirteen and five patients respectively, although two patients reported such events after both vaccine dosages. Myelin oligodendrocyte glycoprotein (MOG) IgG antibodies were positive in eight patients. Tumefactive demyelination was seen in four patients. Management included high-dose methylprednisolone, PLEX, IVIG or a combination of those, with a favourable outcome in the majority of cases. CONCLUSION: Although a rare event, awareness regarding potential demyelinating episodes post-COVID-19 vaccination can help in early diagnosis. The presence of increased MOG-IgG antibodies with temporal association in post-COVID vaccine patients raises a possibility of an immunogenic phenomenon leading to demyelinating disorders.

Schelke, M. W., et al. (2022). "Post-COVID-19 vaccine small-fiber neuropathy and tinnitus treated with plasma exchange." Muscle Nerve **66**(4): E21-E23.

Shirah, B., I. Mulla and Y. Aladdin (2023). "Optic Neuritis Following the BNT162b2 mRNA COVID-19 Vaccine in a Patient with Systemic Lupus Erythematosus Uncovering the Diagnosis of Neuromyelitis Optica Spectrum Disorders." Ocul Immunol Inflamm **31**(6): 1213-1215.

COVID-19 vaccinations have been given worldwide to save the lives of millions. However, several complications following different types of COVID-19 vaccinations were reported previously in the literature. Previous articles have reported multiple ocular complications following different types of COVID-19 vaccinations. In this article, we report a unique case in which the diagnosis of neuromyelitis optica spectrum disorders (NMOSD) was unveiled following vaccination with BNT162b2 mRNA COVID-19 vaccine and manifesting as acute optic neuritis in a patient with systemic lupus erythematosus (SLE). The temporal association of acute optic neuritis after receiving the BNT162b2 mRNA COVID-19 vaccine along with the serological evidence of NMOSD support this theory. The risk of triggering an occult autoimmune disorder in patients with an overactive immune system such as this patient should be studied to calibrate the benefits and risks of vaccination against COVID-19. Screening for aquaporin-4 antibodies in patients with SLE prior to vaccination against COVID-19 may be considered to prevent potentially devastating neurological disability in patients with premorbid occult NMOSD.

Shouman, K., et al. (2021). "Autonomic dysfunction following COVID-19 infection: an early experience." Clin Auton Res **31**(3): 385-394.

PURPOSE: Post-COVID-19 syndrome is a poorly understood aspect of the current pandemic, with clinical features that overlap with symptoms of autonomic/small fiber dysfunction. An early systematic analysis of autonomic dysfunction following COVID-19

is lacking and may provide initial insights into the spectrum of this condition. METHODS: We conducted a retrospective review of all patients with confirmed history of COVID-19 infection referred for autonomic testing for symptoms concerning for para-/postinfectious autonomic dysfunction at Mayo Clinic Rochester or Jacksonville between March 2020 and January 2021. RESULTS: We identified 27 patients fulfilling the search criteria. Symptoms developed between 0 and 122 days following the acute infection and included lightheadedness (93%), orthostatic headache (22%), syncope (11%), hyperhidrosis (11%), and burning pain (11%). Sudomotor function was abnormal in 36%, cardiovagal function in 27%, and cardiovascular adrenergic function in 7%. The most common clinical scenario was orthostatic symptoms without tachycardia or hypotension (41%); 22% of patients fulfilled the criteria for postural tachycardia syndrome (POTS), and 11% had borderline findings to support orthostatic intolerance. One patient each was diagnosed with autoimmune autonomic ganglionopathy, inappropriate sinus tachycardia, vasodepressor syncope, cough/vasovagal syncope, exacerbation of preexisting orthostatic hypotension, exacerbation of sensory and autonomic neuropathy, and exacerbation of small fiber neuropathy. CONCLUSION: Abnormalities on autonomic testing were seen in the majority of patients but were mild in most cases. The most common finding was orthostatic intolerance, often without objective hemodynamic abnormalities on testing. Unmasking/exacerbation of preexisting conditions was seen. The temporal association between infection and autonomic symptoms implies a causal relationship, which however cannot be proven by this study.

Siddig, A., et al. (2022). "AstraZeneca COVID-19 vaccine: A possible risk factor for ischemic stroke and cerebral venous sagittal sinus thrombosis: A case series." Clin Case Rep **10**(7): e6017.
One of the most prevalent neurological impairments is cerebrovascular accident (CVA). Ischemic stroke and CVST have been linked to the AstraZeneca COVID-19 vaccine. Three Sudanese patients developed these diseases after receiving the AstraZeneca COVID-19 vaccine, indicating a relationship between the AstraZeneca COVID-19 vaccine and these conditions.

Sirisuk, W., et al. (2023). "Incidence and clinical characteristics of adverse neurological events and stroke-like syndrome associated with immune stress-related response after COVID-19 vaccination in 2021 from Thailand." Clin Neurol Neurosurg **231**: 107804.
OBJECTIVES: AEFIs (adverse events following immunizations), especially ISRR (immune stress related response) which can cause stroke-like symptoms may affect the vaccine roll-out campaign to prevent the coronavirus 2019 outbreak. METHODS: This study aimed to describe the incidence and clinical characteristics of neurological AEFIs and stroke-like symptoms associated with ISRR after COVID-19 vaccination. Characteristics of ISRR were compared to minor ischemic stroke patients during the same period of the study. During March to September 2021, we retrospectively collected data of participants aged >/= 18 years who received COVID-19 vaccine and developed AEFIs from Thammasat university vaccination center (TUVC). Data of neurological AEFIs patients and minor ischemic stroke patients were collected from hospital electronic medical record system. RESULTS: COVID-19 vaccine were administered at TUVC for

245,799 doses. AEFIs were reported in 129,652 instances (52.6%). ChADOx-1 nCoV-19 viral vector vaccine has the most frequent occurrence of AEFIs (58.0%), and neurological AEFIs (12.6%). 83% of neurological AEFI was headache. Most were mild and did not need medical attention. Of 119 patients who received COVID-19 vaccine from anywhere with neurological AEFIs and presented to TUH, ISRR was diagnosed in 107 patients (89.9%) and all patients who has follow-up data (30.8%) showed clinical improvement. In comparison with minor ischemic stroke (116 patients), ISRR patients had significantly less ataxia, facial weakness, weakness of arm/leg and speech disturbances ($P < 0.001$). CONCLUSION: The incidence of neurological AEFIs after COVID-19 vaccination was higher among recipients of ChAdOx-1 nCoV-19 vaccine (12.6%) than inactivated vaccine (6.2%) and mRNA vaccine (7.5%). However, most neurological AEFIs were ISRR, had mild severity and resolved within 30 days. Stroke-like symptoms occurred less frequently than patients with minor ischemic stroke.

Talotta, R. (2022). "Impaired VEGF-A-Mediated Neurovascular Crosstalk Induced by SARS-CoV-2 Spike Protein: A Potential Hypothesis Explaining Long COVID-19 Symptoms and COVID-19 Vaccine Side Effects?" Microorganisms **10**(12).

Long coronavirus disease-19 (COVID-19) is a newly discovered syndrome characterized by multiple organ manifestations that persist for weeks to months, following the recovery from acute disease. Occasionally, neurological and cardiovascular side effects mimicking long COVID-19 have been reported in recipients of COVID-19 vaccines. Hypothetically, the clinical similarity could be due to a shared pathogenic role of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) spike (S) protein produced by the virus or used for immunization. The S protein can bind to neuropilin (NRP)-1, which normally functions as a coreceptor for the vascular endothelial growth factor (VEGF)-A. By antagonizing the docking of VEGF-A to NRP-1, the S protein could disrupt physiological pathways involved in angiogenesis and nociception. One consequence could be the increase in unbound forms of VEGF-A that could bind to other receptors. SARS-CoV-2-infected individuals may exhibit increased plasma levels of VEGF-A during both acute illness and convalescence, which could be responsible for diffuse microvascular and neurological damage. A few studies suggest that serum VEGF-A may also be a potential biomarker for long COVID-19, whereas evidence for COVID-19 vaccines is lacking and merits further investigation.

Tepmongkol, S., et al. (2022). "Brain perfusion single photon emission computed tomography abnormality in MRI-negative stroke-like patients post COVID-19 vaccination." Medicine (Baltimore) **101**(47): e31965.

Stroke-like symptoms after COVID-19 vaccination was thought to be functional if there was no anatomical image abnormality. We aimed to analyze brain perfusion changes in these patients. A case-control study of brain perfusion single photon emission computed tomography (SPECT) of 12 vaccinated patients with left-sided stroke-like symptoms were compared with 12 age- and gender-matched normal interictal brain SPECTs using voxel-based analysis. Significant hyperperfusion was seen on the right side in postcentral, inferior parietal, mid temporal, parahippocampal, and caudate regions, and on the left

side in the thalamus, hippocampus, and mid temporal areas. In addition, there were hypoperfused bilateral superior frontal gyri and right mid/posterior cingulate cortex (Family-wise-error corrected p-values < .05). Both hypoperfusion and hyperperfusion in the brain are demonstrated. We hypothesize that these findings might be the result of the functional neurological disorder. However, based on other previous studies, circulating spike protein in the patients' plasma early after vaccination might also be the cause.

Ocular Injuries

Bolletta, E., et al. (2021). "Uveitis and Other Ocular Complications Following COVID-19 Vaccination." J Clin Med **10**(24).

Coronavirus disease 2019 (COVID-19) vaccines can cause transient local and systemic post-vaccination reactions. The aim of this study was to report uveitis and other ocular complications following COVID-19 vaccination. The study included 42 eyes of 34 patients (20 females, 14 males), with a mean age of 49.8 years (range 18-83 years). The cases reported were three herpetic keratitis, two anterior scleritis, five anterior uveitis (AU), three toxoplasma retinochoroiditis, two Vogt-Koyanagi-Harada (VKH) disease reactivations, two pars planitis, two retinal vasculitis, one bilateral panuveitis in new-onset Behcet's disease, three multiple evanescent white dot syndromes (MEWDS), one acute macular neuroretinopathy (AMN), five retinal vein occlusions (RVO), one non-arteritic ischemic optic neuropathy (NAION), three activations of quiescent choroidal neovascularization (CNV) secondary to myopia or uveitis, and one central serous chorioretinopathy (CSCR). Mean time between vaccination and ocular complication onset was 9.4 days (range 1-30 days). Twenty-three cases occurred after Pfizer-BioNTech vaccination (BNT162b2 mRNA), 7 after Oxford-AstraZeneca vaccine (ChAdOx1 nCoV-19), 3 after ModernaTX vaccination (mRNA-1273), and 1 after Janssen Johnson & Johnson vaccine (Ad26.COV2). Uveitis and other ocular complications may develop after the administration of COVID-19 vaccine.

Chaturvedi, H. T., et al. (2023). "New acute onset of ocular myasthenia gravis after COVID-19 vaccine: A case report." J Family Med Prim Care **12**(2): 394-396.

Reports have shown the association of coronavirus disease 2019 (COVID-19) with several neuromuscular disorders. Myasthenia gravis (MG) is an autoimmune disease in which antibodies bind to acetyl choline receptors in the postsynaptic membrane at the neuromuscular junction. The characteristic clinical feature of the disease is weakness of the ocular muscle, bulbar muscle, and extremity muscles; when the weakness is limited to the ocular muscle only, the condition is known as ocular myasthenia gravis. Diagnosis is usually confirmed by the acetylcholine receptor antibodies. Symptoms of MG may be aggravated by various types of infections and medications. Here, we are presenting a rare case of a new and acute onset of ocular MG presented after administration of Covishield vaccine.

Chen, X., et al. (2022). "Ocular Adverse Events after Inactivated COVID-19 Vaccination in Xiamen." Vaccines (Basel) **10**(3).

Aims: To report potential vaccine-induced ocular adverse events following inactivated COVID-19 vaccination (Sinopharm and Sinovac). Methods: This case series took place at a tertiary referral center in the southeast of China (Xiamen Eye Center in Fujian Province) from February 2021 to July 2021. Patients who received the first dose of inactivated COVID-19 vaccine and developed vaccine-related ocular adverse events within 10 days were included. The diagnosis of vaccine-related ocular adverse events was guided by the

World Health Organization causality assessment and the Naranjo criteria. Results: Ten eyes of seven patients (two male individuals) presenting with ocular complaints following COVID-19 vaccine were included in the study. The mean (SD) age was 41.4 (9.3) years (range, 30-55 years). The mean time of ocular adverse event manifestations was 4.9 days (range, 1-10 days). Three patients were diagnosed with Vogt-Koyanagi-Harada (VKH)-like uveitis, one with multifocal choroiditis, one with episcleritis, one with iritis, and one with acute idiopathic maculopathy. Two patients received the second dose of vaccine. One patient had exacerbation of VKH, and one patient had no symptoms. An aqueous humor analysis in three patients revealed elevated proinflammatory cytokines and negative virus copy. All the patients had transient ocular disturbance and responded well to steroids. No recurrence was noted during 6 months of follow-up. Conclusions: Potential ocular adverse events should be reported to increase the awareness of the health community for timely detection and proper treatment.

Cunningham, E. T., et al. (2022). "Ocular Complications Following COVID-19 Vaccination - Coincidence, Correlation, or Causation?" Ocul Immunol Inflamm **30**(5): 1031-1034.

Eleiwa, T. K., et al. (2021). "Adverse Ocular Events following COVID-19 Vaccination." Inflamm Res **70**(10-12): 1005-1009.

Fei, P., et al. (2022). "Inflammatory ocular events after inactivated COVID-19 vaccination." Hum Vaccin Immunother **18**(6): 2138051.

To report potential vaccine-induced inflammatory ocular adverse events following inactivated COVID-19 vaccination. Retrospective study of patients with uveitis and other ocular complications following inactivated coronavirus disease 2019 (COVID-19) vaccination at a tertiary referral center between May 2021 and August 2021. Data collection consisted of demographic and clinical data. The study included 8 eyes of 5 patients (4 females, 1 male), with a mean age of 37.2 +/- 12.5 years (range 28-59 years). Mean time between vaccination and ocular complications onset was 13.2 +/- 11.9 days (range 3-30 days), including two patients after the first dose of the vaccine and 3 patients after the second dose. The cases reported were three anterior uveitis, one herpetic keratitis and iridocyclitis, and one posterior uveitis. Patients received treatment with local and/or systemic steroids and all the patients had good visual outcomes. Ocular inflammatory events may occur after vaccination with possible gender preponderance. However, they are rare and manageable. Overall, the efficacy and safety of vaccination should be emphasized.

Haseeb, A. A., et al. (2022). "Ocular Complications Following Vaccination for COVID-19: A One-Year Retrospective." Vaccines (Basel) **10**(2).

Vaccination efforts as a mitigation strategy in the corona virus disease 2019 (COVID-19) pandemic are fully underway. A vital component of understanding the optimal clinical use of these vaccines is a thorough investigation of adverse events following vaccination. To date, some limited reports and reviews have discussed ocular adverse events following COVID-19 vaccination, but a systematic review detailing these reports with

manifestations and clinical courses as well as proposed mechanisms has yet to be published. This comprehensive review one-year into vaccination efforts against COVID-19 is meant to furnish sound understanding for ophthalmologists and primary care physicians based on the existing body of clinical data. We discuss manifestations categorized into one of the following: eyelid, orbit, uveitis, retina, vascular, neuro-ophthalmology, ocular motility disorders, and other.

Jin, W., Y. Tang and C. Wen (2021). "An ocular adverse event in temporal association with COVID-19 vaccination in a patient with systemic lupus erythematosus: a case report." Hum Vaccin Immunother **17**(11): 4102-4104.

After the COVID-19 pandemic, vaccines using inactivated viruses have attracted worldwide attention for the prevention of infectious diseases. Here, we report a patient who suffered from Systemic Lupus Erythematosus (SLE) for six years and developed ocular symptoms within 72 hours after being vaccinated for COVID-19. The patient presented bilateral conjunctival congestion, eyelid edema with pruritus, and suffered from severe headaches. Recovery occurred within 10 days after the onset of symptoms after treatment with anti-infection drugs. The early identification and extensive assessment of side effects help ensuring effective vaccine safety monitoring.

Li, Z., et al. (2022). "Ocular Adverse Events after Inactivated COVID-19 Vaccination." Vaccines (Basel) **10**(6).

Purpose: To report the clinical characteristics of ocular adverse events that have occurred, in China, after vaccination with inactivated COVID-19 vaccines. Methods: A retrospective cross-sectional observational study was conducted of ocular disorders that occurred within 15 days from any dose of an inactivated COVID-19 vaccine. Information on gender, age, the interval between the vaccination and ocular symptoms, laterality, duration of the ocular symptoms, primary visual acuity, and clinical diagnosis were retrospectively collected. Results: Twenty-four patients were involved in the study, including 15 females and 9 males, with a mean age of 41 +/- 16 years (range of 8-71 years). The patients all denied a prior history of COVID-19 infection. Ocular adverse events occurred after the first dose of vaccine in 18 patients and, after the second or third doses, in six patients. The interval between vaccination with the inactivated COVID-19 vaccine and ocular symptoms was 6 +/- 5 days; six patients were bilaterally involved and 18 patients were unilaterally involved. Regarding the diagnosis, 10 patients were diagnosed with white dot syndrome (WDS), 9 patients were diagnosed with uveitis, and 5 patients were diagnosed with retinal vascular disorders. The ages of patients with WDS were younger than those with uveitis or retinal vascular disorders (32 +/- 10 vs. 48 +/- 18, $p < 0.05$). For patients diagnosed with WDS, the best-corrected visual acuity (BCVA) was 0.74 +/- 0.73 LogMAR. For patients diagnosed with retinal vascular disorders or uveitis, the BCVA was 1.44 +/- 1.26 LogMAR. There was no significant difference ($p > 0.05$). Conclusions: A relationship cannot be established between inactivated COVID-19 vaccines and ocular disorders; therefore, further investigation of the clinical spectrum of ocular adverse events after vaccination with an inactivated COVID-19 vaccine is necessary.

Lin, C. Y. and H. J. Chien (2023). "Acute exacerbation of ocular graft-versus-host disease and anterior uveitis after COVID-19 vaccination." BMC Ophthalmol **23**(1): 360.

BACKGROUND: To report a case of simultaneous occurrence of acute exacerbation of ocular graft-versus-host disease (GVHD) and anterior uveitis following coronavirus disease 2019 (COVID-19) vaccination. CASE PRESENTATION: A 60-year-old man with primary myelofibrosis and GVHD after receiving allogeneic hematopoietic stem cell transplantation (HSCT), developed acute exacerbation of ocular GVHD and anterior uveitis after receiving first dose of COVID-19 vaccine. The patient developed erythema of the eyelids, conjunctival hyperemia, superficial punctate keratopathy, and prominent anterior chamber inflammation in both eyes. The ocular GVHD and anterior uveitis were managed with mainly topical corticosteroids, antibiotics, lubricants, and systemic corticosteroids, but were difficult to control. Intravitreal injection of dexamethasone was administered, and the inflammation gradually subsided 6 months after the onset of initial symptoms. CONCLUSIONS: Clinicians should be aware of rare refractory anterior uveitis and acute exacerbation of ocular GVHD after COVID-19 vaccination in patients undergoing HSCT. Early diagnosis and aggressive treatment should be considered to reduce the likelihood of severe complications.

Maher, D. I., D. Hogarty and E. Ben Artsi (2022). "Response to letter to the editor regarding "Acute onset ocular myasthenia gravis after vaccination with the Oxford-AstraZeneca COVID-19 vaccine"." Orbit **41**(5): 662-663.

Ng, X. L., et al. (2021). "Ocular Adverse Events After COVID-19 Vaccination." Ocul Immunol Inflamm **29**(6): 1216-1224.

PURPOSE: The COVID-19 pandemic has galvanized the development of new vaccines at an unprecedented pace. Since the widespread implementation of vaccination campaigns, reports of ocular adverse effects after COVID-19 vaccinations have emerged. This review summarizes ocular adverse effects possibly associated with COVID-19 vaccination, and discusses their clinical characteristics and management. METHODS: Narrative Literature Review. RESULTS: Ocular adverse effects of COVID-19 vaccinations include facial nerve palsy, abducens nerve palsy, acute macular neuroretinopathy, central serous retinopathy, thrombosis, uveitis, multiple evanescent white dot syndrome, Vogt-Koyanagi-Harada disease reactivation, and new-onset Graves' Disease. Studies in current literature are primarily retrospective case series or isolated case reports - these are inherently weak in establishing association or causality. Nevertheless, the described presentations resemble the reported ocular manifestations of the COVID-19 disease itself. Hence, we hypothesize that the human body's immune response to COVID-19 vaccinations may be involved in the pathogenesis of the ocular adverse effects post-COVID-19 vaccination. CONCLUSION: Ophthalmologists and generalists should be aware of the possible, albeit rare, ocular adverse effects after COVID-19 vaccination.

Nyankerh, C. N. A., A. K. Boateng and M. Appah (2022). "Ocular Complications after COVID-19 Vaccination, Vaccine Adverse Event Reporting System." Vaccines (Basel) **10**(6).

In December 2020, the U.S. Food and Drug Administration licensed COVID-19 vaccines for emergency use authorization. We investigated the ocular adverse event reports in patients reported to the Vaccine Adverse Event Reporting System (VAERS) following vaccination against COVID-19. We searched the VAERS database for U.S. reports among persons who received COVID-19 vaccines between December 2020 and December 2021. Our goal was to analyze and quantify the ocular adverse events submitted to VAERS to provide clinicians and researchers with a broader view of these ocular side effects. During the analysis period, VAERS received 55,313 adverse event reports and, after data cleaning, 6688 reports met the inclusion criteria. Note that 2229 (33.33%) adverse events were classified as cases of eyelid swelling, ocular hyperemia and conjunctivitis, 1785 (26.69%) as blurred vision and 1322 (19.77%) as visual impairment. Females accounted for 73.8% of adverse event reports and the age group between 40 and 59 years had the most frequent adverse events. A higher proportion of these adverse events reported to VAERS was linked with the Janssen and Moderna COVID-19 vaccines. At the time of vaccination, a high proportion of patients reported conditions like allergies, hypertension, diabetes, thyroid disease, vascular and other autoimmune diseases. A review of these data suggests a possible association between COVID-19 vaccines and ocular adverse events. Physicians are cautioned not only to be aware of this potential problem, but to check any underlying patient conditions, and to carefully document in VAERS within a few weeks of vaccination. Future COVID-19 vaccine safety studies in healthy subjects would help clarify the vaccine's safety profile.

Pichi, F., et al. (2021). "Association of Ocular Adverse Events With Inactivated COVID-19 Vaccination in Patients in Abu Dhabi." JAMA Ophthalmol **139**(10): 1131-1135.

IMPORTANCE: As vaccinations against COVID-19 continue, potential ocular adverse events should be reported in detail to increase awareness among the medical community, although typically, a causal relationship cannot be established definitively. OBJECTIVE: To describe ocular adverse events that occur soon after receiving an inactivated COVID-19 vaccination (Sinopharm). DESIGN, SETTING, AND PARTICIPANTS: This case series took place from September 2020 to January 2021 at Cleveland Clinic Abu Dhabi, a tertiary referral center. Patients who reported ocular adverse events and presented within 15 days from the first of 2 doses of an inactivated COVID-19 vaccine were analyzed. MAIN OUTCOMES AND MEASURES: Each patient underwent Snellen best-corrected visual acuity that was then converted to logMAR, applanation tonometry, and biomicroscopic examination with indirect ophthalmoscopy. Color fundus photography was obtained with a conventional 9-field fundus photography camera or with a widefield fundus photography system. Optical coherence tomography and optical coherence tomographic angiography images were obtained. Sex, race, age, and clinical data were self-reported. RESULTS: Nine eyes of 7 patients (3 male individuals) presenting with ocular complaints following COVID-19 vaccine were included in the study. The mean (SD) age was 41.4 (9.3) years (range, 30-55 years); the mean best-corrected visual acuity was 0.23 logMAR (range, 0-1 logMAR; approximate Snellen equivalent, 20/32). The mean time of ocular adverse event manifestations was 5.2 days (range, 1-10 days). One patient was diagnosed with episcleritis, 2 with anterior scleritis, 2 with acute

macular neuroretinopathy, 1 with paracentral acute middle maculopathy, and 1 with subretinal fluid. CONCLUSIONS AND RELEVANCE: In this case series study of 7 patients, the timing of transient and ocular complications 5.2 days after vaccination with an inactivated COVID-19 vaccine supported an association with the ocular findings, but a causal relationship cannot be established from this study design.

Pillar, S., T. Weinberg and R. Amer (2023). "Posterior ocular manifestations following BNT162b2 mRNA COVID-19 vaccine: a case series." Int Ophthalmol **43**(5): 1677-1686.

PURPOSE: To report the occurrence of posterior ocular adverse events following the administration of the BNT162b2 mRNA vaccine against SARS-CoV-2. METHODS: A retrospective consecutive case series, in which the medical files of patients presenting with ocular adverse events within 30 days of the vaccine inoculation, were analyzed. RESULTS: Four patients (2 females) were included in the study. The diagnoses included: posterior scleritis, paracentral acute middle maculopathy, herpes panuveitis, and Vogt-Koyanagi-Harada (VKH)-like uveitis. Three of the patients had no relevant ocular history, but the patient who developed scleritis was in remission without medical therapy for four years, until the flare-up, which occurred one day after the vaccine. All patients improved with treatment. CONCLUSION: Though a causal relationship cannot be definitively established, the temporal relationship suggests a possible link between the COVID-19 vaccine and the posterior ocular complications. The benefits of vaccination clearly outweigh the potential adverse effects; however, ophthalmologists should be aware of the potential for vaccine-associated uveitis.

Sadeghi, E., et al. (2023). "Ocular posterior segment complications following COVID-19 vaccination." Int Ophthalmol.

BACKGROUND: The SARS-CoV-2 pandemic has had a significant impact on healthcare, including eye care, worldwide. Effective and safe vaccines have been developed using both conventional and novel technologies to combat SARS-CoV-2 infection. While vaccination has been shown to be remarkably effective in reducing the spread and associated morbidity and mortality of COVID-19 disease, there have been reports of complications to the posterior segment of the eye. METHODS: We present a case-based analysis of reported complications of COVID-19 vaccination to the posterior segment of the eye. The study aims to highlight the diversity of possible complications and discuss the plausible involved pathophysiologic mechanisms. RESULTS: The most significant complications reported were retinal macro or microvascular occlusions, uveitis, and central serous chorioretinopathy. These complications are rare but require prompt diagnosis and management to prevent serious visual morbidity. CONCLUSIONS: Our study highlights the need for ophthalmologists to be aware of possible complications related to COVID-19 vaccination and the importance of prompt diagnosis and management. The findings of this study may help ophthalmologists to better understand and manage these rare complications.

Salem Mahjoubi, Y., et al. (2023). "Acute angle closure glaucoma following COVID-19 vaccination." Therapie.

Singh, R. B., et al. (2022). "Vaccine-associated corneal graft rejection following SARS-CoV-2 vaccination: a CDC-VAERS database analysis." Br J Ophthalmol.

PURPOSE: To evaluate the cases of corneal graft rejection following SARS-CoV-2 vaccination reported to Centers for Disease Control and Prevention Vaccine Adverse Event Reporting System. METHODS: A descriptive analysis of the demographics, clinical history and presentation was performed. We evaluated the correlation between the vaccines and duration of vaccine-associated graft rejection (VAR) onset following vaccination using a one-way analysis of variance test. A post hoc analysis was performed between VAR onset-interval following vaccination dose and vaccine type. Finally, a 30-day cumulative incidence analysis was performed to assess the risk of VAR in short term following different doses, vaccines and type of corneal transplantation. RESULTS: A total of 55 eyes of 46 patients were diagnosed with VAR following vaccination with BNT162b2 (73.91%) and mRNA-1273 (26.09%). The mean age of the patients was 62.76+/-15.83 years, and 28 (60.87%) were female. The patients diagnosed with VAR had undergone penetrating keratoplasty (61.82%), Descemet membrane endothelial keratoplasty (12.73%), descemet stripping endothelial keratoplasty (18.18%), anterior lamellar keratoplasty (3.64%) and corneal limbal allograft transplantation (1.82%). The mean time for VAR since penetrating and endothelial keratoplasty was 8.42+/-9.23 years and 4.18+/-4.40 years, respectively. 45.65% of the cases of VAR were reported after the second dose of vaccine. The duration of VAR onset was significantly shorter after the second dose compared with the first and booster doses (p=0.0165) and in patients who underwent endothelial keratoplasty compared with penetrating keratoplasty (p=0.041). CONCLUSIONS: This study outlines a possible temporal relationship between corneal graft rejection and SARS-CoV-2 vaccination. An earlier onset of VAR was observed in patients who had a history of endothelial keratoplasty and following the second dose of vaccination.

Singh, R. B., et al. (2022). "Glaucoma Cases Following SARS-CoV-2 Vaccination: A VAERS Database Analysis." Vaccines (Basel) **10**(10).

Background: To counter the rapidly spreading severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), global vaccination efforts were initiated in December 2020. We assess the risk of glaucoma following SARS-CoV-2 vaccination and evaluate its onset interval and clinical presentations in patients. Methods: We performed a retrospective analysis of the glaucoma cases reported to the Vaccine Adverse Event Reporting System (VAERS) database between 16 December 2020, and 30 April 2022. We assessed the crude reporting rate of glaucoma, clinical presentations, onset duration, and associated risk factors. Results: During this period, 161 glaucoma cases were reported, with crude reporting rates (per million doses) of 0.09, 0.06, and 0.07 for BNT162b2, mRNA-1273, and Ad26.COV2.S, respectively. The mean age of the patients was 60.41 +/- 17.56 years, and 67.7% were women. More than half (56.6%) of the cases were reported within the first week of vaccination. The cumulative-incidence analysis showed a higher risk of glaucoma in patients who received the BNT162b2 vaccines compared with mRNA-1273 ($p = 0.05$). Conclusions: The incidence of glaucoma following vaccination with BNT162b2,

mRNA-1273, or Ad26.COV2.S is extremely rare. Amongst the patients diagnosed with glaucoma, the onset interval of adverse events was shorter among those who received the BNT162b2 and rAd26.COV2.S vaccines compared with mRNA-1273. Most glaucoma cases were reported within the first week following vaccination in female patients and from the fifth to seventh decade. This study provides insights into the possible temporal association between reported glaucoma events and SARS-CoV-2 vaccines; however, further investigations are required to identify the potential causality link and pathological mechanisms.

Singh, R. B., et al. (2023). "Retinal vascular occlusion following SARS-CoV-2 vaccination: A VAERS database analysis." Ophthalmol Sci: 100354.

PURPOSE: To evaluate the cases of retinal vessel occlusion following COVID-19 vaccination and evaluate the onset interval and clinical presentations in patients diagnosed with vaccine associated retinal artery occlusion (RAO) and retinal vein occlusion (RVO). DESIGN: Retrospective study of the cases reported to the Centers for Disease Control and Prevention (CDC) Vaccine Adverse Events Reporting System (VAERS) between December 11, 2020 and July 1, 2022. PARTICIPANTS: Patients diagnosed with retinal vessel occlusion following vaccination with BNT162b2, mRNA-1273, and Ad26.COV2.S globally. METHODS: We performed a descriptive analysis of the patient demographics and clinical presentation in patients with retinal vessel occlusion. The correlation between the vaccines and continuous and categorical variables were assessed. We performed the post-hoc analysis to evaluated the association between RAO and RVO onset post-vaccination, and vaccine and dosage. Finally, a 30-day reverse analysis for RAO and RVO onset following administration of vaccine. A major limitation in the methods of this study is the lack of control group for assessing the risk of retinal vessel occlusive disease in patients who received the vaccine compared to the patients who were unvaccinated. MAIN OUTCOME MEASURES: The crude reporting rate of retinal vessel occlusion following SARS-CoV-2 vaccine. The ocular and systemic presentations, onset duration and short term risk of RAO and RVO following vaccination. RESULTS: During the study period, 1351 retinal vessel occlusion cases were reported globally. The crude reporting rates of retinal vessel occlusion for BNT162b2, mRNA-1273, and Ad26.COV2.S were 0.36, 0.41, and 0.69, respectively. The majority of the retinal vessel occlusion cases were reported following BNT162b2 (n=606, 74.17%). The mean age of patients with RVO and RAO was 58.54 +/- 16.06 years and 64.63 +/- 16.16 years, respectively. In the cohort, 817 and 433 patients were diagnosed with RVO and RAO, respectively. Most cases of RVO (41.12%) and RAO (48.27%) were reported within the first week post-vaccination. We observed that the mean onset interval for RVO was significantly longer in patients who received Ad26.Cov2.S (54.07 +/- 88.98 days) compared to BNT162b2 (18.07 +/- 28.66 days) and mRNA-1273 (22.85 +/- 38.13 days) vaccines ($p<0.0001$). This was further confirmed by post-hoc analysis, which revealed a significantly longer onset duration for the Ad26.Cov2.S compared to BNT162b2 and mRNA 1273 vaccines ($p<0.0001$). The reverse Kaplan Meier 30-day risk analysis showed a significant a higher risk of RVO onset following BNT162b2 compared to other vaccines($p<0.0001$). CONCLUSIONS: The low crude reporting rate highlights a low safety

concern for retinal vessel occlusion following SARS-CoV-2 vaccination. This study provides insights into possible temporal association between reported retinal vessel occlusion events with SARS-CoV-2 vaccines, however further insights are needed to understand the underlying immunopathological mechanisms that promote thrombosis of retinal vasculature on vaccine administration.

Singh, R. B., et al. (2023). "Herpetic Eye Disease After SARS-CoV-2 Vaccination: A CDC-VAERS Database Analysis." Cornea **42**(6): 731-738.

PURPOSE: The aim of this study was to evaluate the cases of herpes simplex and zoster ophthalmicus after SARS-CoV-2 vaccination and assess the clinical presentations in patients. METHODS: A retrospective analysis of cases reported to the Centers for Disease Control and Prevention (CDC) Vaccine Adverse Event Reporting System (VAERS) between December 11, 2020, and July 1, 2022. Patients diagnosed with herpes simplex ophthalmicus (HSO) and herpes zoster ophthalmicus (HZO) after vaccination with BNT162b2 (Pfizer-BioNTech), mRNA-1273 (Moderna), and Ad26.COV2.S (Janssen) were included in the study. We performed a descriptive analysis of patient demographics, history, and ophthalmic and systemic clinical presentations. The correlations between vaccine type and continuous variables were assessed by the one-way analysis of variance test. In addition, we used the Pearson chi 2 test to assess the association between 3 vaccines and categorical variables. A post hoc analysis was performed between HSO and HZO onset intervals after vaccination, dose, and vaccine type. The 30-day risk analysis was also performed for HSO and HZO onset postvaccination using the reverse Kaplan-Meier analysis. RESULTS: A total of 1180 cases of HZO (983, 83.30%) and HSO (180, 15.25%) were reported. The mean age of patients with HZO and HSO was 59.02 +/- 19.05 and 52.68 +/- 17.83 years, respectively. Most of the cases of HZO (795, 80.87%) and HSO (131, 72.78%) were reported in patients who received BNT162b2. In the cohort, 63.28% and 65.56% diagnosed with HZO and HSO were women. About one third of HZO (36.52%) and HSO (35.56%) cases were reported after the first dose. More than half of the cases of HZO (61.34%) and HSO (64.45%) were reported within the first 2 weeks after vaccination. The estimated crude reporting rate (per million doses) in the United States was 0.25, 0.22, and 0.47 for BNT162b2, mRNA-1273, and Ad26.COV2.S, respectively. The onset interval for HZO was significantly shorter in patients who received BNT162b2 (20.51 +/- 56.20 days, P = 0.030) compared with patients who received mRNA-1273 (36.56 +/- 108.67 days) and Ad26.COV2.S (39.66 +/- 60.15 days) vaccines. The 30-day risk analysis showed a significantly higher risk of HZO after BNT162b2 than the other 2 vaccines (P = 0.011). CONCLUSIONS: The low crude reporting rate suggests that HZO and HSO after SARS-CoV-2 vaccination occur rarely. This study provides insights into the possible temporal association between reported HSO and HZO after SARS-CoV-2 vaccines; however, further investigations are required to delineate the possible underlying immunological mechanisms.

Testi, I., et al. (2022). "Ocular inflammatory events following COVID-19 vaccination: a multinational case series." J Ophthalmic Inflamm Infect **12**(1): 4.

BACKGROUND: Inflammatory adverse events following COVID-19 vaccination are being reported amidst the growing concerns regarding vaccine's immunogenicity and safety, especially in patients with pre-existing inflammatory conditions. METHODS: Multinational case series of patients diagnosed with an ocular inflammatory event within 14 days following COVID-19 vaccination collected from 40 centres over a 3 month period in 2021. RESULTS: Seventy patients presented with ocular inflammatory events within 14 days following COVID-19 vaccination. The mean age was 51 years (range, 19-84 years). The most common events were anterior uveitis (n = 41, 58.6%), followed by posterior uveitis (n = 9, 12.9%) and scleritis (n = 7, 10.0%). The mean time to event was 5 days and 6 days (range, 1-14 days) after the first and second dose of vaccine, respectively. Among all patients, 36 (54.1%) had a previous history of ocular inflammatory event. Most patients (n = 48, 68.6%) were managed with topical corticosteroids. Final vision was not affected in 65 (92.9%), whereas 2 (2.9%) and 3 (4.3%) had reduction in visual acuity reduced by </=3 lines and > 3 lines, respectively. Reported complications included nummular corneal lesions (n = 1, 1.4%), cystoid macular oedema (n = 2, 2.9%) and macular scarring (n = 2, 2.9%). CONCLUSION: Ocular inflammatory events may occur after COVID-19 vaccination. The findings are based on a temporal association that does not prove causality. Even in the possibility of a causal association, most of the events were mild and had a good visual outcome.

Testi, I., et al. (2023). "Ocular Inflammatory Events Following COVID-19 Vaccination in the Paediatric Population: A Multinational Case Series." Ocul Immunol Inflamm: 1-6.

BACKGROUND: Ocular inflammatory events following COVID-19 vaccination have been reported in the adult population. METHODS: Multinational case series of patients under the age of 18 diagnosed with ocular inflammatory events within 28 days of COVID-19 vaccination. RESULTS: Twenty individuals were included. The most common event was anterior uveitis (n = 8, 40.0%), followed by intermediate uveitis (7 patients, 35%), panuveitis (4 patients, 20%), and posterior uveitis (1 patient, 5%). The event was noticed in the first week after vaccination in 11 patients (55.0%). Twelve patients (60.0%) had a previous history of intraocular inflammatory event. Patients were managed with topical corticosteroids (n = 19, 95.0%), oral corticosteroids (n = 10, 50.0%), or increased dose of immunosuppressive treatment (n = 6, 30.0%). Thirteen patients (65.0%) had a complete resolution of the ocular event without complications. All patients had a final visual acuity unaffected or less than three lines of loss. CONCLUSION: Ocular inflammatory events may happen in the paediatric population following COVID-19 vaccination. Most events were successfully treated, and all showed a good visual outcome.

Yasaka, Y., et al. (2023). "A multicenter study of ocular inflammation after COVID-19 vaccination." Jpn J Ophthalmol **67**(1): 14-21.

PURPOSE: To report the characteristics of a case series of ocular inflammatory events following COVID-19 vaccination in Japan. STUDY DESIGN: Retrospective multicenter study METHODS: In this retrospective multicenter survey, a questionnaire was sent to 16 Japanese hospitals that had uveitis specialty clinics. Information on patients who developed ocular inflammatory events within 14 days of COVID-19 vaccination between

February 2021 and December 2021 was collected. RESULTS: Thirty-seven patients were diagnosed with ocular inflammatory events following COVID-19 vaccination. The mean age was 53.4 +/- 16.4 years (range, 26-86 years), and the mean time to onset after vaccination was 6.3 +/- 4.2 days (range, 1-14 days). Vogt-Koyanagi-Harada disease (VKH) was the most common event (n = 17 patients, 46%), followed by anterior uveitis (n = 6), infectious uveitis (n = 3), acute zonal occult outer retinopathy (AZOOR) (n = 2), sarcoidosis-associated uveitis (n = 1), acute posterior multifocal placoid pigment epitheliopathy (APMPPE) (n = 1), optic neuritis (n = 1), multiple evanescent white dot syndrome (MEWDS) (n = 1), Posner-Schlossman syndrome (n = 1), and unclassified uveitis (n = 4). Twenty-eight cases occurred after BNT162b2 vaccination (Pfizer-BioNTech) and 8 after mRNA-1273 vaccination (Moderna), whilst 1 patient had no information about vaccine type. CONCLUSIONS: COVID-19 vaccination can be related to various types of ocular inflammatory events. When we encounter patients with ocular inflammatory disease, we should consider that it may be an adverse effect of COVID-19 vaccination.

Other Adverse Events, including death.

Agrawal, S., et al. (2022). "Reactivation of Herpes Zoster Virus After COVID-19 Vaccination: Is There Any Association?" Cureus **14**(5): e25195.

SARS-CoV-2 disease, COVID-19 infection, is a multi-system illness that has afflicted people all over the world. A number of vaccines have been produced to combat the current COVID-19 pandemic, and a variety of side effects have been recorded following the vaccination. However, there are limited data on the negative effects of immunological reactivation following vaccination. We report 10 incidences of herpes zoster reactivation within 7-21 days of getting the COVID-19 vaccination. Transient immunomodulation following vaccination, similar to that seen in COVID-19 illness, could be one explanation for this reactivation. These cases highlight the significance of continuing to examine vaccine safety during the COVID-19 pandemic's ongoing mass vaccination campaign. We also underline the importance of peripheral health professionals in the management and reporting of any vaccination-associated adverse event.

Akaishi, T., et al. (2022). "Prolonged Diarrhea Following COVID-19 Vaccination: A Case Report and Literature Review." Tohoku J Exp Med **257**(3): 251-259.

Vaccination against coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is currently underway across countries worldwide. However, the prevalence and characteristics of prolonged adverse events lasting for several months after receiving the vaccine remain largely unknown. We herein report a 46-year-old woman with prolonged diarrhea and vomiting after receiving the BNT162b2 mRNA vaccine for COVID-19. She had no notable medical history, including that of gastrointestinal diseases. She developed vomiting several hours after receiving the first vaccine dose and further developed severe diarrhea after 7 days. Several days after the second vaccine dose, her condition deteriorated, unrelieved by symptomatic therapies, including anti-diarrheal drugs. Abdominal computed tomography (CT) revealed inflammatory changes in the entire segment of the small intestine with wall thickening. The upper and lower gastrointestinal and capsule endoscopies were unremarkable. The patient's symptoms persisted for more than 6 months after the second vaccine dose. A Vaccine Adverse Event Reporting System (VAERS) database search suggested that diarrhea is observed in approximately 3% of all vaccine recipients, but a literature review indicated that prolonged gastrointestinal symptoms lasting for several months is very rare. In summary, a case of prolonged unexplained gastrointestinal symptoms, possibly based on inflammatory changes in the small intestine, is described. A literature search revealed that this type of manifestation is very rare, and further evidence is needed to determine the causality between vaccination and gastrointestinal symptoms.

Akpandak, I., et al. (2023). "Risk of herpes zoster ophthalmicus after COVID-19 vaccination in a large US healthcare claims database." Am J Ophthalmol.

PURPOSE: Herpes zoster ophthalmicus (HZO) after COVID-19 vaccination has been reported in numerous case studies. However, no large-scale epidemiologic studies have been conducted to date. The purpose of this study was to determine whether COVID-19 vaccination is associated with an increased risk of HZO. DESIGN: Retrospective before-and-after risk interval analysis. METHODS: Setting: Optum Labs Data Warehouse, a US national de-identified claims-based database. STUDY POPULATION: Patients without a prior history of HZO who received any dose of a COVID-19 vaccine from December 11, 2020 to June 30, 2021. INTERVENTION: Any dose of a COVID-19 vaccine in the defined risk periods. MAIN OUTCOME MEASURE(S): HZO, defined by an International Classification of Disease 10(th) revision code and a prescription or escalation of antivirals. Incidence rate ratios (IRR) were calculated to compare the risk of HZO in the risk intervals after vaccination to the risk of HZO during the control interval. RESULTS: There were 1,959,157 patients who received a dose of a COVID-19 vaccine during the study period and met eligibility criteria. A total of 80 individuals without prior history of HZO were included in the analysis because they developed HZO in the risk or control period. Patients had a mean age of 54.0 years (standard deviation = 12.3). There were 45 cases of HZO in the risk interval following COVID-19 vaccination. There was not an increased risk of HZO following vaccination with BNT162b2 (IRR = 0.90, 95% CI: 0.49 - 1.69, p = 0.74), mRNA-1273 (IRR = 0.74, 95% CI: 0.36 - 1.54, p = 0.42), or Ad26.COV2.S (IRR = 0.50, 95% CI: 0.07-2.56, p = 0.42). CONCLUSIONS: This study found no evidence of increased risk of HZO following COVID-19 vaccination, providing reassurance for patients and providers who may be concerned about the safety profile of the COVID-19 vaccines.

Al-Sawalmeh, K., et al. (2022). "Acute kidney injury after Pfizer COVID-19 vaccine due to crescentic fibrillary glomerulonephritis." Clin Nephrol **98**(4): 205-208.

Fibrillary glomerulonephritis (FGN) is a rare glomerular disease manifesting with proteinuria, renal impairment, hematuria, hypertension, and in a very small proportion can be associated with rapidly progressive glomerulonephritis and, rarely, crescent formation. The main modality for diagnosis is kidney biopsy, which ultrastructurally demonstrates randomly arranged non-branching mesangial and glomerular basement membrane (GBM) fibrils and positive staining for the biomarker DNAJB9. The pathogenesis is largely unknown. It was previously hypothesized to represent an immune-complex-type glomerulonephritis, as most cases show IgG4 restriction. We present the first case of crescentic FGN after mRNA Pfizer vaccine for COVID-19. A strong temporal association between vaccination, elevated creatinine, and diffuse crescentic fibrillary process was found. Immunological, neoplastic, and infectious causes were ruled out. We hypothesized that the vaccine stimulated an immune response that triggered crescentic FGN, however, further investigations will be needed to elucidate the direct role of COVID-19 vaccination in crescentic glomerular disease.

AlAskar, B., A. Alqahtani and S. Alsuhaim (2023). "Chronic Bilateral Anterior Shoulder Fracture-Dislocation Following Febrile Seizure After COVID-19 Vaccine: A Case Report." Cureus **15**(2): e35391.

Although the shoulder is one of the most commonly dislocated joints in the body, bilateral gleno-humeral joint dislocation is considered rare. Due to its complexity and paucity of cases reported in the literature, it represents both a diagnostic and therapeutic challenge. We report a rare case of an adolescent boy who suffered chronic bilateral anterior shoulder dislocations with proximal humerus fracture and Hill-Sachs lesion after febrile seizure following COVID-19 vaccination. An 18-year-old male presented with bilateral proximal humerus fracture with anterior shoulder dislocation following a first-time seizure. He was managed with a bilateral Latarjet procedure and proximal humerus interlocking osteosynthesis (PHILOS) on the left side, and the right-side fracture was fixed with two 3.5 mm cannulated screws. After one year, the patient had a somewhat satisfactory outcome with a DASH (disabilities of the arm, shoulder, and hand) score of 31.8. Bilateral anterior shoulder dislocation with associated proximal humerus fracture remains one of the rare orthopedic injuries. Recurrent shoulder dislocations lead to chronic glenoid bone loss, which needs fixation along with fracture.

Almutairi, N., et al. (2022). "Herpes zoster in the era of COVID 19: A prospective observational study to probe the association of herpes zoster with COVID 19 infection and vaccination." Dermatol Ther **35**(7): e15521.

Herpes zoster (HZ) is caused by reactivation of the latent varicella zoster virus (VZV) following decline in cell-mediated immunity. All over the world, in the past couple of years, the Corona Virus 2019 (COVID-19) has emerged as a viral cause of severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) infection. Based on the current limited evidence, co-infection of COVID-19 with VZV or reactivation of VZV after COVID-19 vaccination has been sporadically reported. All patients diagnosed with HZ, in Farwaniya Hospital in Kuwait, from March 2020 to July 2021, having either (A) a positive COVID-19 polymerase chain reaction (PCR) test, or (B) been vaccinated against SARS-CoV-2 were enrolled in the study. All patients' demographic information, medical history, laboratory findings, and vaccination status was documented. All statistical analyses were performed using SPSS Statistics version 21.0 software. Twelve cases infected with COVID-19 with a positive PCR (group 1) and five cases vaccinated against SARS-CoV-2 (group 2) were documented. Out of the 12 COVID-19 infected patients (group 1), only two patients (16.67%) required hospitalization, while the remaining 10 patients had mild/moderate lymphopenia. Furthermore, amongst the 12 positive COVID-19 cases, four patients with HZ were diagnosed within the first week of COVID-19, while the remaining eight cases were diagnosed within 8 weeks of COVID-19. Thoracic segments were affected in five cases (41.67%), cervical in one case (8.33%), cranial in two cases (16.67%), lumbar in three cases (25%) and sacral in one case (8.33%). In group 2, three patients presented with HZ within 4 weeks of having received the first dose of the vaccine and two patients after the second dose. Blood investigations for all five vaccinated patients did not show any abnormalities. Cervical segments were affected in two patients (40%), and cranial, thoracic, and lumbar segment in the remaining patients respectively (20%). Experts must be aware of the probable increased risk of HZ during the COVID 19 pandemic. We propose appropriate curative and preventive measures against HZ infection, including a

systematic follow-up of these patients to ensure that they stick to extreme safety measures till the diagnosis of COVID-19 is omitted.

Angeli, F., et al. (2022). "[Hypertension after COVID-19 vaccination]." G Ital Cardiol (Rome) **23**(1): 10-14.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) rapidly spread across the world, killing more than 4 million individuals globally, with 240 million individuals being confirmed by laboratory tests. Among different therapeutic strategies to prevent SARS-CoV-2 infection, vaccines are the most promising approach for curbing the pandemic. They elicit an immune neutralizing response and thus offer protection against coronavirus disease 2019 (COVID-19). However, some questions regarding the safety of COVID-19 vaccines have been raised and based on sparse reports of severe systemic reactions after vaccination. Among these, evidences on the potential effect of vaccination on the acute rise in blood pressure have been recently accrued. Approved vaccines in Europe increase the endogenous synthesis of SARS-CoV-2 Spike proteins from a variety of cells. Once synthetized in the cells reached by the vaccine, the Spike proteins first assemble in the cytoplasm and then migrate to the cell surface to protrude with a native-like conformation. Spike proteins are recognized by the immune system which rapidly develops an immune response. Furthermore, the Spike proteins assembled in the cells which are eventually destroyed by the immune response circulate in the blood as free-floating forms. Free-floating Spike proteins may interact with angiotensin-converting enzyme 2 (ACE2) receptors leading to internalization, degradation, and dysregulation of the catalytic activities of these receptors. The consequent loss of ACE2 receptor activity leads to a rapid drop in the generation of angiotensin1,7 resulting from inactivation of angiotensin II. The imbalance between angiotensin II (overactivity) and of angiotensin1,7 (deficiency) might play a role in the genesis of acute elevation in blood pressure.

Bardenheier, B. H., et al. (2021). "Adverse Events Following One Dose of mRNA COVID-19 Vaccination Among US Nursing Home Residents With and Without a Previous SARS-CoV-2 Infection." J Am Med Dir Assoc **22**(11): 2228-2232.

OBJECTIVES: To compare rates of adverse events following Coronavirus Disease 2019 (COVID-19) vaccination among nursing home residents with and without previous severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. DESIGN: Prospective cohort. SETTING AND PARTICIPANTS: A total of 20,918 nursing home residents who received the first dose of messenger RNA COVID-19 vaccine from December 18, 2020, through February 14, 2021, in 284 facilities within Genesis Healthcare, a large nursing home provider spanning 24 US states. METHODS: We screened the electronic health record for adverse events, classified by the Brighton Collaboration, occurring within 15 days of a resident's first COVID-19 vaccine dose. All events were confirmed by physician chart review. To obtain risk ratios, multilevel logistic regression model that accounted for clustering (variability) across nursing homes was implemented. To balance the probability of prior SARS-CoV-2 infection (previous positive test or diagnosis by the International Classification of Diseases, 10(th) Revision, Clinical Modification) more than

20 days before vaccination, we used inverse probability weighting. To adjust for multiplicity of adverse events tested, we used a false discovery rate procedure. RESULTS: Statistically significant differences existed between those without (n = 13,163) and with previous SARS-CoV-2 infection [symptomatic (n = 5617) and asymptomatic (n = 2138)] for all baseline characteristics assessed. Only 1 adverse event was reported among those with previous SARS-CoV-2 infection (asymptomatic), venous thromboembolism [46.8 per 100,000 residents 95% confidence interval (CI) 8.3-264.5], which was not significantly different from the rate reported for those without previous infection (30.4 per 100,000 95% CI 11.8-78.1). Several other adverse events were observed for those with no previous infection, but were not statistically significantly higher than those reported with previous infection after adjustments for multiple comparisons. CONCLUSIONS AND IMPLICATIONS: Although reactogenicity increases with preexisting immunity, we did not find that vaccination among those with previous SARS-CoV-2 infection resulted in higher rates of adverse events than those without previous infection. This study stresses the importance of monitoring novel vaccines for adverse events in this vulnerable population.

Bass, J. R. and G. A. Poland (2022). "Shoulder injury related to vaccine administration (SIRVA) after COVID-19 vaccination." Vaccine **40**(34): 4964-4971.

OBJECTIVE: The global fight against COVID-19 has required mass vaccination clinics as well as mass recruitment of personnel, including many who may not regularly administer intramuscular deltoid immunizations, potentially increasing the incidence of improper intramuscular injection. Shoulder injury related to vaccine administration (SIRVA) is a well-described, preventable injury resulting from improper injection into anatomic structures adjacent to the deltoid muscle leading to mechanical and chemical trauma augmented by an inflammatory immune response to the vaccine and/or adjuvants. SIRVA is best described in the setting of influenza vaccination, and little is known about it as it pertains to COVID-19 vaccination. This study aims to describe SIRVA in the current pandemic, increase clinician awareness, and offer considerations for prevention. METHODS: To identify clinical characteristics of patients with post-COVID-19-vaccination shoulder injuries, we performed a systematic review of the cases of vaccination-related shoulder injuries reported in the literature and conducted a review of the public Vaccine Adverse Event Reporting System (VAERS). RESULTS: We identified 305 cases of SIRVA in the VAERS database and 28 cases of SIRVA in the setting of COVID-19 vaccination from the literature (n = 333). Patients had a mean age of 51.8 years and a median of 51.5 (range: 19-90) years. Of these, 76.3% were female and 23.7% male. Most patients sought medical evaluation with 54 of the 305 VAERS cases reporting utilizing emergency services. Of patients with imaging-confirmed SIRVA (n = 95), the most common diagnoses were adhesive capsulitis and bursitis, and the most common symptoms were pain (97.7%) and limited range of motion (68.1%). Most patients reported requiring treatment with the majority receiving physical therapy (56.3%), followed by cortisone injection (34.4%). Other modalities used were non-steroidal anti-inflammatory drugs, oral steroids, and surgery. Only 5 patients from this group reported recovery while 60 stated they had not yet recovered. Of those, 23.3% reported disability. CONCLUSION:

SIRVA should be regarded as an under-reported, significant cause of post-vaccination morbidity. In the setting of COVID-19 mass vaccination, clinicians must be aware of signs and symptoms of SIRVA as well as appropriate diagnostic modalities and treatment options. Additionally, standardization and proper education regarding injection technique and appropriate needle length is imperative to reducing harm.

Boschi, C., et al. (2022). "SARS-CoV-2 Spike Protein Induces Hemagglutination: Implications for COVID-19 Morbidities and Therapeutics and for Vaccine Adverse Effects." Int J Mol Sci **23**(24).

Experimental findings for SARS-CoV-2 related to the glycan biochemistry of coronaviruses indicate that attachments from spike protein to glycoconjugates on the surfaces of red blood cells (RBCs), other blood cells and endothelial cells are key to the infectivity and morbidity of COVID-19. To provide further insight into these glycan attachments and their potential clinical relevance, the classic hemagglutination (HA) assay was applied using spike protein from the Wuhan, Alpha, Delta and Omicron B.1.1.529 lineages of SARS-CoV-2 mixed with human RBCs. The electrostatic potential of the central region of spike protein from these four lineages was studied through molecular modeling simulations. Inhibition of spike protein-induced HA was tested using the macrocyclic lactone ivermectin (IVM), which is indicated to bind strongly to SARS-CoV-2 spike protein glycan sites. The results of these experiments were, first, that spike protein from these four lineages of SARS-CoV-2 induced HA. Omicron induced HA at a significantly lower threshold concentration of spike protein than the three prior lineages and was much more electropositive on its central spike protein region. IVM blocked HA when added to RBCs prior to spike protein and reversed HA when added afterward. These results validate and extend prior findings on the role of glycan bindings of viral spike protein in COVID-19. They furthermore suggest therapeutic options using competitive glycan-binding agents such as IVM and may help elucidate rare serious adverse effects (AEs) associated with COVID-19 mRNA vaccines, which use spike protein as the generated antigen.

Boskabadi, S. J., et al. (2023). "Acute pancreatitis following COVID-19 vaccine: A case report and brief literature review." Heliyon **9**(1): e12914.

Vaccination is the most effective way to overcome COVID-19 morbidity and mortality. However, Covid-19 vaccines may cause potential adverse effects. We reported a 28-year-old healthy woman who was referred to the emergency department with a chief complaint of severe abdominal pain, nausea and hemoptysis. She has received two doses of COVID-19 vaccine (Sinopharm BIBP). Similar this time, three days after the injection of the second dose of the Sinopharm BIBP COVID-19 vaccine, abdominal and flank pain appeared, for which she has referred to the emergency department. After necessary tests and pancreatitis was confirmed, we started fluid therapy, plasmapheresis, gemfibrozil and insulin for patient management. The COVID-19 vaccines may lead to acute pancreatitis. The mechanism of pancreatitis caused by COVID-19 vaccines is unclear. Acute pancreatitis can develop after COVID-19 vaccination. This process can even happen a few months later. Therefore, to better diagnosis and

prevention of long-term complications, it is necessary to measuring the lipase or amylase in patients that received COVID-19 vaccine if abdominal pain was occurred.

Cantarelli Rodrigues, T., et al. (2021). "Subacromial-subdeltoid bursitis following COVID-19 vaccination: a case of shoulder injury related to vaccine administration (SIRVA)." Skeletal Radiol **50**(11): 2293-2297.

Vaccination injection site adverse reactions are usually mild and transient, and post-vaccination musculoskeletal symptoms, such as myalgia and arthralgia, are very common. Shoulder injury related to vaccine administration (SIRVA), defined as shoulder pain and limited range of motion occurring after the administration of a vaccine intended for intramuscular administration in the upper arm, is a well-established condition in the medical literature, yet underreported. In such cases, subacromial-subdeltoid bursitis may occur, leading to shoulder dysfunction and ongoing pain. Millions of doses of vaccines for the prevention of COVID-19 have been administered to adults worldwide during the pandemic. We report a case of subacromial-subdeltoid bursitis after COVID-19 vaccination, related to the unintentional injection of vaccine solution into the bursa resulting in a robust immune-mediated inflammatory reaction.

Castruita, J. A. S., et al. (2023). "SARS-CoV-2 spike mRNA vaccine sequences circulate in blood up to 28 days after COVID-19 vaccination." APMIS **131**(3): 128-132.

In Denmark, vaccination against Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2) has been with the Pfizer-BioNTech (BTN162b2) or the Moderna (mRNA-1273) mRNA vaccines. Patients with chronic hepatitis C virus (HCV) infection followed in our clinic received mRNA vaccinations according to the Danish roll-out vaccination plan. To monitor HCV infection, RNA was extracted from patient plasma and RNA sequencing was performed on the Illumina platform. In 10 of 108 HCV patient samples, full-length or traces of SARS-CoV-2 spike mRNA vaccine sequences were found in blood up to 28 days after COVID-19 vaccination. Detection of mRNA vaccine sequences in blood after vaccination adds important knowledge regarding this technology and should lead to further research into the design of lipid-nanoparticles and the half-life of these and mRNA vaccines in humans.

Chapin-Bardales, J., et al. (2021). "Reactogenicity within 2 weeks after mRNA COVID-19 vaccines: Findings from the CDC v-safe surveillance system." Vaccine **39**(48): 7066-7073.

BACKGROUND: Post-authorization monitoring of mRNA-based COVID-19 vaccines is needed to better characterize their reactogenicity. We assessed reactions reported during the 2 weeks after receipt of BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna) vaccines. METHODS: We monitored persons who enrolled in v-safe after vaccination health checker(SM), a U.S. smartphone-based vaccine monitoring system, after receiving BNT162b2 or mRNA-1273. V-safe participants received text message prompts to complete web-based surveys. We analyzed responses from persons who received BNT162b2 or mRNA-1273 from December 14, 2020 through March 14, 2021 and completed at least one survey by March 28, 2021. We measured the proportion of participants reporting local and systemic reactions solicited in surveys completed days 0

through 7 post-vaccination. For day 14 surveys, participants described new or worsening symptoms in a free-text response. We assessed the proportion of participants reporting new or worsening local and systemic reactions. RESULTS: One-third of participants were aged <45 years, two-thirds were female, and approximately half received BNT162b2 vaccine. A total of 4,717,908 participants reported during the 7 days after dose 1 and 2,906,377 reported during the 7 days after dose 2. Most reported at least one injection-site reaction (68.5% after dose 1; 72.9% after dose 2) or at least one systemic reaction (50.6% after dose 1; 69.5% after dose 2). Reactogenicity was greater after dose 2 and among mRNA-1273 recipients, persons aged <45 years, and females. New or worsening local and systemic reactions were uncommon during week 2 after either dose; the most frequent were local reactions for dose 1 mRNA-1273 recipients (2.6%). These reactions were reported more often among females after dose 1 mRNA-1273 (3.6%). CONCLUSIONS: During post-authorization monitoring among >4 million vaccinees, local and systemic reactions were commonly reported following mRNA-based vaccines. Reactions were most common during the first week following dose 2 and among persons aged <45 years, females, and mRNA-1273 recipients.

Chavez, A. and C. Pougnier (2021). "A Case of COVID-19 Vaccine Associated New Diagnosis Myasthenia Gravis." J Prim Care Community Health **12**: 21501327211051933.

An 82-year-old man presented with intermittent episodes of slurred speech during his evening meals after receiving the BNT162b2 COVID-19 vaccine. Thorough evaluation was conducted including lab work and EMG confirming a new diagnosis of late-onset myasthenia gravis. Despite treatment, the patient progressed rapidly to severe exacerbation requiring intubation and placement of a PEG tube. Infections provoking new diagnosis and exacerbations of myasthenia gravis have been reported. New diagnosis of myasthenia gravis associated with the COVID-19 vaccine is rarely reported. This case highlights the need for clinicians to be aware of the uncommon presenting symptoms in late-onset myasthenia gravis and the possibility of vaccine provoked diagnoses of immune mediated diseases.

Chow, J. C. K., S. L. Koles and A. J. Bois (2022). "Shoulder injury related to SARS-CoV-2 vaccine administration." CMAJ **194**(2): E46-E49.

Chu, E. C. (2022). "Shoulder Injury Related to Vaccine Administration (SIRVA) in 16 Patients Following COVID-19 Vaccination Who Presented to Chiropractic, Orthopedic, and Physiotherapy Clinics in Hong Kong During 2021." Med Sci Monit **28**: e937430.

BACKGROUND Shoulder injury related to vaccine administration (SIRVA) occurs when an intramuscular deltoid injection is administered into the shoulder joint. This observational study describes clinical features in 16 patients with SIRVA following Coronavirus 2019 (COVID-19) vaccination who presented to chiropractic, orthopedic, and physiotherapy clinics in Hong Kong between January 1, 2021, and January 1, 2022. MATERIAL AND METHODS Adults age >/=18 with new-onset shoulder pain and imaging-confirmed shoulder pathology were retrospectively identified from 35 clinics. Patient demographics and clinical and vaccination details were extracted from the electronic

medical record. Shoulder injury was determined by correlating clinical and imaging features. RESULTS Of 730 patients with shoulder pain, 16 SIRVA cases (mean age, 49+/-10 years, 75% female) were identified; (12/16, 75%) of patients received the Pfizer-BioNTech vaccine while (4/16, 25%) received Sinovac-CoronaVac. The most common diagnosis was adhesive capsulitis (10/16, 63%), followed by bursitis (3/16, 19%) and supraspinatus tear (3/16, 19%). Mean symptom onset was 3.5+/-2.5 days post-vaccination, and always occurred after the 2nd or 3rd vaccination, involving reduced shoulder range of motion (ROM). Mean baseline pain was 8.1+/-1 (out of 10). All patients received conservative care (eg, exercise, manual therapies). At 3-month follow-up, mean pain reduced to 2.4+/-1.4; all patients had normal shoulder ROM. CONCLUSIONS In the past 2 years, millions of intramuscular COVID-19 vaccinations have been administered. It is important that clinicians are aware of SIRVA as a cause of new symptoms of shoulder injury and should ask the patient about recent vaccinations, including for COVID-19.

Conceicao, M. S., et al. (2021). "Maintenance of Muscle Mass and Cardiorespiratory Fitness to Cancer Patients During COVID-19 Era and After SARS-CoV-2 Vaccine." Front Physiol **12**: 655955.

There is emerging evidence that decreased muscle mass and cardiorespiratory fitness (CRF) are associated with increased risk of cancer-related mortality. This paper aimed to present recommendations to prescribe effective and safe exercise protocols to minimize losses, maintain or even improve muscle mass, strength, and CRF of the cancer patients who are undergoing or beyond treatment during the COVID-19 era. Overall, we recommend performing exercises with bodyweight, elastic bands, or suspension bands to voluntary interruption (i.e., interrupt the exercise set voluntarily, according to their perception of fatigue, before concentric muscular failure) to maintain or increase muscle strength and mass and CRF during COVID-19 physical distancing. Additionally, rest intervals between sets and exercises (i.e., long or short) should favor maintaining exercise intensities between 50 and 80% of maxHR and/or RPE of 12. In an exercise program with these characteristics, the progression of the stimulus must be carried out by increasing exercise complexity, number of sets, and weekly frequency. With feasible exercises attainable anywhere, modulating only the work-to-rest ratio and using voluntary interruption, it is possible to prescribe exercise for a wide range of patients with cancer as well as training goals. Exercise must be encouraged; however, exercise professionals must be aware of the patient's health condition even at a physical distance to provide a safe and efficient exercise program. Exercise professionals should adjust the exercise prescription throughout home confinement whenever necessary, keeping in mind that minimal exercise stimuli are beneficial to patients in poor physical condition.

Cruess, S. M., et al. (2023). "Icosapent ethyl (VASCEPA((R))) as treatment for post-acute sequelae of SARS CoV-2 (PASC) vaccine induced injury and infection." J Complement Integr Med **20**(3): 662-664.

OBJECTIVES: As the COVID-19 pandemic continues, a prolonged post-infectious syndrome or "long COVID" has been reported. This is a multi-organ post viral syndrome that persists well after infection. Currently, there is no available treatment. Emerging

evidence credits this "long COVID" syndrome to ongoing inflammatory response following resolution of symptoms during infection. An omega-three fatty acid derivative used in the treatment of hypertriglyceridemia, Icosapent Ethyl (IPE, VASCEPA((R))/Epadel((R))), was previously shown to reduce cardiovascular risk, likely via immunomodulatory effects. This study aims to evaluate the effectiveness of Icosapent Ethyl. METHODS: Following previous publications in treatment of severe acute COVID-19, we analyze two case studies of adults treated with Icosapent Ethyl. RESULTS: After experiencing the symptoms of Long Covid, both individuals analyzed across two case studies experiences a resolution of symptoms after treatment with Icosapent Ethyl. CONCLUSION: After review and analysis we conclude that Icosapent Ethyl may have been a determining factor in Long COVID symptom resolution and should be studied further.

de Souza Campos Fernandes, R. C., et al. (2023). "Henoch-Schonlein purpura in a 6-year-old boy after initial COVID-19 vaccination." Vaccine X **14**: 100333.

The COVID-19 pandemic has significantly impacted global health, and the widespread immunization of adults against SARS-CoV-2 has played a pivotal role in altering the course of the disease. While COVID-19 vaccine adverse events are generally uncommon and mild, the recent vaccination of the pediatric population has emphasized the need for vigilance and reporting of potential side effects. In this case report, we present a 6-year-old boy who developed Henoch-Schonlein purpura following the administration of the first dose of Pfizer-BioNTech BNT16B2b2 mRNA COVID-19 vaccine, making it the earliest reported case of such an adverse event. Our report highlights the importance of continued monitoring and reporting of adverse events in pediatric patients receiving the COVID-19 vaccine, as well as the need for prompt diagnosis and management of potential vaccine-related complications.

Dey, R. K., et al. (2022). "Acute pancreatitis in pregnancy following COVID-19 vaccine: a case report." J Med Case Rep **16**(1): 354.

BACKGROUND: Since the approval of the Pfizer-BioNTech (BNT162b2) mRNA vaccine for COVID-19 infection, a few adverse effects have been reported. Acute pancreatitis has been reported in a few patients. However, there is currently no research showing a direct relationship between the vaccine and acute pancreatitis. Here, we report a case of acute pancreatitis following Pfizer vaccination in a young healthy pregnant woman without any known risk factors. To our knowledge, this is the first case report of possible vaccine-induced pancreatitis in a pregnant woman. CASE PRESENTATION: The patient, a 24-year-old South-Asian female, at 31 weeks of gestation, presented with severe epigastric pain radiating to the back and worsening on lying supine, associated with nausea and vomiting. She was diagnosed with acute pancreatitis with a serum lipase level of 4376 U/L and an ultrasound showing features of pancreatitis. The patient received her first dose of the Pfizer vaccine 1 week prior to these symptoms. Detailed evaluation did not show any etiological cause of pancreatitis. The patient had a spontaneous vaginal delivery and the baby was shifted to the neonatal intensive care unit in a stable condition. A computed tomography scan postpartum (day 2)

demonstrated acute interstitial edematous pancreatitis. The patient was managed conservatively in the intensive care unit and discharged home in a stable condition. CONCLUSION: This report highlights the importance of a detailed history and evaluation, and the close monitoring of any patient presenting with abdominal pain after vaccination. Acute pancreatitis can be fatal if not picked up early.

Edler, C., et al. (2021). "Deaths associated with newly launched SARS-CoV-2 vaccination (Comirnaty(R))." Leg Med (Tokyo) **51**: 101895.

Since 27th December 2020, a mRNA vaccine from BioNTech / Pfizer (Comirnaty(R)) has been used across Germany. As of 12th March 2021, 286 fatalities of vaccinated German individuals were registered at the Paul-Ehrlich-Institute with time intervals after vaccination between one hour to 40 days. From our catchment area in northern Germany, we have so far become aware of 22 deaths in connection with vaccination in a 5 week period (range: 0-28 days after vaccination). Three death cases after vaccination with Comirnaty(R), which were autopsied at the Institute of Legal Medicine Hamburg, are presented in more detail. All three deceased had severe cardiovascular diseases, among other comorbidities, and died in the context of these pre-existing conditions, while one case developed a COVID-19 pneumonia as cause of death. Taking into account the results of the postmortem examination a causal relation between the vaccination and the death was not established in any case. If there are indications of an allergic reaction, histological and postmortem laboratory examinations should be performed subsequent to the autopsy (tryptase, total IgE, CRP, interleukin-6, complement activity C3/C5).

Fernandez Martinez, A. M., M. T. Cuesta Marcos and J. Rodriguez Prieto (2023). "Transarterial Embolization for Shoulder Injury Related to Vaccine COVID-19 Administration." Cardiovasc Intervent Radiol **46**(2): 292-294.

Finsterer, J. and S. Mehri (2023). "The nature and severity of SARS-CoV-2 vaccine side effects in athletes are highly dependent on study design." Hum Vaccin Immunother **19**(2): 2252266.

Fortier, L. M., et al. (2023). "Common Characteristics of Shoulder Injury Related to Vaccine Administration (SIRVA) Following COVID-19 Vaccination: A Comprehensive Systematic Review." J Shoulder Elbow Surg.

BACKGROUND: The pathogenesis of SIRVA is incompletely understood, but it is postulated to be an immune-mediated inflammatory response to a vaccine antigen, leading to shoulder pain and dysfunction. The purpose of this investigation is to systematically review the literature related to SIRVA specifically after the COVID-19 vaccination by describing the diagnostic and clinical characteristics, diagnoses associated with SIRVA, and incidence between vaccine types. METHODS: A systematic review was performed to identify level I to IV studies and case descriptions of shoulder pain occurring after COVID-19 vaccination. To confirm that no studies were missing from the systematic review, references of studies from the initial search were scanned for additional relevant studies. RESULTS: A total of 22 studies, comprised of 81 patients,

were identified meeting the inclusion/exclusion criteria. Reports were most commonly published from countries in Asia (53.1%; n = 43/81). The most commonly described vaccines were Oxford-AstraZeneca at 37.0% (n = 30/81) and Pfizer-BioNTech at 33.3% (n = 27/81). Symptoms occurred most commonly after at least 72 hours of administration (30.9%, n = 25/81). One hundred percent of patients (n = 81/81) described pain as an associated symptom and 90.1% of patients (n = 73/81) described multiple symptoms. The diagnostic modalities utilized to identify a specific pathology consisted of magnetic resonance imaging (MRI) (55.6%; n = 45/81), ultrasound (28.4; n = 23/81), radiograph (25.9%; n = 21/81), and computed tomography (CT) (4.9%; 4/81). Nearly a third of patients (32.1%; n = 26/81) were diagnosed with bursitis, while 22 (27.2%) were diagnosed with adhesive capsulitis, 17 (21.0%) with either rotator cuff tear or tendinopathy, and 14 (17.3%) with polymyalgia rheumatica (PMR) or PMR-like syndrome. The two most common treatment options were physical therapy (34.6%; n = 28/81) and nonsteroidal anti-inflammatory medications (NSAIDs) (33.3%; 27/81). The majority of SIRVA cases (52.1%; n = 38/73) completely resolved within a few weeks to months. CONCLUSION: Despite the limited quality and lack of large-scale studies, it is important for providers to recognize SIRVA as a potential risk factor as the number of patients receiving COVID-19 vaccinations and boosters continues to rise.

Fraiman, J., et al. (2022). "Serious adverse events of special interest following mRNA COVID-19 vaccination in randomized trials in adults." Vaccine **40**(40): 5798-5805.

INTRODUCTION: In 2020, prior to COVID-19 vaccine rollout, the Brighton Collaboration created a priority list, endorsed by the World Health Organization, of potential adverse events relevant to COVID-19 vaccines. We adapted the Brighton Collaboration list to evaluate serious adverse events of special interest observed in mRNA COVID-19 vaccine trials. METHODS: Secondary analysis of serious adverse events reported in the placebo-controlled, phase III randomized clinical trials of Pfizer and Moderna mRNA COVID-19 vaccines in adults (NCT04368728 and NCT04470427), focusing analysis on Brighton Collaboration adverse events of special interest. RESULTS: Pfizer and Moderna mRNA COVID-19 vaccines were associated with an excess risk of serious adverse events of special interest of 10.1 and 15.1 per 10,000 vaccinated over placebo baselines of 17.6 and 42.2 (95 % CI -0.4 to 20.6 and -3.6 to 33.8), respectively. Combined, the mRNA vaccines were associated with an excess risk of serious adverse events of special interest of 12.5 per 10,000 vaccinated (95 % CI 2.1 to 22.9); risk ratio 1.43 (95 % CI 1.07 to 1.92). The Pfizer trial exhibited a 36 % higher risk of serious adverse events in the vaccine group; risk difference 18.0 per 10,000 vaccinated (95 % CI 1.2 to 34.9); risk ratio 1.36 (95 % CI 1.02 to 1.83). The Moderna trial exhibited a 6 % higher risk of serious adverse events in the vaccine group: risk difference 7.1 per 10,000 (95 % CI -23.2 to 37.4); risk ratio 1.06 (95 % CI 0.84 to 1.33). Combined, there was a 16 % higher risk of serious adverse events in mRNA vaccine recipients: risk difference 13.2 (95 % CI -3.2 to 29.6); risk ratio 1.16 (95 % CI 0.97 to 1.39). DISCUSSION: The excess risk of serious adverse events found in our study points to the need for formal harm-benefit analyses, particularly those that are stratified according to risk of serious COVID-19 outcomes. These analyses will require public release of participant level datasets.

Gringeri, M., et al. (2022). "Herpes zoster and simplex reactivation following COVID-19 vaccination: new insights from a vaccine adverse event reporting system (VAERS) database analysis." Expert Rev Vaccines **21**(5): 675-684.

BACKGROUND: A few cases of Herpes Zoster and Simplex reactivation following COVID-19 immunization have been recently described, but the real extent of this suspected adverse event has not been elucidated yet. METHODS: We performed a nested case/control study by using the U.S. Vaccine Adverse Event Reporting System database. We carried out a case-level clinical review of all Herpes reactivation cases following the administration of COVID-19 vaccines. For cases and controls, significance was set at P = 0.05, differential risk of reporting was assessed for each vaccine as reporting odds ratio and incidence was estimated based on the total number of vaccine doses administered. RESULTS: Of 6,195 cases included in the analysis (5,934 and 273 reporting Herpes Zoster and Herpes Simplex, respectively) over 90% were non-serious. We found a slightly higher risk of reporting both for Zoster (ROR = 1.49) and Simplex (ROR = 1.51) infections following the Pfizer-BioNTech vaccine. The estimated incidence was approximately 0.7/100,000 and 0.03/100,000 for Zoster and Simplex, respectively. CONCLUSIONS: The paucity of cases (almost all of non-serious nature) makes the potential occurrence of this adverse effect negligible from clinical standpoints, thus supporting the good safety profile of the COVID-19 vaccination, which remains strongly recommended.

Griss, J., et al. (2022). "A case of COVID-19 vaccination-associated forme fruste purpura fulminans." Br J Dermatol **186**(1): e1.

We report the case of a female, 77 year old patient with multi-localized skin infarctions following vaccination with mRNA-1273 (Moderna). This phenomenon is to our knowledge otherwise only seen in infection-associated purpura fulminans - which was thoroughly ruled out in our patient. This report demonstrates that we need to be vigilant of a wider array of vascular phenomena related to Covid vaccinations.

Gulumsek, E., et al. (2023). "Minimal Change Nephrotic Syndrome with Acute Kidney Injury after the Administration of Pfizer-BioNTech COVID-19 Vaccine." Case Rep Infect Dis **2023**: 5122228.

Nephrotic syndrome progresses with various metabolic disturbances, such as proteinuria over 3.5 grams in 24 hours, hypoalbuminemia, and hypercoagulability. Patients usually complain about diffuse edema throughout the body, which is secondary to hypoalbuminemia. It has many primary and secondary causes. Patients may require a renal biopsy to confirm the diagnosis. Besides, many secondary causes of nephrotic syndrome should be examined and excluded. Although many vaccines were developed due to the COVID-19, many side effects are still reported because of the Pfizer-BioNTech COVID-19 vaccine (COVID-19 mRNA and BNT162b2), which is widely used in Turkey. This study examines a case of nephrotic syndrome with acute renal injury after Pfizer-BioNTech vaccine.

Hamdi, O. A., R. H. Jonas and J. J. Daniero (2022). "Vocal Fold Paralysis Following COVID-19 Vaccination: Query of VAERS Database." J Voice.

OBJECTIVE: Vocal fold paresis or paralysis (VFP) may severely affect quality of life due to dysphonia and respiratory distress. As an increasing percentage of the United States population receives the COVID-19 vaccination, the objective of this study is to determine the correlation of COVID-19 postvaccination recurrent laryngeal neuropathy and resulting VFP. METHODS: The Vaccine Adverse Event Reporting System database was queried for patients exhibiting symptoms of VFP following COVID-19 vaccination. Patient demographics and clinical information including presenting symptoms, time of symptom onset, time of diagnosis and laterality. RESULTS: Twenty patients were found to have laryngoscopy confirmed VFP following COVID-19 vaccination. Vaccinations for Pfizer-BioNTech, Moderna, and Janssen were reported. Of those reported, 13 patients were female (65.0%) and seven were male (35.0%), with a mean age of 61.8 years. The most common presenting symptom was a hoarse voice (30.0%). A majority of these cases were unilateral in nature (64.0%). Mean time from vaccination to symptom onset was 12.1 days and mean time from vaccination to diagnosis was 37.6 days. CONCLUSION: For patients presenting with voice or swallowing complaints after receiving the COVID-19 vaccine, prompt evaluation by an otolaryngologist should occur. However, the potential VFP side effect of vaccination is very rarely cited in the literature and largely outweighed by the benefits of vaccination. Further research is needed to delineate the exact pathophysiology of this complication and determine whether a causal relationship exists.

Heck, E., et al. (2022). "Flagellate purpura associated with COVID-19 vaccination." J Eur Acad Dermatol Venereol **36**(1): e33-e34.

Hermida Perez, B., S. Robles Gaitero and R. Garcia Lopez (2022). "AMA-positive hepatitis induced by the SARS-CoV-2 vaccine." Rev Esp Enferm Dig **114**(5): 297-298.

We present the case of a 56-year-old female admitted to our centre for hepatitis. She had recieved the first dose of the BNT162b2 vaccine against SARS-CoV-2 10 days before the admission. Etiologic study was negative. The patient was diagnosed with vaccine-induced hepatitis.

Honarmand, A. R., J. Mackey and R. Hayeri (2021). "Shoulder injury related to vaccine administration (SIRVA) following mRNA COVID-19 vaccination: Report of 2 cases of subacromial-subdeltoid bursitis." Radiol Case Rep **16**(12): 3631-3634.

Shoulder pain has been reported as a common side-effect after COVID-19 vaccination particularly after administration of mRNA vaccines. Although it is usually mild and self-limiting, occasionally it can become more extensive causing severe pain and marked limited range of motion. Shoulder injury related to vaccine administration has been reported following injection of other routine vaccines. In this case report, we describe 2 cases of shoulder injury related to vaccine administration due to subacromial-subdeltoid bursitis after administration of mRNA COVID-19 vaccines.

Huang, B. D., et al. (2022). "New-Onset Myasthenia Gravis After ChAdOx1 nCOV-19 Vaccine Inoculation." J Neuroophthalmol.

Janssen, E. R. C., et al. (2023). "The prevalence and clinical course of shoulder injury related to vaccine administration (SIRVA) after COVID-19 vaccines in Dutch hospital workers." Vaccine.

INTRODUCTION: Shoulder Injury Related to Vaccine Administration (SIRVA) is a rare disorder characterized by persistent shoulder pain and limited range of motion presenting within 48 h after vaccine administration. With the widespread distribution of the COVID-19 vaccine, the incidence of SIRVA is expected to rise. This sudden rise in vaccine administration presents an ideal opportunity to estimate the prevalence of SIRVA and to better characterize SIRVA. OBJECTIVE: This study aims to investigate the prevalence of SIRVA following COVID-19 vaccine administration among hospital workers in the Netherlands. METHODS: A questionnaire was sent to all hospital workers from a single non-academic hospital in the Netherlands. Respondents who had active SIRVA complaints were invited for an outpatient orthopaedic clinic assessment. Data was collected on participant characteristics and physical examination including assessment of active and passive range of motion (ROM). An ultrasound was performed to identify potential abnormalities. RESULTS: 32 out of 981 (3.3%) respondents reported shoulder pain with limited ROM occurring within 48 h after vaccine administration lasting for at least 7 days. Of these 32 respondents with SIRVA, 18 (56.2%) still reported active symptoms at the time of the survey. Clinical examination of 13 (72.2%) respondents with active SIRVA complaints showed limited glenohumeral ROM, limitations in activities of daily living and injection site pain. Twelve out of thirteen (92.3%) respondents with active SIRVA complaints showed abnormalities of the soft-tissue of the shoulder on ultrasound. Physiotherapy was the most common treatment modality for persistent SIRVA complaints (38.9%). CONCLUSIONS: The prevalence of SIRVA is estimated at 3% in the adult working population. Signs and symptoms of SIRVA are variable in severity, localization and timing. Soft-tissue abnormalities is the most common clinical sign. This study contributes to clinician's knowledge on SIRVA, aiding in early recognition and treatment, which are imperative for prevention of persistent and severe shoulder pathology.

Jena, A., et al. (2022). "Nintedanib-induced liver injury: Not every liver injury is virus or vaccine-induced in the era of COVID-19." Liver Int **42**(5): 1210-1211.

Kaimori, R., et al. (2022). "Histopathologically TMA-like distribution of multiple organ thromboses following the initial dose of the BNT162b2 mRNA vaccine (Comirnaty, Pfizer/BioNTech): an autopsy case report." Thromb J **20**(1): 61.

BACKGROUND: Coronavirus disease 2019 (COVID-19) has spread worldwide. Vaccination is now recommended as one of the effective countermeasures to control the pandemic or prevent the worsening of symptoms. However, its adverse effects have been attracting attention. Here, we report an autopsy case of multiple thromboses after receiving the first dose of the BNT162b2 mRNA vaccine (Comirnaty, Pfizer/BioNTech) in an elderly woman. CASE PRESENTATION: A 72-year-old woman with a history of diffuse large B-cell lymphoma in the stomach and hyperthyroidism received the first dose of the BNT162b2 mRNA vaccine and died 2 days later. The autopsy revealed multiple

microthrombi in the heart, brain, liver, kidneys, and adrenal glands. The thrombi were CD61 and CD42b positive and were located in the blood vessels primarily in the pericardial aspect of the myocardium and subcapsular region of the adrenal glands; their diameters were approximately 5-40 mum. Macroscopically, a characteristic myocardial haemorrhage was observed, and the histopathology of the characteristic thrombus distribution, which differed from that of haemolytic uraemic syndrome and disseminated intravascular coagulation, suggested that the underlying pathophysiology may have been similar to that of thrombotic microangiopathy (TMA). CONCLUSION: This is the first report on a post-mortem case of multiple thromboses after the BNT162b2 mRNA vaccine. The component thrombus and characteristic distribution of the thrombi were similar to those of TMA, which differs completely from haemolytic uraemic syndrome or disseminated intravascular coagulation, after vaccination. Although rare, it is important to consider that fatal adverse reactions may occur after vaccination and that it is vital to conduct careful follow-up.

Kan, A. K. C., et al. (2023). "Adult-onset Still's disease after mRNA COVID-19 vaccination presenting with severe myocarditis with acute heart failure and cardiogenic shock: a case report." Hong Kong Med J **29**(2): 162-164.

Kantar, A., et al. (2021). "Acute Mild Pancreatitis Following COVID-19 mRNA Vaccine in an Adolescent." Children (Basel) **9**(1).

A 17-year-old male was referred to the emergency room with sharp abdominal pain, pallor, sweating, and vomiting 12 h after the administration of his first Pfizer-BioNTech vaccine for coronavirus disease 2019 (COVID-19). He had abdominal pain, an increase in serum lipase value of > 3 times the upper limits of normal, and magnetic resonance imaging (MRI) findings consistent with acute mild pancreatitis (AP). He was started on treatment with fluid therapy and non-steroidal anti-inflammatory drugs for pain management, after which he recovered rapidly and was discharged on the fourth day after hospitalization. The available data are difficult to interpret as AP is a relatively frequent disease, but its occurrence after vaccination seems extremely rare. Although it is a rare event, AP should be considered after COVID-19 vaccination, especially in those exhibiting abdominal tenderness and vomiting, which should be promptly treated and adequately investigated.

Kewan, T., et al. (2021). "Characteristics and outcomes of adverse events after COVID-19 vaccination." J Am Coll Emerg Physicians Open **2**(5): e12565.

OBJECTIVES: BNT-162b2, mRNA-1273, and Ad26.COV2.S vaccines data regarding adverse events (AEs) are scarce. In this report, we aimed to describe fatal and non-fatal possible AEs after COVID-19 vaccine administration. METHODS: An observational multicenter study investigating the causes of emergency department visits and hospital admissions within 10 days of COVID-19 vaccination. Patients who received first or second doses of COVID-19 vaccines and presented to the emergency department (ED), as well as those admitted to the hospitals or intensive care units (ICUs) were included. Causes of ED, hospital, and ICU admissions and discharges were collected based on the International

Classification of Diseases, Tenth Revision (ICD-10) coding system. RESULTS: Between December 2020 and March 2021, 1842 patients visited the ED within 10 days of COVID-19 vaccine administration. The mean age was 70.3 years. Overall, 1221 patients presented after the first dose of the vaccine and 653 after the second dose. Trauma (14.9%), hypertensive emergency/urgency (7.8%), generalized pain and arthralgia (5.7%), and chest pain (4.4%) were the most common causes of presentation to the ED. Of all ED presentations, mortality rate was at 2.2% (41 patients) with a median follow-up time of 68.0 days, versus 2.6% in unvaccinated ED patients. Postvaccination acute hypoxemic respiratory failure (46.3%), septic shock (24.4%), and cardiogenic shock (12.2%) were the most common causes of death. CONCLUSION: Although reported AEs are not necessarily caused by the vaccination, this study provides further information about possible AEs after COVID-19 immunization, especially those requiring hospital admission. This study also supports prior data that serious AEs post vaccination are much lower than primary COVID-19 infections. Further studies are needed to investigate causalities between vaccines and reported AEs across all age groups.

Kim, S. I., et al. (2021). "Leg paralysis after AstraZeneca COVID-19 vaccination diagnosed as neuralgic amyotrophy of the lumbosacral plexus: a case report." J Int Med Res **49**(11): 3000605211056783.

The ongoing global administration of vaccines for coronavirus disease 2019 (COVID-19) means that increasing numbers of patients are likely to present with post-vaccination complications. We describe the first reported case of neuralgic amyotrophy (NA) involving the lumbosacral plexus occurring after AstraZeneca COVID-19 vaccination. The patient presented with acute-onset leg paralysis following administration of the vaccine. Based on the clinical, electrodiagnostic, and radiologic findings, the patient was diagnosed with post-vaccination NA. We speculate that the COVID-19 vaccine elicited an immune-mediated inflammatory response to the injected antigen due to inflammatory immunity in a patient with predisposed susceptibility to NA.

Kostoff, R. N., et al. (2021). "Why are we vaccinating children against COVID-19?" Toxicol Rep **8**: 1665-1684.

This article examines issues related to COVID-19 inoculations for children. The bulk of the official COVID-19-attributed deaths per capita occur in the elderly with high comorbidities, and the COVID-19 attributed deaths per capita are negligible in children. The bulk of the normalized post-inoculation deaths also occur in the elderly with high comorbidities, while the normalized post-inoculation deaths are small, but not negligible, in children. Clinical trials for these inoculations were very short-term (a few months), had samples not representative of the total population, and for adolescents/children, had poor predictive power because of their small size. Further, the clinical trials did not address changes in biomarkers that could serve as early warning indicators of elevated predisposition to serious diseases. Most importantly, the clinical trials did not address long-term effects that, if serious, would be borne by children/adolescents for potentially decades. A novel best-case scenario cost-benefit analysis showed very conservatively that there are five times the number of deaths

attributable to each inoculation vs those attributable to COVID-19 in the most vulnerable 65+ demographic. The risk of death from COVID-19 decreases drastically as age decreases, and the longer-term effects of the inoculations on lower age groups will increase their risk-benefit ratio, perhaps substantially.

Kounis, N. G., V. Mplani and I. Koniari (2022). "Autopsy Histopathologic Cardiac Findings in 2 Adolescents Following the Second COVID-19 Vaccine Dose: Cytokine Storm, Hypersensitivity, or Something Else." Arch Pathol Lab Med **146**(8): 924.

Lam, K. and E. Yim (2022). "Transverse Leukonychia and Beau Lines Following COVID-19 Vaccination." Cutis **110**(2): E28-E31.

Lee, D. Y., et al. (2023). "Adverse events of a third dose of BNT162b2 mRNA COVID-19 vaccine among Korean healthcare workers." Medicine (Baltimore) **102**(11): e33236.

Due to the urgency of controlling the coronavirus disease 2019 pandemic, coronavirus disease 2019 messenger ribonucleic acid (mRNA) vaccines have been expeditiously approved and introduced in several countries without sufficient evaluation for adverse events. We analyzed adverse events among Korean healthcare workers who received all 3 doses of the BNT162b2 mRNA vaccine. This survey was conducted among hospital workers of Inha University Hospital who had received the BNT162b2 mRNA vaccine for their first, second, third rounds, and using a diary card. The surveyed adverse events included local (redness, edema, and injection site pain) and systemic (fever, fatigue, headache, chill, myalgia, arthralgia, vomiting, diarrhea, pruritis, and urticaria) side effects and were divided into 5 grades (Grade 0 = none - Grade 4 = critical). Based on adverse events reported at least once after any of the 3 doses, the most common systemic adverse reactions were chills and headache (respectively, 62.6%, 62.4%), followed by myalgia (55.3%), arthralgia (53.4%), fatigue (51.6%), pruritus (38.1%), and fever (36.5%). The frequency and duration of adverse events were significantly greater in women ($P < .05$) than men. Except for redness, pruritus, urticaria, and most adverse reactions had a higher rate of occurrence after the third dose in subjects who also had reactions with the second dose. However, grade 4 adverse events did occur with the third dose in some patients, even if there were no side effects with the first and second doses. Adverse events experienced with the first and second doses of the BNT162b2 mRNA vaccine in Korean healthcare workers increased the incidence of adverse events at the time of the third dose. On the other hand, grade 4 adverse events could still occur with the third dose even though there were no side effects with the first and second doses.

Lee, J. M., et al. (2023). "Generalized painful papulovesicular eruption following the COVID-19 BNT162b2 mRNA vaccine." J Eur Acad Dermatol Venereol **37**(7): e834-e836.

Li, Z., Y. Hu and Y. Jiang (2023). "The present evidence summary of SARS-CoV-2 vaccine-associated liver injury: A rapid systematic review." J Hepatol **79**(1): e42-e46.

Lien, Y. L., C. Y. Wei and J. S. Liang (2023). "Acute psychosis induced by mRNA-based COVID-19 vaccine in adolescents: A pediatric case report." Pediatr Neonatol **64**(3): 364-365.

Lin, C. W., S. Y. Hung and I. W. Chen (2023). "A study of glycemic perturbations following two doses of COVID-19 vaccination for patients with diabetes: the impacts of vaccine type and anti-diabetes drugs." Diabetol Metab Syndr **15**(1): 81.

BACKGROUND: Glycemic monitoring has become critical during the COVID-19 pandemic because of poor prognosis in diabetes. Vaccines were key in reducing the spread of infection and disease severity but data were lacking on effects on blood sugar levels. The aim of the current study was to investigate the impact of COVID-19 vaccination on glycemic control. METHODS: We performed a retrospective study of 455 consecutive patients with diabetes who completed two doses of COVID-19 vaccination and attended a single medical center. Laboratory measurements of metabolic values were assessed before and after vaccination, while the type of vaccine and administrated anti-diabetes drugs were analyzed to find independent risks associated with elevated glycemic levels. RESULTS: One hundred and fifty-nine subjects received ChAdOx1 (ChAd) vaccines, 229 received Moderna vaccines, and 67 received Pfizer-BioNtech (BNT) vaccines. The average HbA1c was raised in the BNT group from 7.09 to 7.34% (P = 0.012) and non-significantly raised in ChAd (7.13 to 7.18%, P = 0.279) and Moderna (7.19 to 7.27%, P = 0.196) groups. Both Moderna and BNT groups had around 60% of patients with elevated HbA1c following two doses of COVID-19 vaccination, and the ChAd group had only 49%. Under logistic regression modeling, the Moderna vaccine was found to independently predict the elevation of HbA1c (Odds ratio 1.737, 95% Confidence interval 1.12-2.693, P = 0.014), and sodium-glucose co-transporter 2 inhibitor (SGLT2i) was negatively associated with elevated HbA1c (OR 0.535, 95% CI 0.309-0.927, P = 0.026). CONCLUSIONS: Patients with diabetes might have mild glycemic perturbations following two doses of COVID-19 vaccines, particularly with mRNA vaccines. SGLT2i showed some protective effect on glycemic stability. Hesitancy in having vaccinations should not be indicated for diabetic patients with respect to manageable glycemic change. TRIAL REGISTRATION: Not applicable.

Linares-Navarro, R., et al. (2023). "Bullous Pemphigoid Developed after the COVID-19 Vaccine." Skinmed **21**(3): 200-202.

A 91-year-old man presented with pruriginous tense blisters and erosions on the upper and lower extremities (Figures 1A and 1B). Mucous membranes were unaffected and Nikolsky's sign was negative. These lesions appeared 48 hours after the administration of the second dose of the Pfizer-BioNTech COVID-19 vaccine. The patient had received the first dose of the same vaccine 23 days prior to the onset of lesions. He did not suffer from any other post-vaccination adverse effects.

Magnaterra, E., et al. (2023). "Subacute cutaneous lupus erythematosus induced by Pfizer COVID-19 vaccine." Ital J Dermatol Venerol **158**(3): 266-267.

Maliwankul, K., et al. (2022). "Shoulder Injury Related to COVID-19 Vaccine Administration: A Case Series." Vaccines (Basel) **10**(4).

BACKGROUND: A shoulder injury related to vaccine administration (SIRVA) is a vaccination complication that can affect daily life activities. To date, there have been no case series of patients diagnosed as SIRVA following a COVID-19 vaccination. We offer a series of seven SIRVA cases including clinical presentations, investigations and treatment outcomes. METHODS: A retrospective chart review was performed for seven patients who developed SIRVA following a COVID-19 vaccination between April 2021 and October 2021. All patients had no prior shoulder pain before their vaccination and then developed shoulder pain within a few days following the vaccination, which did not spontaneously improve within 1 week. RESULTS: Four of the seven patients were male, and the average age was 62.29 +/- 7.76 years. The average body mass index was 25.1 +/- 2.2 kg/m(2). In all cases, the cause of the SIRVA was from an incorrect COVID-19 vaccine administration technique. Two patients developed shoulder pain immediately following the injection, one patient about 3 h after the injection, and the other four patients within the next few days. Two of the seven patients visited the orthopedic clinic after the persistent shoulder pain for 3 and 4 days and the other five patients 1-9 weeks following their injections. One of the seven patients was treated with combined intravenous antibiotic and oral non-steroidal anti-inflammatory drug (NSAID) because septic arthritis of the shoulder could not initially be ruled out, and recovered within 2 weeks. The other six patients had shoulder pain without acute fever, and five of them were treated with only oral prednisolone 30 mg/day for 5-10 days, following which the pain improved and they all could return to normal activities within 14 days, with no side effects from the prednisolone such as stomachache, nausea, vomiting, headache, or dizziness. DISCUSSION AND CONCLUSION: In our series, the most common cause of SIRVA was an incorrect vaccination technique. Most patients responded well to oral NSAIDs or oral prednisolone. CLINICAL RELEVANCE: All SIRVAs were from an incorrect injection technique and not actually the vaccination, so our series highlights the importance of ensuring all vaccinators understand the importance of taking proper care with the injection technique. Additionally, most of our patients with SIRVA from a COVID-19 injection responded well to oral prednisolone (30 mg/day). If there are no contraindications, we suggest this as the first line treatment for COVID-19-related SIRVA.

Maltezou, H. C., et al. (2023). "Anaphylaxis rates following mRNA COVID-19 vaccination in children and adolescents: Analysis of data reported to EudraVigilance." Vaccine **41**(14): 2382-2386.

AIM: The present study aimed to estimate the anaphylaxis rates following mRNA COVID-19 vaccination in children and adolescents in Europe. METHODS: We retrieved data on 371 anaphylaxis cases following mRNA COVID-19 vaccination in children </= 17 years old notified to EudraVigilance as of October 8, 2022. Overall, 27,120,512 doses of BNT162b2 vaccine and 1,400,300 doses of mRNA-1273 vaccine have been delivered to children during the study period. RESULTS: The overall mean anaphylaxis rate was 12.81 [95% confidence interval (CI): 11.49-14.12] per 10(6) mRNA vaccine doses [12.14 (95% CI: 6.37-17.91) per 10(6) doses for mRNA-1273 and 12.84 (95% CI: 11.49-14.19) per 10(6)

doses for BNT162b2]. Children 12-17 years old accounted for 317 anaphylaxis cases, followed by 48 cases in children 3-11 years old, and 6 cases in children 0-2 years old. Children 10-17 years old had a mean anaphylaxis rate of 13.52 (95% CI: 12.03-15.00) cases per 10(6) mRNA vaccine doses and children 5-9 years old had a mean anaphylaxis rate of 9.51 (95% CI: 6.82-12.20) cases per 10(6) mRNA vaccine doses. There were two fatalities, both in the 12-17 years age group. The fatal anaphylaxis rate was 0.07 cases per 10(6) mRNA vaccine doses. CONCLUSIONS: Anaphylaxis is a rare adverse event after receiving an mRNA COVID-19 vaccine in children. Continuous surveillance of serious adverse events is needed to guide vaccination policies as we move towards SARS-CoV-2 endemicity. Larger real-world studies on COVID-19 vaccination in children, using clinical case confirmation, are imperative.

Mann, R., S. Sekhon and S. Sekhon (2021). "Drug-Induced Liver Injury After COVID-19 Vaccine." Cureus **13**(7): e16491.

The first case of coronavirus disease 2019 (COVID-19) was reported in December 2019 in China. World Health Organization declared it a pandemic on March 11, 2020. It has caused significant morbidity and mortality worldwide. Persistent symptoms and serious complications are being reported in patients who survived COVID-19 infection, but long-term sequelae are still unknown. Several vaccines against COVID-19 have been approved for emergency use around the globe. These vaccines have excellent safety profiles with few reported side effects. Drug-induced hepatotoxicity is mainly seen with different drugs or chemicals. There are only a few reported cases of hepatotoxicity with vaccines. We present a case of liver injury after administration of the vaccine against the COVID-19 infection.

Martora, F., et al. (2023). "Reply to 'A case of pityriasis lichenoides et varioliformis acuta developed after first dose of Oxford-AstraZeneca COVID-19 vaccine'." J Eur Acad Dermatol Venereol **37**(2): e141-e142.

Martora, F., et al. (2023). "Cutaneous adverse reaction following COVID-19 vaccination: Report from a southern Italian referral centre. Comment on "cutaneous adverse reactions following the Pfizer/BioNTech COVID-19 vaccine" by Luo et al." Australas J Dermatol **64**(1): e103-e105.

Meo, S. A., et al. (2021). "COVID-19 vaccines: comparison of biological, pharmacological characteristics and adverse effects of Pfizer/BioNTech and Moderna Vaccines." Eur Rev Med Pharmacol Sci **25**(3): 1663-1669.

OBJECTIVE: The "Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)" disease has caused a worldwide challenging and threatening pandemic (COVID-19), with huge health and economic losses. The US Food and Drug Administration, (FDA) has granted emergency use authorization for treatment with the Pfizer/BioNTech and Moderna COVID-19 vaccines. Many people have a history of a significant allergic reaction to a specific food, medicine, or vaccine; hence, people all over the world have great concerns about these two authorized vaccines. This article compares the pharmacology, indications, contraindications, and adverse effects of the Pfizer/BioNTech

and Moderna vaccines. MATERIALS AND METHODS: The required documents and information were collected from the relevant databases, including Web of Science (Clarivate Analytics), PubMed, EMBASE, World Health Organization (WHO), Food and Drug Authorities (FDA) USA, Local Ministries, Health Institutes, and Google Scholar. The key terms used were: Coronavirus, SARS-COV-2, COVID-19 pandemic, vaccines, Pfizer/BioNTech vaccine, Moderna vaccine, pharmacology, benefits, allergic responses, indications, contraindications, and adverse effects. The descriptive information was recorded, and we eventually included 12 documents including research articles, clinical trials, and websites to record the required information. RESULTS: Based on the currently available literature, both vaccines are beneficial to provide immunity against SARS-CoV-2 infection. Pfizer/BioNTech Vaccine has been recommended to people 16 years of age and older, with a dose of 30 mug (0.3 m) at a cost of $19.50. It provides immunogenicity for at least 119 days after the first vaccination and is 95% effective in preventing the SARS-COV-2 infection. However, Moderna Vaccine has been recommended to people 18 years of age and older, with a dose of 50 mug (0.5 mL) at a cost of $32-37. It provides immunogenicity for at least 119 days after the first vaccination and is 94.5% effective in preventing the SARS-CoV-2 infection. However, some associated allergic symptoms have been reported for both vaccines. The COVID-19 vaccines can cause mild adverse effects after the first or second doses, including pain, redness or swelling at the site of vaccine shot, fever, fatigue, headache, muscle pain, nausea, vomiting, itching, chills, and joint pain, and can also rarely cause anaphylactic shock. The occurrence of adverse effects is reported to be lower in the Pfizer/BioNTech vaccine compared to the Moderna vaccine; however, the Moderna vaccine compared to the Pfizer vaccine is easier to transport and store because it is less temperature sensitive. CONCLUSIONS: The FDA has granted emergency use authorization for the Pfizer/BioNTech and Moderna COVID-19 vaccines. These vaccines can protect recipients from a SARS-CoV- 2 infection by formation of antibodies and provide immunity against a SARS-CoV-2 infection. Both vaccines can cause various adverse effects, but these reactions are reported to be less frequent in the Pfizer/BioNTech vaccine compared to the Moderna COVID-19 vaccine; however, the Moderna vaccine compared to the Pfizer vaccine is easier to transport and store because it is less temperature sensitive.

Moya, D., et al. (2023). "Shoulder injury related to vaccine administration following SARS-CoV-2 inoculation: Case series and review of literature." J Orthop **35**: 79-84.

INTRODUCTION: Shoulder Injuries Related to Vaccine Administration (SIRVA), describes those cases of shoulder severe post-inoculation complications, including pain and prolonged disability. Most of the reported cases have been secondary to influenza vaccination. This study retrospectively describes a series of 18 patients following SARS-CoV-2 inoculation and compares the findings with those previously reported for other vaccines. MATERIALS AND METHODS: Inclusion criteria was onset of symptoms within 48 h after injection, symptoms duration of at least seven days, and restricted range of motion in absence of symptoms prior to vaccination. Average age was 59.4 years old (38-76), and 72.2% were women. RESULTS: In many cases (58%) the initial diagnosis was not clear, which lead to incorrect treatment. The most common pathological finding was

subacromial-subdeltoid bursitis (66.6%). All patients who received depot corticosteroids followed by a gentle rehabilitation program showed strong clinical improvement but did not completely resolve the symptoms at 7.2 months average final follow-up. Surgical intervention was necessary in one of the patients due to the persistence of symptoms despite conservative treatment. CONCLUSIONS: Shoulder injury related to vaccine administration is rare, but when present, its torpid evolution makes it difficult to treat. We have found in our case series a similar pattern to that already described for other vaccines. A high index of suspicion helps to pick up the condition promptly and early treatment can bring satisfactory outcome.

Moya, D., et al. (2022). "Shoulder Injury Related to Vaccine Administration Following Misplaced SARS-CoV-2 Vaccination: A Case Report and Review of Literature." J Orthop Case Rep **12**(3): 100-103.

INTRODUCTION: To confront the SARS-CoV-2 pandemic, a large share of the population must be immunized. Intramuscular vaccination of the shoulder is the preferred technique as it is easily exposed and guarantees a good immune reaction. Local side effects, such as pain and swelling, are common after deltoid inoculation. They usually resolve within 3 days. Shoulder injury related to vaccine administration (SIRVA) should be considered if the symptoms persist. The aim of this presentation is to describe a typical case of SIRVA after SARS-CoV-2 vaccination and provide information to the general orthopedic surgeon to properly diagnose, report, and treat these cases. CASE REPORT: A 69-year-old female health-care professional without history of shoulder pain consulted the senior author for persistent severe left shoulder pain 3 months following the second dose of Sputnik V COVID-19 vaccination. She claimed an improper application technique that caused immediate pain and loss of active range of motion (ROM). She underwent medical treatment with several doctors during 3 months with poor results. A magnetic resonance imaging (MRI) of the left shoulder done 5 days after vaccination showed mild subacromial-subdeltoid bursitis. A follow-up MRI at 2 months after application revealed synovial hypertrophy and distention of the subacromial-subdeltoid bursa. We prescribed a dose of depot betamethasone and home-based program of gentle exercises. Although initial response was quick, the patient required shoulder arthroscopy the following months, due to persistence in pain and functional limitations. CONCLUSION: SIRVA cases may occur and should be suspected in all individuals without a history of shoulder symptoms or dysfunction who experience sudden pain and reduced ROM following deltoid muscle vaccination. Treatment must be initiated early with corticosteroids and rehabilitation. The low probability of this complication does not outweigh the advantages of vaccination.

Mungmunpuntipamtip, R. and V. Wiwanitkit (2021). "Deaths associated with newly launched SARS-CoV-2 vaccination." Leg Med (Tokyo) **53**: 101956.

Murashita, M., et al. (2022). "Subacute thyroiditis associated with thyrotoxic periodic paralysis after COVID-19 vaccination: a case report." Endocrinol Diabetes Metab Case Rep **2022**.

SUMMARY: We report a 26-year-old Japanese man who visited our outpatient clinic presenting fever immediately after i.m. injection of the second dose of a coronavirus disease 2019 (COVID-19) vaccine (Moderna(R)). At the first visit, the patient had a fever of 37.7 degrees C and a swollen thyroid gland with mild tenderness. He was diagnosed with subacute thyroiditis (SAT) based on the presence of thyrotoxicosis (free tri-iodothyronine, 32.3 pg/mL; free thyroxine, >7.77 ng/dL; and thyroid-stimulating hormone (TSH) < 0.01 muIU/mL), high C-reactive protein level (7.40 mg/dL), negative TSH receptor antibody, and characteristic ultrasound findings. His HLA types were A*02:01/24:02, B*15:11/35:01, Cw*03:03, DRB1*09:01/12:01, DQB1*03:03, and DPB1*05: 01/41:01. He was initially administered prednisolone 15 mg/day, following which the fever subsided. After 10 days, he developed limb weakness and could not walk. The serum potassium level decreased to 1.8 mEq/L, which confirmed the diagnosis of thyrotoxic periodic paralysis (TPP). Potassium supplementation was initiated. The muscle weakness gradually decreased. Prednisolone therapy was terminated 6 weeks after the first visit. His thyroid function returned to normal 5 months after the first visit, through a hypothyroid state. To our knowledge, this is the first reported case of TPP-associated SAT following COVID-19 vaccination. Persistent fever following vaccination should be suspected of SAT. Additionally, TPP may be associated with SAT in Asian male patients. LEARNING POINTS: Following coronavirus disease 2019 (COVID-19) vaccination, subacute thyroiditis may develop regardless of the vaccine type. If persistent fever, anterior neck pain, swelling and tenderness of thyroid gland, and symptoms of thyrotoxicosis are observed immediately after the COVID-19 vaccination, examination in consideration of the onset of subacute thyroiditis is recommended. HLA-B35 may be associated with the onset of subacute thyroiditis after the COVID-19 vaccination. Although rare, subacute thyroiditis can be associated with thyrotoxic periodic paralysis, especially in Asian men. Glucocorticoid therapy for subacute thyroiditis may induce thyrotoxic periodic paralysis through hypokalemia.

N, A. M., et al. (2022). "Systemic lupus erythematosus with acute pancreatitis and vasculitic rash following COVID-19 vaccine: a case report and literature review." Clin Rheumatol **41**(5): 1577-1582.

Coronavirus disease-19 (COVID-19) is a global pandemic that is caused by COVID-19 virus, which was initially identified in December 2019 in Wuhan, China. Vaccination is one of the most effective public health interventions, and soon after the Pfizer/BioNTech (BNT162b2) vaccine became available late in 2020, it began to be actively used to fight against COVID-19. Since then, cases of vaccine-associated immune-mediated diseases (IMDs) have been reported. There have been few cases of IMD flare-ups or onset after COVID-19 vaccine administration, and emerging IMDs may be identified over next few years after high use of this vaccine. To this day, few cases of newly diagnosed systemic lupus erythematosus (SLE) following COVID-19 vaccine exposure were reported. Herein, we present the case of a patient diagnosed with SLE, acute pancreatitis, and vasculitic skin rash on the extremities 1 week after the first dose of the Pfizer-BioNTech COVID-19 vaccine. Key Point * COVID-19 Vaccine induced Systemic Lupus Erythematosus.

Naitlho, A., et al. (2021). "A Rare Case of Henoch-Schonlein Purpura Following a COVID-19 Vaccine-Case Report." SN Compr Clin Med **3**(12): 2618-2621.

In the COVID-19 pandemic era, anti-SARS-CoV-2 vaccination is considered to be the most efficient way to overtake the COVID-19 scourge. Like all medicines, vaccines are not devoid of risks and can in rare cases cause some various side effects. The objective of this case report is to highlight this unusual presentation of Henoch-Schonlein purpura following an anti-COVID-19 vaccination in a 62-year-old adult. The 62-year-old patient admitted to the emergency room for a petechial purpuric rash, sloping, occurring within hours, involving both legs and ascending. The clinical signs also included polyarthralgia and hematuria. Reported in the history the notion of an anti-COVID-19 vaccination 8 days prior to the onset of symptomatology. In the case of our patient, we retain the diagnosis of rheumatoid purpura based on the EULAR/PRINTO/PReS diagnostic criteria. Corticosteroid therapy (prednisone) was started, resulting to a rapid regression of clinical and laboratory symptoms, few days after the treatment. Patient was asymptomatic on subsequent visits. The low number of published cases of post-vaccine vasculitis does not question the safety of vaccines, but knowledge of such complications deserves to be known in order to avoid new immunizations that could have more serious consequences, and to avoid aggravating or reactivating a pre-existing vasculitis.

Nakagawa, A., et al. (2023). "Acute pulmonary hypertension due to microthrombus formation following COVID-19 vaccination: a case report." Eur Heart J Case Rep **7**(8): ytad353.

BACKGROUND: Several side effects have been reported after mRNA COVID-19 vaccinations. Nonetheless, the risk of pulmonary hypertension (PH) is rarely reported. Most cases with acute PH following vaccination were due to macropulmonary embolism secondary to deep vein thrombosis. However, acute PH due to microthrombus formation after COVID-19 vaccination has not been reported before, although a microthrombus has been considered to lead to the dysfunction of multiple organs, particularly in patients infected with COVID-19. CASE SUMMARY: A 63-year-old woman without any past medical history presented to our hospital with facial and bilateral pedal oedema and progressive dyspnoea on exertion. Her symptoms began the day after her second COVID-19 vaccination and developed gradually, which prompted her to seek consultation in our hospital 6 weeks later. An echocardiogram revealed substantially elevated right heart pressure, and cardiac catheterization revealed high pulmonary artery pressure (mean PAP, 30 mmHg). Contrast-enhanced computed tomography and venous echography revealed no apparent thrombus, and ventilation/perfusion (V/Q) scintigraphy revealed no V/Q mismatch. However, elevated D-dimer indicated the presence of a coagulation-fibrinolysis system in her body; thus, heparin therapy was initiated intravenously on Day 3 for 4 days, followed by direct oral anticoagulants ended on Day 16. Her symptoms substantially improved as her D-dimer level decreased, and a follow-up cardiac catheterization on Day 14 revealed a decline in mean PAP (15 mmHg). DISCUSSION: Our case suggests that the presence of acute PH is likely due to microangiopathy. Further studies are required to reveal the relationship between immune responses and microthrombus formation after COVID-19 vaccination.

Naoum, C. and M. Hartmann (2022). "Herpes zoster reactivation after COVID-19 vaccination - a retrospective case series of 22 patients." Int J Dermatol **61**(5): 628-629.

Neamatallah, T. (2023). "Delayed inflammatory reaction to hyaluronic acid lip filler after the Pfizer-BioNTech COVID-19 vaccine: A case report." Heliyon **9**(7): e18274.

Hypersensitivity reactions can be a side effect to any vaccine, but they are usually rare. The COVID-19 vaccination may cause hypersensitivity, and several cases of delayed hypersensitivity (DH) to hyaluronic acid (HA) dermal filler have been documented. The current report presents a case of a 36-year-old female patient with DH to HA dermal filler after receiving the Pfizer-BioNTech COVID-19 vaccine. Symptoms, including dryness, swelling, and a painless nodule, appeared after the first and second doses of the vaccine. The patient was treated with intralesional hyaluronidase and triamcinolone in the outpatient clinic. Although HA is relatively safe and routinely used in aesthetic medicine, DH reactions must be considered. Therefore, an appropriate patient history should be obtained, and physicians should provide counselling on the potential reactions to avoid these adverse effects.

Onukak, A. E., et al. (2022). "Acute Kidney Injury after First Dose of AstraZeneca COVID-19 Vaccine Managed in a Nigerian Hospital." West Afr J Med **39**(7): 769-771.

INTRODUCTION: The association of kidney disease and COVID-19 vaccination has been reported with minimal change disease being a common presentation. CASE REPORT: Index patient is a 54-year-old female who presented with a history of reduction in urine output within 3 weeks of receiving the Oxford-AztraZeneca COVID-19 vaccine. Her serum creatinine on admission was 1,057 micromol/L with a premorbid serum creatinine of 78 micromol/L. Her vital signs were stable. She was on antihypertensive and antidiabetic medications for hypertension and diabetes mellitus, respectively. Renal biopsy was precluded by her morbid obesity and she was commenced on oral prednisolone. She had 5 sessions of hemodialysis and her serum creatinine gradually reduced to 106 micromol/L, and she is being followed up on an outpatient basis. CONCLUSION: We report a case of a female patient with acute kidney injury following COVID-19 Oxford-AztraZeneca vaccination. Further studies are required to better understand the pathogenesis of the renal affectation post-vaccination.

Pacheco, I. C. R., et al. (2022). "Kidney injury associated with COVID-19 infection and vaccine: A narrative review." Front Med (Lausanne) **9**: 956158.

The respiratory tract is the main infection site for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), resulting in many admissions to intensive care centers in several countries. However, in addition to lung involvement, kidney injury caused by the novel coronavirus has proven to be a significant factor related to high morbidity and mortality, alarming experts worldwide. The number of deaths has drastically reduced with the advent of large-scale immunization, highlighting the importance of vaccination as the best way to combat the pandemic. Despite the undeniable efficacy of the vaccine, the renal side effects associated with its use deserve to be highlighted, especially the emergence or reactivation of glomerulopathies mentioned in some case reports. This

study aimed to identify the main renal morphological findings correlated with COVID-19 infection and its vaccination, seeking to understand the pathophysiological mechanisms, main clinical features, and outcomes.

Paddock, C. D., et al. (2022). "Autopsy Histopathologic Cardiac Findings in 2 Adolescents Following the Second COVID-19 Vaccine Dose." Arch Pathol Lab Med **146**(8): 921-923.

Pang, E. W., et al. (2023). "COVID-19 vaccination-related exacerbation of seizures in persons with epilepsy." Epilepsy Behav **138**: 109024.

Although vaccines are generally safe in persons with epilepsy (PWE), seizures can be associated with vaccination, including COVID-19. This study assessed the occurrence of COVID-19 vaccination-related seizure exacerbations in PWE. Adult PWE who had received a COVID-19 vaccine were consecutively recruited at a tertiary epilepsy clinic between June 2021 and April 2022. Patient demographics, including epilepsy history, vaccination details, and reported adverse effects were recorded. Seizure exacerbation, defined as occurring within one week of vaccination, was assessed. Five hundred and thirty PWE received the COVID-19 vaccine. 75 % received the Comirnaty (Pfizer) vaccine as their initial dose. Most patients (72 %) were taking >/= 2 antiseizure medications (ASM) and had focal epilepsy (73 %). One-third were 12 months seizure free at their first vaccination. 13 patients (2.5 %) reported a seizure exacerbation following their first vaccination, three of whom required admission. None were seizure-free at baseline. Six of these patients (46 %) had a further exacerbation of seizures with their second vaccine. An additional four patients reported increased seizures only with the second vaccine dose. Seizure exacerbations are infrequently associated with COVID-19 vaccination, mainly in patients with ongoing seizures. The likelihood of COVID-19 infection complications in PWE outweighs the risk of vaccination-related seizure exacerbations.

Papadopoulou, M., et al. (2023). "Myasthenia Gravis Exacerbation Following Immunization With the BNT162b2 mRNA COVID-19 Vaccine: Report of a Case and Review of the Literature." Neurohospitalist **13**(3): 303-307.

Acute exacerbations of Myasthenia Gravis (MG) may be triggered by infections and certain drugs. No consensus has been reached on vaccines and the risk for developing myasthenic crisis. During the COVID-19 pandemic, MG patients are considered at high risk for severe illness, and vaccination is strongly recommended. We report the case of a 70-year-old woman with MG, diagnosed 2 years earlier, that developed myasthenic crisis 10 days after the second dose of the BNT162b2 mRNA COVID-19 vaccine (Pfizer-BioNTech). The patient had no previous MG exacerbations in her history. Following increase of oral pyridostigmine and prednisone treatment, the patient underwent immunoglobulin and plasma exchange therapy. Due to persisting symptoms, immunotherapy was switched to rituximab, under which a clinical remission was achieved. MG patients infected with SARS-CoV-2 may develop severe acute respiratory distress syndrome and have a higher mortality compared to the general population. In addition, reports of new-onset MG following COVID-19 infection accumulate. By contrast, since the beginning of the vaccination program, only 3 cases of new-onset MG

after COVID-19 vaccinations have been published and 2 cases of severe MG exacerbation. Vaccinations in MG patients have always been debated, but most studies confirm their safety. In the era of COVID-19 pandemic, vaccination protects against infection and severe illness, especially in vulnerable populations. The rare occurrence of side effects should not discourage clinicians from recommending COVID-19 vaccination, but close follow-up of MG patients is recommended during the post-vaccination period.

Parkash, O., et al. (2021). "Acute Pancreatitis: A Possible Side Effect of COVID-19 Vaccine." Cureus **13**(4): e14741.

For the first time, the mRNA technology was utilized to produce a vaccine against COVID-19 after the unprecedented pandemic equally affected every part of the world. Pfizer-BioNTech (BNT162b2) mRNA vaccine against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was granted emergency use authorization (EUA) by Food and Drug Administration (FDA) in December 2020. EUA has been widely discussed in the medical literature and the general public. The safety of the BNT162b2 vaccine has been investigated in short-term trials with data available for three months. We present a case of a 96-year-old female with a past surgical history of cholecystectomy who presented with acute onset severe abdominal pain a few days after getting the first dose of Pfizer-BioNTech COVID-19 vaccine. She was diagnosed with acute pancreatitis with a lipase level of 4036 U/L. Extensive history and investigations were unable to find any etiology. The patient was conservatively managed and discharged home without any complications. There has been some data available in medical literature showing an association between acute pancreatitis and COVID-19 infection. Trial data of Pfizer COVID-19 also shows one case of acute pancreatitis in the treatment group. There have also been individual cases of unexplained acute pancreatitis shared by medical professionals on online forums. Our main goal to write this case is to make medical literature aware of possible emerging side effects of the COVID-19 vaccine, one of such side effects being self-resolving uncomplicated acute pancreatitis.

Petrakis, N., et al. (2023). "Shoulder injury following COVID-19 vaccine administration: a case series and proposed diagnostic algorithm." Expert Rev Vaccines **22**(1): 299-306.

BACKGROUND: Shoulder Injury Related to Vaccine Administration (SIRVA) is a preventable adverse event following incorrect vaccine administration, which can result in significant long-term morbidity. There has been a notable surge in reported cases of SIRVA as a rapid national population-based COVID-19 immunization program has been rolled out across Australia. METHODS: Surveillance of Adverse Events Following Vaccination in the Community (SAEFVIC) in Victoria identified 221 suspected cases of SIRVA following the commencement of the COVID-19 vaccination program, reported between February 2021 and February 2022. This review describes the clinical features and outcomes of SIRVA in this population. Additionally, a suggested diagnostic algorithm is proposed, in order to facilitate early recognition and management of SIRVA. RESULTS: 151 cases were confirmed as SIRVA, with 49.0% having received vaccines at state vaccination centers. 75.5% were suspected incorrect administration site, with most patients experiencing shoulder pain and restricted movement within 24 hours of

vaccination, lasting on average 3 months. CONCLUSION: Improved awareness and education regarding SIRVA is imperative in a pandemic vaccine roll-out. The development of a structured framework for evaluating and managing suspected SIRVA will aid in timely diagnosis and treatment, essential to mitigate potential long-term complications.

Rammouz, I., et al. (2023). "Induced Depressive Disorder Following the First Dose of COVID-19 Vaccine." CNS Neurol Disord Drug Targets **22**(4): 618-621.

INTRODUCTION: Several COVID-19 vaccines have been implemented. However, some side effects of the vaccine have been reported, which are sometimes very harmful. Reported cases and data are still very limited regarding the psychiatric side effects of the COVID-19 vaccine. To our knowledge, only one case has been reported. In this paper, we report the case of a patient who presented an acute depressive episode 24 hours after receiving his first dose of the BNT162b2mRNA vaccine. CASE REPORT: The case was a 26-year-old man with a history of Down syndrome with moderately good autonomy for daily routine tasks. The patient, who presented hypothyroidism at 10 years old and schizophrenia at 15 years old, was doing well before the vaccination and received his first dose of the BNT162b2mRNA vaccine. Twenty-four hours later, he presented depressive symptoms that resolved spontaneously after one week. Then, fifteen days later, the symptoms reappeared, and the episode lasted for 5 weeks. The patient received 10 mg/day of escitalopram besides his usual treatment. The depressive symptoms improved considerably by the second day of treatment. DISCUSSION: The presented case illustrated significant diagnostic challenges, especially when taking into account the sequential relationship between the COVID-19 vaccine and the occurrence of depressive symptoms. A single case of depression has been reported after the administration of the COVID-19 vaccine. Scientific evidence suggests the important role of the immune system in the pathophysiology of various psychiatric disorders, including depression. CONCLUSION: Health professionals must take into consideration the potential psychiatric side effects even being rare so far, especially in vulnerable subjects. Further studies are required to establish the causal effects of depressive symptoms occurring during the weeks following the COVID-19 vaccine bolus injection.

Saiz, L. C. and M. Villanueva Alcojol (2023). "Case report: Granulomatosis with polyangiitis (GPA) and facial paralysis after COVID-19 vaccination." Med Clin (Barc) **161**(2): 84-85.

Schubert, R., et al. (2023). "Can Google Trends analysis confirm the public's need for information about the rare association of facial nerve paralysis with COVID-19 or the COVID-19 vaccination?" Rev Neurol (Paris) **179**(3): 218-222.

Facial nerve paralysis or Bell's palsy have been suggested as possible consequences of SARS-CoV-2 infections, as well as possible side effects of COVID-19 vaccinations. Google Trends data have been used to evaluate worldwide levels of public awareness for these topics for pre- and post-pandemic years. The results demonstrate a relatively low public interest in facial nerve paralysis in comparison to other more common COVID-19 related topics. Some peaks of interest in Bell's palsy can most likely be explained as triggered by

the media. Therefore, Google Trends has shown public's relatively low awareness of this rare neurological phenomenon during the pandemic.

Shin, L., et al. (2023). "Adverse Effects of the COVID-19 Vaccine in Patients With Psoriasis." Cutis **111**(2): 80-81.

Singh, R., et al. (2023). "Proposing a standardized assessment of COVID-19 vaccine-associated cutaneous reactions." J Am Acad Dermatol **88**(1): 237-241.

Singh, R. B., et al. (2023). "Vaccine-Associated Uveitis after COVID-19 Vaccination: Vaccine Adverse Event Reporting System Database Analysis." Ophthalmology **130**(2): 179-186.

PURPOSE: To assess the risk of vaccine-associated uveitis (VAU) after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination and evaluate uveitis onset interval and clinical presentations in the patients. DESIGN: A retrospective study from December 11, 2020, to May 9, 2022, using the Centers for Disease Control and Prevention Vaccine Adverse Event Reporting System. PARTICIPANTS: Patients diagnosed with VAU after administration of BNT162b2 (Pfizer-BioNTech, Pfizer Inc/BioNTech SE), mRNA-1273 (Moderna, Moderna Therapeutics Inc), and Ad26.COV2.S (Janssen, Janssen Pharmaceuticals) vaccine worldwide. METHODS: A descriptive analysis of the demographics, clinical history, and presentation was performed. We evaluated the correlation among the 3 vaccines and continuous and categorical variables. A post hoc analysis was performed between uveitis onset interval after vaccination and age, dose, and vaccine type. Finally, a 30-day risk analysis for VAU onset postvaccination was performed. MAIN OUTCOME MEASURES: The estimated global crude reporting rate, observed to expected ratio of VAU in the United States, associated ocular and systemic presentations, and onset duration. RESULTS: A total of 1094 cases of VAU were reported from 40 countries with an estimated crude reporting rate (per million doses) of 0.57, 0.44, and 0.35 for BNT162b2, mRNA-1273, and Ad26.COV2.S, respectively. The observed to expected ratio of VAU was comparable for BNT162b2 (0.023), mRNA-1273 (0.025), and Ad26.COV2.S (0.027). Most cases of VAU were reported in patients who received BNT162b2 (n = 853, 77.97%). The mean age of patients with VAU was 46.24 +/- 16.93 years, and 68.65% (n = 751) were women. Most cases were reported after the first dose (n = 452, 41.32%) and within the first week (n = 591, 54.02%) of the vaccination. The onset interval for VAU was significantly longer in patients who received mRNA-1273 (21.22 +/- 42.74 days) compared with BNT162b2 (11.42 +/- 23.16 days) and rAd26.COV2.S (12.69 +/- 16.02 days) vaccines (P < 0.0001). The post hoc analysis revealed a significantly shorter interval of onset for the BNT162b2 compared with the mRNA 1273 vaccine (P < 0.0001). The 30-day risk analysis showed a significant difference among the 3 vaccines (P < 0.0001). CONCLUSIONS: The low crude reporting rate and observed to expected ratio suggest a low safety concern for VAU. This study provides insights into a possible temporal association between reported VAU events and SARS-CoV-2 vaccines; however, further investigations are required to delineate the associated immunological mechanisms.

Sirufo, M. M., et al. (2021). "Henoch-Schonlein Purpura Following the First Dose of COVID-19 Viral Vector Vaccine: A Case Report." Vaccines (Basel) **9**(10).

A 76 year-old female came to our observation one week after the vaccination with ChAdOx1 nCoV-19 AZD1222 for the onset of purpuric rash on her gluteal and legs regions associated with coxalgia and episodes of macrohaematuria. Henoch-Schonlein purpura (HSP) was diagnosed on the basis of the revised criteria developed by the European League Against Rheumatism, the Paediatric Rheumatology International Trials Organization, and the Paediatric Rheumatology European Society (EULAR/PRINTO/PRES). HSP is a common IgA-mediated small vessel vasculitis, typical of childhood, that affects several systems and is characterized by a tetrad of dermatological, abdominal, joint, and renal manifestations. The Etiology of HSP is not completely understood, but it was observed following upper respiratory tract infections, medications, vaccinations, and malignancies. HSP has previously been reported following immunization with various vaccines, mostly within 12 weeks post, suggesting a possible correlation. To our knowledge, this is the first report of the possible association between COVID-19 ChAdOx1 nCoV-19 AZD1222 and the onset of HSP in a previously healthy woman. No similar cases were reported amongst 23.848 participants in the ChAdOx1 nCoV-19 AZD1222 trial.

Slavin, E., et al. (2022). "New-Onset Myasthenia Gravis Confirmed by Electrodiagnostic Studies After a Third Dose of SARS-CoV-2 mRNA-1273 Vaccine." Am J Phys Med Rehabil **101**(12): e176-e179.

Coronavirus disease 2019 vaccine-related pathology is a rare occurrence with few reported cases. We report on a case of a 60-yr-old man experiencing symptoms of dysphagia, dysarthria, diplopia, and weakness with onset 6 days after receiving a third full dose of SARS-CoV-2 vaccine (mRNA-1273 vaccine) in August 2021, which he received outside of the Center for Disease Control recommended guidelines, at 4 mos after his second dose of the Moderna vaccination course in March 2021. The Food and Drug Administration Emergency Use Authorization for mRNA-1273 booster was established in October 2021.Over the next month, the patient's symptoms progressed including his inability to swallow, requiring hospitalization due to dehydration and malnutrition. Evaluation including laboratory prompted referral for electrodiagnostic studies consisting of repetitive nerve stimulation studies and needle electromyography, confirming a case of new onset bulbar myasthenia gravis.

Son, S. A., et al. (2022). "Bilateral Vocal Fold Paralysis After COVID-19 mRNA Vaccination: A Case Report." J Korean Med Sci **37**(25): e201.

Since severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was noted to cause coronavirus disease 2019 (COVID-19) in 2019, there have been many trials to develop vaccines against the virus. Messenger ribonucleic acid (mRNA) vaccine as a type of the vaccine has been developed and commercialized rapidly, but there was not enough time to verify the long-term safety. An 82-year-old female patient was admitted to the emergency room with dyspnea accompanied by stridor three days after the 3rd COVID-19 mRNA vaccination (Comirnaty, Pfizer-BioNTech, USA). The patient was diagnosed with

bilateral vocal fold paralysis (VFP) by laryngoscope. Respiratory distress was improved after the intubation and tracheostomy in sequence. The brain, chest, and neck imaging tests, serological tests, cardiological analysis, and immunological tests were performed to evaluate the cause of bilateral VFP. However, no definite cause was found except for the precedent vaccination. Because bilateral VFP can lead to a fatal condition, a quick evaluation is necessary in consideration of VFP when dyspnea with stridor occurs after vaccination.

Sookaromdee, P. and V. Wiwanitkit (2022). "Cutaneous adverse events following the inactivated and mRNA COVID-19 vaccines: Correspondence." J Cosmet Dermatol **21**(11): 5338.

Stollberger, C., et al. (2023). "Necrotizing pancreatitis, microangiopathic hemolytic anemia and thrombocytopenia following the second dose of Pfizer/BioNTech COVID-19 mRNA vaccine." Wien Klin Wochenschr **135**(15-16): 436-440.

Implementing vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a major asset in slowing down the coronavirus disease 2019 (COVID-19) pandemic. For mRNA vaccines, the main severe adverse events reported in pharmacovigilance systems and post-authorization studies were anaphylaxis and myocarditis. Pancreatitis after Pfizer/BioNTech COVID-19 vaccination has been reported only in 10 patients.We report a 31-year-old female with a history of borderline personality disorder, intravenous drug abuse, allergic asthma, eating disorder, psoriatic arthritis treated with tofacitinib, neurogenic bladder disturbance, cholecystectomy, recurrent thoracic herpes zoster, vaginal candida infections and urinary tract infections, who developed pancreatitis associated with thrombotic microangiopathy and hemolytic-uremic syndrome 10 days after the second vaccination, whereas the first has been well tolerated. She was treated by plasma exchange, and eventually by transgastric drainage with implantation of a plastic stent to remove fluid abdominal retentions. She was discharged after 19 days. Since then her condition has improved continuously. Computed tomography after 12 months did not reveal retentions anymore.As other causes of pancreatitis have been excluded, this case of acute pancreatitis, microangiopathic hemolytic anemia and thrombocytopenia, temporally associated with the Pfizer-BioNTech COVID-19 vaccine, suggests a causal link.

Subramanian, S. V. and A. Kumar (2021). "Increases in COVID-19 are unrelated to levels of vaccination across 68 countries and 2947 counties in the United States." Eur J Epidemiol.

Sukhija, S., et al. (2022). "Shoulder Injury Related to Vaccine Administration (SIRVA) with COVID-19 vaccination - A case report." J Family Med Prim Care **11**(12): 7937-7940.

The case report evaluates shoulder injury related to COVID-19 vaccine administration. A 26-year-old female patient presented with shoulder pain, which increased on extension and overhead abduction in routine work. Magnetic resonance imaging (MRI) was done based on which, a diagnosis of shoulder injury related to vaccine administration (SIRVA) was reported. Significant improvement was seen after Non-steroidal anti-inflammatory drugs (NSAIDs), topical diclofenac ointment, and serratiopeptidase tablets. Physical

muscle strengthening exercises were advised. Based on Naranjo and World Health Organization (WHO) casualty assessments, the adverse drug reaction (ADR) was categorized under probable. Preventability, Hartwig's scales for severity was assessed, which showed preventability and moderate grade in severity. The total cost (direct and indirect) for management was found to be rupees 7021 and 41,781 in government and private hospital respectively. Thus ADRs not only add to patient suffering but also increase the economic burden. Health care professionals (HCPs) need to be made aware of potentially fatal ADRs associated with the administration of vaccines and should be keen to report such ADRs to drug safety authorities.

Tosunoglu, B., et al. (2023). "Myositis developing after Covid-19 mRNA vaccine: Case Report." Acta Neurol Taiwan **32(2)**: 79-81.

Vaccine-related side effects are common. Usually, pain, edema, redness and tenderness may be seen at the injection site. Symptoms such as fever, fatigue, myalgia may occur. The coronavirus 2019 disease (Covid-19) has affected many people around the world. Although the vaccines that have been used play an active role in the fight against the pandemic, adverse events still continue to be reported. We present a 21-year-old patient who was diagnosed as having myositis after receiving covid vaccine with complaints of pain in her left arm two days after the 2nd dose of BNT162b2 mRNA Covid-19 vaccine, followed by inability to stand up from sitting and squatting and difficulty in going up and down stairs. Keywords: vaccine, myositis, creatine kinase, IVIG.

Tripathy, D. M., et al. (2022). "Postherpetic granulomatous dermatitis and herpes zoster necroticans triggered by Covid-19 vaccination." Dermatol Ther **35**(10): e15707.

Tso, A. C. Y., et al. (2023). "Acquired Thrombotic Thrombocytopenic Purpura: A Rare Coincidence after COVID-19 mRNA Vaccine?" Semin Thromb Hemost **49**(1): 89-91.

Unver, S., A. Haholu and S. Yildirim (2021). "Nephrotic syndrome and acute kidney injury following CoronaVac anti-SARS-CoV-2 vaccine." Clin Kidney J **14**(12): 2608-2611.

A 67-year-old female with Type 2 diabetes mellitus developed nephrotic syndrome within 1 week of receiving the first dose of severe acute respiratory syndrome coronavirus 2 CoronaVac vaccine. A kidney biopsy was consistent with minimal change nephrotic syndrome and treatment was symptomatic with antiproteinuric therapy and improvement in proteinuria. Oedema returned within 1 week of the second dose of CoronaVac. On this occasion, acute kidney injury and massive proteinuria were noted. In kidney biopsy, glomeruli were normal, but tubulointerstitial inflammation consistent with acute tubulointerstitial nephritis was noted. Pulse followed by oral steroids was followed by recovery of kidney function. Proteinuria decreased after initiation of cyclosporine A.

Vallianou, N. G., et al. (2022). "Herpes zoster following COVID-19 vaccination in an immunocompetent and vaccinated for herpes zoster adult: A two-vaccine related event?" Metabol Open **13**: 100171.

Reactivation of varicella-zoster virus (VZV) has been reported after the administration of different vaccine platforms against SARS-CoV-2, also among individuals without known immunosuppressive states. Herein, we describe for the first time a case of herpes zoster after mRNA vaccination against SARS-CoV-2 in a 53-year-old immunocompetent adult without any known comorbidities, who was previously vaccinated with a live attenuated zoster vaccine. The fact that the patient had no history of varicella and had been tested seronegative for VZV prior to immunization with the live attenuated zoster vaccine further contribute to the challenge of this unusual case. This advocates for a high level of vigilance on the part of clinicians regarding this rare complication among receivers of COVID-19 vaccines.

Villa-Zapata, L., et al. (2023). "COVID-19 vaccine adverse events in a population aged 5-17 years: a study from the VAERS database." An Pediatr (Engl Ed) **98**(4): 310-312.

Walton, M., et al. (2023). "Adverse Events Following the BNT162b2 mRNA COVID-19 Vaccine (Pfizer-BioNTech) in Aotearoa New Zealand." Drug Saf.

INTRODUCTION: In February 2021, New Zealand began its largest ever immunisation programme with the BNT162b2 mRNA coronavirus disease 2019 (COVID-19) vaccine. OBJECTIVE: We aimed to understand the association between 12 adverse events of special interest (AESIs) and a primary dose of BNT162b2 in the New Zealand population aged >/=5 years from 19 February 2021 through 10 February 2022. METHODS: Using national electronic health records, the observed rates of AESIs within a risk period (1-21 days) following vaccination were compared with the expected rates based on background data (2014-2019). Standardised incidence ratios (SIRs) were estimated for each AESI with 95% confidence intervals (CIs) using age group-specific background rates. The risk difference was calculated to estimate the excess or reduced number of events per 100,000 persons vaccinated in the risk period. RESULTS: As of 10 February 2022, 4,277,163 first doses and 4,114,364 second doses of BNT162b2 had been administered to the eligible New Zealand population aged >/=5 years. The SIRs for 11 of the 12 selected AESIs were not statistically significantly increased post vaccination. The SIR (95% CI) for myo/pericarditis following the first dose was 2.3 (1.8-2.7), with a risk difference (95% CI) of 1.3 (0.9-1.8), per 100,000 persons vaccinated, and 4.0 (3.4-4.6), with a risk difference of 3.1 (2.5-3.7), per 100,000 persons vaccinated following the second dose. The highest SIR was 25.6 (15.5-37.5) in the 5-19 years age group, following the second dose of the vaccine, with an estimated five additional myo/pericarditis cases per 100,000 persons vaccinated. A statistically significant increased SIR of single organ cutaneous vasculitis (SOCV) was also observed following the first dose of BNT162b2 in the 20-39 years age group only. CONCLUSIONS: A statistically significant association between BNT162b2 vaccination and myo/pericarditis was observed. This association has been confirmed internationally. BNT162b2 was not found to be associated with the other AESIs investigated, except for SOCV following the first dose of BNT162b2 in the 20-39 years age group only, providing reassurances around the safety of the vaccine.

Walton, M., et al. (2023). "Thrombotic events following the BNT162b2 mRNA COVID-19 vaccine (Pfizer-BioNTech) in Aotearoa New Zealand: A self-controlled case series study." Thromb Res **222**: 102-108.

BACKGROUND: An association between thrombotic events and SARS-CoV-2 infection and the adenovirus-based COVID-19 vaccines has been established, leading to concern over the risk of thrombosis after BNT162b2 COVID-19 vaccination. OBJECTIVES: To evaluate the risk of arterial thrombosis, cerebral venous thrombosis (CVT), splanchnic thrombosis, and venous thromboembolism (VTE) following BNT162b2 vaccination in New Zealand. METHODS: This was a self-controlled case series using national hospitalisation and immunisation records to calculate incidence rate ratios (IRR). The study population included individuals aged >/=12 years, unvaccinated, or vaccinated with BNT162b2, who were hospitalised with one of the thrombotic events of interest from 19 February 2021 through 19 February 2022. The risk period was 0-21 days after receiving a primary or booster dose of BNT162b2. RESULTS: 6039 individuals were hospitalised with one of the thrombotic events examined, including 5127 with VTE, 605 with arterial thrombosis, 272 with splanchnic thrombosis, and 35 with CVT. The proportion of individuals vaccinated with at least one dose of BNT162b2 ranged from 82.7 % to 91.4 %. Compared with the control unexposed period, the IRR (95 % CI) of VTE, arterial thrombosis, splanchnic thrombosis, and CVT were 0.87 (0.76-1.00), 0.73 (0.56-0.95), 0.71 (0.43-1.16), and 0.87 (0.31-2.50) in the 21 days after BNT162b2 vaccination, respectively. There was no statistically significant increased risk of thrombosis following BNT162b2 in different ethnic groups in New Zealand. CONCLUSION: The BNT162b2 vaccine was not found to be associated with thrombosis in the general population or different ethnic groups in New Zealand, providing reassurance for the safety of the BNT162b2 vaccine.

Wong, C. Y. and E. J. Rios (2021). "Cutaneous hypersensitivity reaction with acute hepatitis following COVID-19 vaccine." JAAD Case Rep **16**: 44-46.

Yazdi, S. A. M., et al. (2023). "Empyema with an extensive retroperitoneal abscess after the first dose of the COVID-19 vaccine, a case report." Int J Surg Case Rep **107**: 108323.

INTRODUCTION: The most common side effects were mild pain at the injection site and fever after the COVID-19 vaccination. A retroperitoneal abscess is a rare disorder with a deceptive onset and difficult diagnosis. It has various reasons and is related to a high mortality rate. CASE PRESENTATION: A 29-year-old man with a recent history of first-dose Covid-19 vaccination, was referred for dyspnea, chest, and abdominal pain. Chest imaging revealed a lung abscess evacuated to pleural space. Left posterolateral thoracotomy surgery was done. Post-operation abdominopelvic imaging revealed increased fat stranding and fluid collection, suggesting retroperitoneal infection and abscess formation and the patient underwent drainage. CLINICAL DISCUSSION: Common side effects after COVID-19 vaccination were mild and expectable without hospitalization. But in our case, a rare complicated side effect was seen. CONCLUSION: Uncommon side effects should be observed to recognize whether they are related to the vaccine or not.

Yoon, J. P., Y. S. Jung and D. H. Kim (2022). "Local myofascitis of the deltoid muscle after administration of the AstraZeneca (AZD1222) COVID-19 vaccine: two cases, infectious and inflammatory." JSES Rev Rep Tech **2**(3): 376-379.

Yoshimura, Y., et al. (2022). "An autopsy case of COVID-19-like acute respiratory distress syndrome after mRNA-1273 SARS-CoV-2 vaccination." Int J Infect Dis **121**: 98-101.

We report the first case with COVID-19-like acute respiratory distress syndrome after mRNA-1273 SARS-CoV-2 vaccination. An 88-year-old woman developed dyspnea several hours after vaccination with the second dose of mRNA-1273. She was hospitalized on day nine due to worsening dyspnea. Chest computed tomography showed bilateral ground-glass opacities and consolidations, mainly in the peripheral lung areas. Repeat polymerase chain reaction tests for SARS-CoV-2 were negative, although the serum level of antibodies against spike protein was extremely elevated. Her condition did not improve with high-dose corticosteroids and high-flow nasal cannula oxygen therapy; she died on day 18. Autopsy findings revealed very early-phase diffuse alveolar damage in the whole lung without other lung diseases. The clinical and pathological findings suggested vaccine-induced acute respiratory distress syndrome. Serological and pathological tests might be useful to differentiate the disease from COVID-19.

Yuen, W. L. P., S. Y. J. Loh and D. B. Wang (2022). "SIRVA (Shoulder Injury Related to Vaccine Administration) following mRNA COVID-19 Vaccination: Case discussion and literature review." Vaccine **40**(18): 2546-2550.

Shoulder injury related to vaccine administration (SIRVA) is an increasingly recognised complication after vaccination and presents with significant shoulder pain and stiffness. SIRVA is thought to occur as a result of improper administration of vaccine into the subdeltoid bursa or shoulder joint. This results in an inflammatory cascade that damages the structures in the shoulder region. The incidence of SIRVA is relatively higher for influenza vaccination due its widespread administration. We present a reported case of SIRVA following a mRNA COVID-19 vaccination and review the current literature. As we embark on a worldwide scale of COVID-19 vaccination, it is of utmost important that we use proper vaccination techniques and screen patients at risk of SIRVA. This would improve the efficacy of the vaccine and improve the outcomes of the vaccination programme.

Zhang, Q., et al. (2023). "X-linked Charcot-Marie-Tooth disease after SARS-CoV-2 vaccination mimicked stroke-like episodes: A case report." World J Clin Cases **11**(2): 464-471.

BACKGROUND: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccinations have been administered worldwide, with occasional reports of associated neurological complications. Specifically, the impact of vaccinations on individuals with X-linked Charcot-Marie-Tooth disease type 1 (CMTX1) is unclear. Patients with CMTX1 can have stroke-like episodes with posterior reversible encephalopathy syndrome on magnetic resonance imaging (MRI), although this is rare. CASE SUMMARY: A 39-year-old man was admitted with episodic aphasia and dysphagia for 2 d. He received SARS-CoV-2

vaccination 39 d before admission. Physical examination showed pes cavus and reduced tendon reflexes. Brain MRI showed bilateral, symmetrical, restricted diffusion with T2 hyperintensities in the cerebral hemispheres. Nerve conduction studies revealed peripheral nerve damage. He was diagnosed with Charcot-Marie-Tooth disease, and a hemizygous mutation in the GJB1 gene on the X chromosome, known to be pathogenic for CMTX1, was identified. Initially, we suspected transient ischemic attack or demyelinating leukoencephalopathy. We initiated treatment with antithrombotic therapy and immunotherapy. At 1.5 mo after discharge, brain MRI showed complete resolution of lesions, with no recurrence. CONCLUSION: SARS-CoV-2 vaccination could be a predisposing factor for CMTX1 and trigger a sudden presentation.

Reproductive Issues

Al Kadri, H. M., et al. (2023). "COVID-19 vaccination and menstrual disorders among women: Findings from a meta-analysis study." J Infect Public Health **16**(5): 697-704.

BACKGROUND: COVID - 19 vaccine can lead to various local and systemic side effects, including menstrual irregularities in women. There is no robust quantitative evidence of the association between the COVID - 19 vaccine and menstrual irregularities. A meta-analysis was performed to estimate the pooled prevalence of a range of menstrual disorders that may occur in women following COVID - 19 vaccination. METHODS: After searching for epidemiological studies, we systematically performed a meta-analysis on PubMed/Medline, EMBASE, and Science Direct. Sixteen studies were finally included in the study. We estimated the pooled prevalence and corresponding 95 % confidence intervals (CIs) for a group of menstrual disorders, including menorrhagia, polymenorrhea, abnormal cycle length, and oligomenorrhea. Heterogeneity was assessed using the I(2) statistic and the Q test. RESULTS: Overall, the pooled prevalence of menorrhagia was 24.24 % (pooled prevalence 24.24 %; 95 % CI: 12.8-35.6 %). The pooled prevalence of polymenorrhea was 16.2 % (pooled prevalence: 16.2 %; 95 % CI: 10.7-21.6 %). The pooled prevalence of abnormal cycle length was relatively lower than that of the other disorders (pooled prevalence: 6.6 %; 95 % CI: 5.0-8.2 %). The pooled prevalence of oligomenorrhea was 22.7 % (95 % CI: 13.5-32.0 %). CONCLUSION: The findings indicate that menorrhagia, oligomenorrhea, and polymenorrhea were the most common menstrual irregularities after vaccination. The findings also suggest that a relatively high proportion of women suffer from menstrual irregularities. Further longitudinal studies are needed to confirm the causal relationship between COVID-19 vaccination and menstrual irregularities.

Al-Furaydi, A., S. A. Alrobaish and N. Al-Sowayan (2023). "The COVID-19 vaccines and menstrual disorders." Eur Rev Med Pharmacol Sci **27**(3): 1185-1191.

OBJECTIVE: The COVID-19 vaccination has been linked to numerous reports of menstrual disorders as potential side effects. However, menstrual cycle results after vaccination were not collected throughout clinical trials. According to other research, COVID-19 vaccination and menstrual disorders have no discernible connection, and menstrual disorders are temporary. SUBJECTS AND METHODS: We asked questions about menstruation disturbances following the first and second doses of the COVID-19 vaccine in a population-based cohort of adult Saudi women to determine whether the vaccination is linked to menstrual cycle irregularities. RESULTS: According to the results, 63.9% of women experienced variations in their menstrual cycle either after the first or second dose. Such results show that COVID-19 vaccination impacts women's menstrual cycles. However, there is no need for concern because the alterations are relatively minor, and the menstrual cycle usually returns to normal within two months. Additionally, there are no obvious distinctions between the various vaccine types or body mass. CONCLUSIONS: Our findings support and explain the self-reports of menstrual cycle variations. We have discussed reasons for these problems that describe

the mechanism of the relationship between them and the immune response. Such reasons will help prevent hormonal imbalances and the influence of therapies and immunizations on the reproductive system.

Alahmadi, A. M., et al. (2022). "The Effect of the COVID-19 Vaccine on the Menstrual Cycle Among Reproductive-Aged Females in Saudi Arabia." Cureus **14**(12): e32473.

BACKGROUND: A global concern about a possible association between COVID-19 vaccines and menstrual disturbance has been raised. Moreover, women who have experienced menstrual changes are worried about the length of the side effects and are hesitant to receive booster doses. Therefore, the aim of this study is to evaluate the impact of the COVID-19 vaccine on all features of the menstrual cycle, including cycle length, amount of bleeding, and pain. METHODOLOGY: We retrospectively analyzed menstrual cycles following at least two doses of COVID-19 vaccines; the cycle changes within the individual pre-vaccination and post-vaccination were compared. All reproductive-aged females from 18 to 45 years who fit the inclusion criteria were included in the study and categorized into five sub-categories based on age to investigate whether certain age groups were most affected. The data were collected through a well-structured self-administered questionnaire. Participants obtained their vaccination information (date, type of vaccine) from Tawakkalna, the official COVID-19 application in the Kingdom of Saudi Arabia. IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp was performed in data entry and statistical analysis. Variables were described as frequency and percentage, as all were categorical. To investigate the association between menstrual changes and its possible associated factors, we used the Chi-square test, and the statistical significance was determined at $p<0.05$. RESULTS: The online questionnaire received responses from a total of 1092 reproductive females. However, out of which, 419 were not fitting into the inclusion criteria. Thus, a total of 673 females were included in the final report. Overall, the changes in the menstrual cycles after both COVID-19 vaccine doses were observed among 46.7%, mainly more menstrual pain in 22.9% following the first dose compared with 21.4% after the second. Menstrual changes were observed among almost two-thirds of women in the age groups 18-22 years (65.2%) and 38-45 years (65.4%) compared with only 43.5% of those in the age group 23-27 years, $p<0.001$. The Moderna vaccine was associated with the highest rate of menstrual changes (65.4%), whereas Oxford-AstraZeneca was associated with the lowest rate (44.9%), $p=0.040$. The duration of changes in the cycles after the COVID-19 vaccine (one dose or both) was less than one month among 42.5% of females, whereas it was three months or more among 27.1%. CONCLUSION: The COVID-19 vaccination is associated with a minor and transient change in the menstrual cycle, resulting mainly more menstrual pain and increased bleeding.

Alvergne, A., et al. (2023). "Associations Among Menstrual Cycle Length, Coronavirus Disease 2019 (COVID-19), and Vaccination." Obstet Gynecol.

OBJECTIVE: To assess whether coronavirus disease 2019 (COVID-19) is associated with menstrual cycle length changes and, if so, how that compares with those undergoing vaccination or no event (control). METHODS: We conducted a retrospective cohort

analysis in which we analyzed prospectively tracked cycle-length data from users of a period tracker application who also responded to a survey regarding COVID-19 symptoms and vaccination. We restricted our sample to users aged 16-45 years, with normal cycle lengths (24-38 days) and regular tracking behavior during the five cycles around COVID-19 symptoms or vaccination or a similar time period for those experiencing no event (control group). We calculated the within-user change in cycle length (days) from the three consecutive cycles preevent average (either vaccination, disease, or neither; cycles 1-3) to the event (cycle 4) and postevent (cycle 5) cycles. We used mixed-effects models to estimate the age- and country-adjusted difference in change in cycle length across the groups. RESULTS: We included 6,514 users from 110 countries representing 32,570 cycles (COVID-19 symptoms: 1,450; COVID-19 vaccination: 4,643; control: 421). The COVID-19 cohort experienced a 1.45-day adjusted increase in cycle length during cycle 4 (COVID-19) compared with their three preevent cycles (95% CI 0.86-2.04). The vaccinated group experienced a 1.14-day adjusted increase in cycle length during cycle 4 (COVID-19 vaccine) compared with their preevent average (95% CI 0.60-1.69). The control group (neither vaccine nor disease) experienced a 0.68-day decrease (95% CI -1.18 to -0.19) in a similar time period. Post hoc tests showed no significant differences in the magnitude of changes between the COVID-19 and vaccination cohorts. In both cohorts, cycle length changes disappeared in the postevent cycle. CONCLUSION: Experiencing COVID-19 is associated with a small change in cycle length similar to COVID-19 vaccination. These changes resolve quickly within the next cycle.

Alvergne, A., et al. (2023). "A retrospective case-control study on menstrual cycle changes following COVID-19 vaccination and disease." iScience **26**(4): 106401.

There has been increasing public concern that COVID-19 vaccination causes menstrual disturbance regarding the relative effect of vaccination compared to SARS-CoV-2 infection. Our objectives were to test potential risk factors for reporting menstrual cycle changes following COVID-19 vaccination and to compare menstrual parameters following COVID-19 vaccination and COVID-19 disease. We performed a secondary analysis of a retrospective online survey conducted in the UK in March 2021. In pre-menopausal vaccinated participants (n = 4,989), 18% reported menstrual cycle changes after their first COVID-19 vaccine injection. The prevalence of reporting any menstrual changes was higher for women who smoke, have a history of COVID-19 disease, or are not using estradiol-containing contraceptives. In a second sample including both vaccinated and unvaccinated participants (n = 12,579), COVID-19 vaccination alone was not associated with abnormal menstrual cycle parameters, while a history of COVID-19 disease was associated with an increased risk of reporting heavier bleeding, "missed" periods, and inter-menstrual bleeding.

Alvergne, A., E. V. Woon and V. Male (2022). "Effect of COVID-19 vaccination on the timing and flow of menstrual periods in two cohorts." Front Reprod Health **4**: 952976.

COVID-19 vaccination protects against the potentially serious consequences of SARS-CoV-2 infection, but some people have been hesitant to receive the vaccine because of

reports that it could affect menstrual bleeding. To determine whether this occurs we prospectively recruited a cohort of 79 individuals, each of whom recorded details of at least three consecutive menstrual cycles, during which time they each received at least one dose of COVID-19 vaccine. In spontaneously cycling participants, COVID-19 vaccination was associated with a delay to the next period, but this change reversed in subsequent unvaccinated cycles. No delay was detected in those taking hormonal contraception. To explore hypotheses about the mechanism by which these menstrual changes occur, we retrospectively recruited a larger cohort, of 1,273 people who had kept a record of their menstrual cycle and vaccination dates. In this cohort, we found a trend toward use of combined hormonal contraception being protective against reporting a delayed period, suggesting that menstrual changes following vaccination may be mediated by perturbations to ovarian hormones. However, we were unable to detect a clear association between the timing of vaccination within the menstrual cycle and reports of menstrual changes. Our findings suggest that COVID-19 vaccination can lengthen the menstrual cycle and that this effect may be mediated by ovarian hormones. Importantly, we find that the menstrual cycle returns to its pre-vaccination length in unvaccinated cycles.

Amer, A. A., et al. (2022). "Menstrual changes after COVID-19 vaccination and/or SARS-CoV-2 infection and their demographic, mood, and lifestyle determinants in Arab women of childbearing age, 2021." Front Reprod Health **4**: 927211.

BACKGROUND: By September 2, 2021, over 30,000 COVID-19-vaccinated females had reported menstrual changes to the MHRA's Yellow Card surveillance system. As a result, the National Institutes of Health (NIH) is urging researchers to investigate the COVID-19 vaccine's effects on menstruation. Therefore, this study was conducted to explore the menstrual changes after COVID-19 vaccination and/or SARS-CoV-2 infection and their interrelations with demographic, mood, and lifestyle factors in Arab women of childbearing age (CBA). METHODOLOGY: A cross-sectional study was conducted during October 2021 using an Arabic validated and self-administrated questionnaire. In total, 1,254 Women of CBA in the Arabic Population (15-50 y) with regular menstrual cycles were randomly selected from five countries (Saudi Arabia, Egypt, Syria, Libya, and Sudan). RESULTS: The mean (SD) age of the 1,254 studied females was 29.6 (8.5) years old. In total, 634 (50%) were married, 1,104 (88.0%) had a University education or above, 1,064 (84.4%) lived in urban areas, and 573 (45.7%) had normal body weight. Moreover, 524 (41.8%) were COVID-19 cases and 98 women (18.7%) reported menstrual changes (MCs). The 1,044 (83.5%) vaccinated females reported 418 (38.5%) MCs after being vaccinated, and these MCs resolved in 194 women (55.1%) after more than 9 months. Statistically significant relationships were observed between the reported MCs and the following variables: age, marital status, level of education, nationality, residence, and BMI. MCs were reported at 293(80.6) after the 2nd dose, and were mainly reported after 482 (46.1) Pfizer, 254 (24.3) Astrazenica, and 92 (8.8) Senopharm. CONCLUSION: MCs among women of CBA after COVID-19 infection and vaccination are prevalent and complex problems, and had many determinates.

Barabas, K., et al. (2022). "Influence of COVID-19 pandemic and vaccination on the menstrual cycle: A retrospective study in Hungary." Front Endocrinol (Lausanne) **13**: 974788.

Observations of women and clinicians indicated that the prevalence of menstrual cycle problems has escalated during the COVID-19 pandemic. However, it was not clear whether the observed menstrual cycle changes were related to vaccination, the disease itself or the COVID-19 pandemic-induced psychological alterations. To systematically analyze this question, we conducted a human online survey in women aged between 18 and 65 in Hungary. The menstrual cycle of 1563 individuals were analyzed in our study in relation to the COVID-19 vaccination, the COVID-19 infection, the pandemic itself and the mental health. We found no association between the COVID-19 vaccination, the vaccine types or the COVID-19 infection and the menstrual cycle changes. We also evaluated the menstrual cycle alterations focusing on three parameters of the menstrual cycle including the cycle length, the menses length and the cycle regularity in three pandemic phases: the pre-peak, the peak and the post-peak period in Hungary. Our finding was that the length of the menstrual cycle did not change in any of the periods. However, the menses length increased, while the regularity of the menstrual cycle decreased significantly during the peak of the COVID-19 pandemic when comparing to the pre- and post-peak periods. In addition, we exhibited that the length and the regularity of the menstrual cycle both correlated with the severity of depression during the post-peak period, therefore we concluded that the reported menstrual cycle abnormalities during the peak of COVID-19 in Hungary might be the result of elevated depressive symptoms.

Bisgaard Jensen, C., et al. (2023). "Prevalence of and risk factors for self-reported menstrual changes following COVID-19 vaccination: a Danish cohort study." Hum Reprod **38**(9): 1825-1834.

STUDY QUESTION: Are there some characteristics that render individuals more susceptible to report menstrual changes following the Coronavirus disease 2019 (COVID-19) vaccination? SUMMARY ANSWER: We found that 30% of menstruating women reported menstrual changes following COVID-19 vaccination and several potential risk factors including stress, vaccine concerns, severe COVID-19 infection, and immediate vaccine symptoms were associated with these reports. WHAT IS KNOWN ALREADY: Studies suggest that COVID-19 vaccination might temporarily prolong menstrual cycle length by less than 1 day. Specific characteristics may trigger menstrual changes in temporal relation to the vaccination simply by chance or render women more vigilant to potential menstrual changes after being vaccinated. However, research investigating potential risk factors for reporting menstrual changes following COVID-19 vaccination is limited. STUDY DESIGN, SIZE, DURATION: A population-based Danish cohort study. Data were collected from May 2021 to December 2021 as a part of the BiCoVac Cohort with the aim of examining non-specific effects following COVID-19 vaccination. The main study population included 13 648 menstruating women aged 16-65 years who completed all surveys, received their first dose of a COVID-19 vaccine during the data collection period, and completed questions related to their menstrual cycle. PARTICIPANTS/MATERIALS, SETTING, METHODS: Potential risk factors included 14 biological, physical, or psychological measures. Information on most potential risk

factors was self-reported and collected before the participants' first COVID-19 vaccination. Information about any menstrual change following COVID-19 vaccination was self-reported at the end of the data collection period. Logistic regression analyses were used to estimate crude and adjusted odds ratios (ORs) with 95% CIs for the association between each potential risk factor and reporting menstrual changes following COVID-19 vaccination. MAIN RESULTS AND THE ROLE OF CHANCE: Any menstrual change following COVID-19 vaccination was reported by 30% of menstruating women. Most of the potential risk factors were associated with reports of menstrual changes following COVID-19 vaccination. In particular, higher odds were found among women who reported >/=5 immediate vaccine symptoms; OR 1.67 [1.50-1.86], had had a prior severe COVID-19 infection; OR 2.17 [1.40-3.35], had a high-stress level at baseline; OR 1.67 [1.32-2.10], or were concerned about COVID-19 vaccines prior to vaccination; OR 1.92 [1.50-2.45]. Lower odds were found among women with regular menstrual cycles using hormonal contraception; OR 0.71 [0.65-0.78]. LIMITATIONS, REASONS FOR CAUTION: We were unable to address the causal effect of COVID-19 vaccination on the reported menstrual changes, as information about menstrual changes was not available among non-vaccinated women. WIDER IMPLICATIONS OF THE FINDINGS: The study identified several potential risk factors for reporting menstrual changes following COVID-19 vaccination. Further studies are needed to establish causal associations and the clinical impact of self-reported menstrual changes. STUDY FUNDING/COMPETING INTEREST(S): The BiCoVac data collection was funded by TrygFonden (id-number: 153678). No competing interests are declared. TRIAL REGISTRATION NUMBER: N/A.

Blazejewski, G. and J. Witkos (2023). "The Impact of COVID-19 on Menstrual Cycle in Women." J Clin Med **12**(15).

BACKGROUND: The COVID-19 pandemic has become the largest and most diverse to threaten the health of humanity since the 1918 influenza pandemic. METHODS: This study involved 113 women who had suffered from COVID-19. The study was conducted as interviews with each woman during visits to a clinic prior to the start of their post-COVID-19 physiotherapy treatment cycle. The aim of this study was to assess the prevalence of changes in the women's monthly cycles related to COVID-19, as well as to analyse correlations between dependent variables relating to changes in the monthly cycle and independent variables relating to other factors, such as age, weight, number and type of vaccinations, and time since illness. Additionally, the study assesses correlations between the monthly cycle and COVID-19 symptoms persisting after the illness (long COVID). RESULTS: Women who reported more symptoms of COVID-19 were more likely to report changes in their menstrual cycle occurring after the SARS-CoV-2 infection, compared with women whose disease course was mild. Women who declared that COVID-19 affected their monthly cycles most often indicated increases in abdominal, lower abdominal, and joint and muscle pain, as well as in the severity of headaches during monthly bleeding. A small percentage of women indicated that their monthly cycles were longer and their regularity disrupted. CONCLUSIONS: This study shows that the more COVID-19 symptoms a woman had, the more often there were

noted changes in monthly cycle. The same relationship was also found for persistent long COVID symptoms. The longer the time lapse since the COVID-19 infection, the less frequently changes in the monthly cycle were recorded.

Caspersen, I. H., et al. (2023). "Menstrual disturbances in 12- to 15-year-old girls after one dose of COVID-19 Comirnaty vaccine: Population-based cohort study in Norway." Vaccine **41**(2): 614-620.

Chao, M. J., C. Menon and M. Elgendi (2022). "Effect of COVID-19 vaccination on the menstrual cycle." Front Med (Lausanne) **9**: 1065421.

Numerous anecdotal accounts and qualitative research studies have reported on post-vaccination menstrual irregularities in women of reproductive age. However, none have quantified the impact. This is the first systematic review and meta-analysis to quantify and characterize the menstrual irregularities associated with vaccination for women of reproductive age. A search on July 20, 2022, retrieved articles published between December 1, 2019, and July 1, 2022, from MEDLINE, Embase, and Web of Science. The included articles were studies with full texts written in English that reported on menstrual irregularities for vaccinated vs. unvaccinated women of reproductive age. The quality of the studies was evaluated using the Study Quality Assessment Tool for Observation Cohort and Cross-Sectional Studies. Four observational studies were included. Review Manager was used to generating a forest plot with odds ratios (ORs) at the 95% confidence interval (CI), finding statistically significant associations between vaccination and menstrual irregularities for 25,054 women of reproductive age (OR = 1.91, CI: 1.76-2.07) with a significant overall effect of the mean ($Z = 16.01$, $p < 0.0001$). The studies were heterogeneous with significant dispersion of values ($chi(2) = 195.10$ at $df = 3$, $p < 0.00001$, $I (2) = 98\%$). The findings of this systematic review and meta-analysis are limited by the availability of quantitative data. The results have implications for treating women of reproductive age with menstrual irregularities and informing them about the potential side effects of vaccinations.

Darney, B. G., et al. (2023). "Impact of coronavirus disease 2019 (COVID-19) vaccination on menstrual bleeding quantity: An observational cohort study." BJOG **130**(7): 803-812.

OBJECTIVE: To assess whether coronavirus disease 2019 (COVID-19) vaccination impacts menstrual bleeding quantity. DESIGN: Retrospective cohort. SETTING: Five global regions. POPULATION: Vaccinated and unvaccinated individuals with regular menstrual cycles using the digital fertility-awareness application Natural Cycles degrees . METHODS: We used prospectively collected menstrual cycle data, multivariable longitudinal Poisson generalised estimating equation (GEE) models and multivariable multinomial logistic regression models to calculate the adjusted difference between vaccination groups. All regression models were adjusted for confounding factors. MAIN OUTCOME MEASURES: The mean number of heavy bleeding days (fewer, no change or more) and changes in bleeding quantity (less, no change or more) at three time points (first dose, second dose and post-exposure menses). RESULTS: We included 9555 individuals (7401 vaccinated and 2154 unvaccinated). About two-thirds of individuals

reported no change in the number of heavy bleeding days, regardless of vaccination status. After adjusting for confounding factors, there were no significant differences in the number of heavy bleeding days by vaccination status. A larger proportion of vaccinated individuals experienced an increase in total bleeding quantity (34.5% unvaccinated, 38.4% vaccinated; adjusted difference 4.0%, 99.2% CI 0.7%-7.2%). This translates to an estimated 40 additional people per 1000 individuals with normal menstrual cycles who experience a greater total bleeding quantity following the first vaccine dose' suffice. Differences resolved in the cycle post-exposure. CONCLUSIONS: A small increase in the probability of greater total bleeding quantity occurred following the first COVID-19 vaccine dose, which resolved in the cycle after the post-vaccination cycle. The total number of heavy bleeding days did not differ by vaccination status. Our findings can reassure the public that any changes are small and transient.

Duijster, J. W., et al. (2023). "Menstrual abnormalities after COVID-19 vaccination in the Netherlands: A description of spontaneous and longitudinal patient-reported data." Br J Clin Pharmacol.

AIMS: During the COVID-19 vaccination campaigns, the number of reports of menstrual abnormalities increased rapidly. Here, we describe the nature and potential risk factors associated with menstrual abnormalities based on spontaneously reporting data as well as data from a prospective cohort event monitoring (CEM) study as these are poorly studied. METHODS: Reports of menstrual abnormalities received by the Netherlands Pharmacovigilance Centre Lareb in the spontaneous reporting system between February 2021 and April 2022 were summarized. In addition, logistic regression analysis was performed on the reported menstrual abnormalities in the CEM study to assess the association between person characteristics, prior SARS-CoV-2 infection and use of hormonal contraceptives and the occurrence of menstrual abnormalities after vaccination. RESULTS: We analysed over 24 000 spontaneous reports of menstrual abnormalities and over 500 episodes (among 16 929 included women) of menstrual abnormalities in the CEM study. The CEM study showed an incidence of 41.4 per 1000 women aged </=54 years. Amenorrhoea/oligomenorrhoea and heavy menstrual bleeding collectively accounted for about half of all abnormalities reported. Significant associations were observed for the age group 25-34 years (odds ratio 2.18; 95% confidence interval 1.45-3.41) and the Pfizer vaccine (odds ratio 3.04; 95% confidence interval 2.36-3.93). No association was observed for body mass index and presence of most comorbidities assessed. CONCLUSION: The cohort study showed a high incidence of menstrual disorders among women aged </=54 years, and this observation was supported by the analysis of spontaneous reports. This suggests that a relation between COVID-19 vaccination and menstrual abnormalities is plausible and should be further investigated.

Edelman, A., et al. (2022). "Association between menstrual cycle length and covid-19 vaccination: global, retrospective cohort study of prospectively collected data." BMJ Med **1**(1).

OBJECTIVES: To identify whether covid-19 vaccines are associated with menstrual changes in order to address concerns about menstrual cycle disruptions after covid-19

vaccination. DESIGN: Global, retrospective cohort study of prospectively collected data. SETTING: International users of the menstrual cycle tracking application, Natural Cycles. PARTICIPANTS: 19 622 individuals aged 18-45 years with cycle lengths of 24-38 days and consecutive data for at least three cycles before and one cycle after covid (vaccinated group; n=14 936), and those with at least four consecutive cycles over a similar time period (unvaccinated group; n=4686). MAIN OUTCOME MEASURES: The mean change within individuals was assessed by vaccination group for cycle and menses length (mean of three cycles before vaccination to the cycles after first and second dose of vaccine and the subsequent cycle). Mixed effects models were used to estimate the adjusted difference in change in cycle and menses length between the vaccinated and unvaccinated. RESULTS: Most people (n=15 713; 80.08%) were younger than 35 years, from the UK (n=6222; 31.71%), US and Canada (28.59%), or Europe (33.55%). Two thirds (9929 (66.48%) of 14 936) of the vaccinated cohort received the Pfizer-BioNTech (BNT162b2) covid-19 vaccine, 17.46% (n=2608) received Moderna (mRNA-1273), 9.06% (n=1353) received Oxford-AstraZeneca (ChAdOx1 nCoV-19), and 1.89% (n=283) received Johnson & Johnson (Ad26.COV2.S). Individuals who were vaccinated had a less than one day adjusted increase in the length of their first and second vaccine cycles, compared with individuals who were not vaccinated (0.71 day increase (99.3% confidence interval 0.47 to 0.96) for first dose; 0.56 day increase (0.28 to 0.84) for second dose). The adjusted difference was larger in people who received two doses in a cycle (3.70 days increase (2.98 to 4.42)). One cycle after vaccination, cycle length was similar to before the vaccine in individuals who received one dose per cycle (0.02 day change (99.3% confidence interval -0.10 to 0.14), but not yet for individuals who received two doses per cycle (0.85 day change (99.3% confidence interval 0.24 to 1.46)) compared with unvaccinated individuals. Changes in cycle length did not differ by the vaccine's mechanism of action (mRNA, adenovirus vector, or inactivated virus). Menses length was unaffected by vaccination. CONCLUSIONS: Covid-19 vaccination is associated with a small and likely to be temporary change in menstrual cycle length but no change in menses length.

Farah, S., et al. (2023). "Effect of COVID-19 vaccinations on menstrual cycle and postmenopausal bleeding among health care workers: A cross-sectional study." Int J Gynaecol Obstet **162**(2): 532-540.

OBJECTIVE: To determine the effect of coronavirus disease 2019 (COVID-19) vaccination and its association with sociodemographic factors on the menstrual cycle in premenopausal women and on postmenopausal bleeding. METHODS: This is a retrospective cross-sectional study conducted between September 22, 2022, and November 30, 2022, via a questionnaire distributed to 359 health care workers (HCWs) at Lebanese American University Medical Center-Rizk Hospital and St John's Hospital. Inclusion criteria included female Lebanese HCWs who were vaccinated and aged 18 to 65 years. RESULTS: Change in cycle length was significantly associated with age (P = 0.025 after the first dose and P = 0.017 after the second dose), level of education (P = 0.013 after the first dose and P = 0.012 after the second dose), and fibroids (P = 0.006 after the second dose and P = 0.003 after the third dose). The change in cycle flow was

significantly associated with age (P = 0.028), fibroids (P = 0.002 after the second dose and P = 0.002 after the third dose), bleeding disorders (P = 0.000), and chronic medications (P = 0.007). The change in symptoms was associated with polycystic ovary syndrome (P = 0.021), chronic medications (P = 0.019 after the second dose and P = 0.045 after the third dose), and fibroids (P = 0.000). CONCLUSION: COVID-19 vaccination can influence the menstrual cycle. Age, body mass index, level of education, underlying comorbidities, and use of chronic medications are significantly associated with changes in menstrual length, flow, and symptoms following vaccination.

Farland, L. V., et al. (2023). "COVID-19 vaccination and changes in the menstrual cycle among vaccinated persons." Fertil Steril **119**(3): 392-400.

OBJECTIVE: To describe the characteristics of people who experience changes to their menstrual cycle after COVID-19 vaccination. DESIGN: Longitudinal study. PATIENT(S): We recruited a volunteer sample with and without a history of SARS-CoV-2 infection who enrolled in the Arizona COVID-19 Cohort (CoVHORT) study and participated in a reproductive sub-cohort who were pre-menopausal, not pregnant, and had received a COVID-19 vaccine in 2021 (n = 545). EXPOSURE(S): Demographic and reproductive characteristics were collected via self-reports. MAIN OUTCOME MEASURE(S): Information on self-reported changes in the menstrual cycle after COVID-19 vaccination was collected from May 2021 to December 2021. We looked at demographic and reproductive characteristics as predictors of menstrual cycle change. RESULT(S): The majority of our vaccinated sample received the Pfizer-BioNTech vaccine (58%), and were 26-35 years old (51%), non-Hispanic (84%), and White (88%). Approximately 25% of vaccinated participants reported a change in their menstrual cycle after vaccination; the majority reported changes after their second dose (56%) as compared with their first (18%) and third (14%) doses. The most commonly reported changes were irregular menstruation (43%), increased premenstrual symptoms (34%), increased menstrual pain or cramps (30%), and abnormally heavy or prolonged bleeding (31%). High self-reported perceived stress levels compared with low perceived stress (OR, 2.22; 95% CI 1.12-4.37) and greater body mass index (OR, 1.04; 95% CI 1.00-1.07) were associated with greater odds of experiencing the menstrual cycle changes after the vaccination. Participants having a history of SARS-CoV-2 infection were less likely to report changes in their menstrual cycle after vaccination compared with the participants with no history of SARS-CoV-2 infection (OR, 0.58; 95% CI 0.32-1.04). CONCLUSION(S): Among vaccinated participants, approximately 25% of them reported predominantly temporary changes in the menstrual cycle, however, we are unable to determine whether these changes are due to normal cycle variability. The COVID-19 vaccines are safe and effective for everyone, including pregnant people and people trying to conceive; hence, these findings should not discourage vaccination.

Gibson, E. A., et al. (2022). "Covid-19 vaccination and menstrual cycle length in the Apple Women's Health Study." NPJ Digit Med **5**(1): 165.

COVID-19 vaccination may be associated with change in menstrual cycle length following vaccination. We estimated covariate-adjusted differences in mean cycle length (MCL),

measured in days, between pre-vaccination cycles, vaccination cycles, and post-vaccination cycles within vaccinated participants who met eligibility criteria in the Apple Women's Health Study, a longitudinal mobile-application-based cohort of people in the U.S. with manually logged menstrual cycles. A total of 9652 participants (8486 vaccinated; 1166 unvaccinated) contributed 128,094 cycles (median = 10 cycles per participant; inter-quartile range: 4-22). Fifty-five percent of vaccinated participants received Pfizer-BioNTech's mRNA vaccine, 37% received Moderna's mRNA vaccine, and 8% received the Johnson & Johnson/Janssen (J&J) vaccine. COVID-19 vaccination was associated with a small increase in MCL for cycles in which participants received the first dose (0.50 days, 95% CI: 0.22, 0.78) and cycles in which participants received the second dose (0.39 days, 95% CI: 0.11, 0.67) of mRNA vaccines compared with pre-vaccination cycles. Cycles in which the single dose of J&J was administered were, on average, 1.26 days longer (95% CI: 0.45, 2.07) than pre-vaccination cycles. Post-vaccination cycles returned to average pre-vaccination length. Estimated follicular phase vaccination was associated with increased MCL in cycles in which participants received the first dose (0.97 days, 95% CI: 0.53, 1.42) or the second dose (1.43 days, 95% CI: 1.06, 1.80) of mRNA vaccines or the J&J dose (2.27 days, 95% CI: 1.04, 3.50), compared with pre-vaccination cycles. Menstrual cycle change following COVID-19 vaccination appears small and temporary and should not discourage individuals from becoming vaccinated.

Guo, W., et al. (2022). "Profiling COVID-19 Vaccine Adverse Events by Statistical and Ontological Analysis of VAERS Case Reports." Front Pharmacol **13**: 870599.

Since the beginning of the COVID-19 pandemic, vaccines have been developed to mitigate the spread of SARS-CoV-2, the virus that causes COVID-19. These vaccines have been effective in reducing the rate and severity of COVID-19 infection but also have been associated with various adverse events (AEs). In this study, data from the Vaccine Adverse Event Reporting System (VAERS) was queried and analyzed via the Cov19VaxKB vaccine safety statistical analysis tool to identify statistically significant (i.e., enriched) AEs for the three currently FDA-authorized or approved COVID-19 vaccines. An ontology-based classification and literature review were conducted for these enriched AEs. Using VAERS data as of 31 December 2021, 96 AEs were found to be statistically significantly associated with the Pfizer-BioNTech, Moderna, and/or Janssen COVID-19 vaccines. The Janssen COVID-19 vaccine had a higher crude reporting rate of AEs compared to the Moderna and Pfizer COVID-19 vaccines. Females appeared to have a higher case report frequency for top adverse events compared to males. Using the Ontology of Adverse Event (OAE), these 96 adverse events were classified to different categories such as behavioral and neurological AEs, cardiovascular AEs, female reproductive system AEs, and immune system AEs. Further statistical comparison between different ages, doses, and sexes was also performed for three notable AEs: myocarditis, GBS, and thrombosis. The Pfizer vaccine was found to have a closer association with myocarditis than the other two COVID-19 vaccines in VAERS, while the Janssen vaccine was more likely to be associated with thrombosis and GBS AEs. To support standard AE representation and study, we have also modeled and classified the newly identified thrombosis with thrombocytopenia syndrome (TTS) AE and its subclasses in the OAE by incorporating the

Brighton Collaboration definition. Notably, severe COVID-19 vaccine AEs (including myocarditis, GBS, and TTS) rarely occur in comparison to the large number of COVID-19 vaccinations administered in the United States, affirming the overall safety of these COVID-19 vaccines.

Kareem, R., et al. (2022). "The effect of COVID-19 vaccination on the menstrual pattern and mental health of the medical students: A mixed-methods study from a low and middle-income country." PLoS One **17**(11): e0277288.

OBJECTIVE: To assess the effect of COVID-19 vaccination on menstrual patterns and mental health of medical students and to explore the students' perspective regarding this effect. MATERIALS AND METHODS: This mixed-method study was conducted on the medical and dental students of the private and public sector institutions of Peshawar from September 2021 to March 2022. A Menstrual symptom questionnaire (MSQ) and hospital anxiety and depression scale (HADS) were used. This was followed by qualitative interviews with the students who faced problems in their menstruation after the COVID-19 vaccination. RESULTS: A total of 953 students were included, with a mean age of 20.67+/-1. 56 years. More than half (n = 512, 53.7%) experienced menstrual cycle abnormalities post-vaccination. The majority having disturbances in their menstrual cycle had significantly higher levels of anxiety (p = 0.000). Results on the menstrual symptom questionnaire, anxiety, and depression subtype of HADS showed a negative and statistically significant relationship with changes after COVID-19 vaccination (p<0.05). In the qualitative interviews, 10 (58.8%) students each had problems with frequency and flow, followed by 7 (41.2%) students, who had dysmenorrhea. Seven (41.2%) consulted a gynecologist for management. The majority (n = 14, 82.4%) stated that these issues had an adverse impact on their mental health and almost half (n = 8, 47.1%) suggested consulting a gynecologist while facing such situations. CONCLUSION: This study showed the impact of the COVID-19 vaccine on women;s menstrual patterns and subsequent mental health status. Although the majority of the students experienced menstrual cycle abnormalities and subsequent mental health adversities post COVID-19 vaccination but these were temporary and self-limiting and were attributed to the psychological impact of the vaccination. Therefore, it is imperative to alert health care professionals about possible side effects and prior counseling is expected to play an important role in this context.

Katz, A., et al. (2022). "Web and social media searches highlight menstrual irregularities as a global concern in COVID-19 vaccinations." Sci Rep **12**(1): 17657.

Delineation of public concerns that prevent vaccine compliance is a major step in generating assurances and enhancing the success of COVID-19 prevention programs. We therefore sought to identify public concerns associated with COVID-19 vaccines, as reflected by web and social media searches, with a focus on menstrual irregularities. We used trajectory analyses of web and social media search data in combination with global COVID-19 data to reveal time-dependent correlations between vaccination rates and the relative volume of vaccine and period related searches. A surge of period and vaccine related Google searches followed the introduction of Covid vaccines around the world,

and the commencement of vaccination programs in English speaking countries and across the United States. The relative volume of searches such as "Covid vaccine menstrual irregularities", "Covid vaccine menstrual period", "Pfizer vaccine menstruation", and "Moderna vaccine menstruation" was each significantly correlated with vaccination rates (Spearman r = 0.42-0.88, P = 4.33 x 10(-34)-1.55 x 10(-5)), and significantly different before and after the introduction of Covid vaccines (Mann-Whitney P = 2.00 x 10(-21)-7.10 x 10(-20)). TikTok users were more engaged in period problems in 2021 than ever before. International, national, and state-level correlations between COVID-19 vaccinations and online activity demonstrate a global major concern of vaccine-related menstrual irregularities. Whether it is a potential side effect or an unfounded worry, monitoring of web and social media activity could reveal the public perception of COVID-19 prevention efforts, which could then be directly addressed and translated into insightful public health strategies.

Madaan, S., et al. (2022). "Post-COVID-19 menstrual abnormalities and infertility: Repercussions of the pandemic." J Educ Health Promot **11**: 170.

While battling the life-threatening complications of COVID-19, its effect on the menstrual cycle and infertility has been somewhat ignored. This brief review aims on highlighting the importance of menstrual abnormalities being experienced during the post-COVID period and to make the clinicians aware about what to expect in regard of menstrual abnormalities by learning from various studies that have been conducted worldwide. This review article was written with systematic literature review with the help of data search machine such as PubMed, Scopus, Web of Sciences, and Google Scholar. A search strategy leads to the extraction of 160 related articles that after the removal of inappropriate and duplicate articles, 33 articles were selected for the review. To find other potentially relevant articles, the references of the extracted articles were thoroughly examined. The search was carried out using keywords including "COVID-19," "Menstrual abnormalities," and "Infertility." Using OR and AND, the keywords mentioned above were combined and then utilized in the search box of the databases. Articles published from January 2020 to September 2021 were included in this study. It includes worldwide data ranging from studies done in China, India, Ireland, Turkey, Jordan, and Germany. During the post-COVID period, there is a significant alteration in the sex hormones of females infected by COVID-19 which may manifest as menstrual cycle abnormalities such as decreased cycle length or prolonged menstrual cycle bleeding. It may also manifest as infertility due to ovarian failure due to suppression of ovarian function COVID-19 a novel coronavirus which is presently a pandemic has affected the world in manner reminding the world of 1918 Spanish flu. However, while battling the deadly pandemic, the clinicians should also be aware of the repercussions of the effect this infection has on multiple organs such as ovarian suppression leading to infertility, oligomenorrhea, or menorrhagia.

Minguez-Esteban, I., et al. (2022). "Association between RNAm-Based COVID-19 Vaccines and Permanency of Menstrual Cycle Alterations in Spanish Women: A Cross-Sectional Study." Biology (Basel) **11**(11).

Introduction: The purpose of this study was to delve more deeply into the medium and long-term relation between mRNA-based vaccines and changes in menstrual pain, cycle length, and amount of bleeding in Spanish women. Material and Methods: A total of 746 women (63% between 18-30 and 37% between 31-45 years old) participated in the study. A numerical rating scale was used for recording pain intensity, a pictorial chart for menstrual bleeding, and data from menstrual cycle duration, type of vaccine, number of doses and time from vaccination. Results: Sixty-five per cent of the women perceived changes in their menstrual cycle after receiving the vaccines, irrespective of type of vaccine or number of doses; all p values were >0.05. Most of them (n = 316 out of 484) reported more than one alteration in their menstrual cycle. Almost half of the participants had been vaccinated over 5 months (45%), 3-4 months (15%) 2-3 months (26%), and one month or less (13%) before. The percentage of women that reported alterations remained strongly constant across time, p > 0.05, ranging from 64 to 65%. Conclusions: Reported alterations in Spanish women after COVID vaccination remained more than 5 months after the last dose.

Nazir, M., et al. (2022). "Menstrual abnormalities after COVID-19 vaccines: A systematic review." Vacunas **23**: S77-S87.

The objective of this systematic review is to give a comprehensive interpretation of menstrual cycle changes after the COVID-19 vaccination. Additionally, it is imperative to assess reports of menstrual changes following vaccination to dispel concerns that COVID-19 vaccines hinder the likelihood of pregnancy in the long run. A literature review was conducted using digital databases to systematically identify the studies reporting any menstrual abnormalities after the COVID-19 vaccine. Detailed patient-level study characteristics including the type of study, sample size, administered vaccines, and menstrual abnormalities were abstracted. A total of 78 138 vaccinated females were included in this review from 14 studies. Of these, 39 759 (52.05%) had some form of a menstrual problem after vaccination. Due to the lack of published research articles, preprints were also included in this review. Menorrhagia, metrorrhagia, and polymenorrhea were the most commonly observed problems and the overall study-level rate of menstrual abnormality ranged from 0.83% to 90.9%. Age, history of pregnancy, systemic side-effects of COVID-19, smoking, and second dose of COVID-19 vaccine were predictors of menstrual problems after vaccination.

Qashqari, F. S. I., et al. (2022). "Effect of the COVID-19 Vaccine on the Menstrual Cycle among Females in Saudi Arabia." Ethiop J Health Sci **32**(6): 1083-1092.

BACKGROUND: The number of reports of menstrual changes after COVID-19 vaccination in the Saudi population is still unknown. Therefore, this study aimed to assess the effect of the COVID-19 vaccine(Pfizer, AstraZeneca, and Moderna) on the menstrual cycle among females in Saudi Arabia. METHODS: This descriptive cross-sectional study was conducted in Saudi Arabia at Umm Al-Qura University (UQU) from August 2021 to February 2022. Data was collected through a previously validated online questionnaire. RESULTS: A total of 2338 participants who received the first dose of the COVID-19 vaccine participated in this study; 1606 (68.7%) of them received the second dose in

addition to the first. The mean age of the study participants was 35.4+/-9.5 years. No significant associations were found between the type of COVID-19 vaccine and the impact on the menstrual cycle, either for the first or second dose (P-values > 0.05). A significant association was found only between the first dose vaccination day and the impact on the menstrual cycle in the second question of "After receiving the COVID-19 vaccine, your next period was" (P-value </= 0.05). Significant associations were found between the second dose vaccination day and the impact on the menstrual cycle in the first and second questions of "After receiving the COVID-19 vaccine, your next period was", and "After receiving the first dose, your next period was," respectively (P-values </= 0.05). CONCLUSION: The study found a potential association between the COVID-19 vaccine and menstrual cycle irregularities, which could impact females' quality of life.

Roncati, L. and A. Manenti (2022). "Apropos of menstrual changes and abnormal uterine bleeding after COVID-19 vaccination." Brain Hemorrhages.

It is news of 28 October 2022 that the Pharmacovigilance Risk Assessment Committee of the European Medicines Agency has recommended to add heavy menstrual bleeding among the side effects of unknown frequency inside the package insert of nucleoside-modified messenger ribonucleic acid vaccines to prevent coronavirus disease 2019 (COVID-19). The decision has been made in the light of the numerous reports of unexpected menstrual changes or abnormal uterine bleeding following COVID-19 vaccination. Here we advance a possible involvement of the particular adenohypophyseal microcirculation in these strange and still unexplained events.

Saleem, A., S. O. Javed and F. Malik (2022). "COVID-19 vaccine related menstrual irregularities: A cause of vaccine hesitation?" J Pak Med Assoc **72**(8): 1683-1684.

Sarfraz, A., et al. (2022). "Menstrual irregularities following COVID-19 vaccination: A global cross-sectional survey." Ann Med Surg (Lond) **81**: 104220.

INTRODUCTION: The coronavirus disease 2019 (COVID-19) vaccination generates protective immunity against SARS-CoV-2 infection. There is no clear evidence of COVID-19 vaccine-induced menstrual irregularities. OBJECTIVE: To identify potential menstrual irregularities following COVID-19 vaccine among females. METHODS: A worldwide cross-sectional survey study was conducted from June 10, 2021, to July 10, 2021 using online mediums. The survey consisted of 15 questions divided into baseline characteristics, vaccination status and dosage, menstruation and relate factors, and thoughts and knowledge about menstrual irregularities. Non-probability convenience sampling method was used including 510 responses. The results were tabulated, with bivariate analysis and chi-square test results. The sensitivity and specificity test of factors associated to knowledge about menstrual irregularities post COVID-19 vaccination were analyzed by receiver operating characteristic analysis. RESULTS: The associations between healthcare worker (HCW) status and perceptions (chi2 = 10.422; p = 0.064), and knowledge about menstrual irregularities post-vaccination (chi2 = 1.966; p = 0.161) were found. Vaccinated compared to non-vaccinated women had a higher risk of change in inter-cycle length between periods (OR = 3.172; 95% CI = 0.470-21.431). Of 314 HCW

vs. 196 non-HCW, 60 (19.1%) vs. 28 (14.3%) were knowledgeable about menstrual irregularities (OR = 1.338, 95% CI = 0.886-2.019 vs. OR = 0.944; 95% CI = 0.873-1.021). On asking the HCW vs. non-HCW about perceptions of COVID-19 vaccine-induced menstrual irregularities, 24 (7.6%) vs. 9 (4.6%) agreed, 139 (44.3%) vs. 67 (34.2%) disagreed, and 151 (48.1%) vs. 120 (61.2%) did not know or chose not applicable. CONCLUSION: There is a gap in the current understanding of menstrual irregularities, even if temporary, following COVID-19 vaccination that requires further exploration. Misinformation may also be the culprit for the observed proportion of women that noticed changes in their menstrual periods after COVID-19 vaccination.

Sualeh, M., et al. (2022). "Impact of COVID-19 Vaccination on Menstrual Cycle: A Cross-Sectional Study From Karachi, Pakistan." Cureus **14**(8): e28630.

Background The coronavirus disease 2019 (COVID-19) disease triggered a worldwide health catastrophe. To deal with this deadly situation multiple vaccines were developed and a mass immunization program started globally. However, vaccine hesitancy was seen, especially among women of reproductive age, having concerns that the vaccine might affect their menstrual cycle. This study investigated the link between COVID-19 vaccination and menstrual abnormalities. It is essential for us to understand the effects of vaccines on menstruation as menstrual distress can have effects on everyday life, and mental and reproductive health. Methods A cross-sectional study was performed using self-administered online forms to collect data from all over Karachi. The sample included 384 females aged 18 years and above. The data were collected from November 2021 to February 2022. Results Majority of the participants were aged 21 years and had a normal body mass index (BMI). Most were moderately stressed (n=245) with 146 reporting menstrual changes post-vaccination. The difference between the post-vaccine menstruation affected (n=146) and the unaffected cohort (n=238) was significant. Other factors which likely contributed to the post-vaccine menstrual changes included Perceived Stress Scale (PSS) score, strenuous physical activity, and the pre-vaccine menstrual flow. Conclusions Among the women vaccinated for COVID-19, strenuous physical activity and high perceived stress levels affected the menstrual cycle. There is no denying that existing data are inadequate, which is one of the grounds for vaccination apprehension, particularly among menstruating women. To minimize this hesitation, the spread of disinformation about the vaccine's influence on the menstrual cycle must be avoided. In future research and clinical trials, menstruation-related side effects should also be investigated when developing vaccines.

Taskaldiran, I., et al. (2022). "Menstrual Changes after COVID-19 Infection and COVID-19 Vaccination." Int J Clin Pract **2022**: 3199758.

BACKGROUND: Several factors such as stress, depression, infection, and vaccination influenced the menstrual cycle in women during the coronavirus disease 2019 (COVID-19) pandemic. We investigated whether there were changes in the menstrual cycle in women after COVID-19 vaccination or infection and, if so, the nature of the change. METHODS: This study was designed as a descriptive, cross-sectional study. A face-to-face survey was conducted among menstruating women aged 18-50 years from May 31 to

July 31, 2022. Women were inquired about their first three menstrual cycles that occurred after COVID-19 infection or vaccination. RESULTS: Of 241 women with COVID-19 infection, 86 (35.7%) mentioned that they experienced various changes in their menstrual patterns in the first three cycles after infection. Of 537 participants who received various COVID-19 vaccines, 82 (15.1%) stated that they experienced changes in their menstrual patterns after vaccination. The incidence of postvaccination menstrual change was higher in women who received Pfizer-BioNTech and Sinovac (CoronaVac) vaccines. Only 10.9% of women who reported a change in their menstrual pattern after vaccination or infection consulted a physician. CONCLUSION: COVID-19 infection and vaccination can affect the menstrual cycle in women. It is important to be aware of the menstrual changes after COVID-19 infection and vaccination and to warn and inform women about this issue.

Trogstad, L., et al. (2022). "Covid-19 vaccines and menstrual changes." BMJ Med **1**(1): e000357.

Wong, K. K., et al. (2022). "Menstrual irregularities and vaginal bleeding after COVID-19 vaccination reported to v-safe active surveillance, USA in December, 2020-January, 2022: an observational cohort study." Lancet Digit Health **4**(9): e667-e675.

BACKGROUND: Anecdotal reports of menstrual irregularities after receiving COVID-19 vaccines have been observed in post-authorisation and post-licensure monitoring. We aimed to identify and classify reports of menstrual irregularities and vaginal bleeding after COVID-19 vaccination submitted to a voluntary active surveillance system. METHODS: This observational cohort study included recipients of a COVID-19 vaccine who were aged 18 years and older and reported their health experiences to v-safe, a voluntary smartphone-based active surveillance system for monitoring COVID-19 vaccine safety in the USA, from Dec 14, 2020, to Jan 9, 2022. Responses to survey questions on reactions after vaccination were extracted, and a pre-trained natural language inference model was used to identify and classify free-text comments related to menstruation and vaginal bleeding in response to an open-ended prompt about any symptoms at intervals after vaccination. Related responses were further categorised into themes of timing, severity, perimenopausal and postmenopausal bleeding, resumption of menses, and other responses. We examined associations between symptom theme and respondent characteristics, including vaccine type and dose number received, solicited local and systemic reactions reported, and health care sought. FINDINGS: 63 815 respondents reported on menstrual irregularities or vaginal bleeding, which included 62 679 female respondents (1.0% of 5 975 363 female respondents aged >/=18 years). Common themes identified included timing of menstruation (70 981 [83.6%] responses) and severity of menstrual symptoms (56 890 [67.0%] responses). Other themes included menopausal bleeding (3439 [4.0%] responses) and resumption of menses (2378 [2.8%] responses). Respondents submitting reports related to menopausal bleeding were more likely to seek health care than were those submitting reports related to other menstruation and vaginal bleeding themes. INTERPRETATION: Reports of heterogeneous symptoms related to menstruation or vaginal bleeding after COVID-19 vaccination are being submitted to v-safe, although this study is unable to characterise the relationship

of these symptoms to COVID-19 vaccination. Methods that leverage pretrained models to interpret and classify unsolicited signs and symptoms in free-text reports offer promise in the initial evaluation of unexpected adverse events potentially associated with use of newly authorised or licensed vaccines. FUNDING: Centers for Disease Control and Prevention.

Zhang, B., et al. (2022). "COVID-19 vaccine and menstrual conditions in female: data analysis of the Vaccine Adverse Event Reporting System (VAERS)." BMC Womens Health **22**(1): 403.
BACKGROUND: In reports of adverse reactions following vaccination with the coronavirus disease 2019(COVID-19) vaccines, there have been fewer reports of concern for menstrual disorders in female. OBJECTIVE: Our study employed Vaccine Adverse Event Reporting System (VAERS) to investigate and analyze the relationship between COVID-19 Vaccines and menstrual disorders in female. METHODS: We collected reports of menstrual disorders in VAERS from July 2, 1990 to November 12, 2021, and performed a stratified analysis. The potential relationship between COVID-19 vaccine and reports of menstrual disorders was evaluated using the Reporting Odds Ratio (ROR) method. RESULTS: A total of 14,431 reports of menstrual disorders were included in the study, and 13,118 were associated with COVID-19 vaccine. The ROR was 7.83 (95% confidence interval [95%CI]: 7.39-8.28). The most commonly reported event was Menstruation irregular (4998 reports), and a higher percentage of female aged 30-49 years reported menstrual disorders (42.55%) after exposure to COVID-19 Vaccines. Both for all reports of menstrual disorders (ROR = 5.82; 95%CI: 4.93-6.95) and excluding reports of unknown age (ROR = 13.02; 95%CI: 10.89-15.56),suggest that female age may be associated with menstrual disorders after vaccination with the COVID-19 Vaccines. CONCLUSION: There is a potential safety signal when the COVID-19 vaccine is administered to young adult female (30-49 years old), resulting in menstrual disorders in. However, due to the well-known limitations of spontaneous reporting data, it is challenging to explicity classify menstrual disorders as an adverse event of the COVID-19 Vaccines, and reports of adverse reactions to COVID-19 Vaccines in this age group should continue to be tracked.

Rhabdomyolysis

Ajmera, K. M. (2021). "Fatal Case of Rhabdomyolysis Post-COVID-19 Vaccine." Infect Drug Resist **14**: 3929-3935.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or COVID-19 pandemic has taken away the lives of many people (>4 million per WHO) around the world as of July 2021. With the advancement of the vaccine against COVID-19, in less than a year since the start of the pandemic, the infection rate has come under control in certain regions but is still rising in many more. However, with time, we are also learning a lot more about the adverse events related to the vaccine. This report documents the first fatal case of rhabdomyolysis potentially associated with the COVID-19 vaccine and supports the possibility that autoimmunity is a major risk factor for covid vaccine-related rhabdomyolysis.

Al-Rasbi, S., et al. (2022). "Myocarditis, Pulmonary Hemorrhage, and Extensive Myositis with Rhabdomyolysis 12 Days After First Dose of Pfizer-BioNTech BNT162b2 mRNA COVID-19 Vaccine: A Case Report." Am J Case Rep **23**: e934399.

BACKGROUND The COVID-19 pandemic is a current global crisis, and there are hundreds of millions of individuals being vaccinated worldwide. At present, there have been few reports of COVID-19 vaccine-induced autoimmune processes manifested as myositis, thrombocytopenia, and myocarditis. CASE REPORT A 37-year-old man presented to the Emergency Department (ED) with a 3-day history of back pain and a 1-day history of left upper limb swelling with paresthesia and shortness of breath, 12-days after receiving the first dose of Pfizer/BioNTech BNT162b2 mRNA COVID-19 vaccine. He was diagnosed with severe myositis complicated with rhabdomyolysis and non-oliguric acute kidney injury, thrombocytopenia, myocarditis with pulmonary edema, and pulmonary hemorrhage. Screens for potential toxic, infectious, paraneoplastic, and autoimmune disorders were unremarkable. The patient was treated with a 5-day course of intravenous methylprednisolone and intravenous immunoglobulin, with a good response. He was hospitalized for 16 days and discharged home on a tapering dose of oral prednisolone for 6 weeks. CONCLUSIONS The case describes a possible link between Pfizer/BioNTech BNT162b2 mRNA COVID-19 vaccine and immune-mediated myocarditis, pulmonary vasculitis, myositis, and thrombocytopenia. However, further data are required to confirm such an association.

Banamah, T. A., et al. (2022). "Severe Rhabdomyolysis Complicated With Acute Kidney Injury Required Renal Replacement Therapy After Pfizer COVID-19 Vaccine " Cureus **14**(5): e25199.

The adverse effects of coronavirus disease 2019 (COVID-19) vaccines are somewhat common but rarely life-threatening. Diagnosing life-threatening vaccine-related adverse effects is heavily dependent on history taking and ruling out the other possible causes. Vaccine-related complications vary, so awareness of possible complications can lead to efficient management. We present the case of a 58-year-old woman with a history of schizophrenia who received the COVID-19 Pfizer vaccine and developed severe

rhabdomyolysis. She required renal replacement therapy and fully recovered with possible transient autoimmune activity. This case highlights the importance of early awareness of adverse effects following vaccine administration and careful history taking and monitoring to avoid life-threatening conditions.

Faissner, S., et al. (2022). "COVID-19 mRNA vaccine induced rhabdomyolysis and fasciitis." J Neurol **269**(4): 1774-1775.

Hakroush, S. and B. Tampe (2021). "Case Report: ANCA-Associated Vasculitis Presenting With Rhabdomyolysis and Pauci-Immune Crescentic Glomerulonephritis After Pfizer-BioNTech COVID-19 mRNA Vaccination." Front Immunol **12**: 762006.

As the coronavirus disease 2019 (COVID-19) pandemic is ongoing and new variants of severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) are emerging, there is an urgent need for COVID-19 vaccines to control disease outbreaks by herd immunity. Surveillance of rare safety issues related to these vaccines is progressing, since more granular data emerge with regard to adverse events of COVID-19 vaccines during post-marketing surveillance. Interestingly, four cases of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) presenting with pauci-immune crescentic glomerulonephritis (GN) after COVID-19 mRNA vaccination have already been reported. We here expand our current knowledge of this rare but important association and report a case of AAV presenting with massive rhabdomyolysis and pauci-immune crescentic GN after Pfizer-BioNTech COVID-19 mRNA vaccination. As huge vaccination programs are ongoing worldwide, post-marketing surveillance systems must continue to assess vaccine safety important for the detection of any events associated with COVID-19 vaccination. This is especially relevant in complex diseases where diagnosis is often challenging, as in our patient with AAV presenting with massive rhabdomyolysis and pauci-immune crescentic GN.

Kalekar, T. M., R. K. Jaipuria and R. S. Navani (2022). "MRI Findings in Case of Post-COVID-19 Vaccination Rhabdomyolysis: A Rare Postvaccination Adverse Effect." Indian J Radiol Imaging **32**(2): 256-259.

In the era of this pandemic, without any proper and efficacious availability of antiviral agents against the novel coronavirus disease 2019 (COVID-19), vaccines have come as a hope for humankind. Although adverse reactions are common after getting the COVID-19 vaccine, serious or life-threatening side effects are very uncommon in these new emergency-approved vaccines. In this case report, we describe an unusual case of adverse reaction in a patient who received the COVID-19 vaccination. The patient who received the COVID-19 vaccination presented with progressive right lower limb pain and swelling, which further progressed to bilateral shoulder pain and swelling. Ultrasonography, Doppler, and magnetic resonance imaging of right lower limb were done for the patient.

Mack, M., L. Nichols and D. M. Guerrero (2021). "Rhabdomyolysis Secondary to COVID-19 Vaccination." Cureus **13**(5): e15004.

Rhabdomyolysis has been described as a complication of coronavirus disease 2019 (COVID-19) infection, but few cases of rhabdomyolysis associated with COVID-19 vaccination have been reported. We described a case of an 80-year-old male who developed rhabdomyolysis two days after receiving his second dose of the Moderna COVID-19 vaccine. He presented with severe weakness, myalgias, and an initial creatinine kinase (CK) of 6,546 IU/L that improved with intravenous fluids. Common causes of rhabdomyolysis were excluded including statin use, strenuous exercise, and trauma. With the increasing immunization efforts against COVID-19, physicians should consider the possibility of rhabdomyolysis when a patient presents with neuromuscular complaints following vaccination.

Nassar, M., et al. (2021). "COVID-19 vaccine induced rhabdomyolysis: Case report with literature review." Diabetes Metab Syndr **15**(4): 102170.

Pucchio, A., et al. (2023). "Severe rhabdomyolysis secondary to COVID-19 mRNA vaccine in a teenager." Pediatr Nephrol **38**(6): 1979-1983.

BACKGROUND: Rhabdomyolysis, the breakdown of skeletal muscles following an insult or injury, has been established as a possible complication of SARS-CoV-2 infection. Despite being highly effective in preventing COVID-19-related morbidity and mortality, several cases of COVID-19 mRNA vaccination-induced rhabdomyolysis have been identified. We provide the second description of a pediatric case of severe rhabdomyolysis presenting after COVID-19 mRNA vaccination. CASE: DIAGNOSIS/TREATMENT: A 16-year-old male reported to the emergency department with a 2-day history of bilateral upper extremity myalgias and dark urine 2 days after his first dose of COVID-19 vaccine (Pfizer-BioNtech). The initial blood work showed an elevated creatinine kinase (CK) of 141,300 units/L and a normal creatinine of 69 umol/L. The urinalysis was suggestive of myoglobinuria, with the microscopy revealing blood but no red blood cells. Rhabdomyolysis was diagnosed, and the patient was admitted for intravenous hydration, alkalinization of urine, and monitoring of kidney function. CK levels declined with supportive care, while his kidney function remained normal, and no electrolyte abnormalities developed. The patient was discharged 5 days after admission as his symptoms resolved. CONCLUSION: While vaccination is the safest and most effective way to prevent morbidity from COVID-19, clinicians should be aware that rhabdomyolysis could be a rare but treatable adverse event of COVID-19 mRNA vaccination. With early recognition and diagnosis and supportive management, rhabdomyolysis has an excellent prognosis.

Ruijters, V. J., et al. (2022). "Rhabdomyolysis after COVID-19 Comirnaty Vaccination: A Case Report." Case Rep Neurol **14**(3): 429-432.

Rhabdomyolysis is an acute disruption in skeletal muscle integrity, leading to the rapid release of 4 muscle contents into the bloodstream, such as creatine kinase (CK). It can have various causes, including infections. Throughout the pandemic, multiple cases of rhabdomyolysis following COVID-19 infections have been reported. However, rhabdomyolysis subsequent to COVID-19 vaccinations appears to be relatively rare.

Here, we report such a case after a second COVID-19 Comirnaty (BioNTech/Pfizer) vaccination. Our patient developed rhabdomyolysis 1 day after the second Comirnaty vaccination with high creatine kinase (CK) levels, generalized weakness, and kidney failure. CK levels and muscle weakness resolved after treatment with intravenous fluids, but unfortunately, he remained hemodialysis dependent after discharge. To our knowledge, this is one of the first case reports describing a patient with rhabdomyolysis after a Comirnaty vaccination. However, as millions of people have received the Comirnaty vaccine, it is unclear whether the rhabdomyolysis in our patient is a rare side effect or an unrelated, coincidental event. Large observational studies are needed to elucidate the causality between the Comirnaty vaccination and rhabdomyolysis. Awareness is warranted in patients with myalgia and muscle weakness shortly after COVID-19 vaccination, in order to initiate treatment early and prevent life-threatening complications.

Sheka, M., et al. (2023). "A severe case of rhabdomyolysis after Moderna mRNA anti-COVID-19 vaccine with a literature review." Clin Case Rep **11**(5): e7184.

The identification of rhabdomyolysis as a potential fatal adverse reaction to recent COVID-19 vaccines is essential. As the symptoms of rhabdomyolysis are not specific, the threshold to actively search for this complication should be low.

Sutcu, M., et al. (2022). "Rhabdomyolysis after BNT162b2 mRNA Covid-19 vaccine in an adolescent male." Malawi Med J **34**(2): 154-156.

Pfizer-BioNTech COVID-19 (BNT162b2) conferred a high level of protection against Covid-19 with a proven short-term safety profile. Although cases of vaccine-associated myopericarditis have been reported, the existence of rhabdomyolysis without myocarditis has not yet been published. A 16-year-old, healthy male patient, who did not use any herbal or illegal drugs before, was admitted with muscle pain that developed after the second dose of BNT162b2 vaccine. Cardiac examination and heart enzymes were normal and the patient had significantly higher creatinine kinase levels. The patient, whose enzymes returned to normal with only force hydration therapy, recovered without complications. Reporting the side effects of the vaccine, which has a short history of application to large populations, is of vital importance in the conduct of vaccine development studies and in identifying the risky group in terms of side effects.

Unger, K., C. D. Ponte and D. Anderson (2022). "A Possible Case of COVID-19 Booster Vaccine-Associated Rhabdomyolysis and Acute Kidney Injury." J Pharm Technol **38**(4): 247-250.

Background: Nearly 10 billion doses of the various messenger ribonucleic acid (mRNA) and viral vector vaccines against Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) have been administered worldwide. Adverse drug reactions (ADRs) have been overwhelmingly mild to moderate in nature. Rare side effects have included myocarditis/pericarditis, thrombosis with thrombocytopenia syndrome (TTS), Guillain-Barre Syndrome (GBS), and death. However, vaccine-related ADR data are still being collected using a variety of reporting systems. Purpose: We will describe a case of suspected mRNA coronavirus disease 2019 (COVID-19) booster-related rhabdomyolysis

in a woman who developed signs and symptoms 10 days after administration of the vaccine dose. With a Naranjo ADR probability score of 4, the vaccine was deemed to be a possible cause of our patient's rhabdomyolysis. Methods: A search of the VAERS (Vaccine Adverse Event Reporting System) mined in November 2021 revealed 386 reported cases of COVID-19 vaccine-related rhabdomyolysis. However, system limitations make the utility of the information problematic. Conclusions: It is vitally important that clinicians, scientists, and patients are aware of rhabdomyolysis as a potential side effect of vaccination. Suspected vaccine-related ADRs should be promptly and accurately reported via VAERS or other surveillance systems to support the ongoing effort to ensure vaccine safety.

Stroke

Alammar, M. A. (2021). "Ischemic stroke after AstraZeneca (Covid-19) vaccination." Saudi Med J **42**(10): 1136-1139.

Vaccination against SARS-COV-2 is considered an effective preventive strategy to halt COVID-19 pandemic. Reports of thromboembolic events in vaccine recipients has jolted some of the European countries to pause the vaccination process temporarily. It is still unclear whether the events are actually due to the vaccines or it is just a coincidence. The gravity of events particularly in young and previously normal patients merits further research to reach some conclusion. Here we present a similar case who sustained ischemic stroke shortly after receiving the first dose of his vaccine.

Andrews, N., et al. (2023). "BA.1 Bivalent COVID-19 Vaccine Use and Stroke in England." JAMA **330**(2): 184-185.

This study investigates the association between bivalent COVID-19 vaccines and ischemic stroke, as well as the effect of simultaneous influenza vaccination on the association.

eng Department in her directorate provides vaccine manufacturers (including Pfizer) with postmarketing surveillance reports about pneumococcal and meningococcal disease, which the companies are required to submit to the UK Licensing authority in compliance with their risk management strategy. A cost recovery charge is made for these reports. No other disclosures were reported.

Bardenheier, B. H., et al. (2022). "Adverse events following third dose of mRNA COVID-19 vaccination among nursing home residents who received the primary series." J Am Geriatr Soc **70**(6): 1642-1647.

BACKGROUND: We sought to compare rates of adverse events among nursing home residents who received an mRNA COVID-19 vaccine booster dose with those who had not yet received their booster. METHODS: We assessed a prospective cohort of 11,200 nursing home residents who received a primary COVID-19 mRNA vaccine series at least 6 months prior to September 22, 2021 and received a third "booster dose" between September 22, 2021 and February 2, 2022. Residents lived in 239 nursing homes operated by Genesis HealthCare, spanning 21 U.S. states. We screened electronic health records for 20 serious vaccine-related adverse events that are monitored following receipt of COVID-19 vaccination by the CDC's Vaccine Safety Datalink. We matched boosted and yet-to-be boosted residents during the same time period, comparing rates of events occurring 14 days after booster administration with those occurring 14 days prior to booster administration. To supplement previously reported background rates of adverse events, we report background rates of medical conditions among nursing home residents during 2020, before COVID-19 vaccines were administered in nursing homes. Events occurring in 2021-2022 were confirmed by physician chart review. We report unadjusted rates of adverse events and used a false discovery rate procedure to adjust for multiplicity of events tested. RESULTS: No adverse events were reported during the 14 days post-booster. A few adverse events occurred prior to booster (ischemic stroke:

49.4 per 100,000 residents, 95% CI: 21.2, 115.7; venous thromboembolism: 9.9 per 100,000 residents, 95% CI: 1.7, 56.0), though differences in event rates pre- versus post-booster were not statistically significant ($p < 0.05$) after adjusting for multiple comparisons. No significant differences were detected between post-booster vaccination rates and prior year 14-day background rates of medical conditions. CONCLUSIONS: No safety signals were detected following a COVID-19 mRNA vaccine booster dose in this large multi-state sample of nursing home residents.

Behers, B. J., et al. (2022). "Myocarditis Following COVID-19 Vaccination: A Systematic Review of Case Reports." Yale J Biol Med **95**(2): 237-247.

Introduction: COVID-19, the infectious disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), often presents with a spectrum of symptoms at varying levels of severity, ranging from asymptomatic patients to those with fatal complications, such as myocarditis. With increased availability of COVID-19 vaccines, the awareness of possible side effects has expanded as reports surface. This study reviewed cases of myocarditis following COVID-19 vaccination and with existing literature on COVID-19 infection-induced myocarditis to compare clinical courses and analyze possible mechanisms of action. Methods: A systematic review of literature was conducted to identify published case reports (as of February 3, 2022) pertaining to the development of myocarditis following COVID-19 vaccination with either Pfizer or Moderna for an in-depth analysis. Additional subgroup analyses were conducted based on age, past medical history, vaccine manufacturer, and dose number. Results: There were 53 eligible case reports that were included in this study. Patients were mostly male with a median age of 24 years, and the most reported symptom upon presentation was chest pain. Seventy percent of the cases involved the Pfizer vaccine with a majority of myocarditis developing subsequent to second dose. Resolution of symptoms was achieved in all but one patient. Clinical severity, as measured primarily by left ventricular ejection fraction, appeared to be worse among adult patients than pediatric, as well as for patients with comorbidities. Conclusion: This study revealed an observable association between COVID-19 vaccines and myocarditis. However, the clinical course and prognosis seem favorable and less prevalent than those conferred from natural infection.

Blauenfeldt, R. A., et al. (2021). "Thrombocytopenia with acute ischemic stroke and bleeding in a patient newly vaccinated with an adenoviral vector-based COVID-19 vaccine." J Thromb Haemost **19**(7): 1771-1775.

We describe the first Danish case of presumed inflammatory and thrombotic response to vaccination with an adenoviral (ChAdOx1) vector-based COVID-19 vaccine (AZD1222). The case describes a 60-year-old woman who was admitted with intractable abdominal pain 7 days after receiving the vaccine. Computed tomography of the abdomen revealed bilateral adrenal hemorrhages. On the following day, she developed a massive right-sided ischemic stroke and magnetic resonance imaging angiography showed occlusion of the right internal carotid artery. The ischemic area was deemed too large to offer reperfusion therapy. During admission, blood tests showed a remarkable drop in platelet counts from 118,000 to 5000 per mul and a substantial increase in D-dimer. The patient

died on the sixth day of hospitalization. Blood tests revealed platelet factor 4 reactive antibodies, imitating what is seen in heparin-induced thrombocytopenia. This may be a novel immune-mediated response to the vaccine.

Cascio Rizzo, A., G. Giussani and E. C. Agostoni (2022). "Ischemic Stroke and Vaccine-Induced Immune Thrombotic Thrombocytopenia following COVID-19 Vaccine: A Case Report with Systematic Review of the Literature." Cerebrovasc Dis **51**(6): 722-734.

INTRODUCTION: Vaccine-induced immune thrombotic thrombocytopenia (VITT) is a prothrombotic syndrome observed after adenoviral vector-based vaccines for severe acute respiratory syndrome coronavirus 2. It is characterized by thrombocytopenia, systemic activation of coagulation, extensive venous thrombosis, and anti-platelet factor 4 antibodies. Arterial thrombosis is less common and mainly affects the aorta, peripheral arteries, heart, and brain. Several cases of ischemic stroke have been reported in VITT, often associated with large vessel occlusion (LVO). Here, we describe a case of ischemic stroke with LVO after Ad26.COV2.S vaccine, then we systematically reviewed the published cases of ischemic stroke and VITT following COVID-19 vaccination. METHODS: We describe a 58-year-old woman who developed a thrombotic thrombocytopenia syndrome with extensive splanchnic vein thrombosis and ischemic stroke due to right middle cerebral artery (MCA) occlusion, 13 days after receiving Ad26.COV2.S vaccination. Then, we performed a systematic review of the literature until December 3, 2021 using PubMed and EMBASE databases. The following keywords were used: ("COVID-19 vaccine") AND ("stroke"), ("COVID-19 vaccine") AND ("thrombotic thrombocytopenia"). We have selected all cases of ischemic stroke in VITT. RESULTS: Our study included 24 patients. The majority of the patients were females (79.2%) and younger than 60 years of age (median age 45.5 years). Almost all patients (96%) received the first dose of an adenoviral vector-based vaccine. Ischemic stroke was the presenting symptom in 18 patients (75%). Splanchnic venous thrombosis was found in 10 patients, and cerebral venous thrombosis in 5 patients (21%). Most patients (87.5%) had an anterior circulation stroke, mainly involving MCA. Seventeen patients (71%) had an intracranial LVO. We found a high prevalence of large intraluminal thrombi (7 patients) and free-floating thrombus (3 patients) in extracranial vessels, such as the carotid artery, in the absence of underlying atherosclerotic disease. Acute reperfusion therapy was performed in 7 of the 17 patients with LVO (41%). One patient with a normal platelet count underwent intravenous thrombolysis with alteplase, while 6 patients underwent mechanical thrombectomy. A malignant infarct occurred in 9 patients and decompressive hemicraniectomy was performed in 7 patients. Five patients died (21%). CONCLUSION: Our study points out that, in addition to cerebral venous thrombosis, adenoviral vector-based vaccines also appear to have a cerebral arterial thrombotic risk, and clinicians should be aware that ischemic stroke with LVO, although rare, could represent a clinical presentation of VITT.

Cho, J. Y., et al. (2023). "COVID-19 vaccination-related myocarditis: a Korean nationwide study." Eur Heart J **44**(24): 2234-2243.

AIMS: A comprehensive nationwide study on the incidence and outcomes of COVID-19 vaccination-related myocarditis (VRM) is in need. METHODS AND RESULTS: Among 44 276 704 individuals with at least 1 dose of COVID-19 vaccination, the incidence and clinical courses of VRM cases confirmed by the Expert Adjudication Committee of the Korea Disease Control and Prevention Agency were analyzed. COVID-19 VRM was confirmed in 480 cases (1.08 cases per 100 000 persons). Vaccination-related myocarditis incidence was significantly higher in men than in women (1.35 vs. 0.82 per 100 000 persons, $P < 0.001$) and in mRNA vaccines than in other vaccines (1.46 vs. 0.14 per 100 000 persons, $P < 0.001$). Vaccination-related myocarditis incidence was highest in males between the ages of 12 and 17 years (5.29 cases per 100 000 persons) and lowest in females over 70 years (0.16 cases per 100 000 persons). Severe VRM was identified in 95 cases (19.8% of total VRM, 0.22 per 100 000 vaccinated persons), 85 intensive care unit admission (17.7%), 36 fulminant myocarditis (7.5%), 21 extracorporeal membrane oxygenation therapy (4.4%), 21 deaths (4.4%), and 1 heart transplantation (0.2%). Eight out of 21 deaths were sudden cardiac death (SCD) attributable to VRM proved by an autopsy, and all cases of SCD attributable to VRM were aged under 45 years and received mRNA vaccines. CONCLUSION: Although COVID-19 VRM was rare and showed relatively favorable clinical courses, severe VRM was found in 19.8% of all VRM cases. Moreover, SCD should be closely monitored as a potentially fatal complication of COVID-19 vaccination.

Chu, W. M., C. Y. Wang and J. C. Wei (2023). "Vaccination, Acute Myocardial Infarction, and Ischemic Stroke After COVID-19 Infection." JAMA **329**(5): 426.

Chui, C. S. L., et al. (2022). "Thromboembolic events and hemorrhagic stroke after mRNA (BNT162b2) and inactivated (CoronaVac) covid-19 vaccination: A self-controlled case series study." EClinicalMedicine **50**: 101504.

BACKGROUND: This study aims to evaluate the association between thromboembolic events and hemorrhagic stroke following BNT162b2 and CoronaVac vaccination. METHODS: Patients with incident thromboembolic events or hemorrhagic stroke within 28 days of covid-19 vaccination or SARS-CoV-2 positive test during 23 February to 30 September 2021 were included. The incidence per 100,000 covid-19 vaccine doses administered and SARS-CoV-2 test positive cases were estimated. A modified self-controlled case series (SCCS) analysis using the data from the Hong Kong territory-wide electronic health and vaccination records. Seasonal effect was adjusted by month. FINDINGS: A total of 5,526,547 doses of BNT162b2 and 3,146,741 doses of CoronaVac were administered. A total of 334 and 402 thromboembolic events, and 57 and 49 hemorrhagic stroke cases occurred within 28 days after BNT162b2 and CoronaVac vaccination, respectively. The crude incidence of thromboembolic events and hemorrhagic stroke per 100,000 doses administered for both covid-19 vaccines were smaller than that per 100,000 SARS-CoV-2 test positive cases. The modified SCCS detected an increased risk of hemorrhagic stroke in BNT162b2 14-27 days after first dose with adjusted IRR of 2.53 (95% CI 1.48-4.34), and 0-13 days after second dose with adjusted IRR 2.69 (95% CI 1.54-4.69). No statistically significant risk was observed for

thromboembolic events for both vaccines. INTERPRETATION: We detected a possible safety signal for hemorrhagic stroke following BNT162b2 vaccination. The incidence of thromboembolic event or hemorrhagic stroke following vaccination is lower than that among SARS-CoV-2 test positive cases; therefore, vaccination against covid-19 remains an important public health intervention. FUNDING: This study was funded by a research grant from the Food and Health Bureau, The Government of the Hong Kong Special Administrative Region (reference COVID19F01).

Dionne, A., et al. (2021). "Association of Myocarditis With BNT162b2 Messenger RNA COVID-19 Vaccine in a Case Series of Children." JAMA Cardiol **6**(12): 1446-1450.

IMPORTANCE: The BNT162b2 (Pfizer-BioNTech) messenger RNA COVID-19 vaccine was authorized on May 10, 2021, for emergency use in children aged 12 years and older. Initial reports showed that the vaccine was well tolerated without serious adverse events; however, cases of myocarditis have been reported since approval. OBJECTIVE: To review results of comprehensive cardiac imaging in children with myocarditis after COVID-19 vaccine. DESIGN, SETTING, AND PARTICIPANTS: This study was a case series of children younger than 19 years hospitalized with myocarditis within 30 days of BNT162b2 messenger RNA COVID-19 vaccine. The setting was a single-center pediatric referral facility, and admissions occurred between May 1 and July 15, 2021. MAIN OUTCOMES AND MEASURES: All patients underwent cardiac evaluation including an electrocardiogram, echocardiogram, and cardiac magnetic resonance imaging. RESULTS: Fifteen patients (14 male patients [93%]; median age, 15 years [range, 12-18 years]) were hospitalized for management of myocarditis after receiving the BNT162b2 (Pfizer) vaccine. Symptoms started 1 to 6 days after receipt of the vaccine and included chest pain in 15 patients (100%), fever in 10 patients (67%), myalgia in 8 patients (53%), and headache in 6 patients (40%). Troponin levels were elevated in all patients at admission (median, 0.25 ng/mL [range, 0.08-3.15 ng/mL]) and peaked 0.1 to 2.3 days after admission. By echocardiographic examination, decreased left ventricular (LV) ejection fraction (EF) was present in 3 patients (20%), and abnormal global longitudinal or circumferential strain was present in 5 patients (33%). No patient had a pericardial effusion. Cardiac magnetic resonance imaging findings were consistent with myocarditis in 13 patients (87%) including late gadolinium enhancement in 12 patients (80%), regional hyperintensity on T2-weighted imaging in 2 patients (13%), elevated extracellular volume fraction in 3 patients (20%), and elevated LV global native T1 in 2 patients (20%). No patient required intensive care unit admission, and median hospital length of stay was 2 days (range 1-5). At follow-up 1 to 13 days after hospital discharge, 11 patients (73%) had resolution of symptoms. One patient (7%) had persistent borderline low LV systolic function on echocardiogram (EF 54%). Troponin levels remained mildly elevated in 3 patients (20%). One patient (7%) had nonsustained ventricular tachycardia on ambulatory monitor. CONCLUSIONS AND RELEVANCE: In this small case series study, myocarditis was diagnosed in children after COVID-19 vaccination, most commonly in boys after the second dose. In this case series, in short-term follow-up, patients were mildly affected. The long-term risks associated with

postvaccination myocarditis remain unknown. Larger studies with longer follow-up are needed to inform recommendations for COVID-19 vaccination in this population.

Doi, K., et al. (2022). "Cervical Transverse Myelitis Following COVID-19 Vaccination." NMC Case Rep J **9**: 145-149.

Various COVID-19 vaccines are associated with numerous adverse side effects. Associations between vaccinations and neurological disorders, such as transverse myelitis, stroke, Bell's palsy, acute disseminated encephalomyelitis, and Guillain-Barre syndrome, have been reported. A 27-year-old Japanese woman presented with paresthesia four days after receiving a second dose of the COVID-19 vaccine. One month after vaccination, she started to feel left lower limb weakness, and her symptoms almost improved after two steroid pulse therapies. Spinal cord tumor biopsy could potentially help make a definitive diagnosis in clinical situations. However, it is very important to review the patient's medical history, including vaccinations received, before performing a direct spinal cord biopsy, which is invasive and does not guarantee a definitive diagnosis.

Du, L., Z. Li and Y. Zhao (2023). "Reader Response: Acute Arterial Ischemic Stroke Following COVID-19 Vaccination: A Systematic Review and Meta-analysis." Neurology **100**(9): 446-447.

Elaidouni, G., et al. (2022). "Acute ischemic stroke after first dose of inactivated COVID-19 vaccine: A case report." Radiol Case Rep **17**(6): 1942-1945.

The acute cerebral ischemia induced by the COVID-19 vaccine is one of the side effects. We report the first case of a patient who suffered from a neurological deficit mimicking a stroke after receiving his 1st dose of the inactivated COVID-19 vaccine BIBP (Sinopharm) and who mainly developed cerebral venous thrombosis. Our reported case is a 36-year-old man who was admitted to our intensive care unit 2 days after his first injection dose of the inactivated COVID-19 vaccine BIBP (Sinopharm). He presented a numbness in his left arm and legs with headaches 24 hours after the vaccine injection. In the second day, he had asymmetry of the face which was aggravated by the installation of disturbance of consciousness and a state of agitation. His vital signs were normal. A brain CT scan without injection was done showing a right deep parietal ischemic stroke. The treatment was initiated by aspirin. cerebral MRI showed a very extensive stroke ischemic in the superficial and deep right parietal territory with the onset of hemorrhagic rearrangement of the right basal ganglia, magnetic resonance imaging angiography of the supra-aortic trunks was normal. The patient gradually improved and was discharged after 15 days of his stay in the intensive care unit. The installation of ischemic stroke reported in our young patient after receiving his first dose of inactivated COVID-19 vaccine BIBP; could be a new immune response to the vaccine.

Famularo, G. (2022). "Stroke after COVID-19 vaccination." Acta Neurol Scand **145**(6): 787-788.

Ferro, J. M., et al. (2021). "European stroke organization interim expert opinion on cerebral venous thrombosis occurring after SARS-CoV-2 vaccination." Eur Stroke J **6**(3): CXVI-CXXI.

Severe cases of cerebral venous thrombosis (CVT) with thrombocytopenia and anti-platelet factor 4 (PF4) antibodies occurring after adenoviral vector anti-SARS-CoV-2 vaccines have been recently reported. We aim to present a guidance document on the diagnosis and treatment of patients presenting with CVT after vaccination against SARS-CoV-2 infection. We reviewed the available evidence which consists on case reports, small case series, expert opinion and analogy with heparin-induced thrombocytopenia (HIT) management. Because of the low level of evidence, this is an interim document, based only on expert opinion consensus. In patients presenting with CVT after being vaccinated against SARS-CoV-2 infection, if there is thrombocytopenia a reliable HIT PF4 Antibody ELISA test should be performed, to confirm vaccine-induced immune thrombotic thrombocytopenia (VITT). In patients with CVT and thrombocytopenia, in whom VITT is suspected or confirmed, heparin (unfractionated or low molecular weight) should be avoided and non-heparin anticoagulants are preferred. If possible, platelet transfusions should be avoided. If the diagnosis of VITT is confirmed or suspected, early intravenous immunoglobulins are indicated. This expert opinion is supported by low quality evidence. It should be periodically updated, or changed to a formal guideline, as new and higher quality evidence is eventually produced. Because of their potential unfavourable clinical course, patients developing symptoms and signs suggestive of CVT after being vaccinated against SARS-CoV-2 virus should undergo urgent clinical and neuroimaging evaluation. In cases of suspected or confirmed VITT, non-heparin anticoagulants should be used, platelet transfusions avoided and intravenous immunoglobulin started early.

Finsterer, J. (2022). "Stroke four days after vaccination with a vector-based SARS-CoV-2 vaccine." J Family Med Prim Care **11**(11): 7491-7492.

Finsterer, J. (2023). "Symmetric DWI hyperintensities in CMT1X patients after SARS-CoV-2 vaccination should not be classified as stroke-like lesions." World J Clin Cases **11**(16): 3929-3931.

The interesting case report by Zhang et al on a 39 years-old male with Charcot-Marie-Tooth disease type 1X has several limitations. The causal relation between the two episodes of asyndesis, dysphagia, and dyspnea 37 d after the second dose of the inactivated severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) vaccine (Beijing Institute of Biological Products Co., Ltd., Beijing, China) remains unproven. SARS-CoV-2 vaccination cannot trigger a genetic disorder. It also remains unsupported that the patient had a stroke-like episode (SLE). SLEs occur in mitochondrial disorders but not in hereditary neuropathies. Because of the episodic nature of the neurological symptoms, it is critical to rule out seizures. Overall, the causal relation between vaccination and the neurological complications remains unsupported and the interpretation of symmetric diffusion-weighted imaging lesions on cerebral magnetic resonance imaging should be carefully revised.

Finsterer, J. and F. A. Scorza (2021). "Letter to the Editor: Ischemic Stroke of the Corpus Callosum after SARS-CoV-2 Vaccination." J Korean Med Sci **36**(40): e288.

Fiorini, A. C., et al. (2023). "Stroke seven hours after SARS-CoV-2 vaccination." Clinics (Sao Paulo) **78**: 100193.

Fronza, M., et al. (2022). "Myocardial Injury Pattern at MRI in COVID-19 Vaccine-Associated Myocarditis." Radiology **304**(3): 553-562.

Background There are limited data on the pattern and severity of myocardial injury in patients with COVID-19 vaccination-associated myocarditis. Purpose To describe myocardial injury following COVID-19 vaccination and to compare these findings to other causes of myocarditis. Materials and Methods In this retrospective cohort study, consecutive adult patients with myocarditis with at least one T1-based and at least one T2-based abnormality at cardiac MRI performed at a tertiary referral hospital from December 2019 to November 2021 were included. Patients were classified into one of three groups: myocarditis following COVID-19 vaccination, myocarditis following COVID-19 illness, and other myocarditis not associated with COVID-19 vaccination or illness. Results Of the 92 included patients, 21 (23%) had myocarditis following COVID-19 vaccination (mean age, 31 years +/- 14 [SD]; 17 men; messenger RNA-1273 in 12 [57%] and BNT162b2 in nine [43%]). Ten of 92 (11%) patients had myocarditis following COVID-19 illness (mean age, 51 years +/- 14; three men) and 61 of 92 (66%) patients had other myocarditis (mean age, 44 years +/- 18; 36 men). MRI findings in the 21 patients with vaccine-associated myocarditis included late gadolinium enhancement (LGE) in 17 patients (81%) and left ventricular dysfunction in six (29%). Compared with other causes of myocarditis, patients with vaccine-associated myocarditis had a higher left ventricular ejection fraction and less extensive LGE, even after controlling for age, sex, and time from symptom onset to MRI. The most frequent location of LGE in all groups was subepicardial at the basal inferolateral wall, although septal involvement was less common in vaccine-associated myocarditis. At short-term follow-up (median, 22 days [IQR, 7-48 days]), all patients with vaccine-associated myocarditis were asymptomatic with no adverse events. Conclusion Cardiac MRI demonstrated a similar pattern of myocardial injury in vaccine-associated myocarditis compared with other causes, although abnormalities were less severe, with less frequent septal involvement and no adverse events over the short-term follow-up. (c) RSNA, 2022 Online supplemental material is available for this article. See also the editorial by Raman and Neubauer in this issue.

Ganesh, A. and S. Galetta (2023). "Editors' Note: Acute Arterial Ischemic Stroke Following COVID-19 Vaccination: A Systematic Review and Meta-analysis." Neurology **100**(9): 446.

Garcia-Grimshaw, M., S. I. Valdes-Ferrer and A. Arauz (2022). "Author Response: Stroke Among SARS-CoV-2 Vaccine Recipients in Mexico: A Nationwide Descriptive Study." Neurology **99**(15): 674.

Giovane, R. and J. Campbell (2021). "Bilateral Thalamic Stroke: A Case of COVID-19 Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT) or a Coincidence Due to Underlying Risk Factors?" Cureus **13**(10): e18977.

Vaccine-induced immune thrombotic thrombocytopenia (VITT) is a rare but potentially life-threatening side effect that has only been observed in adenovirus-based vaccines for coronavirus disease 2019 (COVID-19). VITT is an immune-mediated condition that generally presents within five to 10 days post-vaccination with thrombosis, thrombocytopenia, and coagulation abnormalities. A diagnosis of VITT is made clinically and through laboratory testing. Although VITT is an important differential to consider, it is believed that more emphasis should be placed on vaccination due to the safety and efficacy in overcoming COVID-19.

Gorenflo, M. P., et al. (2023). "Ischemic stroke after COVID-19 bivalent vaccine administration in patients aged 65 years and older: analysis of nation-wide patient electronic health records in the United States." medRxiv.

IMPORTANCE: The Centers for Disease Control and Prevention (CDC) announced in January 2023 that they were investigating a potential connection between administration of the Pfizer novel coronavirus disease-2019 (COVID-19) bivalent vaccine booster and ischemic stroke (IS). OBJECTIVE: To explore the relationship between Pfizer bivalent booster administration and IS in older patients in the United States and compare it to other COVID-19 vaccines. DESIGN: A retrospective cohort study was conducted to compare hazard of IS among patients aged 65 years or over who received the Pfizer bivalent, Moderna bivalent, or Pfizer/Moderna monovalent COVID-19 booster vaccine 1-21 and 22-42 days after vaccination. SETTING: Patient data were collected from TriNetX, a cloud-based analytics platform that includes electronic health record data from over 90 million unique patients in the United States. PARTICIPANTS: Patients in the United States aged 65 years or over at the time of administration of a Pfizer bivalent (n = 43,216), Moderna bivalent (n = 4,267), or Pfizer/Moderna monovalent (n = 100,583) booster were included for analysis. Cohorts were propensity-score matched by demographic factors and risk factors for IS and severe COVID-19. EXPOSURES: Pfizer bivalent, Moderna bivalent, or Pfizer/Moderna monovalent COVID-19 booster administration. MAIN OUTCOMES: The hazard ratio (HR) and 95% confidence interval (CI) for IS in the cohorts at 1-21 and 22-42 days after administration. RESULTS: After matching, the Pfizer bivalent cohort included 4,267 patients, with an average age of 73.7 years (44.43% male, 76.59% white). The Moderna bivalent cohort included 4,267 patients, with an average age of 74.0 years (44.08% male, 77.39% white). There was no significant difference in the hazard of IS encounters between the Pfizer bivalent versus Moderna bivalent cohorts at 1-21- or 22-42-days post-administration: HR = 0.59 (0.31, 1.11), 0.73 (0.33, 1.60). The hazard for IS was lower in the Pfizer bivalent cohort than in the Pfizer/Moderna monovalent cohort at both timepoints: HR = 0.24 (0.19, 0.29), 0.25 (0.20, 0.31). CONCLUSIONS AND RELEVANCE: Older adults administered the Pfizer bivalent booster had similar hazard for IS encounters compared to those administered the Moderna bivalent booster vaccine, but lower hazard than those administered the Pfizer/Moderna monovalent boosters. KEY POINTS: Question: What is the comparative hazard of ischemic stroke in American patients ages 65 years and over after administration of the Pfizer bivalent, Moderna bivalent, or Pfizer/Moderna monovalent COVID-19 booster vaccine?Findings: A retrospective cohort study was conducted. There

was no significant difference in the hazard of ischemic stroke encounters between the Pfizer bivalent versus Moderna bivalent cohorts, but lower hazard for the Pfizer bivalent than the monovalent boosters at 1-21 or 22-42 days post-administration.Meaning: There is no evidence from these results that the Pfizer bivalent booster is associated with increased hazard for ischemic stroke.

Haaf, P., et al. (2021). "The very low risk of myocarditis and pericarditis after mRNA COVID-19 vaccination should not discourage vaccination." Swiss Med Wkly **151**: w30087.

The benefits of vaccination - regarding COVID-19 infection and transmission, as well as COVID-associated complications - clearly outweigh the potential risk of vaccine-associated inflammation of the heart and other adverse events. Given the current state of knowledge, the outcome of myocarditis and pericarditis following vaccination is generally good. This review aims to guide physicians in the early diagnosis and management of suspected myocarditis following mRNA COVID vaccination. The initial work-up should include detailed history, a 12-lead electrocardiogram and serological biomarkers (high-sensitivity cardiac troponin T/I, natriuretic peptides and markers of inflammation) in accordance with the assessments recommended in current clinical practice guidelines for patients presenting with acute chest pain. In patients with suspected myocarditis, further assessment with transthoracic echocardiography and cardiovascular magnetic resonance imaging should be undertaken to confirm peri-/myocarditis and to distinguish the findings from other diseases with similar presentation. Patients with mRNA vaccine-associated myocarditis should be followed-up at least once to exclude chronic myocardial inflammation and deterioration of left ventricular ejection fraction. Consultation with an expert such as an immunologist with experience in vaccination regarding further mRNA vaccinations is advised in all patients with mRNA vaccine-associated perimyocarditis. Reporting of mRNA vaccine-associated myocarditis to Swissmedic is mandatory. Cohort studies prospectively follow-up on young adult and paediatric populations following immunisation with an mRNA COVID vaccine to monitor cardiac and immune parameters would generate valuable knowledge to better understand pathogenesis and risk factors for vaccine-associated perimyocarditis.

Huh, K., Y. E. Kim and J. Jung (2023). "Vaccination, Acute Myocardial Infarction, and Ischemic Stroke After COVID-19 Infection-Reply." JAMA **329**(5): 426-427.

Ihle-Hansen, H., et al. (2023). "Stroke After SARS-CoV-2 mRNA Vaccine: A Nationwide Registry Study." Stroke **54**(5): e190-e193.

BACKGROUND: Whether the SARS-CoV-2 mRNA vaccines may cause a transient increased stroke risk is uncertain. METHODS: In a registry-based cohort of all adult residents at December 27, 2020, in Norway, we linked individual-level data on COVID-19 vaccination, positive SARS-CoV-2 test, hospital admissions, cause of death, health care worker status, and nursing home resident status extracted from the Emergency Preparedness Register for COVID-19 in Norway. The cohort was followed for incident intracerebral bleeding, ischemic stroke, and subarachnoid hemorrhage within the first

28 days after the first/second or third dose of mRNA vaccination until January 24, 2022. Stroke risk after vaccination relative to time not exposed to vaccination was assessed by Cox proportional hazard ratio, adjusted for age, sex, risk groups, health care personnel, and nursing home resident. RESULTS: The cohort included 4 139 888 people, 49.8% women, and 6.7% were >/=80 years of age. During the first 28 days after an mRNA vaccine, 2104 people experienced a stroke (82% ischemic stroke, 13% intracerebral hemorrhage, and 5% subarachnoid hemorrhage). Adjusted hazard ratios (95% CI) after the first/second and after the third mRNA vaccine doses were 0.92 (0.85-1.00) and 0.89 (0.73-1.08) for ischemic stroke, 0.81 (0.67-0.98) and 1.05 (0.64-1.71) for intracerebral hemorrhage, and 0.64 (0.46-0.87) and 1.12 (0.57-2.19) for subarachnoid hemorrhage, respectively. CONCLUSIONS: We did not find increased risk of stroke during the first 28 days after an mRNA SARS-CoV-2 vaccine.

Ilonze, O. J. and M. E. Guglin (2022). "Myocarditis following COVID-19 vaccination in adolescents and adults: a cumulative experience of 2021." Heart Fail Rev **27**(6): 2033-2043.

Clinical course and outcomes of myocarditis after COVID-19 vaccination remain variable. We retrospectively collected data on patients > 12 years old from 01/01/2021 to 12/30/2021 who received COVID-19 messenger RNA (mRNA) vaccination and were diagnosed with myocarditis within 60 days of vaccination. Myocarditis cases were based on case definitions by authors. We report on 238 patients of whom most were male (n = 208; 87.1%). The mean age was 27.4 +/- 16 (range 12-80) years. Females presented at older ages (41.3 +/- 21.5 years) than men 25.7 +/- 14 years (p = 0.001). In patients > 20 years of age, the mean duration from vaccination to symptoms was 4.8 days +/- 5.5 days, but in < 20, it was 3.0 +/- 3.3 days (p = 0.04). Myocarditis occurred most commonly after the Pfizer-BioNTech mRNA vaccine (n = 183; 76.45) and after the second dose (n = 182; 80%). Symptoms started 3.95 +/- 4.5 days after vaccination. The commonest symptom was chest pain (n = 221; 93%). Patients were treated with non-steroidal anti-inflammatory drugs (n = 105; 58.3%), colchicine (n = 38; 21.1%), or glucocorticoids (n = 23; 12.7%). About 30% of the patients had left ventricular ejection fraction but more than half recovered the on repeat imaging. Abnormal cardiac MRIs were common; 168 patients (96% of 175 patients that had MRI) had late gadolinium enhancement, while 120 patients (68.5%) had myocardial edema. Heart failure guideline-directed medical therapy use was common (n = 27; 15%). Eleven patients had cardiogenic shock; and 4 patients required mechanical circulatory support. Five patients (1.7%) died; of these, 3 patients had endomyocardial biopsy/autopsy-confirmed myocarditis. Most cases of COVID-19 vaccine myocarditis are mild. Females presented at older ages than men and duration from vaccination to symptoms was longer in patients > 20 years. Cardiogenic shock requiring mechanical circulatory support was seen and mortality was low. Future studies are needed to better evaluate risk factors, and long-term outcomes of COVID-19 mRNA vaccine myocarditis.

Jabagi, M. J., et al. (2022). "Myocardial Infarction, Stroke, and Pulmonary Embolism After BNT162b2 mRNA COVID-19 Vaccine in People Aged 75 Years or Older." JAMA **327**(1): 80-82.

This population-based study evaluates the short-term risk of severe cardiovascular events among French residents aged 75 years or older after receipt of the BNT162b2 mRNA COVID-19 vaccination.

Kahn, F., O. Shannon and L. Bjorck (2021). "Thrombocytopenia with acute ischemic stroke and bleeding in a patient newly vaccinated with an adenoviral vector-based COVID-19 vaccine: COMMENT from Gruel et al.: RESPONSE from Kahn et al." J Thromb Haemost **19**(10): 2633.

Khan, E., et al. (2022). "Acute transverse myelitis following SARS-CoV-2 vaccination: a case report and review of literature." J Neurol **269**(3): 1121-1132.
OBJECTIVE: To report a unique case and literature review of post COVID-19 vaccination associated transverse myelitis and with abnormal MRI findings. BACKGROUND: Coronavirus disease have been reported to be associated with several neurological manifestations such as stroke, Guillain-Barre syndrome, meningoencephalitis amongst others. There are only a few reported cases of transverse myelitis with the novel coronavirus (n-CoV-2). Here, we identify a post COVID-19 vaccination patient diagnosed with acute transverse myelitis. METHOD: A retrospective chart review of a patient diagnosed with post SARS-CoV-2 vaccination acute transverse myelitis, and a review of literature of all the reported cases of other post vaccination and transverse myelitis, from December 1st, 2010 till July 15th, 2021, was performed. CONCLUSION: To our knowledge, this is the one of early reported case of transverse myelitis and with post SARS-CoV-2 vaccination, who responded well to plasmapheresis. Further studies would be recommended to identify the underlying correlation between COVID-19 vaccination and transverse myelitis.

Kim, Y. E., et al. (2022). "Association Between Vaccination and Acute Myocardial Infarction and Ischemic Stroke After COVID-19 Infection." JAMA **328**(9): 887-889.
This retrospective cohort study examines the incidence of acute myocardial infarction and ischemic stroke after COVID-19 infection among vaccinated vs unvaccinated adults in Korea.

Kobayashi, K., et al. (2023). "Multisystem inflammatory syndrome and lymphohistiocytic myocarditis after Covid-19 vaccine in a middle-aged woman." ESC Heart Fail **10**(2): 1435-1439.
We describe a 51-year-old otherwise healthy woman hospitalized for hypotension, fever, and weakness 4 days after the second-dose Covid-19 mRNA vaccine. Elevated inflammatory markers, natriuretic peptide levels and troponin levels, and slightly reduced left ventricular ejection fraction of 50% were noted. We also found the multiple organ damage, including mucocutaneous, gastrointestinal, and neurologic systems. In addition, we revealed the positive results for anti-nucleocapsid SARS-CoV-2 IgG, albeit negative for SARS-CoV-2 polymerase chain reaction testing, suggesting the prior asymptomatic Covid-19 infection. We finally diagnosed her as multisystem inflammatory syndrome after vaccination. Of note, we obtained myocardial specimen from the patients and demonstrated the lymphohistiocytic myocarditis, which is a rare form of myocarditis.

Kolahchi, Z., M. Khanmirzaei and A. Mowla (2022). "Acute ischemic stroke and vaccine-induced immune thrombotic thrombocytopenia post COVID-19 vaccination; a systematic review." J Neurol Sci **439**: 120327.

INTRODUCTION: One of the rare but potentially serious side effects of COVID-19 vaccination is arterial and venous thrombosis. Acute ischemic stroke (AIS) cases have been reported post COVID-19 vaccination. Herein, we systematically reviewed the reported cases of AIS after COVID-19 vaccination. METHOD: This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline. We searched PubMed and Scopus until April 14, 2022 to find studies that reported AIS post COVID-19 vaccination. RESULTS: We found 447 articles. From those, 140 duplicates were removed. After screening and excluding irrelevant articles, 29 studies (43 patients) were identified to be included. From all cases, 22 patients (51.1%) were diagnosed with AIS associated with Vaccine-induced immune thrombotic thrombocytopenia (VITT). Among AIS associated with VITT group, all received viral vector vaccines except one. The majority of cases with AIS and VITT were female (17 cases, 77.2%) and aged below 60 years (15 cases, 68%). Fourteen patients (32.5%) had additional thrombosis in other sites. Four of them (0.09%) showed concurrent CVST and ischemic stroke. Hemorrhagic transformation following AIS occurred in 7 patients (16.27%). Among 43 patients with AIS, at least 6 patients (14%) died during hospital admission. CONCLUSION: AIS has been reported as a rare complication within 4 weeks post COVID-19 vaccination, particularly with viral vector vaccines. Health care providers should be familiar with this rare consequence of COVID-19 vaccination in particular in the context of VITT to make a timely diagnosis and appropriate treatment plan.

Kukreti, S., et al. (2023). "The association of care burden with motivation of vaccine acceptance among caregivers of stroke patients during the COVID-19 pandemic: mediating roles of problematic social media use, worry, and fear." BMC Psychol **11**(1): 157.

BACKGROUND: The aim of the present study was to investigate the relationship between care burden and motivation of COVID-19 vaccine acceptance among caregivers of patients who have experienced a stroke and to explore the mediating roles of social media use, fear of COVID-19, and worries about infection in this relationship. METHODS: A cross-sectional survey study with 172 caregivers of patients who had experienced a stroke took part in a Taiwan community hospital. All participants completed the Zarit Burden Interview, Bergen Social Media Addiction Scale, Worry of Infection Scale, Fear of COVID-19 Scale, and Motors of COVID-19 Vaccine Acceptance Scale. Multiple linear regression model was applied to construct and explain the association among the variables. Hayes Process Macro (Models 4 and 6) was used to explain the mediation effects. RESULTS: The proposed model significantly explained the direct association of care burden with motivation of COVID-19 vaccine acceptance. Despite the increased care burden associated with decreased vaccine acceptance, problematic social media use positively mediated this association. Moreover, problematic social media use had sequential mediating effects together with worry of infection or fear of COVID-19 in the

association between care burden and motivation of vaccine acceptance. Care burden was associated with motivation of vaccine acceptance through problematic social media use followed by worry of infection. CONCLUSIONS: Increased care burden among caregivers of patients who have experienced a stroke may lead to lower COVID-19 vaccines acceptance. Moreover, problematic social media use was positively associated with their motivation to get COVID-19 vaccinated. Therefore, health experts and practitioners should actively disseminate accurate and trustworthy factual information regarding COVID-19, while taking care of the psychological problems among caregivers of patients who have experienced a stroke.

Liu, J., et al. (2023). "Stroke Following COVID-19 Vaccination: Evidence Based on Different Designs of Real-World Studies." J Infect Dis.

BACKGROUND: We aimed to evaluate the association between coronavirus disease 2019 (COVID-19) vaccination and the risk of stroke. METHOD: We conducted a systematic meta-analysis of studies published until December 24, 2022, using PubMed and the Cochrane database; real-world studies using cohort, self-controlled case series (SCCS), and case-crossover study (CCOS) designs were identified to evaluate the incidence risk ratios (IRRs) and 95% confidence intervals (CIs) of ischemic stroke (IS), hemorrhagic stroke (HS), and cerebral venous sinus thrombosis (CVST) following COVID-19 vaccination. Random-effects meta-analyses were performed to pool the risks of IS and HS among subpopulations categorized by vaccine type, dose, age, and sex. Sensitivity analysis was performed after stratification by defined risk periods. RESULTS: Fourteen observational studies involving 79,918,904 individuals were included. Cohort studies showed decreased risks of IS (IRR [95% CI], 0.82 [0.75-0.90]) and HS (IRR [95% CI], 0.75 [0.67-0.85]) post-vaccination, but no association with CVST was found (IRR [95% CI], 1.18 [0.70-1.98]). SCCS identified increased risks 1-21 days (IRR [95% CI]IS, 1.05 [1.00-1.10]; IRR [95% CI]HS, 1.16 [1.06-1.26]) or 1-28 days (IRR [95% CI]IS, 1.04 [1.00-1.08]; IRR [95% CI]HS, 1.37 [1.15-1.64]) post-vaccination, similar to CVST (IRR [95% CI], 1.58 [1.08-2.32]). A CCOS reported an increased risk of CVST after vaccination using ChAdOx1 (IRR [95% CI], 2.9 [1.1-7.2]). DISCUSSION: Although different study designs yielded inconsistent findings, considering the relatively low background incidence of stroke and benefits of vaccination, even a potentially increased risk of stroke post-vaccination should not justify vaccine hesitancy.

Lopez-Mena, D., et al. (2022). "Stroke Among SARS-CoV-2 Vaccine Recipients in Mexico: A Nationwide Descriptive Study." Neurology **98**(19): e1933-e1941.

BACKGROUND AND OBJECTIVES: Information on stroke among severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccines remains scarce. We report stroke incidence as an adverse event following immunization (AEFI) among recipients of 79,399,446 doses of 6 different SARS-CoV-2 vaccines (BNT162b2, ChAdOx1 nCov-19, Gam-COVID-Vac, CoronaVac, Ad5-nCoV, and Ad26.COV2-S) between December 24, 2020, and August 31, 2021, in Mexico. METHODS: This retrospective descriptive study analyzed stroke incidence per million doses among hospitalized adult patients (>/=18 years) during an 8-month interval. According to the World Health Organization, AEFIs were

defined as clinical events occurring within 30 days after immunization and categorized as either nonserious or serious, depending on severity, treatment, and hospital admission requirements. Acute ischemic stroke (AIS), intracerebral hemorrhage (ICH), subarachnoid hemorrhage (SAH), and cerebral venous thrombosis (CVT) cases were collected through a passive epidemiologic surveillance system in which local health providers report potential AEFI to the Mexican General Board of Epidemiology. Data were captured with standardized case report formats by an ad hoc committee appointed by the Mexican Ministry of Health to evaluate potential neurologic AEFI against SARS-COV-2. RESULTS: We included 56 patients (31 female patients [55.5%]) for an overall incidence of 0.71 cases per 1,000,000 administered doses (95% CI 0.54-0.92). Median age was 65 years (interquartile range [IQR] 55-76 years); median time from vaccination to stroke (of any subtype) was 2 days (IQR 1-5 days). In 27 (48.2%) patients, the event was diagnosed within the first 24 hours after immunization. The most frequent subtype was AIS in 43 patients (75%; 0.54 per 1,000,000 doses, 95% CI 0.40-0.73), followed by ICH in 9 (16.1%; 0.11 per 1,000,000 doses, 95% CI 0.06-0.22) and SAH and CVT, each with 2 cases (3.6%; 0.03 per 1,000,000 doses, 95% CI 0.01-0.09). Overall, the most common risk factors were hypertension in 33 (58.9%) patients and diabetes in 22 (39.3%). Median hospital length of stay was 6 days (IQR 4-13 days). At discharge, functional outcome was good (modified Rankin Scale score 0-2) in 41.1% of patients; in-hospital mortality rate was 21.4%. DISCUSSION: Stroke is an exceedingly rare AEFI against SARS-CoV-2. Preexisting stroke risk factors were identified in most patients. Further research is needed to evaluate causal associations between SARS-COV-2 vaccines and stroke.

Luisa, V., et al. (2022). "Ischemic stroke shortly after vaccination against SARS-CoV-2: A case-control study." J Neurol Sci **436**: 120209.

BACKGROUND AND PURPOSE: Vaccination against SARS-CoV-2 has been associated with rare occurrences of severe venous thromboses. Very little data exist about arterial ischemic strokes. We have assessed the features of ischemic strokes occurring shortly after vaccination against SARS-CoV-2 in the Cremona area, Italy. METHODS: From February 1, to July 31, 2021, all patients with ischemic stroke within four weeks of vaccination against COVID-19 admitted to our stroke unit were consecutively collected, and their main features were compared with those of all other patients with ischemic strokes admitted during the same period. RESULTS: Sixteen strokes after vaccination were collected. They represented 10.5% of all ischemic strokes. Median interval from vaccination was 12 days (range 1-24). Fifteen (93.8%) had received the BNT162b2 (Pfizer-BioNTech) vaccine and 1 (6.2%) the ChAdOx1 nCoV-19 (AstraZeneca). Two patients (12.5%) had a mild thrombocytopenia on admission (128,000 and 142,000/ml), without any evidence of bleeding or venous thrombosis. Thrombolysis and/or thrombectomy were carried out in 4 cases (25.0%). When compared with 137 strokes without recent vaccination, none of the demographic, clinical, and laboratory features of post-vaccination strokes were significantly different. CONCLUSIONS: Ischemic strokes occurring shortly after COVID-19 vaccination at our center were similar to those of non-vaccinated patients. Therefore, the relatively high percentage of such patients probably

relates to the very high fraction of elderly people vaccinated against SARS-CoV-2 in the Cremona area, rather than to a consequence of vaccination.

Markus, H. S. (2021). "Ischaemic stroke can follow COVID-19 vaccination but is much more common with COVID-19 infection itself." J Neurol Neurosurg Psychiatry **92**(11): 1142.

McMillan, N., et al. (2023). "Fatal Post COVID mRNA-Vaccine Associated Cerebral Ischemia." Neurohospitalist **13**(2): 156-158.

BACKGROUND: Venous thromboses have been linked to several COVID-19 vaccines, but there is limited information on the Moderna vaccine's effect on the risk of arterial thrombosis. Here we describe a case of post-Moderna COVID-19 vaccination arterial infarct with vaccine-associated diffuse cortical edema that was complicated by refractory intracranial hypertension. CASE SUMMARY: 24 hrs after receiving her first dose of the Moderna COVID-19 vaccine, a 30-year-old female developed severe headache. Three weeks later she was admitted with subacute headache and confusion. Imaging initially showed scattered cortical thrombosis with an elevated opening pressure on lumbar puncture. An external ventricular drain was placed, but she continued to have elevated intracranial pressure. Ultimately, she required a hemicraniectomy, but intractable cerebral edema resulted in her death. Pathology was consistent with thrombosis and associated inflammatory response. CONCLUSION: Though correlational, her medical team surmised that the mRNA vaccine may have contributed to this presentation. The side effects of COVID-19 infection and vaccination are still incompletely understood. Though complications are rare, clinicians should be aware of presentations like this one.

Merchant, H. (2022). "Inadvertent injection of COVID-19 vaccine into deltoid muscle vasculature may result in vaccine distribution to distance tissues and consequent adverse reactions." Postgrad Med J **98**(1161): e5.

Mesa-Gamarra, K., et al. (2022). "Acute Thalamic Ischemic Stroke in an Older Patient Newly Vaccinated with COVID-19 Vaccine Based on Adenoviral Vectors." Innov Clin Neurosci **19**(4-6): 48-50.

INTRODUCTION: Recent reports have shown several cases of cerebrovascular events after vaccination against COVID-19. The effects have been described mainly in women within the first two weeks of receiving the vaccine. CLINICAL CASE: We describe here the first Colombian case of a cerebrovascular event after vaccination against COVID-19 in a 67-year-old woman with a vascular history. Four days after application of the messenger ribonucleic acid (mRNA) vaccine, she exhibited deviation of the labial commissure, ipsilateral ptosis, and limitation of march with lateralization. The event was associated with a subacute ischemic event in the right thalamus in parasagittal situation, changes in chronic ischemic microangiopathy of small vessels, and vascular crossing in the right cerebellar angle, without other alternative causes. CONCLUSION: The development and rapid use of vaccines has allowed the hospitalization and mortality statistics associated with COVID-19 to be reduced, but at the same time, it has generated concern about the potential side effects, generating controversy among the general population, especially

in individuals with cardiovascular diseases. In our case, we provided evidence for the discussion of potential cerebrovascular events related to the application of vaccines in older people with a history of cerebrovascular diseases. This was done in order to analyze and control in subsequent studies the modulation of medical history on the likely effects of vaccination. However, despite the unavoidable side effects, the benefits of vaccination are superior.

Mustafa Alhussein, M., et al. (2022). "Natural History of Myocardial Injury After COVID-19 Vaccine-Associated Myocarditis." Can J Cardiol **38**(11): 1676-1683.

BACKGROUND: Acute myocarditis is a rare complication of mRNA-based COVID-19 vaccination. Little is known about the natural history of this complication. METHODS: Baseline and convalescent (>/= 90 days) cardiac magnetic resonance (CMR) imaging assessments were performed in 20 consecutive patients meeting Updated Lake Louise Criteria for acute myocarditis within 10 days of mRNA-based vaccination. CMR-based changes in left ventricular volumes, mass, ejection fraction (LVEF), markers of tissue inflammation (native T1 and T2 mapping), and fibrosis (late gadolinium enhancement [LGE] and extracellular volume [ECV]) were assessed between baseline and convalescence. Cardiac symptoms and clinical outcomes were captured. RESULTS: Median age was 23.1 years (range 18-39 years), and 17 (85%) were male. Convalescent evaluations were performed at a median (IQR) 3.7 (3.3-6.2) months. The LVEF showed a mean 3% absolute improvement, accompanied by a 7% reduction in LV end-diastolic volume and 5% reduction in LV mass (all P < 0.015). Global LGE burden was reduced by 66% (P < 0.001). Absolute reductions in global T2, native T1, and ECV of 2.1 ms, 58 ms, and 2.9%, repectively, were documented (all P </= 0.001). Of 5 patients demonstrating LVEF </= 50% at baseline, all recovered to above this threshold in convalescence. A total of 18 (90%) patients showed persistence of abnormal LGE although mean fibrosis burden was < 5% of LV mass in 85% of cases. No patient experienced major clinical outcomes. CONCLUSIONS: COVID-19 mRNA vaccine-associated myocarditis showed rapid improvements in CMR-based markers of edema, contractile function, and global LGE burden beyond 3 months of recovery in this young patient cohort. However, regional fibrosis following edema resolution was commonly observed, justifying need for ongoing surveillance.

Nahab, F., et al. (2023). "Factors associated with stroke after COVID-19 vaccination: a statewide analysis." Front Neurol **14**: 1199745.

BACKGROUND: The objective of our study was to evaluate vaccine type, COVID-19 infection, and their association with stroke soon after COVID-19 vaccination. METHODS: In a retrospective cohort study, we estimated the 21-day post-vaccination incidence of stroke among the recipients of the first dose of a COVID-19 vaccine. We linked the Georgia Immunization Registry with the Georgia Coverdell Acute Stroke Registry and the Georgia State Electronic Notifiable Disease Surveillance System data to assess the relative risk of stroke by the vaccine type. RESULTS: Approximately 5 million adult Georgians received at least one COVID-19 vaccine between 1 December 2020 and 28 February 2022: 54% received BNT162b2, 41% received mRNA-1273, and 5% received

Ad26.COV2.S. Those with concurrent COVID-19 infection within 21 days post-vaccination had an increased risk of ischemic (OR = 8.00, 95% CI: 4.18, 15.31) and hemorrhagic stroke (OR = 5.23, 95% CI: 1.11, 24.64) with no evidence for interaction between the vaccine type and concurrent COVID-19 infection. The 21-day post-vaccination incidence of ischemic stroke was 8.14, 11.14, and 10.48 per 100,000 for BNT162b2, mRNA-1273, and Ad26.COV2.S recipients, respectively. After adjusting for age, race, gender, and COVID-19 infection status, there was a 57% higher risk (OR = 1.57, 95% CI: 1.02, 2.42) for ischemic stroke within 21 days of vaccination associated with the Ad26.COV2.S vaccine compared to BNT162b2; there was no difference in stroke risk between mRNA-1273 and BNT162b2. CONCLUSION: Concurrent COVID-19 infection had the strongest association with early ischemic and hemorrhagic stroke after the first dose of COVID-19 vaccination. Although not all determinants of stroke, particularly comorbidities, were considered in this analysis, the Ad26.COV2.S vaccine was associated with a higher risk of early post-vaccination ischemic stroke than BNT162b2.

Pandey, S., et al. (2022). "A case of ischemic stroke and transient thrombocytopenia in a young female following adenoviral vector-based COVID-19 vaccination: Was the association incidental or causal?" J Family Med Prim Care **11**(10): 6556-6559.

Since March 2021, cases with unusual clots, particularly cerebral venous sinus thrombosis and splanchnic vein thrombosis, have been reported worldwide following adenoviral vector-based coronavirus disease 2019 (COVID-19) vaccination. This entity has been termed vaccine-induced thrombotic thrombocytopenia (VITT). We report a 23-year-old healthy female who developed seizures, altered sensorium, and left hemiparesis, 20 days after receiving the first dose of adenoviral vector-based COVID-19 vaccine "Covishield." The patient had transient thrombocytopenia. The D-dimer level was 2460 ng/mL. Magnetic resonance imaging (MRI) demonstrated occlusion of M2 segment of the middle cerebral artery and cerebral infarction. Platelet factor-4 antibodies level was normal. Treatment with aspirin and antiepileptic drugs resulted in a remarkable recovery. This is the first Indian case report of ischemic stroke and transient thrombocytopenia following SARS-CoV-2 ChAdOx1 nCoV-19 vaccination. Our case had clinical features consistent with the diagnosis of probable VITT. Familiarity with VITT is crucial because timely treatment with non-heparin anticoagulants and intravenous immunoglobulin improves the outcome.

Patel, T., et al. (2022). "Comparison of Multisystem Inflammatory Syndrome in Children-Related Myocarditis, Classic Viral Myocarditis, and COVID-19 Vaccine-Related Myocarditis in Children." J Am Heart Assoc **11**(9): e024393.

Background Although rare, classic viral myocarditis in the pediatric population is a disease that carries significant morbidity and mortality. Since 2020, myocarditis has been a common component of multisystem inflammatory syndrome in children (MIS-C) following SARS-CoV-2 infection. In 2021, myocarditis related to mRNA COVID-19 vaccines was recognized as a rare adverse event. This study aims to compare classic, MIS-C, and COVID-19 vaccine-related myocarditis with regard to clinical presentation, course, and outcomes. Methods and Results In this retrospective cohort study, we compared

patients aged <21 years hospitalized at our institution with classic viral myocarditis from 2015 to 2019, MIS-C myocarditis from March 2020 to February 2021, and vaccine-related myocarditis from May 2021 to June 2021. Of 201 total participants, 43 patients had classic myocarditis, 149 had MIS-C myocarditis, and 9 had vaccine-related myocarditis. At presentation, ejection fraction was lowest for those with classic myocarditis, with ejection fraction <55% present in 58% of patients. Nearly all patients with MIS-C myocarditis (n=139, 93%) and all patients with vaccine-related myocarditis (n=9, 100%) had normal left ventricular ejection fraction at the time of discharge compared with 70% (n=30) of the classic myocarditis group (P<0.001). At 3 months after discharge, of the 21 children discharged with depressed ejection fraction, none of the 10 children with MIS-C myocarditis had residual dysfunction compared with 3 of the 11 (27%) patients in the classic myocarditis group. Conclusions Compared with classic myocarditis, those with MIS-C myocarditis had better clinical outcomes, including rapid recovery of cardiac function. Patients with vaccine-related myocarditis had prompt resolution of symptoms and improvement of cardiac function.

Rahmig, J., et al. (2022). "Acute Ischemic Stroke in the Context of SARS-CoV-2 Vaccination: A Systematic Review." Neuropsychiatr Dis Treat **18**: 1907-1916.

BACKGROUND: There have been reports suggesting an increased incidence of acute ischemic stroke among anti-SARS-CoV-2 vaccinees. We aimed to systematically review the literature to summarize the available evidence on the association between SARS-CoV-2 vaccination and acute ischemic stroke. METHODS: A systematic literature search on MEDLINE, LitCovid and LIVIVO databases was performed for eligible randomized controlled trials, observational studies, registries and case reports that reported on imaging-confirmed acute ischemic stroke in the context of any SARS-CoV-2 vaccination with BNT162b2, mRNA-1273, Ad26.COV2.S, ChAdOx1 or Gam-COVID-Vac. Literature search was limited to English and German languages and publication date before October 19, 2021. RESULTS: We identified a total of 395,105,670 individuals who underwent vaccination. We found 21 sources, including 2 cohort studies, 4 registry studies, 3 randomized clinical trials, and 12 case reports. Individuals included in these studies were at least 16 years old. Cari et al observed a higher likelihood of acute ischemic stroke in vaccinees aged 18-64 years, compared to Whiteley et al observing vaccinees older than 70 years when vaccinated. In addition, differences in the likelihood of acute ischemic stroke were found among the vaccines studied, although no overall increased stroke incidence was demonstrated with vaccination. CONCLUSION: In this systematic review of the available literature, we found that the risk of acute ischemic stroke does not appear to be increased in vaccinated individuals who have received any of the currently licensed SARS-CoV-2 vaccines compared with the baseline incidence of stroke.

Rattanawong, W., et al. (2021). "Acute prolonged motor aura resembling ischemic stroke after COVID - 19 vaccination (CoronaVac): the first case report." J Headache Pain **22**(1): 93.

BACKGROUND: We report the first case of a patient who suffered transient focal neurological deficit mimicking stroke following CoronaVac vaccination. However, instead

of an ischemic stroke, motor aura was suspected. CASE PRESENTATIONS: A 24 year-old Thai female presented with left hemiparesis fifteen minutes after receiving CoronaVac. She also had numbness of her left arm and legs, flashing lights, and headaches. On physical examination, her BMI was 32.8. Her vital signs were normal. She had moderate left hemiparesis (MRC grade III), numbness on her left face, arms, and legs. Her weakness continued for 5 days. A brain CT scan was done showing no evidence of acute infarction. Acute treatment with aspirin was given. MRI in conjunction with MRA was performed in which no restricted diffusion was seen. A SPECT was performed to evaluate the function of the brain showing significant hypoperfusion of the right hemisphere. The patient gradually improved and was discharged. DISCUSSIONS: In this study, we present the first case of stroke mimic after CoronaVac vaccination. After negative imaging studies had been performed repeatedly, we reach a conclusion that stroke is unlikely to be the cause. Presumably, this phenomenon could possibly have abnormal functional imaging study. Therefore, we believed that it might be due to cortical spreading depression, like migraine aura, which we had conducted a literature review.

Rizzo, P. A., et al. (2022). "COVID-19 Vaccination Is Associated with a Better Outcome in Acute Ischemic Stroke Patients: A Retrospective Observational Study." J Clin Med **11**(23).

Background: It is unclear whether and how COVID-19 vaccination may affect the outcome of patients with acute ischemic stroke (AIS). We investigated this potential association in a retrospective study by comparing previously vaccinated (VAX) versus unvaccinated (NoVAX) stroke patients. Methods: We collected clinical reports for all consecutive AIS patients admitted to our hospital and evaluated the outcome predictors in VAX and NoVAX groups. Adjustments were made for possible confounders in multivariable logistic regression analysis, and adjusted hazard ratios were calculated. Results: A total of 466 AIS patients (287 VAX and 179 NoVAX) were included in this study. The NIHSS score at discharge and mRS score at a 3-month follow-up visit were significantly lower in VAX patients compared to NoVAX patients ($p < 0.001$). Good outcomes (mRS 0-2) were significantly associated with COVID-19 vaccination before AIS (adjusted hazard ratio, 0.400 [95% CI = 0.216-0.741]). Conclusions: The observation that COVID-19 vaccination can influence the outcome of AIS provides support for further studies investigating the role of immunity in ischemic brain damage.

Rojko, M., et al. (2023). "Patent Foramen Ovale-associated Stroke and COVID-19 Vaccination." Interv Cardiol **18**: e10.

Background: COVID-19 infection has been associated with paradoxical thromboembolism through a patent foramen ovale (PFO) and ischaemic stroke. Such events have not been reported after COVID-19 vaccination. The aim of the present study was to investigate PFO-associated stroke during the mass COVID-19 vaccination in Slovenia. Methods: This prospective study, conducted between 26 December 2020 and 31 March 2022, enrolled consecutive patients (>/=18 years) with PFO-associated stroke referred for a percutaneous closure to a single interventional facility in Slovenia. Results: A total of 953,546 people aged between 18 and 70 years received at least one dose of a COVID-19 vaccine approved by the European Medicines Agency. Of the 28 patients

presenting with PFO-associated stroke, 12 patients (42.9%) were vaccinated prior to the event, of whom nine were women and three were men, aged between 21 and 70 years. Stroke occurred within 35 days after vaccination in six patients (50%). Clinical presentation included motor dysphasia, paresis, vertigo, ataxia, paraesthesia, headache, diplopia and hemianopia. At hospital discharge, 11 patients (91.6%) had at least one residual ischaemic lesion. Conclusion: A temporal coincidence of COVID-19 vaccination and PFO-associated stroke has been described. A potential cause-effect relationship may only be hypothesised.

Roongpiboonsopit, D., et al. (2022). "Inactivated COVID-19 vaccine induced acute stroke-like focal neurologic symptoms: a case series." BMC Neurol **22**(1): 210.

BACKGROUND: A subgroup of individuals experienced stroke-like symptoms after receiving an inactivated COVID-19 vaccine. We present clinical characteristics, neuroimaging, and outcome of these patients. METHODS: Medical personals who had neurological symptoms after receiving inactivated COVID-19 vaccine were enrolled. Clinical, laboratory investigation and neuroimaging were collected. Subjects were prospectively followed-up on clinical and neuroimaging to detect brain parenchymal or cerebrovascular abnormality. RESULTS: Nineteen out of 385 subjects (4.9%) developed neurological symptoms after vaccination. There was a female predominance (89.5%) with mean age of 34 +/- 7.5 years. Majority of patients (52.6%) had symptoms within 60 min after vaccination. The most common neurological symptoms were numbness (94.7%) followed by headache (52.6%) and weakness (47.4%). The most common neurological signs were sensory deficit (79%) followed by motor weakness (52.6%) and tongue deviation (26.3%). Recurrent headache was observed in most patients (89.5%) during followed up. Serial brain imaging was done in all patients with median follow-up interval of 18 days. There was no evidence of acute brain infarction in any of the patients, 84.2% had no vascular abnormality, 15.8% had transient focal narrowing of cerebral vessels. Outcome was favorable, modified ranking scale 0-1 for all patients at 4 weeks after vaccination. CONCLUSIONS: Transient focal neurological symptoms and deficits can be found after COVID-19 vaccination. However, benefit to stop COVID-19 pandemic by vaccination is outweighed by these seemingly reversible side effects. The pathophysiology underlined these phenomena should be further investigated.

Salah, H. M. and J. L. Mehta (2021). "COVID-19 Vaccine and Myocarditis." Am J Cardiol **157**: 146-148.

Samimisedeh, P., et al. (2022). "Cardiac MRI Findings in COVID-19 Vaccine-Related Myocarditis: A Pooled Analysis of 468 Patients." J Magn Reson Imaging **56**(4): 971-982.

Understanding the pattern and severity of myocarditis caused by the coronavirus disease 2019 (COVID-19) vaccine is imperative for improving the care of the patients, and cardiac evaluation by MRI plays a key role in this regard. Our systematic review and meta-analysis aimed to summarize cardiac MRI findings in COVID-19 vaccine-related myocarditis. We performed a comprehensive systematic review of literature in PubMed, Scopus, and Google Scholar databases using key terms covering COVID-19 vaccine,

myocarditis, and cardiac MRI. Individual-level patient data (IPD) and aggregated-level data (AD) studies were pooled through a two-stage analysis method. For this purpose, all IPD were first gathered into a single data set and reduced to AD, and then this AD (from IPD studies) was pooled with existing AD (from the AD studies) using fixed/random effect models. I(2) was used to assess the degree of heterogeneity, and the prespecified level of statistical significance (P value for heterogeneity) was <0.1. Based on meta-analysis of 102 studies (n = 468 patients), 79% (95% confidence interval [CI]: 54%-97%) of patients fulfilled Lake Louise criteria (LLC) for diagnosis of myocarditis. Cardiac MRI abnormalities included elevated T2 in 72% (95% CI: 50%-90%), myocardial late gadolinium enhancement (LGE) in 93% (95% CI: 83%-99%; nearly all with a subepicardial and/or midwall pattern), impaired left ventricular ejection fraction (LVEF) (<50%) in 4% (95% CI: 1.0%-9.0%). Moreover, elevated T1 and extracellular volume fraction (ECV) (>30), reported only by some IPD studies, were detected in 74.5% (76/102) and 32% (16/50) of patients, respectively. In conclusion, our findings may suggest that over two-thirds of patients with clinically suspected myocarditis following COVID-19 vaccination meet the LLC. COVID-19 vaccine-associated myocarditis may show a similar pattern compared to other acute myocarditis entities. Notably, preserved LVEF is probably a common finding in these patients. EVIDENCE LEVEL: 4 TECHNICAL EFFICACY: Stage 3.

Schmitt, P., et al. (2021). "Acute Myocarditis after COVID-19 vaccination: A case report." Rev Med Interne **42**(11): 797-800.

INTRODUCTION: The etiology of myocarditis often remains undetermined. A large variety of infectious agents, systemic diseases, drugs, and toxins can cause the disease. We report the case of a 19-year-old man who developed myocarditis three days after Pfizer-BioNTech COVID-19 booster vaccination. CASE REPORT: A 19-year-old man, presenting with troponin-positive acute chest pain, was referred to our department. He had received the Pfizer-BioNTech COVID-19 vaccine three days prior to his admission. The diagnosis of acute myocarditis was confirmed by cardiovascular magnetic resonance imaging. Patient hemodynamic status remained stable during hospitalization. The left ventricular ejection fraction was preserved during hospital stay and at one-month follow-up. We found no evidence for another infectious or autoimmune etiology. CONCLUSION: Although imputability of the vaccine cannot be formally established on the basis of this case report, the findings raise the possibility of an association between mRNA COVID-19 vaccination and acute myocarditis.

Siddig, A., et al. (2022). "AstraZeneca COVID-19 vaccine: A possible risk factor for ischemic stroke and cerebral venous sagittal sinus thrombosis: A case series." Clin Case Rep **10**(7): e6017.

One of the most prevalent neurological impairments is cerebrovascular accident (CVA). Ischemic stroke and CVST have been linked to the AstraZeneca COVID-19 vaccine. Three Sudanese patients developed these diseases after receiving the AstraZeneca COVID-19 vaccine, indicating a relationship between the AstraZeneca COVID-19 vaccine and these conditions.

Sirisuk, W., et al. (2023). "Incidence and clinical characteristics of adverse neurological events and stroke-like syndrome associated with immune stress-related response after COVID-19 vaccination in 2021 from Thailand." Clin Neurol Neurosurg **231**: 107804.

OBJECTIVES: AEFIs (adverse events following immunizations), especially ISRR (immune stress related response) which can cause stroke-like symptoms may affect the vaccine roll-out campaign to prevent the coronavirus 2019 outbreak. METHODS: This study aimed to describe the incidence and clinical characteristics of neurological AEFIs and stroke-like symptoms associated with ISRR after COVID-19 vaccination. Characteristics of ISRR were compared to minor ischemic stroke patients during the same period of the study. During March to September 2021, we retrospectively collected data of participants aged >/= 18 years who received COVID-19 vaccine and developed AEFIs from Thammasat university vaccination center (TUVC). Data of neurological AEFIs patients and minor ischemic stroke patients were collected from hospital electronic medical record system. RESULTS: COVID-19 vaccine were administered at TUVC for 245,799 doses. AEFIs were reported in 129,652 instances (52.6%). ChADOx-1 nCoV-19 viral vector vaccine has the most frequent occurrence of AEFIs (58.0%), and neurological AEFIs (12.6%). 83% of neurological AEFI was headache. Most were mild and did not need medical attention. Of 119 patients who received COVID-19 vaccine from anywhere with neurological AEFIs and presented to TUH, ISRR was diagnosed in 107 patients (89.9%) and all patients who has follow-up data (30.8%) showed clinical improvement. In comparison with minor ischemic stroke (116 patients), ISRR patients had significantly less ataxia, facial weakness, weakness of arm/leg and speech disturbances ($P < 0.001$). CONCLUSION: The incidence of neurological AEFIs after COVID-19 vaccination was higher among recipients of ChAdOx-1 nCoV-19 vaccine (12.6%) than inactivated vaccine (6.2%) and mRNA vaccine (7.5%). However, most neurological AEFIs were ISRR, had mild severity and resolved within 30 days. Stroke-like symptoms occurred less frequently than patients with minor ischemic stroke.

Stefanou, M. I., et al. (2022). "Acute Arterial Ischemic Stroke Following COVID-19 Vaccination: A Systematic Review and Meta-analysis." Neurology.

BACKGROUND: Acute arterial-ischemic-stroke (AIS) has been reported as a rare adverse-event following COVID-19-vaccination with mRNA or viral-vector vaccines. However, data are sparse regarding the risk of post-vaccination AIS and its potential association with thrombotic-thrombocytopenia-syndrome (TTS). METHODS: A systematic review and meta-analysis of randomized-controlled clinical trials (RCTs), pharmacovigilance registries, registry-based studies, observational cohorts and case-series was performed with the aim to calculate: (1) the pooled proportion of patients presenting with AIS following COVID-19-vaccination; (2) the prevalence of AIS after mRNA and vector-based vaccination; (3) the proportion of TTS among post-vaccination AIS-cases. Patient characteristics were assessed as secondary outcomes. RESULTS: Two RCTs, three cohort and eleven registry-based studies comprising 17,481 AIS-cases among 782,989,363 COVID-19-vaccinations were included in the meta-analysis. The pooled proportion of AIS following exposure to any COVID-19-vaccine type was 4.7 cases per 100,000 vaccinations (95%CI:2.2-8.1; I(2)=99.9%). The pooled proportion of AIS following mRNA-vaccination

(9.2 cases per 100,000 vaccinations; 95%CI: 2.5-19.3; I(2)=99.9%) did not differ compared to adenovirus-based-vaccination (2.9 cases per 100,000 vaccinations; 95%CI: 0.3-7.8; I(2)=99.9%). No differences regarding demographics were disclosed between patients with AIS following mRNA- or vector-based vaccination. The pooled proportion of TTS among post-vaccination AIS-cases was 3.1% (95%CI: 0.7-7.2%; I(2)=78.8%). CONCLUSIONS: The pooled proportion of AIS following COVID-19 vaccination is comparable to the prevalence of AIS in the general population and much lower than the AIS prevalence among SARS-CoV-2-infected patients. TTS is very uncommonly reported in patients with AIS following COVID-19 vaccination.

Stoiloudis, P., et al. (2022). "Reader Response: Stroke Among SARS-CoV-2 Vaccine Recipients in Mexico: A Nationwide Descriptive Study." Neurology **99**(15): 673-674.

Taccetta, C. A. (2022). "Reader Response: Stroke Among SARS-CoV-2 Vaccine Recipients in Mexico: A Nationwide Descriptive Study." Neurology **99**(15): 672.

Tepmongkol, S., et al. (2022). "Brain perfusion single photon emission computed tomography abnormality in MRI-negative stroke-like patients post COVID-19 vaccination." Medicine (Baltimore) **101**(47): e31965.

Stroke-like symptoms after COVID-19 vaccination was thought to be functional if there was no anatomical image abnormality. We aimed to analyze brain perfusion changes in these patients. A case-control study of brain perfusion single photon emission computed tomography (SPECT) of 12 vaccinated patients with left-sided stroke-like symptoms were compared with 12 age- and gender-matched normal interictal brain SPECTs using voxel-based analysis. Significant hyperperfusion was seen on the right side in postcentral, inferior parietal, mid temporal, parahippocampal, and caudate regions, and on the left side in the thalamus, hippocampus, and mid temporal areas. In addition, there were hypoperfused bilateral superior frontal gyri and right mid/posterior cingulate cortex (Family-wise-error corrected p-values < .05). Both hypoperfusion and hyperperfusion in the brain are demonstrated. We hypothesize that these findings might be the result of the functional neurological disorder. However, based on other previous studies, circulating spike protein in the patients' plasma early after vaccination might also be the cause.

Thomas, M. G., A. Dermawan and S. Teh (2023). "Cerebellar and brainstem stroke possibly associated with booster dose of BNT162b2 (Pfizer-BioNTech) COVID-19 vaccine." BMJ Case Rep **16**(5).

As COVID-19 vaccination becomes widely available and administered globally, there have been several reports of side effects attributed to the vaccine. This report highlights a patient who developed stroke 2 days following the administration of the COVID-19 vaccine, although its association remains uncertain. A man in his late 30s developed acute neurological symptoms 2 days after receiving the booster dose of the BNT162b2 (Pfizer-BioNTech) mRNA COVID-19 vaccine. History and neurological examination suggested a posterior circulation stroke, which was confirmed by MRI, as a right-sided

posterior inferior cerebellar artery stroke. Full workup did not suggest other causes of the stroke. Due to the patient's age and well-controlled risk factors, it was presumed to be a rare adverse effect of the vaccine. Medical management with aspirin, statin therapy and rehabilitation led to the improvement of symptoms and enabled ongoing restoration of function. Further cases of stroke following administration of COVID-19 vaccine have been documented in the literature, but the association is yet to be established.

Titheradge, P. J., P. S. Micalos and F. E. Marino (2022). "Increased heart rate response to exercise following Pfizer COVID-19 vaccination with no change in cardiac output or stroke volume?" J Appl Physiol (1985) **133**(4): 985.

Turner, G. M., et al. (2022). "Stroke and TIA Survivors' Perceptions of the COVID-19 Vaccine and Influences on Its Uptake: Cross Sectional Survey." Int J Environ Res Public Health **19**(21).

BACKGROUND: People who have experienced a stroke or transient ischaemic attack (TIA) have greater risks of complications from COVID-19. Therefore, vaccine uptake in this vulnerable population is important. To prevent vaccine hesitancy and maximise compliance, we need to better understand individuals' views on the vaccine. OBJECTIVES: We aimed to explore perspectives of the COVID-19 vaccine and influences on its uptake from people who have experienced a stroke or TIA. METHOD: A cross-sectional, electronic survey comprising multiple choice and free text questions. Convenience sampling was used to recruit people who have experienced a stroke/TIA in the UK/Ireland. RESULTS: The survey was completed by 377 stroke/TIA survivors. 87% (328/377) had either received the first vaccine dose or were booked to have it. The vaccine was declined by 2% (7/377) and 3% (11/377) had been offered the vaccine but not yet taken it up. 8% (30/377) had not been offered the vaccine despite being eligible. Some people expressed concerns around the safety of the vaccine (particularly risk of blood clots and stroke) and some were hesitant to have the second vaccine. Societal and personal benefits were motivations for vaccine uptake. There was uncertainty and lack of information about risk of COVID-19 related complications specifically for people who have experienced a stroke or TIA. CONCLUSION: Despite high uptake of the first vaccine, some people with stroke and TIA have legitimate concerns and information needs that should be addressed. Our findings can be used to identify targets for behaviour change to improve vaccine uptake specific to stroke/TIA patients.

Wu, G., et al. (2022). "A survey on the safety of the SARS-CoV-2 vaccine among a population with stroke risk in China." Front Med (Lausanne) **9**: 859682.

BACKGROUND: The safety of the COVID-19 vaccine in patients at stroke risk is poorly understood. METHODS: A survey was conducted on risk factors related to stroke and adverse reactions to vaccines. The participants were divided into low-, medium-, and high-risk groups, according to the stroke risk scorecard recommended by the Stroke Prevention and Control Engineering Committee of the National Health and Family Planning Commission. Factors associated with adverse reactions were analyzed. Reasons for non-vaccination and the aggravation of underlying diseases after vaccination were

investigated. RESULTS: 1747 participants participated (138 unvaccinated) and 36.8, 22.1, 41.1% of the vaccinated participants had low, medium, high risk of stroke, respectively. The incidence of adverse reactions after the first and second injection was 16.6, 13.7%, respectively. There was no difference in the incidence of adverse reactions among different risk groups. Sex, vaccine type, sleep quality, worry of adverse reactions, age, and education level were significantly related to adverse reactions to vaccination. The most popular reason for non-vaccination for medium- or high risk-participants was the aggravation of the existing disease. Only 0.3% of vaccinated participants reported slight changes in blood pressure, sugar levels, and lipid levels. No aggravation of stroke sequelae, atrial fibrillation, or transient ischemic attack was reported. CONCLUSIONS: Vaccination against COVID-19 (inactive virus) is safe for people at risk of stroke when the existing disease condition is stable. It is suggested to strengthen vaccine knowledge and ensure good sleep before vaccination.

Ye, X., et al. (2023). "Sex-based differences in risk of ischaemic stroke or systemic embolism after BNT162b2 or CoronaVac COVID-19 vaccination in patients with atrial fibrillation: a self-controlled case series and nested case-control study." Eur Heart J Cardiovasc Pharmacother **9**(5): 403-412.

AIMS: Patients with atrial fibrillation (AF) have a higher risk of ischaemic stroke or systemic embolism, with a greater risk for female patients. This study aims to evaluate the risk of ischaemic stroke or systemic embolism and bleeding following COVID-19 vaccination in patients with AF and the sex differences. METHODS AND RESULTS: Self-controlled case series (SCCS) analysis was conducted to evaluate the risk of ischaemic stroke or systemic embolism and bleeding following BNT162b2 or CoronaVac in patients with AF, using the territory-wide electronic medical records from the Hospital Authority and vaccination records from the Department of Health in Hong Kong. Patients with a primary diagnosis of ischaemic stroke, systemic embolism, or bleeding in the inpatient setting between 23 February 2021 and 31 March 2022 were included. A nested case-control analysis was also conducted with each case randomly matched with 10 controls according to sex, age, Charlson comorbidity index, and date of hospital admission. Conditional Poisson regression was used in the SCCS analysis, and conditional logistic regression was used in the nested case-control analysis to assess the risks, and all analyses were stratified by sex and type of vaccines. Among 51 158 patients with AF, we identified an increased risk of ischaemic stroke or systemic embolism after the first dose of BNT162b2 in SCCS analysis during 0-13 days [incidence rate ratio 6.60, 95% confidence interval (CI) 1.51-28.77] and 14-27 days (6.53, 95% CI 1.31-32.51), and nested case-control analysis during 0-13 days (adjusted odds ratio 6.21, 95% CI 1.14-33.91) and 14-27 days (5.52, 95% CI 1.12-27.26) only in female patients. The increased risk in female patients following the first dose of CoronaVac was only detected during 0-13 days (3.88, 95% CI 1.67-9.03) in the nested case-control analysis. No increased risk of ischaemic stroke or systemic embolism was identified in male patients, and no increased risk of bleeding was detected in all patients with AF for both vaccines. An increased risk of ischaemic stroke or systemic embolism after COVID-19 was also observed in both females (17.42, 95% CI 5.08-59.73) and males (6.63, 95% CI 2.02-21.79). CONCLUSIONS:

The risk of ischaemic stroke or systemic embolism after COVID-19 vaccination was only increased in female patients with AF. However, as the risk after COVID-19 was even higher, proactive uptake of COVID-19 vaccines is recommended to prevent the potential severe outcomes after infection.

Yoshida, K., et al. (2022). "Repeated Cardioembolic Stroke after COVID-19 mRNA Vaccination: A Case Report." J Stroke Cerebrovasc Dis **31**(2): 106233.

OBJECTIVE: There have been no reports suggesting a relationship between the COVID-19 mRNA vaccines that encodes the spike glycoprotein of SARS-CoV-2 and cerebrovascular disease. A case of repeated cardioembolic stroke after vaccination with the BNT162b2 (Pfizer) COVID-19 mRNA vaccine is presented. METHODS: Imaging and laboratory findings, treatment decisions, and the outcome of this case are presented. RESULTS: An 83-year-old Japanese woman developed right hemiplegia and motor aphasia three days after receiving her first dose of the BNT162b2 (Pfizer) COVID-19 mRNA vaccine. She had been taking rivaroxaban for persistent atrial fibrillation for 10 years, but had no symptomatic ischemic strokes. On magnetic resonance imaging (MRI) the left middle cerebral artery (MCA) was occluded. Intravenous recombinant tissue-plasminogen activator (rt-PA) therapy and mechanical thrombectomy were performed, and she recovered almost fully. However, three days after the second dose, she developed left hemiplegia and left hemispatial neglect. MRI showed occlusion of the right MCA. Only mechanical thrombectomy was performed again, but it could not be resumed due to the hard thrombus. DISCUSSION: In this case, it is difficult to exclude a causal relationship between the COVID-19 mRNA vaccine and ischemic stroke. This association needs to be carefully monitored.

Tachycardia

Abdallah, W., et al. (2022). "Fetal supraventricular tachycardia and maternal COVID-19 vaccination: is there any relationship?" Future Sci OA **8**(7): FSO812.

Fetal supraventricular tachycardia accounts for 60-80% of the fetal tachyarrhythmias with prevalence ranging from 1/1000 to 1/25 000 pregnancies. It may be secondary to fetal anomalies or maternal factors. By reviewing the literature, there is no previous article that reports fetal arrhythmia after maternal vaccination. We present herein two cases of fetal supraventricular tachycardia following the administration of the Pfizer-BioNTech COVID-19 vaccine during pregnancy. Continued safety monitoring and more longitudinal follow-up are needed to evaluate the fetal impact after maternal COVID-19 vaccination.

Bassareo, P. P., K. Mihali and K. P. Walsh (2022). "Ventricular tachycardia triggered by the first dose of an adenoviral vector-based COVID-19 vaccine in an adult patient with congenital heart disease." Clin Case Rep **10**(9): e6064.

A unique adverse event of adenoviral COVID-19 vaccine in an adult patient with congenital heart disease is reported.

Dionne, A., et al. (2021). "Association of Myocarditis With BNT162b2 Messenger RNA COVID-19 Vaccine in a Case Series of Children." JAMA Cardiol **6**(12): 1446-1450.

IMPORTANCE: The BNT162b2 (Pfizer-BioNTech) messenger RNA COVID-19 vaccine was authorized on May 10, 2021, for emergency use in children aged 12 years and older. Initial reports showed that the vaccine was well tolerated without serious adverse events; however, cases of myocarditis have been reported since approval. OBJECTIVE: To review results of comprehensive cardiac imaging in children with myocarditis after COVID-19 vaccine. DESIGN, SETTING, AND PARTICIPANTS: This study was a case series of children younger than 19 years hospitalized with myocarditis within 30 days of BNT162b2 messenger RNA COVID-19 vaccine. The setting was a single-center pediatric referral facility, and admissions occurred between May 1 and July 15, 2021. MAIN OUTCOMES AND MEASURES: All patients underwent cardiac evaluation including an electrocardiogram, echocardiogram, and cardiac magnetic resonance imaging. RESULTS: Fifteen patients (14 male patients [93%]; median age, 15 years [range, 12-18 years]) were hospitalized for management of myocarditis after receiving the BNT162b2 (Pfizer) vaccine. Symptoms started 1 to 6 days after receipt of the vaccine and included chest pain in 15 patients (100%), fever in 10 patients (67%), myalgia in 8 patients (53%), and headache in 6 patients (40%). Troponin levels were elevated in all patients at admission (median, 0.25 ng/mL [range, 0.08-3.15 ng/mL]) and peaked 0.1 to 2.3 days after admission. By echocardiographic examination, decreased left ventricular (LV) ejection fraction (EF) was present in 3 patients (20%), and abnormal global longitudinal or circumferential strain was present in 5 patients (33%). No patient had a pericardial effusion. Cardiac magnetic resonance imaging findings were consistent with myocarditis in 13 patients (87%) including late gadolinium enhancement in 12 patients (80%),

regional hyperintensity on T2-weighted imaging in 2 patients (13%), elevated extracellular volume fraction in 3 patients (20%), and elevated LV global native T1 in 2 patients (20%). No patient required intensive care unit admission, and median hospital length of stay was 2 days (range 1-5). At follow-up 1 to 13 days after hospital discharge, 11 patients (73%) had resolution of symptoms. One patient (7%) had persistent borderline low LV systolic function on echocardiogram (EF 54%). Troponin levels remained mildly elevated in 3 patients (20%). One patient (7%) had nonsustained ventricular tachycardia on ambulatory monitor. CONCLUSIONS AND RELEVANCE: In this small case series study, myocarditis was diagnosed in children after COVID-19 vaccination, most commonly in boys after the second dose. In this case series, in short-term follow-up, patients were mildly affected. The long-term risks associated with postvaccination myocarditis remain unknown. Larger studies with longer follow-up are needed to inform recommendations for COVID-19 vaccination in this population.

Dykes, K. C. and C. M. Kessler (2022). "First report of COVID-19 vaccine induced flare of compensated congenital thrombotic thrombocytopenic purpura." Blood Coagul Fibrinolysis **33**(1): 71-73.

Eldokla, A. M. and M. T. Numan (2022). "Postural orthostatic tachycardia syndrome after mRNA COVID-19 vaccine." Clin Auton Res **32**(4): 307-311.

Garcia, M. T. M., et al. (2023). "[Reply to "Tachycardia, adverse effect, COVID-19 vaccine"]." Enferm Infecc Microbiol Clin **41**(1): 65-66.

Gomez-Moyano, E., et al. (2023). "Postural orthostatic tachycardia syndrome and other related dysautonomic disorders after SARS-CoV-2 infection and after COVID-19 messenger RNA vaccination." Front Neurol **14**: 1221518.

The COVID-19 pandemic has caused a challenge for our society due to the post-acute sequelae of the disease. Persistent symptoms and long-term multiorgan complications, known as post-acute COVID-19 syndrome, can occur beyond 4 weeks from the onset of the COVID-19 infection. Postural orthostatic tachycardia syndrome (POTS) is considered a variety of dysautonomia, which is characterized by chronic symptoms that occur with standing and a sustained increase in heart rate, without orthostatic hypotension. POTS can lead to debilitating symptoms, significant disability, and impaired quality of life. In this narrative review, the etiopathogenic basis, epidemiology, clinical manifestations, diagnosis, treatment, prognosis, and socioeconomic impact of POTS, as well as other related dysautonomic disorders, after COVID-19 infection and SARS-CoV-2 postvaccination, were discussed. After a search conducted in March 2023, a total of 89 relevant articles were selected from the PubMed, Google Scholar, and Web of Science databases. The review highlights the importance of recognizing and managing POTS after COVID-19 infection and vaccination, and the approach to autonomic disorders should be known by all specialists in different medical areas. The diagnosis of POTS requires a comprehensive clinical assessment, including a detailed medical history, physical examination, orthostatic vital signs, and autonomic function tests. The treatment of

POTS after COVID-19 infection or vaccination is mainly focused on lifestyle modifications, such as increased fluid and salt intake, exercise, and graduated compression stockings. Pharmacotherapy, such as beta-blockers, fludrocortisone, midodrine, and ivabradine, may also be used in selected cases. Further research is needed to understand the underlying mechanisms, risk factors, and optimal treatment strategies for this complication.

Guglin, M. E., et al. (2023). "Fulminant Myocarditis and Cardiogenic Shock Following COVID-19 Infection Versus COVID-19 Vaccination: A Systematic Literature Review." J Clin Med **12**(5).

BACKGROUND: Myocarditis, diagnosed by symptoms and troponin elevation, has been well-described with COVID-19 infection, as well as shortly after COVID-19 vaccination. The literature has characterized the outcomes of myocarditis following COVID-19 infection and vaccination, but clinicopathologic, hemodynamic, and pathologic features following fulminant myocarditis have not been well-characterized. We aimed to compare clinical and pathological features of fulminant myocarditis requiring hemodynamic support with vasopressors/inotropes and mechanical circulatory support (MCS), in these two conditions. METHODS: We analyzed the literature on fulminant myocarditis and cardiogenic shock associated with COVID-19 and COVID-19 vaccination and systematically reviewed all cases and case series where individual patient data were presented. We searched PubMed, EMBASE, and Google Scholar for "COVID", "COVID-19", and "coronavirus" in combination with "vaccine", "fulminant myocarditis", "acute heart failure", and "cardiogenic shock". The Student's t-test was used for continuous variables and the chi2 statistic was used for categorical variables. For non-normal data distributions, the Wilcoxon Rank Sum Test was used for statistical comparisons. RESULTS: We identified 73 cases and 27 cases of fulminant myocarditis associated with COVID-19 infection (COVID-19 FM) and COVID-19 vaccination (COVID-19 vaccine FM), respectively. Fever, shortness of breath, and chest pain were common presentations, but shortness of breath and pulmonary infiltrates were more often present in COVID-19 FM. Tachycardia, hypotension, leukocytosis, and lactic acidosis were seen in both cohorts, but patients with COVID-19 FM were more tachycardic and hypotensive. Histologically, lymphocytic myocarditis dominated both subsets, with some cases of eosinophilic myocarditis in both cohorts. Cellular necrosis was seen in 44.0% and 47.8% of COVID-19 FM and COVID-19 vaccine FM, respectively. Vasopressors and inotropes were used in 69.9% of COVID-19 FM and in 63.0% of the COVID-19 vaccine FM. Cardiac arrest was observed more in COVID-19 FM ($p = 0.008$). Venoarterial extracorporeal membrane oxygenation (VA-ECMO) support for cardiogenic shock was also used more commonly in the COVID-19 fulminant myocarditis group ($p = 0.0293$). Reported mortality was similar (27.7%) and 27.8%, respectively) but was likely worse for COVID-19 FM as the outcome was still unknown in 11% of cases. CONCLUSIONS: In the first series to retrospectively assess fulminant myocarditis associated with COVID-19 infection versus COVID-19 vaccination, we found that both conditions had a similarly high mortality rate, while COVID-19 FM had a more malignant course with more symptoms on presentation, more profound hemodynamic decompensation (higher heart rate, lower blood pressure), more cardiac arrests, and higher temporary MCS requirements including VA-ECMO. In terms of

pathology, there was no difference in most biopsies/autopsies that demonstrated lymphocytic infiltrates and some eosinophilic or mixed infiltrates. There was no predominance of young males in COVID-19 vaccine FM cases, with male patients representing only 40.9% of the cohort.

Han, J., et al. (2022). "Case report: Myocarditis with nonsustained ventricular tachycardia following COVID-19 mRNA vaccination in a female adolescent." Front Pediatr **10**: 995167.

Children with underlying medical conditions potentially develop severe illness from Coronavirus disease 2019 (COVID-19). The use of vaccines against COVID-19 is currently recommended for the pediatric population. The COVID-19 vaccine has a temporal association with the occurrence of myocarditis. Although most patients with COVID-19 vaccination-associated myocarditis (C-VAM) exhibit a mild clinical course and rapid recovery, C-VAM potentially causes electrical instability and sudden cardiac death. Herein, we report the case of a 17-year-old woman who presented with chest pain and syncope following the first dose of the messenger RNA COVID-19 vaccine. The patient's heart function was impaired, and nonsustained ventricular tachycardia was frequent. Cardiac magnetic resonance (CMR) imaging satisfied the criteria for myocarditis. Despite the administration of immunomodulatory drugs, the patient's heart function was not fully restored, and the concentration of cardiac enzymes remained above the normal range. Persistence of late gadolinium enhancement was observed on short-term follow-up CMR imaging. Although most patients with C-VAM exhibit mild symptoms, significant cardiac arrhythmias potentially occur. Furthermore, some patients with C-VAM demonstrate prolonged impaired heart function and sustained late gadolinium enhancement on follow-up CMR imaging. Therefore, monitoring of electrical and functional cardiac abnormalities in patients with C-VAM is crucial and the long-term outcomes and prognosis of patients with C-VAM require further investigation.

Hermel, M., et al. (2022). "COVID-19 Vaccination Might Induce Postural Orthostatic Tachycardia Syndrome: A Case Report." Vaccines (Basel) **10**(7).

We report a case of new-onset postural orthostatic tachycardia syndrome in a healthy 46-year-old female after a single dose of the BNT162b2 (Pfizer-BioNTech) SARS-CoV-2 vaccine. There have been three prior reports of new-onset postural orthostatic tachycardia syndrome after COVID-19 vaccination. Predominant symptoms noted included fatigue, brain fog, headache, sinus tachycardia, and dizziness. Management includes noninvasive therapies, behavioral approaches, and pharmacologic regimens. Here, the patient presented with fatigue, palpitations, dizziness, and presyncope, with symptoms beginning 7 days after vaccination. Presenting vitals included temperature within normal limits, inappropriate tachycardia, up to 120 beats per minute, blood pressure of 128/87 mm of mercury, and 100% saturation in room air. Her management included lifestyle changes, dietary supplements, and ivabradine. Further studies are needed to evaluate prevalence, etiology, and optimal management.

Horiuchi, K., et al. (2022). "Fulminant myocarditis after the first dose of mRNA-1273 vaccination in a patient with previous COVID-19: a case report." Eur Heart J Case Rep **6**(7): ytac290.

BACKGROUND: COVID-19 vaccines have shown success in protecting people worldwide, although serious adverse effects have been reported in very rare cases. CASE SUMMARY: A 32-year-old male with a prior medical history of mild COVID-19 infection developed fulminant myocarditis five days after mRNA-1273 vaccination (first dose), which was confirmed using endomyocardial biopsy. He acutely developed respiratory failure and cardiogenic shock with ventricular tachycardia, but recovered completely with short-term high-dose steroid therapy and mechanical cardiac support, which is the recommended treatment for fulminant lymphocytic myocarditis. DISCUSSION: COVID-19 vaccine-induced myocarditis varies from mild to severe. In the present case, the patient was treated as for fulminant lymphocytic myocarditis and recovered relatively quickly. The mechanism of COVID-19 vaccine-associated myocarditis needs to be urgently investigated.

Kwan, A. C., et al. (2022). "Apparent Risks of Postural Orthostatic Tachycardia Syndrome Diagnoses After COVID-19 Vaccination and SARS-Cov-2 Infection." Nat Cardiovasc Res **1**(12): 1187-1194.

Postural orthostatic tachycardia syndrome (POTS) has been previously described after SARS-CoV-2 infection; however, limited data is available on the relation of POTS with COVID-19 vaccination. Here we show in a cohort of 284,592 COVID-19 vaccinated individuals using a sequence-symmetry analysis, that the odds of POTS are higher 90 days after vaccine exposure than 90 days prior to exposure, and that the odds for POTS are higher than referent conventional primary care diagnoses, but lower than the odds of new POTS diagnosis after SARS-CoV-2 infection. Our results identify a possible association between COVID-19 vaccination and incidence of POTS. Notwithstanding the probable low incidence of POTS after COVID-19 vaccination, particularly when compared to SARS-Cov-2 post-infection odds which were five times higher, our results suggest that further studies, are needed to investigate the incidence and etiology of POTS occurring after COVID-19 vaccination.

Kyaw, H., et al. (2022). "COVID-19 mRNA Vaccine-Associated Myocarditis." Cureus **14**(1): e21009.

Coronavirus disease 2019 (COVID-19) has been reported to cause cardiovascular complications including myocarditis, pericardial effusion, pericarditis, and arrhythmias. With the introduction of the vaccine, there have been reports of myocarditis possibly associated with the mRNA COVID-19 vaccine. We report a case of cardiac involvement following the second dose of Pfizer-BioNTech COVID-19 vaccine in a young male. A healthy 24-year-old male presented to the emergency department with complaints of non-radiating mid-sternal chest pain and pressure. He noticed his symptoms started six hours after he received the second dose of Pfizer COVID vaccine. Laboratory tests revealed elevated cardiac troponin I-CtNI levels. Computed tomography angiography of the chest did not show evidence of pulmonary embolism. Given his presentation of acute chest pain associated with elevated troponin levels, a coronary angiogram was performed which revealed normal coronary arteries. He was subsequently treated for acute peri-myocarditis with colchicine, non-steroidal anti-inflammatory drugs (NSAIDs),

and beta-blockers for tachycardia and the prevention of arrhythmia. Although rare, clinicians should be aware of the risk for myocarditis and pericarditis, which should be considered in individuals presenting with chest pain within a week after vaccination, especially in the younger population. Although the long-term risk in these patients is uncertain, early diagnosis and treatment are key to minimizing complications.

Lee, D. Y., C. Y. Lin and S. S. Huang (2022). "Ventricular tachycardia because of myocardial infarction after COVID-19 vaccination." J Arrhythm **38**(5): 824-826.

Lin, W., et al. (2022). "Ventricular tachycardia from myocarditis following COVID-19 vaccination with tozinameran (BNT162b2, Pfizer-BioNTech)." Pacing Clin Electrophysiol **45**(9): 1097-1100.

To combat the coronavirus disease 2019 (COVID-19) pandemic, many countries have started population vaccination programs using messenger ribonucleic acid (mRNA) vaccines. With the widespread use of such vaccines, reports are emerging worldwide, of the vaccine's association with the development of myocarditis. Younger men are more likely to develop postvaccine myocarditis, which usually presents as self-limiting chest pain within a week after the second dose. We present a case of myocarditis following vaccination with tozinameran (BNT162b2, Pfizer-BioNTech), which presented late, with ventricular tachycardia (VT) reduced left ventricular ejection fraction (LVEF).

Lin, Y. T., P. Y. Chen and Y. J. Su (2022). "Paroxysmal supra-ventricular ventricular tachycardia after AstraZeneca COVID-19 vaccine injection." New Microbes New Infect **45**: 100965.

Maharaj, N., et al. (2023). "Suspected COVID-19 mRNA Vaccine-Induced Postural Orthostatic Tachycardia Syndrome." Cureus **15**(1): e34236.

We present a case of a 15-year-old South Asian male who developed suspected postural orthostatic tachycardia syndrome (POTS) two weeks after receiving the Pfizer-BioNTech coronavirus disease 2019 (COVID-19) vaccine booster, which was successfully managed with low-dose fludrocortisone and ivabradine. Clinicians should be aware of the Pfizer-BioNTech COVID-19 vaccine being implicated with the onset of POTS.

Manfredi, R., et al. (2022). "Clinical Profiles and CMR Findings of Young Adults and Pediatrics with Acute Myocarditis Following mRNA COVID-19 Vaccination: A Case Series." Vaccines (Basel) **10**(2).

Messenger RNA (mRNA) coronavirus disease of 2019 (COVID-19) vaccines have been recently associated with acute myocarditis, predominantly in healthy young males. Out of 231,989 vaccines administrated in our region (Marche, Italy), we report a case series of six healthy patients (four males and two females, 16.5 years old (Q1, Q3: 15, 18)) that experienced mRNA-COVID-19-vaccines side effects. All patients were hospitalized due to fever and troponins elevation following the second dose of an mRNA-based COVID-19 vaccine. Cardiovascular magnetic resonance (CMR) was performed 72-96 h after vaccination. All patients were treated with colchicine and ibuprofen. Myocarditis was prevalent in males. It was characterized by myocardial edema and late gadolinium enhancement (LGE) in the lateral wall of the left ventricle (LV). One patient showed sole

right ventricular involvement, while the females presented with myopericarditis (myocarditis + pericardial effusion). All patients in our series had preserved LV ejection fraction and remained clinically stable during a relatively short inpatient hospital stay. One case presented with atrial tachycardia. At the follow-up, no significant CMR findings were documented after a three-month medical treatment. According to other recently published case series, our report suggests a possible association between acute myocarditis and myopericarditis with mRNA COVID-19 vaccination in healthy young adults and pediatric patients. Not only males are involved, while some arrhythmic manifestations are possible, such as atrial tachycardia. Conversely, we here highlight the benign nature of such complications and the absence of CMR findings after a three-month medical treatment with colchicine and ibuprofen.

Marco Garcia, M. T., et al. (2021). "Tachycardia as an undescribed adverse effect to the Comirnaty(c) vaccine (BNT162b2 Pfizer-BioNTech Covid-19 vaccine): Description of 3 cases with a history of SARS-CoV-2 disease." Enferm Infecc Microbiol Clin (Engl Ed) **40**(5): 276-277.

Marco Garcia, M. T., et al. (2022). "Tachycardia as an undescribed adverse effect to the Comirnaty(c) vaccine (BNT162b2 Pfizer-BioNTech Covid-19 vaccine): Description of 3 cases with a history of SARS-CoV-2 disease." Enferm Infecc Microbiol Clin (Engl Ed) **40**(5): 276-277.

Martins-Filho, P. R. (2023). "Tachycardia following Pfizer-BioNTech COVID-19 vaccine." Enferm Infecc Microbiol Clin (Engl Ed) **41**(1): 62-63.

Miri, C., et al. (2022). "Pulmonary embolism with junctional tachycardia: A serious complication after COVID-19 vaccination." Ann Med Surg (Lond) **80**: 103983.

INTRODUCTION: the association between the development of a thromboembolic event following COVID-19 vaccination is very rare, it represents less than 0.1% of vaccinated cases. Until now this association remains to be discussed. CASE PRESENTATION: A 49-year-old man presented to the Emergency Department a 7-day after receiving her second dose of BNT162b2 mRNA COVID-19 (Pfizer-BioNTech), and he was diagnosed with pulmonary embolism (PE) with junctional tachycardia on ECG. The biological workup showed an increase in CRP with elevated D-dimer, but no abnormalities in cardiac markers, including troponin and BNP, the COVID-19 testing was negative and absence of thrombocytopenia. The patient was put under curative anticoagulation by rivaroxabon. DISCUSSION: Studies have reported the association of venous thrombosis after administration of the COVID-19 vaccine with negative FP4 antibodies and normal platelet count which is similar with our patient. Moreover, spike proteins generated by mRNA vaccines can produce a pro-inflammatory state, a cascade of events guiding to endothelial dysfunction and afterwards to the development of venous thrombosis. CONCLUSION: All the same that some studies association COVID-19 immunizations to the development of VTE, we nevertheless recommend COVID-19 vaccination, due to the rarity of these events, compared to the hypercoagulable effects and other serious complications of COVID-19 infection.

Ojo, A., et al. (2023). "Recurrent ventricular tachycardia in a patient with COVID-19 vaccine-associated myocarditis: a case report." Ann Transl Med **11**(6): 267.

BACKGROUND: The development of coronavirus disease 2019 (COVID-19) vaccine-associated myocarditis has been reported. Most of the reported cases are mild, with quick clinical recovery and excellent short-term outcomes. Cases of COVID-19 vaccine-associated myocarditis presenting with sustained ventricular tachycardia (VT) are rare. CASE DESCRIPTION: A 46-year-old male patient with no prior cardiac history presented following two episodes of syncope. Two days earlier, he had received his second dose of COVID-19 mRNA vaccine (Pfizer)-first dose was administered three weeks earlier. He had an episode of VT while in the emergency room. His cardiac magnetic resonance imaging (MRI) findings were consistent with myocarditis. He was eventually diagnosed with COVID-19 vaccine-associated myocarditis after all other work up were unremarkable [echocardiogram, coronary angiogram, diagnostic electrophysiology study and later (18)F-fluorodeoxyglucose (FDG) metabolism cardiac sarcoid positron emission tomography (PET) study]. An implantable cardiac monitor was implanted to monitor for recurrence of VT. Seven months after initial presentation, he had recurrent VT and he underwent implantation of an implantable cardioverter defibrillator (ICD). He has received appropriate ICD therapies on account of recurrent VT and he is currently maintained on an antiarrhythmic medication. CONCLUSIONS: Excellent short-term outcomes have been reported in patients with COVID-19 vaccine associated myocarditis. Our case shows that long-term outcomes may not be benign in everyone, particularly in those who develop myocardial scar.

Park, J., et al. (2022). "A case of transient POTS following COVID-19 vaccine." Acta Neurol Belg **122**(4): 1081-1083.

Reddy, S., S. Reddy and M. Arora (2021). "A Case of Postural Orthostatic Tachycardia Syndrome Secondary to the Messenger RNA COVID-19 Vaccine." Cureus **13**(5): e14837.

Postural orthostatic tachycardia syndrome (POTS) is an impaction of the autonomic nervous system initiating orthostatic tachycardia. There are numerous triggers for POTS including viruses, vaccines, and an autoimmune basis. This case report is clinically relevant to better understand the pathophysiology behind the messenger RNA (mRNA) coronavirus disease 2019 (COVID-19) vaccine and the mechanism that triggers autonomic nervous system dysfunction. Furthermore, the overall goal of this case study is to report a unique side effect associated with the novel mRNA COVID-19 vaccine. A 42-year-old male, with no prior symptoms of sinus tachycardia and presyncope episodes, is diagnosed with POTS secondary to the first dose of the mRNA COVID-19 vaccine. Symptoms to this date include sinus tachycardia, dizziness, headaches, and fatigue that are often triggered after a large meal or standing for a longer duration. Numerous diagnostic tests and images failed to confirm any other diagnosis other than POTS. There was a sequential connection between the onset of symptoms approximately one week after taking the first dose of the mRNA COVID-19 vaccine. Currently, POTS in this patient is controlled by lifestyle modification. This case report has broader implications as it can help us understand how the mRNA vaccine works on the body relative to the immune

system. Our theory is that the development of antibodies activates an autoimmune reaction that triggers POTS disease. The prevalence of the POTS dysautonomia post-vaccination will be clearer as more data and research are conducted on the side effects from the innovative mRNA vaccines created to combat severe acute respiratory syndrome coronavirus 2.

Rubin, R. (2023). "Large Cohort Study Finds Possible Association Between Postural Orthostatic Tachycardia Syndrome and COVID-19 Vaccination but Far Stronger Link With SARS-CoV-2 Infection." JAMA **329**(6): 454-456.

This Medical News story discusses a study that found possible associations between postural orthostatic tachycardia syndrome (POTS) and COVID-19 vaccination and SARS-CoV-2 infection.

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Sanada, Y., et al. (2022). "Overlapping Myocarditis and Postural Orthostatic Tachycardia Syndrome After COVID-19 Messenger RNA Vaccination: A Case Report." Cureus **14**(11): e31006.

The worldwide spread of the coronavirus disease 2019 (COVID-19) pandemic and the significant morbidity and mortality rate associated with it led to the rapid development of several COVID-19 vaccines. While serious side effects related to the vaccines are rare, various adverse events have been reported to occur after COVID-19 messenger RNA (mRNA) vaccination, including myocarditis, Guillain-Barre syndrome, and thrombosis. Postural orthostatic tachycardia syndrome (POTS) is a chronic cardiovascular dysautonomia among young and middle-aged individuals. Although the pathophysiology of POTS is thought to be heterogeneous, vaccine-induced immune-mediated autonomic dysfunction is hypothesized to be one cause of the syndrome. In this report, we present a case of myocarditis and POTS occurring in a 13-year-old male following COVID-19 mRNA vaccination. He presented with persistent severe fatigue and headache. The patient's symptoms improved after intravenous immunoglobulin for myocarditis, non-pharmacologic interventions, and multiple medications for POTS.

Sheth, S. P. and R. Gandhi (2023). "Ventricular Arrhythmia and COVID-19 Vaccine-associated Myocarditis." Pediatr Infect Dis J **42**(4): e112-e113.

17-year-old male presented with COVID-19 vaccine-associated myocarditis. Six months later, due to chest discomfort with exercise, the patient underwent an exercise stress test that revealed a 3-beat run of nonsustained ventricular tachycardia at 230 bpm at peak exercise. The long-term outcomes of COVID-19 vaccine-associated myocarditis are unclear. This patient had nonsustained ventricular tachycardia over 6 months after diagnosis.

Shouman, K., et al. (2021). "Autonomic dysfunction following COVID-19 infection: an early experience." Clin Auton Res **31**(3): 385-394.

PURPOSE: Post-COVID-19 syndrome is a poorly understood aspect of the current pandemic, with clinical features that overlap with symptoms of autonomic/small fiber dysfunction. An early systematic analysis of autonomic dysfunction following COVID-19

is lacking and may provide initial insights into the spectrum of this condition. METHODS: We conducted a retrospective review of all patients with confirmed history of COVID-19 infection referred for autonomic testing for symptoms concerning for para-/postinfectious autonomic dysfunction at Mayo Clinic Rochester or Jacksonville between March 2020 and January 2021. RESULTS: We identified 27 patients fulfilling the search criteria. Symptoms developed between 0 and 122 days following the acute infection and included lightheadedness (93%), orthostatic headache (22%), syncope (11%), hyperhidrosis (11%), and burning pain (11%). Sudomotor function was abnormal in 36%, cardiovagal function in 27%, and cardiovascular adrenergic function in 7%. The most common clinical scenario was orthostatic symptoms without tachycardia or hypotension (41%); 22% of patients fulfilled the criteria for postural tachycardia syndrome (POTS), and 11% had borderline findings to support orthostatic intolerance. One patient each was diagnosed with autoimmune autonomic ganglionopathy, inappropriate sinus tachycardia, vasodepressor syncope, cough/vasovagal syncope, exacerbation of preexisting orthostatic hypotension, exacerbation of sensory and autonomic neuropathy, and exacerbation of small fiber neuropathy. CONCLUSION: Abnormalities on autonomic testing were seen in the majority of patients but were mild in most cases. The most common finding was orthostatic intolerance, often without objective hemodynamic abnormalities on testing. Unmasking/exacerbation of preexisting conditions was seen. The temporal association between infection and autonomic symptoms implies a causal relationship, which however cannot be proven by this study.

Sookaromdee, P. and V. Wiwanitkit (2023). "Tachycardia, adverse effect, COVID-19 vaccine: Correspondence." Enferm Infecc Microbiol Clin (Engl Ed) **41**(1): 65.

Tate, C., L. Demashkieh and W. Hakmeh (2021). "Isolated Tachycardia Presenting After Pfizer-BioNTech COVID-19 Vaccination." Cureus **13**(7): e16706.

A 29-year-old woman presented to the emergency department with palpitations and a heart rate of over 140 beats per minute that started approximately six to eight hours after administration of her second COVID-19 vaccination. Many side effects have been associated with the administration of vaccines. We present the first documented case of tachycardia and palpitations, in the absence of other signs or symptoms, presenting within hours of receiving the Pfizer-BioNTech COVID-19 vaccination. Clinicians should be aware that this appears to be benign and resolved within 24 hours in our patient.

Teresa Marco Garcia, M., et al. (2023). "Reply to "Tachycardia, adverse effect, COVID-19 vaccine"." Enferm Infecc Microbiol Clin (Engl Ed) **41**(1): 65-66.

Truong, D. T., et al. (2022). "Clinically Suspected Myocarditis Temporally Related to COVID-19 Vaccination in Adolescents and Young Adults: Suspected Myocarditis After COVID-19 Vaccination." Circulation **145**(5): 345-356.

BACKGROUND: Understanding the clinical course and short-term outcomes of suspected myocarditis after the coronavirus disease 2019 (COVID-19) vaccination has important public health implications in the decision to vaccinate youth. METHODS: We

retrospectively collected data on patients <21 years old presenting before July 4, 2021, with suspected myocarditis within 30 days of COVID-19 vaccination. Lake Louise criteria were used for cardiac MRI findings. Myocarditis cases were classified as confirmed or probable on the basis of the Centers for Disease Control and Prevention definitions. RESULTS: We report on 139 adolescents and young adults with 140 episodes of suspected myocarditis (49 confirmed, 91 probable) at 26 centers. Most patients were male (n=126, 90.6%) and White (n=92, 66.2%); 29 (20.9%) were Hispanic; and the median age was 15.8 years (range, 12.1-20.3; interquartile range [IQR], 14.5-17.0). Suspected myocarditis occurred in 136 patients (97.8%) after the mRNA vaccine, with 131 (94.2%) after the Pfizer-BioNTech vaccine; 128 (91.4%) occurred after the second dose. Symptoms started at a median of 2 days (range, 0-22; IQR, 1-3) after vaccination. The most common symptom was chest pain (99.3%). Patients were treated with nonsteroidal anti-inflammatory drugs (81.3%), intravenous immunoglobulin (21.6%), glucocorticoids (21.6%), colchicine (7.9%), or no anti-inflammatory therapies (8.6%). Twenty-six patients (18.7%) were in the intensive care unit, 2 were treated with inotropic/vasoactive support, and none required extracorporeal membrane oxygenation or died. Median hospital stay was 2 days (range, 0-10; IQR, 2-3). All patients had elevated troponin I (n=111, 8.12 ng/mL; IQR, 3.50-15.90) or T (n=28, 0.61 ng/mL; IQR, 0.25-1.30); 69.8% had abnormal ECGs and arrhythmias (7 with nonsustained ventricular tachycardia); and 18.7% had left ventricular ejection fraction <55% on echocardiogram. Of 97 patients who underwent cardiac MRI at a median 5 days (range, 0-88; IQR, 3-17) from symptom onset, 75 (77.3%) had abnormal findings: 74 (76.3%) had late gadolinium enhancement, 54 (55.7%) had myocardial edema, and 49 (50.5%) met Lake Louise criteria. Among 26 patients with left ventricular ejection fraction <55% on echocardiogram, all with follow-up had normalized function (n=25). CONCLUSIONS: Most cases of suspected COVID-19 vaccine myocarditis occurring in persons <21 years have a mild clinical course with rapid resolution of symptoms. Abnormal findings on cardiac MRI were frequent. Future studies should evaluate risk factors, mechanisms, and long-term outcomes.

Tv, P., et al. (2023). "Postural orthostatic tachycardia syndrome-like symptoms following COVID-19 vaccination: An overview of clinical literature." Hum Antibodies **31**(1-2): 9-17.

BACKGROUND: Postural Orthostatic Tachycardia Syndrome (POTS) is a common condition affecting more than 170 people per 100,000 population. However, POTS following COVID-19 vaccination remains a rare reporting in the medical literature. OBJECTIVE: We, herein, summarize and highlight the evidence that has been reported regarding POTS-like symptoms following COVID-19 vaccination. METHODS: We conducted a literature search and summarized the findings in the form of a narrative commentary. All types of publications (case reports/series, original articles, letters to editors, brief communications etc.) in English language were included. RESULTS: Whilst the exact pathogenetic mechanism behind POTS is yet to elucidated, there has been increasing evidence pointing towards an autoimmune dysfunction. Females were found to be predominantly affected (72%) with age range from 17 years to 52 years. Additionally, it seems that POTS-like symptoms could be triggered after immunization

with Pfizer- BioNTech, Moderna, and Oxford-AstraZeneca COVID-19 vaccines. The symptoms typically appear within the first week, depending upon previous exposure to the virus and presence of other systemic conditions. In some patients, the condition is self-resolving. However, in others, non-pharmacological interventions coupled with negative ionotropic medications can be used for symptomatic management of the patients. CONCLUSIONS: Timely diagnosis and proper treatment are quintessential for ensuring early alleviation (and in some cases complete resolution) of symptoms. Furthermore, there may be episodes of relapse. Overall prognosis of the new-onset POTS-like symptoms is difficult to predict based on current literature.

Visclosky, T., et al. (2021). "Myocarditis Following mRNA COVID-19 Vaccine." Pediatr Emerg Care **37**(11): 583-584.

A growing number of adolescents are being diagnosed with acute myocarditis following mRNA COVID-19 vaccinations. This case describes an adolescent who presented to the emergency department with chest pain and tachycardia following the Pfizer-BioNTech COVID-19 vaccination. Point-of-care ultrasound was performed prior to the return of laboratory studies and revealed depressed left ventricular systolic function. Point-of-care ultrasound may be a tool used to rapidly diagnose or risk stratify patients with potential post-COVID-19 vaccine myocarditis.

Yamamoto, J., et al. (2023). "Myocarditis with ventricular tachycardia following bivalent COVID-19 mRNA vaccination." CJC Open.

Thrombocytopenia

Ahmed, S. H., et al. (2022). "SARS-CoV-2 vaccine-associated-tinnitus: A review." Ann Med Surg (Lond) **75**: 103293.

The global vaccination drive against severe acute respiratory syndrome coronavirus-2 is being pursued at a historic pace. Unexpected adverse effects have been reported following vaccination, including thrombotic thrombocytopenia, myocarditis, amongst others. More recently, some cases of tinnitus are reported post-vaccination. According to the Vaccine Adverse Events Reporting System (VAERS), 12,247 cases of coronavirus post-vaccination tinnitus have been reported till September 14, 2021. To the best of our knowledge, this is the first review evaluating any otologic manifestation following vaccine administration and aims to evaluate the potential pathophysiology, clinical approach, and treatment. Although the incidence is infrequent, there is a need to understand the precise mechanisms and treatment for vaccine-associated-tinnitus.

Al-Rasbi, S., et al. (2022). "Myocarditis, Pulmonary Hemorrhage, and Extensive Myositis with Rhabdomyolysis 12 Days After First Dose of Pfizer-BioNTech BNT162b2 mRNA COVID-19 Vaccine: A Case Report." Am J Case Rep **23**: e934399.

BACKGROUND The COVID-19 pandemic is a current global crisis, and there are hundreds of millions of individuals being vaccinated worldwide. At present, there have been few reports of COVID-19 vaccine-induced autoimmune processes manifested as myositis, thrombocytopenia, and myocarditis. CASE REPORT A 37-year-old man presented to the Emergency Department (ED) with a 3-day history of back pain and a 1-day history of left upper limb swelling with paresthesia and shortness of breath, 12-days after receiving the first dose of Pfizer/BioNTech BNT162b2 mRNA COVID-19 vaccine. He was diagnosed with severe myositis complicated with rhabdomyolysis and non-oliguric acute kidney injury, thrombocytopenia, myocarditis with pulmonary edema, and pulmonary hemorrhage. Screens for potential toxic, infectious, paraneoplastic, and autoimmune disorders were unremarkable. The patient was treated with a 5-day course of intravenous methylprednisolone and intravenous immunoglobulin, with a good response. He was hospitalized for 16 days and discharged home on a tapering dose of oral prednisolone for 6 weeks. CONCLUSIONS The case describes a possible link between Pfizer/BioNTech BNT162b2 mRNA COVID-19 vaccine and immune-mediated myocarditis, pulmonary vasculitis, myositis, and thrombocytopenia. However, further data are required to confirm such an association.

Alislambouli, M., et al. (2022). "Acquired thrombotic thrombocytopenic purpura following Pfizer COVID-19 vaccination." EJHaem **3**(1): 207-210.

Acquired thrombotic thrombocytopenic purpura (aTTP) is a rare disease and has occasionally been described after vaccination, especially against viral agents. We present a case of a patient who presents with the classic pentad of TTP a few days after receiving the first dose of the mRNA Pfizer COVID-19 vaccine. To our knowledge, this is the second report of a de novo TTP following mRNA Pfizer COVID-19 vaccination.

Asaduzzaman, M., et al. (2022). "COVID-19 mRNA vaccine-associated encephalopathy, myocarditis, and thrombocytopenia with excellent response to methylprednisolone: A case report." J Neuroimmunol **368**: 577883.

INTRODUCTION: Large-scale vaccination is considered one of the most effective strategies to control the pandemic of COVID-19. Since its start, different complications have been described thought to be related to vaccination. Here, we present a rare case where encephalopathy, myocarditis, and thrombocytopenia developed simultaneously following the second dose of Pfizer-BioNTech mRNA vaccine (BNT162b2). CASE PRESENTATION: A 15-years-old female presented with fever, altered consciousness, and convulsions after taking the second shot of the vaccine. Clinical and laboratory workup was notable for the presence of thrombocytopenia and myocarditis. No alternative causes of encephalitis were found. The patient responded significantly to methylprednisolone suggesting underlying immune pathogenesis responsible for the clinical features. The diagnostic criteria for possible autoimmune encephalitis were also fulfilled. CONCLUSION: Although rare, the clinician should be aware of the possible adverse events following COVID-19 vaccination. Further research with large pooled data is needed to get more insight into its pathogenesis and causal relationship.

Bae, D. H., et al. (2022). "Simultaneous Occurrence of Immune-Mediated Thrombocytopenia and Myocarditis After mRNA-1273 COVID-19 Vaccination: A Case Report." J Korean Med Sci **37**(21): e169.

With the global spread of severe acute respiratory syndrome coronavirus 2, several vaccines were developed; messenger RNA (mRNA) vaccines have recently been widely used worldwide. However, the incidence of myocarditis following mRNA vaccination is increasing; although the cause of myocarditis has not yet been clearly identified, it is presumed to be caused by a problem in the innate immune system. Immune-mediated thrombocytopenia (ITP) after vaccination is rare but has been reported and is also assumed to occur by the same mechanism. We report the first case of simultaneous myocarditis and ITP after mRNA vaccination. A 38-year-old woman presented with chest pain, mild dyspnea, and sweating after vaccination with mRNA-1273 vaccine (Moderna) 4 days prior to admission. Upon admission to the emergency department, cardiac enzymes were elevated; blood test performed 5 months ago showed normal platelet count, but severe thrombocytopenia was observed upon admission. After administration of intravenous immunoglobulin, the platelet count improved; subsequently, myocarditis was observed on endomyocardial biopsy. Thus, myocarditis and ITP were judged to have occurred simultaneously due to the expression of the innate immune system markers after mRNA vaccination. The patient was discharged on day 6 of admission.

Barda, N., et al. (2021). "Safety of the BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting." N Engl J Med **385**(12): 1078-1090.

BACKGROUND: Preapproval trials showed that messenger RNA (mRNA)-based vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) had a good safety profile, yet these trials were subject to size and patient-mix limitations. An evaluation of

the safety of the BNT162b2 mRNA vaccine with respect to a broad range of potential adverse events is needed. METHODS: We used data from the largest health care organization in Israel to evaluate the safety of the BNT162b2 mRNA vaccine. For each potential adverse event, in a population of persons with no previous diagnosis of that event, we individually matched vaccinated persons to unvaccinated persons according to sociodemographic and clinical variables. Risk ratios and risk differences at 42 days after vaccination were derived with the use of the Kaplan-Meier estimator. To place these results in context, we performed a similar analysis involving SARS-CoV-2-infected persons matched to uninfected persons. The same adverse events were studied in the vaccination and SARS-CoV-2 infection analyses. RESULTS: In the vaccination analysis, the vaccinated and control groups each included a mean of 884,828 persons. Vaccination was most strongly associated with an elevated risk of myocarditis (risk ratio, 3.24; 95% confidence interval [CI], 1.55 to 12.44; risk difference, 2.7 events per 100,000 persons; 95% CI, 1.0 to 4.6), lymphadenopathy (risk ratio, 2.43; 95% CI, 2.05 to 2.78; risk difference, 78.4 events per 100,000 persons; 95% CI, 64.1 to 89.3), appendicitis (risk ratio, 1.40; 95% CI, 1.02 to 2.01; risk difference, 5.0 events per 100,000 persons; 95% CI, 0.3 to 9.9), and herpes zoster infection (risk ratio, 1.43; 95% CI, 1.20 to 1.73; risk difference, 15.8 events per 100,000 persons; 95% CI, 8.2 to 24.2). SARS-CoV-2 infection was associated with a substantially increased risk of myocarditis (risk ratio, 18.28; 95% CI, 3.95 to 25.12; risk difference, 11.0 events per 100,000 persons; 95% CI, 5.6 to 15.8) and of additional serious adverse events, including pericarditis, arrhythmia, deep-vein thrombosis, pulmonary embolism, myocardial infarction, intracranial hemorrhage, and thrombocytopenia. CONCLUSIONS: In this study in a nationwide mass vaccination setting, the BNT162b2 vaccine was not associated with an elevated risk of most of the adverse events examined. The vaccine was associated with an excess risk of myocarditis (1 to 5 events per 100,000 persons). The risk of this potentially serious adverse event and of many other serious adverse events was substantially increased after SARS-CoV-2 infection. (Funded by the Ivan and Francesca Berkowitz Family Living Laboratory Collaboration at Harvard Medical School and Clalit Research Institute.).

Bidari, A., et al. (2023). "Immune thrombocytopenic purpura secondary to COVID-19 vaccination: A systematic review." Eur J Haematol **110**(4): 335-353.

INTRODUCTION: This systematic review aimed to retrieve patients diagnosed with de novo immune thrombocytopenic purpura (ITP) after COVID-19 immunization to determine their epidemiological characteristics, clinical course, therapeutic strategies, and outcome. MATERIALS AND METHODS: We conducted the review using four major databases, comprising PubMed, Scopus, Web of Science, and the Cochrane library, until April 2022. A systematic search was performed in duplicate to access eligible articles in English. Furthermore, a manual search was applied to the chosen papers' references to enhance the search sensitivity. Data were extracted and analyzed with the SPSS 20.1 software. RESULTS: A total of 77 patients with de novo COVID-19 vaccine-associated ITP were identified from 41 studies, including 31 case reports and 10 case series. The median age of patients who developed COVID-19 vaccine-associated ITP was 54 years (IQR 36-72 years). The mRNA-based COVID-19 vaccines, including BNT16B2b2 and

mRNA-1273, were most implicated (75.4%). Those were followed by the adenovirus vector-based vaccines, inclusive of ChAdOx1 nCoV-19 and vAd26.COV2.S. No report was found relating ITP to other COVID-19 vaccines. Most cases (79.2%) developed ITP after the first dose of COVID-19 vaccination. 75% of the patients developed ITP within 12 days of vaccination, indicating a shorter lag time compared to ITP after routine childhood vaccinations. Sixty-seven patients (87%) patients were hospitalized. The management pattern was similar to primary ITP, and systemic glucocorticoids, IVIg, or both were the basis of the treatment in most patients. Most patients achieved therapeutic goals; only two individuals required a secondary admission, and one patient who presented with intracranial hemorrhage died of the complication. CONCLUSIONS: De novo ITP is a rare complication of COVID-19 vaccination, and corresponding reports belong to mRNA-based and adenovirus vector-based vaccines, in order of frequency. This frequency pattern may be related to the scale of administration of individual vaccines and their potency in inducing autoimmunity. The more the COVID-19 vaccine is potent to induce antigenic challenge, the shorter the lag time would be. Most patients had a benign course and responded to typical treatments of primary ITP.

Blauenfeldt, R. A., et al. (2021). "Thrombocytopenia with acute ischemic stroke and bleeding in a patient newly vaccinated with an adenoviral vector-based COVID-19 vaccine." J Thromb Haemost **19**(7): 1771-1775.

We describe the first Danish case of presumed inflammatory and thrombotic response to vaccination with an adenoviral (ChAdOx1) vector-based COVID-19 vaccine (AZD1222). The case describes a 60-year-old woman who was admitted with intractable abdominal pain 7 days after receiving the vaccine. Computed tomography of the abdomen revealed bilateral adrenal hemorrhages. On the following day, she developed a massive right-sided ischemic stroke and magnetic resonance imaging angiography showed occlusion of the right internal carotid artery. The ischemic area was deemed too large to offer reperfusion therapy. During admission, blood tests showed a remarkable drop in platelet counts from 118,000 to 5000 per mul and a substantial increase in D-dimer. The patient died on the sixth day of hospitalization. Blood tests revealed platelet factor 4 reactive antibodies, imitating what is seen in heparin-induced thrombocytopenia. This may be a novel immune-mediated response to the vaccine.

Cascio Rizzo, A., G. Giussani and E. C. Agostoni (2022). "Ischemic Stroke and Vaccine-Induced Immune Thrombotic Thrombocytopenia following COVID-19 Vaccine: A Case Report with Systematic Review of the Literature." Cerebrovasc Dis **51**(6): 722-734.

INTRODUCTION: Vaccine-induced immune thrombotic thrombocytopenia (VITT) is a prothrombotic syndrome observed after adenoviral vector-based vaccines for severe acute respiratory syndrome coronavirus 2. It is characterized by thrombocytopenia, systemic activation of coagulation, extensive venous thrombosis, and anti-platelet factor 4 antibodies. Arterial thrombosis is less common and mainly affects the aorta, peripheral arteries, heart, and brain. Several cases of ischemic stroke have been reported in VITT, often associated with large vessel occlusion (LVO). Here, we describe a case of ischemic stroke with LVO after Ad26.COV2.S vaccine, then we systematically reviewed the

published cases of ischemic stroke and VITT following COVID-19 vaccination. METHODS: We describe a 58-year-old woman who developed a thrombotic thrombocytopenia syndrome with extensive splanchnic vein thrombosis and ischemic stroke due to right middle cerebral artery (MCA) occlusion, 13 days after receiving Ad26.COV2.S vaccination. Then, we performed a systematic review of the literature until December 3, 2021 using PubMed and EMBASE databases. The following keywords were used: ("COVID-19 vaccine") AND ("stroke"), ("COVID-19 vaccine") AND ("thrombotic thrombocytopenia"). We have selected all cases of ischemic stroke in VITT. RESULTS: Our study included 24 patients. The majority of the patients were females (79.2%) and younger than 60 years of age (median age 45.5 years). Almost all patients (96%) received the first dose of an adenoviral vector-based vaccine. Ischemic stroke was the presenting symptom in 18 patients (75%). Splanchnic venous thrombosis was found in 10 patients, and cerebral venous thrombosis in 5 patients (21%). Most patients (87.5%) had an anterior circulation stroke, mainly involving MCA. Seventeen patients (71%) had an intracranial LVO. We found a high prevalence of large intraluminal thrombi (7 patients) and free-floating thrombus (3 patients) in extracranial vessels, such as the carotid artery, in the absence of underlying atherosclerotic disease. Acute reperfusion therapy was performed in 7 of the 17 patients with LVO (41%). One patient with a normal platelet count underwent intravenous thrombolysis with alteplase, while 6 patients underwent mechanical thrombectomy. A malignant infarct occurred in 9 patients and decompressive hemicraniectomy was performed in 7 patients. Five patients died (21%). CONCLUSION: Our study points out that, in addition to cerebral venous thrombosis, adenoviral vector-based vaccines also appear to have a cerebral arterial thrombotic risk, and clinicians should be aware that ischemic stroke with LVO, although rare, could represent a clinical presentation of VITT.

Congiu, T., et al. (2022). "Ultrastructural findings of lung injury due to Vaccine-induced Immune Thrombotic Thrombo- cytopenia (VITT) following COVID-19 vaccination: a scanning electron microscopic study." Eur Rev Med Pharmacol Sci **26**(1): 270-277.

Vaccine-induced immune thrombotic thrombocytopenia (VITT) is a rare new syndrome occurring after the ChAdOx1 nCoV-19 vaccine immunization. Patients with VITT are characterized by a variable clinical presentation, likewise also the outcome of these patients is very variable. Here we report the lung ultrastructural findings in the course of VITT of a 58-year-old male patient. Alveoli were mainly dilated, irregular in shape, and occupied by a reticular network of fibrin, while interalveolar septa appeared thickened. The proliferation of small capillaries gave rise to plexiform structures and pulmonary capillary hemangiomatosis-like features. Near the alveoli occupied by a dense fibrin network, the medium-sized arteries showed a modified wall and an intraluminal thrombus. This scenario looks quite similar to that found during COVID-19, where the lungs suffer from the attack of the antigen-antibodies complexes and the virus respectively. In both diseases, the final outcome is a severe inflammation, activation of the haemostatic system and fibrinolysis.

Deucher, W., S. Sukumar and S. R. Cataland (2022). "Clinical relapse of immune-mediated thrombotic thrombocytopenic purpura following COVID-19 vaccination." Res Pract Thromb Haemost **6**(1): e12658.

De novo and relapsed immune-mediated thrombotic thrombocytopenic purpura (iTTP) have been documented to have occurred following severe acute respiratory syndrome coronavirus 2 (COVID-19) vaccination. Here, we present a case of a 28-year-old woman who received the tozinameran (BNT162b2, Pfizer-BioNtech) vaccine for COVID-19 and experienced an iTTP relapse during longitudinal follow-up. She received the vaccine 30 months after her initial diagnosis, while she was in clinical remission. She was not in complete ADAMTS-13 remission, as she had undetectable ADAMTS-13 activity during follow-up except for one isolated measurement of 48%. Shortly after vaccination, she developed complaints of bruising, petechiae, ataxia, and an episode of slurred speech. Laboratory testing demonstrated thrombocytopenia, schistocytes, and eventually undetectable ADAMTS-13 activity. She was successfully treated with caplacizumab, rituximab, and corticosteroids without plasma exchange. She achieved complete clinical and ADAMTS-13 remission after treatment. We recommend caution in the administration of COVID-19 vaccines for survivors of iTTP in remission with severely deficient ADAMTS-13 activity.

Elrashdy, F., et al. (2021). "Autoimmunity roots of the thrombotic events after COVID-19 vaccination." Autoimmun Rev **20**(11): 102941.

Although vaccination represents the most promising way to stop or contain the coronavirus disease 2019 (COVID-19) pandemic and safety and effectiveness of available vaccines were proven, a small number of individuals who received anti-SARS-CoV-2 vaccines developed a prothrombotic syndrome. Vaccine-induced immune thrombotic thrombocytopenia (VITT) can be triggered by the adenoviral vector-based vaccine, whereas lipid nanoparticle-mRNA-based vaccines can induce rare cases of deep vein thrombosis (DVT). Although the main pathogenic mechanisms behind this rare phenomenon have not yet been identified, both host and vaccine factors might be involved, with pathology at least in part being related to the vaccine-triggered autoimmune reaction. In this review, we are considering some aspects related to pathogenesis, major risk factors, as well as peculiarities of diagnosis and treatment of this rare condition.

Fang, F., B. Tse and K. Pavenski (2022). "Relapse of immune thrombotic thrombocytopenic purpura (iTTP) possibly triggered by COVID-19 vaccination and/or concurrent COVID-19 infection." BMJ Case Rep **15**(7).

Thrombotic thrombocytopenic purpura (TTP) is a life-threatening disease that may be triggered by inflammation, including infection or vaccination. Since the start of the COVID-19 pandemic, several case reports were published on de novo or relapsed immune TTP (iTTP) in COVID-19-infected patients. Case reports of iTTP episodes following vaccination against COVID-19 are also emerging. We report a case of relapsed iTTP in a patient who received Moderna mRNA-1273 SARS-CoV-2 vaccine and developed concurrent severe COVID-19 infection. The patient's iTTP was successfully managed with

caplacizumab, therapeutic plasma exchange and high-dose steroids. We summarise published cases of iTTP associated with COVID-19 infection or vaccination.

Ferro, J. M., et al. (2021). "European stroke organization interim expert opinion on cerebral venous thrombosis occurring after SARS-CoV-2 vaccination." Eur Stroke J **6**(3): CXVI-CXXI.

Severe cases of cerebral venous thrombosis (CVT) with thrombocytopenia and anti-platelet factor 4 (PF4) antibodies occurring after adenoviral vector anti-SARS-CoV-2 vaccines have been recently reported. We aim to present a guidance document on the diagnosis and treatment of patients presenting with CVT after vaccination against SARS-CoV-2 infection. We reviewed the available evidence which consists on case reports, small case series, expert opinion and analogy with heparin-induced thrombocytopenia (HIT) management. Because of the low level of evidence, this is an interim document, based only on expert opinion consensus. In patients presenting with CVT after being vaccinated against SARS-CoV-2 infection, if there is thrombocytopenia a reliable HIT PF4 Antibody ELISA test should be performed, to confirm vaccine-induced immune thrombotic thrombocytopenia (VITT). In patients with CVT and thrombocytopenia, in whom VITT is suspected or confirmed, heparin (unfractionated or low molecular weight) should be avoided and non-heparin anticoagulants are preferred. If possible, platelet transfusions should be avoided. If the diagnosis of VITT is confirmed or suspected, early intravenous immunoglobulins are indicated. This expert opinion is supported by low quality evidence. It should be periodically updated, or changed to a formal guideline, as new and higher quality evidence is eventually produced. Because of their potential unfavourable clinical course, patients developing symptoms and signs suggestive of CVT after being vaccinated against SARS-CoV-2 virus should undergo urgent clinical and neuroimaging evaluation. In cases of suspected or confirmed VITT, non-heparin anticoagulants should be used, platelet transfusions avoided and intravenous immunoglobulin started early.

Galassi, G., et al. (2022). "Coincidental Onset of Ocular Myasthenia Gravis Following ChAdOx1 n-CoV-19 Vaccine against Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)." Isr Med Assoc J **24**(1): 9-10.

The Oxford-AstraZeneca vaccine ChAdOx1 (AZD1222, Vaxzevria) is playing a crucial role in counteracting the coronavirus disease-2019 (COVID-19) pandemic [1]. Since March 2021, reports of unexpected thrombotic events associated with thrombocytopenia and vaccination have been published [2]. To the best of our knowledge there is only one report about vaccination-associated myasthenia gravis (MG) occurring after a second dose of BNT162b2 (Pfizer-BioNTech).

Giovane, R. and J. Campbell (2021). "Bilateral Thalamic Stroke: A Case of COVID-19 Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT) or a Coincidence Due to Underlying Risk Factors?" Cureus **13**(10): e18977.

Vaccine-induced immune thrombotic thrombocytopenia (VITT) is a rare but potentially life-threatening side effect that has only been observed in adenovirus-based vaccines for coronavirus disease 2019 (COVID-19). VITT is an immune-mediated condition that

generally presents within five to 10 days post-vaccination with thrombosis, thrombocytopenia, and coagulation abnormalities. A diagnosis of VITT is made clinically and through laboratory testing. Although VITT is an important differential to consider, it is believed that more emphasis should be placed on vaccination due to the safety and efficacy in overcoming COVID-19.

Giuffrida, G., et al. (2022). "Relapse of immune-mediated thrombotic thrombocytopenic purpura following mRNA COVID-19 vaccination: a prospective cohort study." Haematologica **107**(11): 2661-2666.

Immune-mediated thrombotic thrombocytopenic purpura (iTTP) is a rare and life-threatening disease. Vaccination has been reported to be a trigger of onset and relapse of autoimmune diseases. We evaluated after mRNA COVID-19 vaccination 32 adult patients previously diagnosed with iTTP by means of weekly monitoring of complete blood count and ADAMTS13 testing. Thirty of 32 patients received at least one dose of Pfizer-BioNTech, the remaining two received Moderna. A total of five patients, all vaccinated with Pfizer-BioNTech, had a biochemical relapse at a median post-vaccination time of 15 days following the second or third vaccine dose, presenting without measurable ADAMTS13 activity and a median anti- ADAMTS13 autoantibody value of 34 U/mL. Four of five cases had concomitant clinical relapse and were treated with corticosteroids alone or daily sessions of plasma exchange and caplacizumab, while one patient was closely monitored with ADAMTS13 with no onset of anemia and thrombocytopenia. Although the benefits of vaccination exceed its potential risks, clinicians should be aware that iTTP relapse might follow COVID-19 vaccination. Therefore, laboratory and clinical monitoring of iTTP patients should be done in the first post-vaccination month, in order to promptly diagnose and treat any relapse.

Goldman, M. and C. Hermans (2021). "Thrombotic thrombocytopenia associated with COVID-19 infection or vaccination: Possible paths to platelet factor 4 autoimmunity." PLoS Med **18**(5): e1003648.

Michel Goldman and Cedric Hermans discuss thrombotic mechanisms in COVID-19 and rare adverse reactions to SARS-CoV-2 vaccinations.

Guo, W., et al. (2022). "Profiling COVID-19 Vaccine Adverse Events by Statistical and Ontological Analysis of VAERS Case Reports." Front Pharmacol **13**: 870599.

Since the beginning of the COVID-19 pandemic, vaccines have been developed to mitigate the spread of SARS-CoV-2, the virus that causes COVID-19. These vaccines have been effective in reducing the rate and severity of COVID-19 infection but also have been associated with various adverse events (AEs). In this study, data from the Vaccine Adverse Event Reporting System (VAERS) was queried and analyzed via the Cov19VaxKB vaccine safety statistical analysis tool to identify statistically significant (i.e., enriched) AEs for the three currently FDA-authorized or approved COVID-19 vaccines. An ontology-based classification and literature review were conducted for these enriched AEs. Using VAERS data as of 31 December 2021, 96 AEs were found to be statistically significantly associated with the Pfizer-BioNTech, Moderna, and/or Janssen COVID-19 vaccines. The

Janssen COVID-19 vaccine had a higher crude reporting rate of AEs compared to the Moderna and Pfizer COVID-19 vaccines. Females appeared to have a higher case report frequency for top adverse events compared to males. Using the Ontology of Adverse Event (OAE), these 96 adverse events were classified to different categories such as behavioral and neurological AEs, cardiovascular AEs, female reproductive system AEs, and immune system AEs. Further statistical comparison between different ages, doses, and sexes was also performed for three notable AEs: myocarditis, GBS, and thrombosis. The Pfizer vaccine was found to have a closer association with myocarditis than the other two COVID-19 vaccines in VAERS, while the Janssen vaccine was more likely to be associated with thrombosis and GBS AEs. To support standard AE representation and study, we have also modeled and classified the newly identified thrombosis with thrombocytopenia syndrome (TTS) AE and its subclasses in the OAE by incorporating the Brighton Collaboration definition. Notably, severe COVID-19 vaccine AEs (including myocarditis, GBS, and TTS) rarely occur in comparison to the large number of COVID-19 vaccinations administered in the United States, affirming the overall safety of these COVID-19 vaccines.

Harris, D. A., et al. (2023). "Comparative Risks of Potential Adverse Events Following COVID-19 mRNA Vaccination Among Older US Adults." JAMA Netw Open **6**(8): e2326852.

IMPORTANCE: Head-to-head safety comparisons of the mRNA vaccines for SARS-CoV-2 are needed for decision making; however, current evidence generalizes poorly to older adults, lacks sufficient adjustment, and inadequately captures events shortly after vaccination. Additionally, no studies to date have explored potential variation in comparative vaccine safety across subgroups with frailty or an increased risk of adverse events, information that would be useful for tailoring clinical decisions. OBJECTIVE: To compare the risk of adverse events between mRNA vaccines for COVID-19 (mRNA-1273 and BNT162b2) overall, by frailty level, and by prior history of the adverse events of interest. DESIGN, SETTING, AND PARTICIPANTS: This retrospective cohort study was conducted between December 11, 2020, and July 11, 2021, with 28 days of follow-up following the week of vaccination. A novel linked database of community pharmacy and Medicare claims data was used, representing more than 50% of the US Medicare population. Community-dwelling, fee-for-service beneficiaries aged 66 years or older who received mRNA-1273 vs BNT162b2 as their first COVID-19 vaccine were identified. Data analysis began on October 18, 2022. EXPOSURE: Dose 1 of mRNA-1273 vs BNT162b2 vaccine. MAIN OUTCOMES AND MEASURES: Twelve potential adverse events (eg, pulmonary embolism, thrombocytopenia purpura, and myocarditis) were assessed individually. Frailty was measured using a claims-based frailty index, with beneficiaries being categorized as nonfrail, prefrail, and frail. The risk of diagnosed COVID-19 was assessed as a secondary outcome. Generalized linear models estimated covariate-adjusted risk ratios (RRs) and risk differences (RDs) with 95% CIs. RESULTS: This study included 6 388 196 eligible individuals who received the mRNA-1273 or BNT162b2 vaccine. Their mean (SD) age was 76.3 (7.5) years, 59.4% were women, and 86.5% were White. A total of 38.1% of individuals were categorized as prefrail and 6.0% as frail. The risk of all outcomes was low in both vaccine groups. In adjusted models, the mRNA-1273

vaccine was associated with a lower risk of pulmonary embolism (RR, 0.96 [95% CI, 0.93-1.00]; RD, 9 [95% CI, 1-16] events per 100 000 persons) and other adverse events in subgroup analyses (eg, 11.0% lower risk of thrombocytopenia purpura among individuals categorized as nonfrail). The mRNA-1273 vaccine was also associated with a lower risk of diagnosed COVID-19 (RR, 0.86 [95% CI, 0.83-0.87]), a benefit that was attenuated by frailty level (frail: RR, 0.94 [95% CI, 0.89-0.99]). CONCLUSIONS AND RELEVANCE: In this cohort study of older US adults, the mRNA-1273 vaccine was associated with a slightly lower risk of several adverse events compared with BNT162b2, possibly due to greater protection against COVID-19. Future research should seek to formally disentangle differences in vaccine safety and effectiveness and consider the role of frailty in assessments of COVID-19 vaccine performance.

Hines, A., et al. (2021). "Immune thrombocytopenic purpura and acute liver injury after COVID-19 vaccine." BMJ Case Rep **14**(7).

A 26-year-old woman was sent to the emergency room by her primary care physician for a new petechial rash and thrombocytopenia 2 weeks after receiving the Moderna mRNA-1273 SARS-CoV-2 vaccine. Her hospital course was complicated by transaminitis. Her platelet count improved to normal on hospital day 5 after receiving intravenous steroids and intravenous immunoglobulin to treat her suspected diagnosis of immune thrombocytopenic purpura. Extensive workup for her thrombocytopenia and transaminitis was unremarkable including ruling out infectious, autoimmune and toxic causes. A liver biopsy was unrevealing and her transaminitis was improved on discharge. Although not proven, the temporal relationship of her vaccination with thrombocytopenia and abnormal liver enzymes points towards the Moderna mRNA-1273 SARS-CoV-2 vaccine as the most likely inciting factor.

Jasaraj, R. B., et al. (2021). "Immune Thrombocytopenic Purpura Following Pfizer-BioNTech COVID-19 Vaccine in an Elderly Female." Cureus **13**(8): e16871.

Mass vaccination campaigns are being run all over the globe to combat the ongoing COVID-19 pandemic. There have been several reports of immune thrombocytopenic purpura (ITP) occurrence following COVID-19 vaccination. However, ITP due to the Pfizer-BioNTech vaccine has been rarely reported, and a causal link has not been identified. The pathophysiology behind immune thrombocytopenia is similar to heparin-induced thrombocytopenia. The management is also similar to other secondary immune thrombocytopenia. We present a case of a 67-year old female diagnosed with immune thrombocytopenia following Pfizer-BioNTech vaccination. The treatment was resistant to high-dose steroids, intravenous immunoglobulin (IVIG), and rituximab and eventually responded to a thrombopoietin-stimulating agent.

Julian, J. A., D. R. Mathern and D. Fernando (2021). "Idiopathic Thrombocytopenic Purpura and the Moderna Covid-19 Vaccine." Ann Emerg Med **77**(6): 654-656.

Kahn, F., O. Shannon and L. Bjorck (2021). "Thrombocytopenia with acute ischemic stroke and bleeding in a patient newly vaccinated with an adenoviral vector-based COVID-19 vaccine: COMMENT from Gruel et al.: RESPONSE from Kahn et al." J Thromb Haemost **19**(10): 2633.

Karabulut, K., A. Andronikashvili and A. H. Kapici (2021). "Recurrence of Thrombotic Thrombocytopenic Purpura after mRNA-1273 COVID-19 Vaccine Administered Shortly after COVID-19." Case Rep Hematol **2021**: 4130138.

Thrombotic thrombocytopenic purpura (TTP) is a potentially life-threatening consumptive coagulopathy requiring emergent diagnosis and timely treatment. It is characterized by microangiopathic hemolytic anemia and thrombocytopenia with the development of microthrombi caused by inherited or acquired deficiency of the von Willebrand factor-cleaving protease ADAMTS13 and resulting end-organ damage. Most of the cases are the result of acquired deficiency of ADAMTS13, for which the exact etiology is unknown but reported to be related to various autoimmune disorders, infections, and medications. Our case report features of a patient with a history of idiopathic thrombocytopenic purpura and thrombotic thrombocytopenic purpura, who developed a recurrence of TTP 5 days after his first dose of the mRNA Coronavirus disease 2019 (COVID-19) vaccine (mRNA-1273 vaccine) in the setting of recent COVID-19. The close temporal association between vaccine administration, recent COVID-19, and relapse of remitted TTP raises concern for an enhanced immune reaction to COVID-19 vaccine in the setting of recent COVID-19 and underlying autoimmune disease. The association is not absolute, but given the novelty of COVID-19 and the mRNA COVID-19 vaccine and the relapse timing, it leads us to pose this hypothesis. Vaccine distribution to a larger and more diverse population will allow for an increased rate of adverse event reporting. This case report exemplifies potential safety issues that may be encountered with new vaccine administration in patients with recent COVID-19 and underlying autoimmune disease. There are no specific recommendations for COVID-19 vaccine administration in such patients.

Kim, C. S., et al. (2022). "A call for vigilance: thrombotic thrombocytopenic syndrome caused by mRNA COVID-19 vaccine associated with muscle weakness." Blood Res **57**(1): 1-3.

Kolahchi, Z., M. Khanmirzaei and A. Mowla (2022). "Acute ischemic stroke and vaccine-induced immune thrombotic thrombocytopenia post COVID-19 vaccination; a systematic review." J Neurol Sci **439**: 120327.

INTRODUCTION: One of the rare but potentially serious side effects of COVID-19 vaccination is arterial and venous thrombosis. Acute ischemic stroke (AIS) cases have been reported post COVID-19 vaccination. Herein, we systematically reviewed the reported cases of AIS after COVID-19 vaccination. METHOD: This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline. We searched PubMed and Scopus until April 14, 2022 to find studies that reported AIS post COVID-19 vaccination. RESULTS: We found 447 articles. From those, 140 duplicates were removed. After screening and excluding irrelevant articles, 29 studies (43 patients) were identified to be included. From all cases,

22 patients (51.1%) were diagnosed with AIS associated with Vaccine-induced immune thrombotic thrombocytopenia (VITT). Among AIS associated with VITT group, all received viral vector vaccines except one. The majority of cases with AIS and VITT were female (17 cases, 77.2%) and aged below 60 years (15 cases, 68%). Fourteen patients (32.5%) had additional thrombosis in other sites. Four of them (0.09%) showed concurrent CVST and ischemic stroke. Hemorrhagic transformation following AIS occurred in 7 patients (16.27%). Among 43 patients with AIS, at least 6 patients (14%) died during hospital admission. CONCLUSION: AIS has been reported as a rare complication within 4 weeks post COVID-19 vaccination, particularly with viral vector vaccines. Health care providers should be familiar with this rare consequence of COVID-19 vaccination in particular in the context of VITT to make a timely diagnosis and appropriate treatment plan.

Kounis, N. G., et al. (2022). "Encephalitis, myocarditis, and thrombocytopenia after COVID-19 mRNA vaccination: Clinical and pathophysiological considerations." J Neuroimmunol **373**: 577988.

Krajewski, P. K. and J. C. Szepietowski (2021). "Immune thrombocytopenic purpura associated with COVID-19 Pfizer-BioNTech BNT16B2b2 mRNA vaccine." J Eur Acad Dermatol Venereol **35**(10): e626-e627.

Lane, S., A. Yeomans and S. Shakir (2022). "Reports of myocarditis and pericarditis following mRNA COVID-19 vaccination: a systematic review of spontaneously reported data from the UK, Europe and the USA and of the scientific literature." BMJ Open **12**(5): e059223.

OBJECTIVES: To combine spontaneously reported data from multiple countries to estimate reporting rate, and better understand risk factors for myocarditis and pericarditis following COVID-19 messenger RNA (mRNA) vaccines. DESIGN: Systematic review of spontaneously reported data from UK, USA and European Union/European Economic Area (EU/EEA) and of the scientific literature. DATA SOURCES: UK Yellow Card scheme, Vaccine Adverse Event Reporting System (VAERS), EudraVigilance were searched from date of vaccine launch to 14 March 2022-16 March 2022. PubMed/MEDLINE and Embase were searched to 15 March 2022. ELIGIBILITY CRITERIA: We included publicly available spontaneous reporting data for 'Myocarditis' and 'Pericarditis' from UK, USA and EU/EEA following COVID-19 mRNA vaccines. Pharmacoepidemiological observational studies investigating myocarditis/pericarditis following mRNA COVID-19 vaccines were included (no restrictions on language or date). Critical Appraisal Skills Programme tools assessed study quality. DATA EXTRACTION AND SYNTHESIS: Two researchers extracted data. Events of myocarditis and pericarditis were presented for each data source, stratified by vaccine, age, sex and dose (where available). Reporting rates were calculated for myocarditis and pericarditis for each population. For published pharmacoepidemiological studies, design, participant characteristics, and study results were tabulated. RESULTS: Overall, 18 204 myocarditis and pericarditis events were submitted to the UK, USA and EU/EEA regulators during the study period. Males represented 62.24% (n=11 331) of myocarditis and pericarditis

reports. In the UK and USA, most reports concerned vaccinees aged <40 years (59.7% and 47.3% of reported events, respectively); trends in age were less clear for EU/EEA. Reports were more frequent following a second dose (47.1% of reports, where data available). Reporting rates were consistent between the data sources. Thirty-two pharmacoepidemiological studies were included; results were consistent with our spontaneous report analyses. CONCLUSIONS: Younger vaccinees more frequently report myocarditis and pericarditis following mRNA COVID-19 vaccines than older vaccinees. Results from published literature supported the results of our analyses.

Lane, S., A. Yeomans and S. Shakir (2022). "Systematic review of spontaneous reports of myocarditis and pericarditis in transplant recipients and immunocompromised patients following COVID-19 mRNA vaccination." BMJ Open **12**(7): e060425.

OBJECTIVES: To determine whether spontaneous reporting rates of myocarditis and pericarditis differed in immunocompromised patients compared with the whole population overall, and in terms of demographics, vaccine dose and time-to-onset. DESIGN: Systematic review of spontaneously reported data from the European Union/European Economic Area (EU/EEA), the USA and the UK. DATA SOURCES: EudraVigilance (EU/EEA), Vaccine Adverse Event Reporting System (VAERS; USA) and the Medicines and Healthcare products Regulatory Agency (UK) spontaneous reporting databases were searched from date of vaccine launch to 1 December 2021. ELIGIBILITY CRITERIA: Publicly available spontaneous reporting data for 'myocarditis' and 'pericarditis' from EU/EEA and USA following COVID-19 messenger RNA vaccines. Reports with comorbidities or concurrent medication indicative of transplantation, HIV infection or cancer ('immunocompromised' population) were compared with each overall database population. DATA EXTRACTION AND SYNTHESIS: Two researchers extracted data. Spontaneously reported events of myocarditis and pericarditis were presented for immunocompromised populations for each data source, stratified by age, sex, dose and time-to-onset (where available). Seriousness of each event was determined according to the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guideline E2A definition. Proportional reporting ratio (PRR) was calculated. RESULTS: There were 178 reports of myocarditis and pericarditis among immunocompromised individuals overall. Seriousness was comparable between the immunocompromised and overall populations in both databases. No trends in age or sex were observed among immunocompromised individuals. Most reports followed a second vaccine dose and occurred within 14 days. The frequency of reporting was similar to the wider population (PRR=1.36 (95% CI=0.89 to 1.82) for VAERS population). CONCLUSIONS: Myocarditis and pericarditis following COVID-19 vaccination are very rare, and benefits of COVID-19 vaccination continue to outweigh any perceived risks. Reporting rates of myocarditis and pericarditis were similar in immunocompromised individuals, however defining characteristics differed compared with the whole population; therefore, continued monitoring of adverse events following vaccination remains vital to understand differences between population subgroups.

Lin, T. C., et al. (2023). "Vaccine-Induced Immune Thrombotic Thrombocytopenia following BNT162b2 mRNA COVID-19 Booster: A Case Report." Vaccines (Basel) **11**(6).

Vaccine-induced immune thrombotic thrombocytopenia (VITT) is a life-threatening complication caused by platelet activation via platelet factor 4 (PF4) antibodies. We report a healthy 28-year-old man who developed hemoptysis, bilateral leg pain, and headaches three weeks after his third dose of the COVID-19 vaccine with the first BNT162b2 (from Pfizer-BioNTech) injection. He had previously had the first and second doses with ChAdOx1 nCov-19 without any discomfort. Serial investigations demonstrated pulmonary embolisms, cerebral sinus, and deep iliac venous thrombosis. Positive PF4 antibody assay (ELISA) confirmed the diagnosis of VITT. He had a prompt response to intravenous immunoglobulins (IVIGs) at a total dose of 2 g/kg and his symptoms are now in remission with anticoagulant. Although the definite mechanism is unknown, the VITT was most likely triggered by his COVID-19 vaccine. We report this case of VITT following BNT162b2, a mRNA-based vaccine, and suggest that VITT could still happen without the adenoviral vector vaccines.

Luisa, V., et al. (2022). "Ischemic stroke shortly after vaccination against SARS-CoV-2: A case-control study." J Neurol Sci **436**: 120209.

BACKGROUND AND PURPOSE: Vaccination against SARS-CoV-2 has been associated with rare occurrences of severe venous thromboses. Very little data exist about arterial ischemic strokes. We have assessed the features of ischemic strokes occurring shortly after vaccination against SARS-CoV-2 in the Cremona area, Italy. METHODS: From February 1, to July 31, 2021, all patients with ischemic stroke within four weeks of vaccination against COVID-19 admitted to our stroke unit were consecutively collected, and their main features were compared with those of all other patients with ischemic strokes admitted during the same period. RESULTS: Sixteen strokes after vaccination were collected. They represented 10.5% of all ischemic strokes. Median interval from vaccination was 12 days (range 1-24). Fifteen (93.8%) had received the BNT162b2 (Pfizer-BioNTech) vaccine and 1 (6.2%) the ChAdOx1 nCoV-19 (AstraZeneca). Two patients (12.5%) had a mild thrombocytopenia on admission (128,000 and 142,000/ml), without any evidence of bleeding or venous thrombosis. Thrombolysis and/or thrombectomy were carried out in 4 cases (25.0%). When compared with 137 strokes without recent vaccination, none of the demographic, clinical, and laboratory features of post-vaccination strokes were significantly different. CONCLUSIONS: Ischemic strokes occurring shortly after COVID-19 vaccination at our center were similar to those of non-vaccinated patients. Therefore, the relatively high percentage of such patients probably relates to the very high fraction of elderly people vaccinated against SARS-CoV-2 in the Cremona area, rather than to a consequence of vaccination.

Malayala, S. V., et al. (2021). "A Case of Idiopathic Thrombocytopenic Purpura After Booster Dose of BNT162b2 (Pfizer-Biontech) COVID-19 Vaccine." Cureus **13**(10): e18985.

Vaccination is now considered the best measure in minimizing the morbidity and mortality from the Covid-19 pandemic. Almost all the vaccines are considered safe except for minor and occasional side effects. Some of the commonly reported

complications from the COVID-19 vaccines are vaccine-induced thrombotic thrombocytopenia (VITT)/thrombosis with thrombocytopenia syndrome/vaccine-induced pro-thrombotic immune thrombocytopenia syndrome. In this case report, we present a case of a 75-year-old female who had an uncomplicated first and second vaccine dose but developed VITT after the booster dose of the vaccine. The patient was treated with dexamethasone and platelet transfusions. So far no such cases have been reported after the third (booster) dose of the Pfizer-Biontech vaccine. With this case report, we present the case of the patient and discuss the literature related to vaccine-induced thrombocytopenia.

Mekheal, E. M., et al. (2022). "Coincidental or causal? A case report of acquired thrombotic thrombocytopenic purpura following mRNA-1273 Covid-19 vaccination." Hematol Transfus Cell Ther.

Miri, C., et al. (2022). "Pulmonary embolism with junctional tachycardia: A serious complication after COVID-19 vaccination." Ann Med Surg (Lond) **80**: 103983.

INTRODUCTION: the association between the development of a thromboembolic event following COVID-19 vaccination is very rare, it represents less than 0.1% of vaccinated cases. Until now this association remains to be discussed. CASE PRESENTATION: A 49-year-old man presented to the Emergency Department a 7-day after receiving her second dose of BNT162b2 mRNA COVID-19 (Pfizer-BioNTech), and he was diagnosed with pulmonary embolism (PE) with junctional tachycardia on ECG. The biological workup showed an increase in CRP with elevated D-dimer, but no abnormalities in cardiac markers, including troponin and BNP, the COVID-19 testing was negative and absence of thrombocytopenia. The patient was put under curative anticoagulation by rivaroxabon. DISCUSSION: Studies have reported the association of venous thrombosis after administration of the COVID-19 vaccine with negative FP4 antibodies and normal platelet count which is similar with our patient. Moreover, spike proteins generated by mRNA vaccines can produce a pro-inflammatory state, a cascade of events guiding to endothelial dysfunction and afterwards to the development of venous thrombosis. CONCLUSION: All the same that some studies association COVID-19 immunizations to the development of VTE, we nevertheless recommend COVID-19 vaccination, due to the rarity of these events, compared to the hypercoagulable effects and other serious complications of COVID-19 infection.

Ntelis, S. and K. Champ (2022). "Recurrence of Thrombotic Thrombocytopenic Purpura After Vaccination with mRNA-1273 COVID-19 vaccine." J Community Hosp Intern Med Perspect **12**(4): 80-84.

Thrombotic thrombocytopenic purpura (TTP) is a rare disease characterized by thrombocytopenia, microangiopathic hemolytic anemia, and ischemic organ damage. Several cases of TTP associated with administration of COVID-19 vaccines have been reported. We report a case of a 63-year-old woman with a past medical history of hypertension, diabetes mellitus, chronic kidney disease, HIV infection, and remote history of TTP who presented with several days of shortness of breath on exertion, chest

tightness, low-grade fever, and bruising thirty-three days after receiving the second dose of the mRNA-1273 COVID-19 vaccine. Thrombocytopenia and hemolytic anemia with schistocytes were noted on testing, and ADAMTS13 activity was <5%. Temporizing treatment with fresh frozen plasma was started immediately on presentation, and treatment was continued with daily therapeutic plasma exchange and corticosteroids. TTP should be considered in patients who present with thrombocytopenia after COVID-19 vaccination, especially if there is a past history of TTP.

Ozcan, F., et al. (2023). "Thrombotic thrombocytopenic purpura after vaccination for COVID-19: lesson for the clinical nephrologist." J Nephrol **36**(3): 647-649.

Pandey, S., et al. (2022). "A case of ischemic stroke and transient thrombocytopenia in a young female following adenoviral vector-based COVID-19 vaccination: Was the association incidental or causal?" J Family Med Prim Care **11**(10): 6556-6559.

Since March 2021, cases with unusual clots, particularly cerebral venous sinus thrombosis and splanchnic vein thrombosis, have been reported worldwide following adenoviral vector-based coronavirus disease 2019 (COVID-19) vaccination. This entity has been termed vaccine-induced thrombotic thrombocytopenia (VITT). We report a 23-year-old healthy female who developed seizures, altered sensorium, and left hemiparesis, 20 days after receiving the first dose of adenoviral vector-based COVID-19 vaccine "Covishield." The patient had transient thrombocytopenia. The D-dimer level was 2460 ng/mL. Magnetic resonance imaging (MRI) demonstrated occlusion of M2 segment of the middle cerebral artery and cerebral infarction. Platelet factor-4 antibodies level was normal. Treatment with aspirin and antiepileptic drugs resulted in a remarkable recovery. This is the first Indian case report of ischemic stroke and transient thrombocytopenia following SARS-CoV-2 ChAdOx1 nCoV-19 vaccination. Our case had clinical features consistent with the diagnosis of probable VITT. Familiarity with VITT is crucial because timely treatment with non-heparin anticoagulants and intravenous immunoglobulin improves the outcome.

Patel, J., et al. (2022). "Acute Thrombotic Thrombocytopenic Purpura: Rare and Life-Threatening Side Effect of Recent BNT-162b2 COVID-19 Vaccination." HCA Healthc J Med **3**(6): 343-348.

Description Thrombotic thrombocytopenic purpura (TTP) is a rare, potentially life-threatening disorder characterized by uncontrolled and spontaneous clot formation throughout the body. Known secondary causes of TTP include malignancy, bone marrow transplantation, pregnancy, various medications, and HIV infection. TTP in the setting of COVID-19 vaccination is rare and not well reported. Reported cases have been confined primarily to the AstraZeneca and Johnson and Johnson COVID-19 Vaccines. TTP in the setting of Pfizer BNT-162b2 vaccination has only recently been reported. We present a patient with no obvious risk factors for TTP who presented with acute altered mental status and was found to have objective evidence of TTP. To our knowledge, there are very few reported cases of TTP in the setting of a recent Pfizer COVID-19 vaccination.

Paulsen, F. O., et al. (2021). "Immune thrombocytopenic purpura after vaccination with COVID-19 vaccine (ChAdOx1 nCov-19)." Blood **138**(11): 996-999.

Pomara, C., et al. (2021). "COVID-19 Vaccine and Death: Causality Algorithm According to the WHO Eligibility Diagnosis." Diagnostics (Basel) **11**(6).

The current challenge worldwide is the administration of anti-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccines. Even if rarely, severe vascular adverse reactions temporally related to vaccine administration have induced diffidence in the population at large. In particular, researchers worldwide are focusing on the so-called "thrombosis and thrombocytopenia after COVID-19 vaccination". This study aims to establish a practical workflow to define the relationship between adverse events following immunization (AEFI) and COVID-19 vaccination, following the basic framework of the World Health Organization (WHO). Post-mortem investigation plays a pivotal role to support this causality relationship when death occurs. To demonstrate the usefulness and feasibility of the proposed workflow, we applied it to two exemplificative cases of suspected AEFI following COVID-19 vaccination. Based on the proposed model, we took into consideration any possible causality relationship between COVID-19 vaccine administration and AEFI. This led us to conclude that vaccination with ChAdOx1 nCov-19 may cause the rare development of immune thrombocytopenia mediated by platelet-activating antibodies against platelet factor 4 (PF4), which clinically mimics heparin-induced autoimmune thrombocytopenia. We suggest the adoption of the proposed methodology in order to confirm or rule out a causal relationship between vaccination and the occurrence of AEFI.

Reza, R. R., et al. (2023). "Takotsubo Cardiomyopathy Following COVID-19 Vaccine Booster Dose: A Case Report." Cureus **15**(8): e43295.

Although the efficacy and safety of the coronavirus disease 2019 (COVID-19) vaccine have been established, side effects and adverse events related to the COVID-19 vaccine are still coming out. COVID-19 vaccine also has the potential to cause acute and long-term cardiovascular effects, which include myocarditis, pericarditis, myopericarditis, myocardial infarction, pulmonary embolism, thrombotic thrombocytopenia, and pulmonary hemorrhage. Although uncommon, takotsubo cardiomyopathy (TCM) has also been reported following COVID-19 vaccination. We report a case of TCM following the COVID-19 vaccine in a 59-year-old female who presented with intermittent chest pain and dyspnea following the COVID-19 vaccine booster dose. She had no identifiable triggers for TCM, no risk factors for cardiovascular disease, and normal cardiac enzyme levels, ruling out other causes of cardiac dysfunction. The diagnosis of TCM was supported by imaging findings and the absence of obstructive or thrombotic lesions on angiography.

Root-Bernstein, R. (2021). "COVID-19 coagulopathies: Human blood proteins mimic SARS-CoV-2 virus, vaccine proteins and bacterial co-infections inducing autoimmunity: Combinations of bacteria and SARS-CoV-2 synergize to induce autoantibodies targeting cardiolipin, cardiolipin-

binding proteins, platelet factor 4, prothrombin, and coagulation factors." Bioessays **43**(12): e2100158.

Severe COVID-19 is often accompanied by coagulopathies such as thrombocytopenia and abnormal clotting. Rarely, such complications follow SARS-CoV-2 vaccination. The cause of these coagulopathies is unknown. It is hypothesized that coagulopathies accompanying SARS-CoV-2 infections and vaccinations result from bacterial co-infections that synergize with virus-induced autoimmunity due to antigenic mimicry of blood proteins by both bacterial and viral antigens. Coagulopathies occur mainly in severe COVID-19 characterized by bacterial co-infections with Streptococci, Staphylococci, Klebsiella, Escherichia coli, and Acinetobacter baumannii. These bacteria express unusually large numbers of antigens mimicking human blood antigens, as do both SARS-CoV-2 and adenoviruses. Bacteria mimic cardiolipin, prothrombin, albumin, and platelet factor 4 (PF4). SARS-CoV-2 mimics complement factors, Rh antigens, platelet phosphodiesterases, Factors IX and X, von Willebrand Factor (VWF), and VWF protease ADAMTS13. Adenoviruses mimic prothrombin and platelet factor 4. Bacterial prophylaxis, avoidance of vaccinating bacterially infected individuals, and antigen deletion for vaccines may reduce coagulopathy risk. Also see the video abstract here: https://youtu.be/zWDOsghrPg8.

Ruhe, J., et al. (2022). "Acquired thrombotic thrombocytopenic purpura after first vaccination dose of BNT162b2 mRNA COVID-19 vaccine." Ann Hematol **101**(3): 717-719.

Saluja, P., et al. (2022). "Thrombotic thrombocytopenic purpura (TTP) after COVID-19 vaccination: A systematic review of reported cases." Thromb Res **214**: 115-121.

INTRODUCTION: With the advent of COVID-19 vaccines, hospitalization rates and progression to severe COVID-19 disease have reduced drastically. Most of the adverse events reported by the vaccine recipients were minor. However, autoimmune hematological complications such as vaccine-induced immune thrombotic thrombocytopenia (VITT), immune thrombocytopenic purpura (ITP) and TTP have also been reported post-COVID-19 vaccination. Given this, we sought to reflect on the existing cases of TTP, whether de novo or relapsing, reported after COVID-19 vaccination to further gain insight into any association, if present, and outcomes. METHODS: We searched PubMed, Embase, and Ebsco databases for published individual case reports on the occurrence or relapse of TTP after receiving any COVID-19 vaccine. A total of 23 articles (27 patients) were included in this qualitative analysis. RESULTS: The mean age for the patients who developed de novo TTP post-COVID-19 vaccination was 51.3 years. TTP episodes were seen mostly after BNT162b2 vaccine, followed by mRNA-1273 vaccine. All patients with immune TTP except one received plasma exchange (PLEX) and steroids. One patient passed away after two days of hospitalization, likely due to a sudden cardiovascular event. CONCLUSION: Our review underscores the importance of in-depth anamnesis before vaccination and outlines characteristics of predisposed individuals. Evaluation of post-vaccine thrombocytopenia must include the possibility of TTP given the associated fatality with this condition.

Seneff, S., et al. (2022). "Innate immune suppression by SARS-CoV-2 mRNA vaccinations: The role of G-quadruplexes, exosomes, and MicroRNAs." Food Chem Toxicol **164**: 113008.

The mRNA SARS-CoV-2 vaccines were brought to market in response to the public health crises of Covid-19. The utilization of mRNA vaccines in the context of infectious disease has no precedent. The many alterations in the vaccine mRNA hide the mRNA from cellular defenses and promote a longer biological half-life and high production of spike protein. However, the immune response to the vaccine is very different from that to a SARS-CoV-2 infection. In this paper, we present evidence that vaccination induces a profound impairment in type I interferon signaling, which has diverse adverse consequences to human health. Immune cells that have taken up the vaccine nanoparticles release into circulation large numbers of exosomes containing spike protein along with critical microRNAs that induce a signaling response in recipient cells at distant sites. We also identify potential profound disturbances in regulatory control of protein synthesis and cancer surveillance. These disturbances potentially have a causal link to neurodegenerative disease, myocarditis, immune thrombocytopenia, Bell's palsy, liver disease, impaired adaptive immunity, impaired DNA damage response and tumorigenesis. We show evidence from the VAERS database supporting our hypothesis. We believe a comprehensive risk/benefit assessment of the mRNA vaccines questions them as positive contributors to public health.

Sessa, F., et al. (2021). "Autopsy Findings and Causality Relationship between Death and COVID-19 Vaccination: A Systematic Review." J Clin Med **10**(24).

The current challenge worldwide is the administration of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine. Considering that the COVID-19 vaccination represents the best possibility to resolve this pandemic, this systematic review aims to clarify the major aspects of fatal adverse effects related to COVID-19 vaccines, with the goal of advancing our knowledge, supporting decisions, or suggesting changes in policies at local, regional, and global levels. Moreover, this review aims to provide key recommendations to improve awareness of vaccine safety. All studies published up to 2 December 2021 were searched using the following keywords: "COVID-19 Vaccine", "SARS-CoV-2 Vaccine", "COVID-19 Vaccination", "SARS-CoV-2 Vaccination", and "Autopsy" or "Post-mortem". We included 17 papers published with fatal cases with post-mortem investigations. A total of 38 cases were analyzed: 22 cases were related to ChAdOx1 nCoV-19 administration, 10 cases to BNT162b2, 4 cases to mRNA-1273, and 2 cases to Ad26.COV2.S. Based on these data, autopsy is very useful to define the main characteristics of the so-called vaccine-induced immune thrombotic thrombocytopenia (VITT) after ChAdOx1 nCoV-19 vaccination: recurrent findings were intracranial hemorrhage and diffused microthrombi located in multiple areas. Moreover, it is fundamental to provide evidence about myocarditis related to the BNT162B2 vaccine. Finally, based on the discussed data, we suggest several key recommendations to improve awareness of vaccine safety.

Shibata, K., et al. (2021). "[Development of thrombocytopenic purpura following BNT162b2 mRNA COVID-19 vaccination]." Rinsho Ketsueki **62**(10): 1519-1521.

Because the coronavirus disease 2019 (COVID-19) pandemic is still rampant, vaccination is being promoted worldwide. However, the safety of various COVID-19 vaccines remains poorly understood. We herein report the case of a 37-year-old woman who experienced thrombocytopenia following BNT162b2 mRNA COVID-19 vaccination. The patient presented with purpura on the extremities 10 days after the first vaccination. She had marked thrombocytopenia and no thrombosis. Thrombocytopenia resolved spontaneously. Given the possibility of occurrence of post-vaccination thrombocytopenia, vaccinated persons should be instructed to consult a medical institution if they experience bleeding symptoms.

Tejaswi, G. M., K. Sriganesh and V. Sriram (2023). "COVID 19 vaccine induced thrombotic thrombocytopenia, cerebral venous thrombosis and neurogenic stunned myocardium." Indian J Anaesth **67**(2): 224-225.

Unger, K., C. D. Ponte and D. Anderson (2022). "A Possible Case of COVID-19 Booster Vaccine-Associated Rhabdomyolysis and Acute Kidney Injury." J Pharm Technol **38**(4): 247-250.

Background: Nearly 10 billion doses of the various messenger ribonucleic acid (mRNA) and viral vector vaccines against Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) have been administered worldwide. Adverse drug reactions (ADRs) have been overwhelmingly mild to moderate in nature. Rare side effects have included myocarditis/pericarditis, thrombosis with thrombocytopenia syndrome (TTS), Guillain-Barre Syndrome (GBS), and death. However, vaccine-related ADR data are still being collected using a variety of reporting systems. Purpose: We will describe a case of suspected mRNA coronavirus disease 2019 (COVID-19) booster-related rhabdomyolysis in a woman who developed signs and symptoms 10 days after administration of the vaccine dose. With a Naranjo ADR probability score of 4, the vaccine was deemed to be a possible cause of our patient's rhabdomyolysis. Methods: A search of the VAERS (Vaccine Adverse Event Reporting System) mined in November 2021 revealed 386 reported cases of COVID-19 vaccine-related rhabdomyolysis. However, system limitations make the utility of the information problematic. Conclusions: It is vitally important that clinicians, scientists, and patients are aware of rhabdomyolysis as a potential side effect of vaccination. Suspected vaccine-related ADRs should be promptly and accurately reported via VAERS or other surveillance systems to support the ongoing effort to ensure vaccine safety.

Welsh, K. J., et al. (2021). "Thrombocytopenia including immune thrombocytopenia after receipt of mRNA COVID-19 vaccines reported to the Vaccine Adverse Event Reporting System (VAERS)." Vaccine **39**(25): 3329-3332.

BACKGROUND: The objective of this study is to assess cases of thrombocytopenia, including immune thrombocytopenia (ITP), reported to the Vaccine Adverse Event Reporting System (VAERS) following vaccination with mRNA COVID-19 vaccines. METHODS: This case-series study analyzed VAERS reports of thrombocytopenia after vaccination with Pfizer-BioNTech COVID-19 Vaccine or Moderna COVID-19 Vaccine. RESULTS: Fifteen cases of thrombocytopenia were identified among 18,841,309 doses of

Pfizer-BioNTech COVID-19 Vaccine and 13 cases among 16,260,102 doses of Moderna COVID-19 Vaccine. The reporting rate of thrombocytopenia was 0.80 per million doses for both vaccines. Based on an annual incidence rate of 3.3 ITP cases per 100,000 adults, the observed number of all thrombocytopenia cases, which includes ITP, following administration of mRNA COVID-19 vaccines is not greater than the number of ITP cases expected. CONCLUSIONS: The number of thrombocytopenia cases reported to VAERS does not suggest a safety concern attributable to mRNA COVID-19 vaccines at this time.

Wong, J. S. Y., J. H. Kang and K. Z. Maw (2022). "Acute immune thrombocytopenic purpura post first dose of COVID-19 vaccination." Postgrad Med J **98**(e2): e129-e130.

Yasmin, F., et al. (2023). "Adverse events following COVID-19 mRNA vaccines: A systematic review of cardiovascular complication, thrombosis, and thrombocytopenia." Immun Inflamm Dis **11**(3): e807.

BACKGROUND AND OBJECTIVES: Since publishing successful clinical trial results of mRNA coronavirus disease 2019 (COVID-19) vaccines in December 2020, multiple reports have arisen about cardiovascular complications following the mRNA vaccination. This study provides an in-depth account of various cardiovascular adverse events reported after the mRNA vaccines' first or second dose including pericarditis/myopericarditis, myocarditis, hypotension, hypertension, arrhythmia, cardiogenic shock, stroke, myocardial infarction/STEMI, intracranial hemorrhage, thrombosis (deep vein thrombosis, cerebral venous thrombosis, arterial or venous thrombotic events, portal vein thrombosis, coronary thrombosis, microvascular small bowel thrombosis), and pulmonary embolism. METHODS: A systematic review of original studies reporting confirmed cardiovascular manifestations post-mRNA COVID-19 vaccination was performed. Following the PRISMA guidelines, electronic databases (PubMed, PMC NCBI, and Cochrane Library) were searched until January 2022. Baseline characteristics of patients and disease outcomes were extracted from relevant studies. RESULTS: A total of 81 articles analyzed confirmed cardiovascular complications post-COVID-19 mRNA vaccines in 17,636 individuals and reported 284 deaths with any mRNA vaccine. Of 17,636 cardiovascular events with any mRNA vaccine, 17,192 were observed with the BNT162b2 (Pfizer-BioNTech) vaccine, 444 events with mRNA-1273 (Moderna). Thrombosis was frequently reported with any mRNA vaccine (n = 13,936), followed by stroke (n = 758), myocarditis (n = 511), myocardial infarction (n = 377), pulmonary embolism (n = 301), and arrhythmia (n = 254). Stratifying the results by vaccine type showed that thrombosis (80.8%) was common in the BNT162b2 cohort, while stroke (39.9%) was common with mRNA-1273 for any dose. The time between the vaccination dosage and the first symptom onset averaged 5.6 and 4.8 days with the mRNA-1273 vaccine and BNT162b2, respectively. The mRNA-1273 cohort reported 56 deaths compared to the 228 with BNT162b2, while the rest were discharged or transferred to the ICU. CONCLUSION: Available literature includes more studies with the BNT162b2 vaccine than mRNA-1273. Future studies must report mortality and adverse cardiovascular events by vaccine types.

Tinnitus

Ahmed, S. H., et al. (2022). "SARS-CoV-2 vaccine-associated-tinnitus: A review." Ann Med Surg (Lond) **75**: 103293.

The global vaccination drive against severe acute respiratory syndrome coronavirus-2 is being pursued at a historic pace. Unexpected adverse effects have been reported following vaccination, including thrombotic thrombocytopenia, myocarditis, amongst others. More recently, some cases of tinnitus are reported post-vaccination. According to the Vaccine Adverse Events Reporting System (VAERS), 12,247 cases of coronavirus post-vaccination tinnitus have been reported till September 14, 2021. To the best of our knowledge, this is the first review evaluating any otologic manifestation following vaccine administration and aims to evaluate the potential pathophysiology, clinical approach, and treatment. Although the incidence is infrequent, there is a need to understand the precise mechanisms and treatment for vaccine-associated-tinnitus.

Canales Medina, M. and M. Ramirez Gomez (2022). "Tinnitus, Sudden Sensorineural Hearing Loss, and Vestibular Neuritis As Complications of the Astra Zeneca COVID-19 Vaccine." Cureus **14**(1): e20906.

BACKGROUND: Sudden sensorineural hearing loss is most commonly defined as a sensorineural hearing loss of 30dB or greater over at least three contiguous audiometric frequencies occurring within a 72-hr period. The Astra Zeneca COVID-19 vaccine is suspicious of causing thrombotic complications following its administration, and could theoretically induce hearing loss by damaging the hearing organs through this mechanism, as well as vestibular damage through similar mechanisms. MATERIAL AND METHODS: We reviewed the files of patients with otological symptoms after exposure to the Astra Zeneca COVID-19 vaccine during the year 2021. CASE SERIES: We studied a total of six cases with otologic symptoms temporally related to the Astra Zeneca COVID-19 vaccine. We report four cases of patients presenting with hearing loss and tinnitus a few days after the second dose of the Astra Zeneca vaccine, and one case with the same symptoms after the first dose. Four cases were successfully treated with steroids; however, one case presented to the office two months after the onset of symptoms and did not improve with treatment. We also report the first case of vestibular neuritis temporally related to the administration of the first dose of the vaccine, which also had a good outcome after medical treatment. CONCLUSIONS: Prompt treatment in the present cases was a factor associated with a good prognosis.

Chen, J. J., et al. (2022). "Pfizer-BioNTech COVID-19 vaccine-associated tinnitus and treatment with transcranial magnetic stimulation." QJM **115**(9): 623-624.

Finsterer, J. and R. Edmonds (2022). "Persisting, unilateral tinnitus 22 days after first dose of an mRNA-based SARS-CoV-2 vaccine." J Family Med Prim Care **11**(6): 3330-3332.

OBJECTIVES: Although vaccination with vector-based or mRNA-based SARS-CoV-2 vaccines is usually well tolerated, they are not free of side effects. Some of these side effects can be severe and concern the primary care physician, otorhinolaryngologist, and the neurologist. Persisting, unilateral tinnitus time-linked to the first dose and worsening after the second dose of an mRNA-based SARS-CoV-2 vaccine has not been reported. STUDY DESIGN: Case report. METHODS: Routine tests were applied to investigate the patient. RESULTS: A 35-year-old male experienced sudden onset of right-sided tinnitus, diffuse headache, and ear respectively facial pressure 22 days after the first dose of an mRNA-based SARS-CoV-2 vaccine. Since symptoms worsened after the second dose, 28 days later, the patient started a self-medication with non-steroidal anti-inflammatory drugs, without benefit. After an otolaryngologist suspected Meniere's disease, prednisone was given for 5 days with significant improvement. After discontinuation of steroids, however, previous symptoms recurred with similar intensity as before. Cetirizin and loratadin were started resulting in complete resolution of headache and pressures but persistence of tinnitus. After exclusion of various differentials, a causal relation between clinical presentation and vaccination was suspected. CONCLUSIONS: SARS-CoV-2 vaccination can be followed by unilateral persisting tinnitus, headache, and ear respectively facial pressure. Since steroids and anti-histamines had a beneficial effect, an immunological pathophysiology is quite likely.

Lin, D. and A. M. Selleck (2023). "Tinnitus cases after COVID-19 vaccine administration, one institution's observations." Am J Otolaryngol **44**(4): 103863.

OBJECTIVE: After the role out of the COVID-19 vaccine in the United States, there has been increase in case reports of tinnitus attributed to the vaccine reported. We present our institution's experience over the initial 13 month period the vaccines were available. STUDY DESIGN: Retrospective chart review. SETTING: Tertiary academic otology and general otolaryngology practice. PATIENTS: Patients who received a COVID-19 vaccine and a tinnitus diagnosis code. INTERVENTIONS: Observation, steroids (oral and intratympanic), diagnostic imaging and audiometry. MAIN OUTCOME MEASURES: Patients who received a COVID-19 vaccine in the time frame of 12/1/2020-12/31/21 with a diagnosis of tinnitus, an audiogram, and at least one visit with one of our Otolaryngologists were included in the study. Twenty-seven of the 1254 patients identified met these criteria. The patients ranged in age from 41 to 84 years old including seven male and twenty female patients. Sixteen received the Pfizer vaccine, seven received the Moderna vaccine and four patients received the Janssen vaccine. CONCLUSIONS: No definite correlation could be established between COVID-19 vaccine and tinnitus. Any concurrent sudden hearing loss should be treated as usual with oral or intratympanic steroids. Health care providers should be aware of the tinnitus onset and if new or recent onset, to refer for prompt audiogram and Otolaryngology evaluation.

Schelke, M. W., et al. (2022). "Post-COVID-19 vaccine small-fiber neuropathy and tinnitus treated with plasma exchange." Muscle Nerve **66**(4): E21-E23.

Transverse Myelitis

Alabkal, J., et al. (2021). "Incomplete Subacute Transverse Myelitis Following Vaccination With Pfizer-BioNTech COVID-19 mRNA Vaccine: A Case Report." Cureus **13**(12): e20460.

In response to the coronavirus disease 2019 (COVID-19) pandemic, rapid development, clinical testing, and regulatory approval of vaccines occurred. The tozinameran COVID-19 vaccine is the first mRNA vaccine approved for use in humans. Transverse myelitis is a rare inflammatory disorder of the spinal cord that is associated with traditional vaccinations. There are rare case reports describing an association between mRNA vaccines and transverse myelitis. Herein, we describe a case of transverse myelitis following mRNA vaccination. A healthy 26-year-old woman developed saddle anesthesia, numbness, and allodynia in the S1-S4 distribution within three days of receiving the first dose of tozinameran COVID-19 vaccine. She had decreased sensation to pinprick, temperature, and light touch in S1-S4 distribution and a positive Rhomberg test. An MRI brain and spine demonstrated a short segment T2 hyperintense and diffusely enhancing lesion at T5. Cerebrospinal fluid studies demonstrated pleocytosis and elevated IgG index. A five-day course of IV methylprednisolone resulted in minimal improvements in her symptoms. Stage III clinical trials may be underpowered to detect more rare adverse effects such as transverse myelitis. Therefore, it is imperative to have ongoing surveillance and reporting of adverse events associated with COVID-19 vaccines to ensure transparency with regard to potential risks to patients obtaining the vaccine and algorithms in place for detection and urgent treatment if required. Nonetheless, the safety and efficacy of vaccination against COVID-19 are well established and greatly outweigh any potential risks associated with the vaccine. Given the individual, societal, and global health benefits of vaccination we strongly advocate for ongoing vaccinations against COVID-19.

Chen, Y., Y. Li and T. Zhan (2022). "A case report of possible concurrent vasculitis in vertebral bodies and partial transverse myelitis following COVID-19 vaccination." Medicine (Baltimore) **101**(39): e30814.

INTRODUCTION: Cases with organ-specific and systemic vasculitis associated with corona virus disease 2019 (COVID-19) vaccination have been reported. However, acute partial transverse myelitis (APTM) is rare adverse events following received COVID-19 vaccines. To the best of our knowledge, there is no report on vaccine-associated APTM accompanied by possible concurrent vasculitis. Herein we present a case with possible concurrent spinal vasculitis and APTM following the second dose of inactivated COVID-19 vaccine. CASE SUMMARY: A 33-year-old man presented with weakness of left lower limb and aberrant sensation of his left lower trunk and limb (from T9 level to toes) for 2 days following receipt of an inactivated COVID-19 vaccine. Remarkable demyelinating lesion at T7 spinal cord was showed by 3.0T magnetic resonance imaging (MRI) scan. Moreover, vertebral bodies of T3-T7 also presented high signal in T-2 weighted imaging (T2WI) accompanied by multiple sites of flowing void effect indicating possible vasculitis. Oligoclonal band was positive in cerebrospinal fluid (CSF) while it was negative in sera.

Intravenous methylprednisolone (1 g/d) was administrated for 5 days followed by subsequent dose-tapering prednisone. His limb weakness and aberrant sensation both improved and he was able to walk unaided after treatment. The MRI recheck also showed remarkable improvement on the lesions in spinal cord and vertebral bodies. CONCLUSION: this case illustrates the concurrence of possible vasculitis in vertebral bodies and acute transverse myelitis (ATM) following COVID-19 vaccination.

Cho, S. Y., et al. (2023). "Transverse myelitis caused by herpes zoster following COVID-19 vaccination: A case report." World J Clin Cases **11**(6): 1419-1425.

BACKGROUND: Transverse myelitis (TM) is characterized by sudden lower extremity progressive weakness and sensory impairment, and most patients have a history of advanced viral infection symptoms. A variety of disorders can cause TM in association with viral or nonviral infection, vascular, neoplasia, collagen vascular, and iatrogenic, such as vaccination. Vaccination has become common through the global implementation against coronavirus disease 2019 (COVID-19) and reported complications like herpes zoster (HZ) activation has increased. CASE SUMMARY: This is a 68-year-old woman who developed multiple pustules and scabs at the T6-T9 dermatome site 1 wk after vaccination with the COVID-19 vaccine (Oxford/AstraZeneca ([ChAdOx1Srecombinant]). The patient had a paraplegia aggravation 3 wk after HZ symptoms started. Spinal magnetic resonance imaging (MRI) showed transverse myelitis at the T6-T9 Level. Treatment was acyclovir with steroids combined with physical therapy. Her neurological function was slowly restored by Day 17. CONCLUSION: HZ developed after COVID-19 vaccination, which may lead to more severe complications. Therefore, HZ treatment itself should not be delayed. If neurological complications worsen after appropriate management, an immediate diagnostic procedure, such as magnetic resonance imaging and laboratory tests, will start and should treat the neurological complications.

da Gama, P. D., et al. (2022). "Extensive Longitudinal Transverse Myelitis Temporally Related to the Use of AZD1222, AstraZeneca COVID-19 Vaccine: Cerebrospinal Fluid Analysis and Recent Data Review." Case Rep Neurol Med **2022**: 8999853.

While mass immunization against coronavirus disease 2019 (COVID-19) rolls out around the globe, safety concerns and adverse events that need prompt evaluation are also emerging. Neurological complications such as transverse myelitis raise concerns as cases were observed in clinical trials. Cerebrospinal fluid analysis is routine in these cases and the characteristics of the abnormalities found are of great help not only in establishing the diagnosis but also in understanding this rare condition. We present a case of extensive longitudinal transverse myelitis after vaccination with AZD1222, AstraZeneca COVID-19 vaccine, which was the first case reported in Brazil. The abnormalities found in the study of the cerebrospinal fluid in our case are reported and discussed using data from recent publications.

Do, K., et al. (2023). "Onset of Guillain-Barre Syndrome and Transverse Myelitis Following COVID-19 Vaccination." Cureus **15**(6): e41009.

Guillain-Barre syndrome (GBS) and transverse myelitis (TM) are both neuro-inflammatory disorders that are attributed to dysfunctions of the peripheral nervous system and spinal cord, respectively. The two conditions involve immune-mediated destruction and inflammation of the nervous system and may present clinically as a weakness in the muscles, loss of normal sensations, and even paralysis of the body or extremities. Although the incidence of GBS and TM is quite rare, there have been reports of the two diseases developing in patients, either independently or concurrently, following COVID-19 vaccinations. In this case report, we present a patient (male) who lost functions and sensations in his lower extremities 60 days after he received the COVID-19 booster vaccine. The patient's blood work was unremarkable. Magnetic resonance imaging (MRI) of his thoracic spine and an electromyography study revealed evidence of nerve demyelination, which supports the diagnosis of GBS/TM overlap syndrome. He was ultimately treated with intravenous immunoglobulins (IVIGs) and gained back functions in his lower extremities.

Doi, K., et al. (2022). "Cervical Transverse Myelitis Following COVID-19 Vaccination." NMC Case Rep J **9**: 145-149.

Various COVID-19 vaccines are associated with numerous adverse side effects. Associations between vaccinations and neurological disorders, such as transverse myelitis, stroke, Bell's palsy, acute disseminated encephalomyelitis, and Guillain-Barre syndrome, have been reported. A 27-year-old Japanese woman presented with paresthesia four days after receiving a second dose of the COVID-19 vaccine. One month after vaccination, she started to feel left lower limb weakness, and her symptoms almost improved after two steroid pulse therapies. Spinal cord tumor biopsy could potentially help make a definitive diagnosis in clinical situations. However, it is very important to review the patient's medical history, including vaccinations received, before performing a direct spinal cord biopsy, which is invasive and does not guarantee a definitive diagnosis.

Eom, H., et al. (2022). "Case Reports of Acute Transverse Myelitis Associated With mRNA Vaccine for COVID-19." J Korean Med Sci **37**(7): e52.

Acute transverse myelitis (ATM) has been reported as rare complication of vaccination. Herein, we report 2 cases of ATM after the administration of an mRNA vaccine for coronavirus disease 2019 (COVID-19). The first one is an 81-year-old man who received the BNT162b2 vaccine. He presented with bilateral hand weakness. Spine magnetic resonance imaging (MRI) showed high signal intensity from the C1 to C3 vertebrae. The second is a 23-year-old woman who received the BNT162b2 vaccine and experienced tingling in her legs. Spine MRI showed a high signal intensity lesion at the conus medullaris. These patients were treated with intravenous methylprednisolone and their symptoms improved slightly. Careful follow-up is needed to identify adverse events after the administration of mRNA vaccines for COVID-19.

Erdem, N. S., et al. (2021). "Acute transverse myelitis after inactivated COVID-19 vaccine." Ideggyogy Sz **74**(7-08): 273-276.

Vaccines against the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been rapidly developed to prevent coronavirus disease 2019 (COVID-19) pandemic. There is increasing safety concerns regarding COVID-19 vaccines. We report a 78-year old woman who was presented with tetraparesis, paresthesias of bilateral upper extremities, and urinary retention of one-day duration. Three weeks before these symptoms, she was vaccinated with CoronaVAC vaccine (Sinovac Life Sciences, China). Spine magnetic resonance imaging showed longitudinally extensive transverse myelitis (TM) from the C1 to the T3 spinal cord segment. An extensive diagnostic workup was performed to exclude other possible causes of TM. We suggest that longitudinally extensive TM may be associated with COVID-19 vaccination in this case. To the best of our knowledge, this is the first report of longitudinally extensive TM developing after CoronaVac vaccination. Clinicians should be aware of neurological symptoms after vaccination of COVID-19.

Esechie, A., et al. (2022). "A case report of longitudinal extensive transverse myelitis: immunotherapy related adverse effect vs. COVID-19 related immunization complications." Int J Neurosci: 1-4.

Background: Transverse myelitis (TM) is a rare, acquired neuro-immunological spinal cord disorder that occurs with rapid onset of motor weakness, sensory deficits with bowel and bladder dysfunction. Patients being treated with immune checkpoint inhibitors (ICIs) for advanced malignancy have a known higher propensity of developing neuro immune complications. With the advent of COVID-19 pandemic there have been reported cases of TM with COVID-19 immunization. The reported infrequency of TM with both of the aforementioned causes makes delineation of the etiology challenging.Methods: We present a patient with metastatic small cell lung cancer (SCLC) on maintenance Atezolizumab immunotherapy who developed longitudinal extensive transverse myelitis (LETM) after administration of second dose of COVID-19 mRNA vaccine one day prior to presenting symptoms of acute paralysis of the lower extremity, sensory loss from chest down with overflow incontinence. A clinical diagnosis of myelopathy was supported by MRI of the spine illustrating enhancing lesions from C7-T7 concerning for LETM.Results: A 5-day course of pulsed methylprednisolone followed by therapeutic plasma exchange for 3 days resulted in only minimal improvement in the neurologic exam with increased strength in his lower extremities while the sensory level remained unchanged.Conclusions: This case demonstrates the complication and symptomatology of TM in the setting of anti-PD-L1 monoclonal antibody with coincidental COVID-19 mRNA vaccine administration. The causal relationship between the vaccine and LETM is difficult to establish. However, the presence of a known inciting factor hints at a possible exaggeration of the existing neuro-inflammatory process.

Finsterer, J. and D. Matovu (2022). "Consider Transverse Myelitis as a Complication of a SARS-CoV-2 Vaccination." J Korean Med Sci **37**(18): e150.

Fitzsimmons, W. E. (2022). "COVID-19 vaccine associated transverse myelitis-Evusheld as an option when vaccination is not recommended due to severe adverse events." Hum Vaccin Immunother **18**(5): 2068338.

Individuals who experience severe COVID-19-vaccine-related adverse reactions such as transverse myelitis may be precluded from receiving further vaccination to protect from SARS-CoV-2 infection. Although the mechanism of autoimmune spinal cord inflammation resulting in transverse myelitis is unclear, it may be safe to administer antibody therapy for preventing COVID-19. Recently, Evusheld, tixagevimab with cilgavimab, two spike-protein directed monoclonal antibodies were authorized by the U.S. FDA and U.K. MHRA for administration to individuals when vaccination is not recommended. We report the safe administration of Evusheld to a patient who experienced transverse myelitis 11 months previously as a result of receiving the Moderna mRNA vaccine. This patient has experienced no adverse events to Evusheld. Additional experience and data collection are warranted to determine the safety of this prophylactic therapy.

Gao, J. J., et al. (2021). "Acute Transverse Myelitis Following COVID-19 Vaccination." Vaccines (Basel) **9**(9).

An increasing number of people are undergoing vaccination for COVID-19 because of the ongoing pandemic. The newly developed, genetically engineered mRNA vaccines are critical for controlling the epidemic disease. However, major adverse effects, including neuroimmunological disorders, are being attributed to this vaccine. For instance, several cases of acute transverse myelitis (ATM) after COVID-19 vaccination have been reported in clinical trials. Here, we report an exceedingly rare case of longitudinally extensive transverse myelitis (LETM), a rare subtype of ATM involving three or more vertebral segments, that occurred shortly after vaccination with the Moderna COVID-19 (mRNA-1273) vaccine, with a comorbidity of vitamin B12 deficiency. The findings of subsequent investigations suggest the possibility that autoimmune responses are triggered by the reactions between anti-SARS-CoV-2 spike protein antibodies and tissue proteins, as well as the interaction between spike proteins and angiotensin-converting enzyme 2 receptors.

Helmchen, C., et al. (2022). "Acute bilateral optic/chiasm neuritis with longitudinal extensive transverse myelitis in longstanding stable multiple sclerosis following vector-based vaccination against the SARS-CoV-2." J Neurol **269**(1): 49-54.

Hirose, S., et al. (2021). "Acute autoimmune transverse myelitis following COVID-19 vaccination: A case report." Medicine (Baltimore) **100**(51): e28423.

RATIONALE: Transverse myelitis is an infectious or noninfectious inflammatory spinal cord syndrome. We report a rare case of transverse myelitis following vaccination against COVID-19. PATIENT CONCERNS: A 70-year-old male presented with progressive sensorimotor dysfunction of the bilateral lower limbs 7 days after receiving the mRNA-1273 vaccine against COVID-19. Spinal magnetic resonance imaging revealed intramedullary lesions with gadolinium enhancement on the Th1/2 and Th5/6 vertebral levels. Cerebrospinal fluid (CSF) testing showed a mildly increased level of total protein

and positive oligoclonal bands (OCB). DIAGNOSIS: The patient was diagnosed with acute transverse myelitis. INTERVENTION: The patient received 5 days of intravenous methylprednisolone pulse (1000 mg/day) followed by oral prednisolone (30 mg/day with gradual tapering). OUTCOMES: The patient fully recovered from muscle weakness of the lower limbs. He was discharged from our hospital and able to independently walk without unsteadiness. LESSON: This is a rare case of transverse myelitis following COVID-19 vaccination. Positive OCB in CSF in the present case highlights the possibility of autoimmune processes, including polyclonal activation of B lymphocytes, following vaccination.

Hsiao, Y. T., et al. (2021). "Acute Transverse Myelitis after COVID-19 Vaccination." Medicina (Kaunas) **57**(10).

The adverse effects of the COVID-19 vaccine have been discovered as the rapid application of the vaccines continues. Neurological complications such as transverse myelitis raise concerns as cases were observed in clinical trials. Transverse myelitis is a rare immune-mediated disease with spinal cord neural injury, resulting in neurological deficits in the motor, sensory, and autonomic system. Vaccine-related transverse myelitis is even rarer. We present a case of acute transverse myelitis after vaccination against COVID-19 with the ChAdOx1 nCOV-19 vaccine (AZD1222), which was the first case reported in Taiwan. Although it rarely occurs, post-vaccination neurological complications should not be ignored. As the pandemic of SARS-CoV-2 continues to spread and concern about vaccination efficacy and safety rises, heterologous vaccination were implemented in health public policy in several countries. A literature review of several clinical trials shows promising effects of mix-and-match vaccination. Further study on different combinations of vaccines can be expected.

Kc, O., et al. (2022). "A Rare Case of Longitudinally Extensive Transverse Myelitis Following Pfizer-BioNTech COVID-19 Vaccination with a Favourable Outcome." Eur J Case Rep Intern Med **9**(9): 003553.

INTRODUCTION: mRNA COVID-19 vaccines are very safe, but rare adverse events such as transverse myelitis have been reported after COVID-19 vaccination. CASE DESCRIPTION: We report the case of 50-year-old man who presented with progressive lower extremity weakness, back pain and urinary retention after his second dose of the Pfizer COVID-19 vaccine. MRI of the spine revealed longitudinally extensive transverse myelitis (LETM). He recovered completely after treatment with intravenous methylprednisone and physical therapy. DISCUSSION: This case highlights the rare association between LETM and COVID-19 vaccines and encourages clinicians to maintain a high index of suspicion for prompt diagnosis and treatment. LEARNING POINTS: Longitudinally extensive transverse myelitis (LETM) is rare adverse events after mRNA COVID-19 vaccination.Clinicians should maintain a high index of suspicion for prompt diagnosis of vaccine-induced transverse myelitis.Vaccine-induced LETM should show marked clinical improvement after appropriate treatment.

Khan, E., et al. (2022). "Acute transverse myelitis following SARS-CoV-2 vaccination: a case report and review of literature." J Neurol **269**(3): 1121-1132.

OBJECTIVE: To report a unique case and literature review of post COVID-19 vaccination associated transverse myelitis and with abnormal MRI findings. BACKGROUND: Coronavirus disease have been reported to be associated with several neurological manifestations such as stroke, Guillain-Barre syndrome, meningoencephalitis amongst others. There are only a few reported cases of transverse myelitis with the novel coronavirus (n-CoV-2). Here, we identify a post COVID-19 vaccination patient diagnosed with acute transverse myelitis. METHOD: A retrospective chart review of a patient diagnosed with post SARS-CoV-2 vaccination acute transverse myelitis, and a review of literature of all the reported cases of other post vaccination and transverse myelitis, from December 1st, 2010 till July 15th, 2021, was performed. CONCLUSION: To our knowledge, this is the one of early reported case of transverse myelitis and with post SARS-CoV-2 vaccination, who responded well to plasmapheresis. Further studies would be recommended to identify the underlying correlation between COVID-19 vaccination and transverse myelitis.

Khan, Z., et al. (2022). "Interstitial Lung Disease and Transverse Myelitis: A Possible Complication of COVID-19 Vaccine." Cureus **14**(2): e21875.

The clinical impact of the severe acute respiratory syndrome 2 (SARS-CoV-2) pandemic is growing, and vaccine-associated complications are becoming more evident. Although global vaccination against coronavirus disease 19 (COVID-19) is an outstanding accomplishment, safety concerns and adverse outcomes are also emerging that need to be addressed promptly. The most reported side effects of the COVID-19 vaccine include fever, myalgia, headache, and injection site reactions. Acute transverse myelitis (ATM) and interstitial lung disease (ILD) following the CoronaVac vaccine are rarely reported. We report a case of ILD followed by acute myelopathy in a female who presented with dyspnea, cough, and fever after the second dose of the COVID-19 vaccine. On the third day of admission, she developed paresthesia and bilateral upper and lower limb weakness. She was diagnosed with ILD and ATM due to the COVID-19 vaccine based on imaging and detailed investigations after ruling out all possible causes. Her neurological and respiratory manifestations improved gradually after starting intravenous methylprednisolone.

Marginean, C. O., et al. (2022). "COVID-19 Vaccine-A Potential Trigger for MOGAD Transverse Myelitis in a Teenager-A Case Report and a Review of the Literature." Children (Basel) **9**(5).

MOGAD-transverse myelitis is a rare disorder in children and adults, but with a higher incidence in pediatric patients. We report a case of MOGAD-transverse myelitis in a boy who was admitted to hospital with bilateral motor deficit of the lower limbs associated with the impossibility of defecating and urinating. The symptoms progressively developed with severe fatigue within the week prior to admission, with the impossibility to stand occurring 36 h before admission. The anamnesis found that he was vaccinated for COVID-19 approximately 6 weeks before admission to our clinic. The laboratory tests revealed a normal complete cellular blood count, without any signs of inflammation or

infection, except for both cryoglobulins and IgG anti-MOG antibodies. MRI showed a T2 hypersignal on vertebral segments C2-C5, Th2-Th5 and Th7-Th11, confirming the diagnosis of longitudinally extensive transverse myelitis. The patient received intravenous high-dose methylprednisolone (1 g) for 5 days, associated with prophylactic antibiotic treatment, subcutaneous low-molecular-weight heparin and other supportive treatment. The patient was discharged on the 12th day of admission, able to walk without support and with no bladder or bowel dysfunction. We can conclude that an early diagnosis was essential for improving the patient's long-term outcome.

Maroufi, S. F., et al. (2022). "Longitudinally extensive transverse myelitis after Covid-19 vaccination: case report and review of literature." Hum Vaccin Immunother **18**(1): 2040239.
Mass vaccination has been the main policy to overcome the Covid-19 pandemic. Several vaccines have been approved by the World Health Organization. With growing vaccination, safety concerns and adverse events that need prompt evaluation are also emerging. Herein, we report a case of a healthy woman with longitudinally extensive transverse myelitis after vaccination with the AstraZeneca vaccine. The patient was successfully treated after ruling out all the possible causes.

Mathew, E., et al. (2022). "Transverse myelitis after Johnson & Johnson COVID-19 vaccine: illustrative case." J Neurosurg Case Lessons **4**(24).
BACKGROUND: Transverse myelitis is a rare neurological occurrence with varied presentation. Imaging is necessary to properly diagnose this condition; however, identifying the cause of this condition may often be difficult. OBSERVATIONS: An otherwise healthy patient presented to the clinic with peculiar neurological symptoms without an obvious underlying cause. Imaging evidenced no significant structural defects but did lead to discovery of cord enhancement compatible with a diagnosis of transverse myelitis. Corticosteroid treatment was initiated rapidly to address this pathology, and the patient recovered without deficits. To identify the underlying cause, patient medical history was reviewed thoroughly and compared with existing literature. Previous tuberculosis infection could be a less likely cause of the neurological symptoms. However, recent vaccination with the Johnson & Johnson coronavirus disease 2019 (COVID-19) vaccine could be a more likely cause of the transverse myelitis, which has been rarely reported. LESSONS: Transverse myelitis after COVID-19 infection has been an escalating phenomenon. However, transverse myelitis after COVID-19 vaccination is a rare occurrence that is also on the rise. Given the increased rates of vaccination, transverse myelitis should not be overlooked as a potential pathology, due to the severity of neurological impairment if this condition is not treated rapidly.

Nakano, H., et al. (2022). "Acute transverse myelitis after BNT162b2 vaccination against COVID-19: Report of a fatal case and review of the literature." J Neurol Sci **434**: 120102.

Nguyen, S., et al. (2022). "Transverse Myelitis Following SARS-CoV-2 Vaccination: A Pharmacoepidemiological Study in the World Health Organization's Database." Ann Neurol **92**(6): 1080-1089.

BACKGROUND: Transverse myelitis (TM) has recently been associated by health authorities with Ad26.COV2.S (Janssen/Johnson & Johnson), one of the 5 US Food and Drug Administration (FDA) or European Medicines Agency (EMA) labeled severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) vaccines. It is unknown whether a similar association exists for the other FDA or EMA labeled SARS-CoV-2 vaccines (BNT162b2 [Pfizer/BioNTech], mRNA-1273 [Moderna], ChAdOx1nCov-19 [Oxford-AstraZeneca], and NVX-CoV2373 [Novavax]). This study aimed to evaluate the association between SARS-CoV-2 vaccine class and TM. METHODS: This observational, cross-sectional, pharmacovigilance cohort study examined individual case safety reports from VigiBase, the World Health Organization's pharmacovigilance database. We first conducted a disproportionality analysis with the information component (IC) using the reports of TM that occurred within 28 days following exposure to the FDA or EMA labeled SARS-CoV-2 vaccines, from December 1, 2020 (first adverse event related to a SARS-CoV-2 vaccine) to March 27, 2022. Second, we analyzed the clinical features of SARS-CoV-2 vaccine-associated TM cases reported in VigiBase. RESULTS: TM was significantly associated both with the messenger ribonucleic acid (mRNA)-based (n = 364; IC(025) = 0.62) and vector-based (n = 136; IC(025) = 0.52) SARS-CoV-2 vaccines that are authorized by the FDA or the EMA. CONCLUSIONS: Findings from this observational, cross-sectional pharmacovigilance study showed that mRNA-based and vector-based FDA/EMA labeled SARS-CoV-2 vaccines can be associated with TM. However, because TM remains a rare event, with a previously reported rate of 0.28 cases per 1 million vaccine doses, the risk-benefit ratio in favor of vaccination against SARS-CoV-2 virus remains unchallenged. Rather, this study suggests that clinicians should consider the diagnosis of TM in patients presenting with early signs of spinal cord dysfunction after SARS-CoV-2 vaccination. ANN NEUROL 2022;92:1080-1089.

Notghi, A. A., J. Atley and M. Silva (2021). "Lessons of the month 1: Longitudinal extensive transverse myelitis following AstraZeneca COVID-19 vaccination." Clin Med (Lond) **21**(5): e535-e538.

Longitudinal extensive transverse myelitis (LETM) is a rare but recognised complication of vaccination. We report the case of a 58-year-old man admitted to hospital 10 days after his first AstraZeneca COVID-19 vaccination with progressive neurological symptoms and signs, and investigations and imaging consistent with LETM.This case reviews the literature and the investigative process behind excluding other diagnoses given the patient's background of pulmonary sarcoidosis. It is unique in being the first UK report of a case of LETM with a strong temporal link to COVID-19 vaccination.

Ostovan, V. R., et al. (2022). "Clinical characteristics, radiological features and prognostic factors of transverse myelitis following COVID-19 vaccination: A systematic review." Mult Scler Relat Disord **66**: 104032.

BACKGROUND: Since introducing COVID-19 vaccines, many neurological complications such as acute transverse myelitis have been reported in the literature. This study aims to identify the clinical characteristics, radiological findings, and prognostic factors in patients with COVID-19 vaccine-associated transverse myelitis (TM). METHODS: We

systematically reviewed Scopus, Pubmed, Cochrane library, Google Scholar, and preprint databases using appropriate keywords from inception till 8th April 2022. Besides, we manually searched the reference lists of the included studies and relevant previous reviews. RESULTS: We included 28 studies identifying 31 post-COVID-19 vaccination myelitis patients (17 female and 14 male). The mean age of the included patients was 52+/-19 years. ChAdOx1 nCoV-19 vaccine (Oxford-AstraZeneca) was the most common type of vaccine in association with myelitis (12 out of 31), followed by Pfizer (8 out of 31), Moderna (7 out of 31), Sinopharm (3 out of 31), and Janssen vaccine (1 out of 31). The myelitis occurred in 24 and 7 patients after administering the first and second dose of the vaccine, respectively. 21 and 10 patients had good recovery (Modified Rankin Score (MRS) <3 at the follow-up) and poor recovery (MRS>/=3 at the follow-up) from myelitis, respectively. Age (OR 1.09, 95%CI 1.01-1.18, p(value) 0.02), and MRS at admission (OR 17.67, 95%CI 1.46-213.76, p(value) 0.024) were two independent risk factors for poor recovery from myelitis. CONCLUSION: The patients with higher age and MRS at admission had a worse prognosis and needed timely and more aggressive therapeutic strategies.

Pagenkopf, C. and M. Sudmeyer (2021). "A case of longitudinally extensive transverse myelitis following vaccination against Covid-19." J Neuroimmunol **358**: 577606.

BACKGROUND: Longitudinally extensive transverse myelitis (LETM) is a rare subtype of transverse myelitis (TM) that potentially results in relevant disability. Apart from association to neuromyelitis optica and other chronic demyelinating diseases of the central nervous system, many other aetiologies are known. Particularly systemic infections and vaccination are considered potential triggers for immune mediated inflammation of the spinal cord. In the course of the current Covid-19 pandemic several cases of TM following Covid-19 infection have been described. Here we present a case of LETM following vaccination against Covid-19 with AZD1222, AstraZeneca. An extensive diagnostic work up was performed to rule out alternative causes, including prior and current Covid-19 infection. CONCLUSION: To our knowledge this is first case of LETM possibly related to Covid-19 vaccination that is published after marketing authorisation of various vaccine candidates.

Roman, G. C., et al. (2021). "Acute Transverse Myelitis (ATM):Clinical Review of 43 Patients With COVID-19-Associated ATM and 3 Post-Vaccination ATM Serious Adverse Events With the ChAdOx1 nCoV-19 Vaccine (AZD1222)." Front Immunol **12**: 653786.

INTRODUCTION: Although acute transverse myelitis (ATM) is a rare neurological condition (1.34-4.6 cases per million/year) COVID-19-associated ATM cases have occurred during the pandemic. CASE-FINDING METHODS: We report a patient from Panama with SARS-CoV-2 infection complicated by ATM and present a comprehensive clinical review of 43 patients with COVID-19-associated ATM from 21 countries published from March 2020 to January 2021. In addition, 3 cases of ATM were reported as serious adverse events during the clinical trials of the COVID-19 vaccine ChAdOx1 nCoV-19 (AZD1222). RESULTS: All patients had typical features of ATM with acute onset of paralysis, sensory level and sphincter deficits due to spinal cord lesions demonstrated by

imaging. There were 23 males (53%) and 20 females (47%) ranging from ages 21- to 73-years-old (mean age, 49 years), with two peaks at 29 and 58 years, excluding 3 pediatric cases. The main clinical manifestations were quadriplegia (58%) and paraplegia (42%). MRI reports were available in 40 patients; localized ATM lesions affected </=3 cord segments (12 cases, 30%) at cervical (5 cases) and thoracic cord levels (7 cases); 28 cases (70%) had longitudinally-extensive ATM (LEATM) involving >/=4 spinal cord segments (cervicothoracic in 18 cases and thoracolumbar-sacral in 10 patients). Acute disseminated encephalomyelitis (ADEM) occurred in 8 patients, mainly women (67%) ranging from 27- to 64-years-old. Three ATM patients also had blindness from myeloneuritis optica (MNO) and two more also had acute motor axonal neuropathy (AMAN). CONCLUSIONS: We found ATM to be an unexpectedly frequent neurological complication of COVID-19. Most cases (68%) had a latency of 10 days to 6 weeks that may indicate post-infectious neurological complications mediated by the host's response to the virus. In 32% a brief latency (15 hours to 5 days) suggested a direct neurotropic effect of SARS-CoV-2. The occurrence of 3 reported ATM adverse effects among 11,636 participants in the AZD1222 vaccine trials is extremely high considering a worldwide incidence of 0.5/million COVID-19-associated ATM cases found in this report. The pathogenesis of ATM remains unknown, but it is conceivable that SARS-CoV-2 antigens - perhaps also present in the AZD1222 COVID-19 vaccine or its chimpanzee adenovirus adjuvant- may induce immune mechanisms leading to the myelitis.

Tahir, N., et al. (2021). "SARS-CoV-2 Vaccination-Induced Transverse Myelitis." Cureus **13**(7): e16624.

While mass immunization against coronavirus disease 2019 (COVID-19) rolls out around the globe, safety concerns and adverse events that need prompt evaluation are also emerging. We report a case of transverse myelitis and Bell's palsy after receiving Johnson and Johnson COVID-19 vaccination under the emergency use authorization in a healthy young woman with no past medical history. Other possible etiologies of her symptoms were ruled out, and she was treated successfully with steroids and plasma exchange.