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TABLE OF CONTENTS

AGRICULTURAL SCIENCES

1. *Horodyska O. P., Storozh O. V.* 13
WHEAT SEED DURABILITY DURING STORAGE AND METHODS OF ITS ASSESSMENT
2. *Кудрик Н. А., Туринський В. М.* 16
МЕТОДОЛОГІЧНІ АСПЕКТИ СТВОРЕННЯ АСКАНІЙСЬКОЇ КАРАКУЛЬСЬКОЇ ПОРОДИ ОВЕЦЬ
3. *Куліш О. О., Богданова Н. В.* 20
РІВЕНЬ ПРОДУКТИВНОСТІ ОВЕЦЬ РОМАНІВСЬКОЇ ПОРОДИ
4. *Соколовська І. М.* 26
ЕФЕКТИВНІСТЬ ВИРОЩУВАННЯ НАСІННЄВОЇ КАРТОПЛІ ЗАЛЕЖНО ВІД ЗАСТОСУВАННЯ МІКРОЕЛЕМЕНТІВ ЗА РІЗНИХ НОРМ ВНЕСЕННЯ МІНЕРАЛЬНИХ ДОБРИВ
5. *Туринський В. М.* 31
ШЛЯХИ ПІДВИЩЕННЯ ЕКОНОМІЧНОЇ ЕФЕКТИВНОСТІ ВЕДЕННЯ ВІВЧАРСТВА ВОВНОВОГО НАПРЯМУ ПРОДУКТИВНОСТІ

BIOLOGICAL SCIENCES

6. *Андрійчук Н. Б., Гудзенко Т. В., Горшкова О. Г., Ракитська С. І.* 36
ЖИРНО-КИСЛОТНИЙ СКЛАД ЗАГАЛЬНИХ ЛІПІДІВ ШТАМУ AEROMONAS ICHTHIOSMIA ONU 552 – ДЕСТРУТОРА ФЕНОЛА
7. *Островська С. С., Абрамов С. В., Носуля І. М., Тищенко Т. Д., Борець А. О.* 41
ЕФЕКТИ ВПЛИВУ СВИНЦЮ НА КІСТКОВОМОЗКОВЕ КРОВОТВОРЕННЯ

MEDICAL SCIENCES

8. *Abrar Elfatih Galaleldeen Hassan, Glukhova O.* 44
SEPTIC ARTHRITIS – EVALUATION OF MIMICKED PATHOLOGIES, MANIFESTATIONS AND MANAGEMENT
9. *Horodnov Ye.* 48
MANIFESTATIONS OF ANXIETY IN PATIENTS WITH GENERALIZED PERIODONTIS WHEN PROVIDING DENTAL CARE
10. *Pingili Deepthi, Pavliukovych N., Pavliukovych O.* 53
POST-COVID-19 MYOCARDITIS: ITS INCIDENCE AND MECHANISMS OF DEVELOPMENT
11. *Алієв Р. Б., Шаповалова А. С., Шекера І. А.* 58
ПРОФІЛАКТИЧНІ ЗАХОДИ І РАННЄ ДІАГНОСТУВАННЯ, ЯК ГОЛОВНІ МЕТОДИ ЗНИЖЕННЯ КІЛЬКОСТІ ВИПАДКІВ ТУБЕРКУЛЬОЗНОГО МЕНІНГІТУ

POST-COVID-19 MYOCARDITIS: ITS INCIDENCE AND MECHANISMS OF DEVELOPMENT

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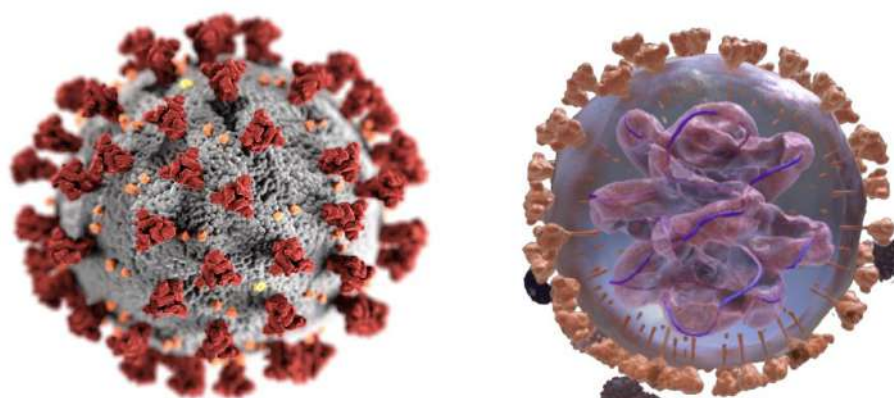
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The Coronavirus disease (COVID-19) is an infectious disease caused by the SARS-CoV-2 virus



Pic. 1. Ultrastructure of the SARS-CoV-2 coronavirus

This model depicts ultrastructure of the SARS-CoV-2 coronavirus:

- a positive-sense single-stranded RNA virus (+ssRNA).
- internally, helical RNA is enveloped by N protein, forming the nucleocapsid.
- on the surface – spike glycoproteins mediate infection by binding to angiotensin-converting enzyme 2 (ACE-2), which is a transmembrane glycoprotein of lung, intestine, kidney, and blood vessel epithelium.

COVID-19 was first reported in late 2019 in Wuhan, China and spread

extensively worldwide. It is caused by SARS-CoV-2, a coronavirus discovered in 2019. SARS-CoV-2 infection causes a spectrum of severity of disease, from asymptomatic to acute respiratory failure and death. Risk factors for severe disease include older age, immunocompromised, comorbidities (e.g., diabetes, chronic kidney disease), and pregnancy.

As of June 28, 2021, more than 12.3 million doses of the Janssen vaccine have been administered in the United States. The CDC and the FDA identified 38 confirmed reports of people who got this vaccine and later developed TTS. Women younger than 50 years should especially be aware of the rare but increased risk of this adverse event. For the AstraZeneca vaccine, thrombosis seems to be a complication of the vaccine especially in people younger than 60 years. In one Italian case, a young girl (18 years) died three days after the vaccination.

Myocarditis and pericarditis after Covid-19 vaccines are rare. As of June 28, 2021, VAERS (Vaccine Adverse Events Reporting System) has received 780 reports of myocarditis or pericarditis among people 30 years and younger who received a Covid-19 vaccine.

Myocarditis 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.

Case reports and surveillance signals of myocarditis (including myopericarditis) and pericarditis after covid-19 vaccination appeared as early as April 2021, leading to the surveillance of adverse events of special interest after vaccination with mRNA vaccines manufactured by Pfizer/BioNTech (BNT162b2) and Moderna (mRNA-1273). Estimated rates of myocarditis are 11 per 100 000 person years in the UK and 1-2 cases per 100 000 person years in the US regardless of age.

In the US, estimated background rates or expected rates after COVID-19 vaccination of myocarditis is 0.2 per one million people and of pericarditis is 1.4 per one million people, after adjustment for a 7-day risk period where most cases appear.

Males are notably more likely to develop myocarditis and pericarditis following COVID-19 vaccination than females (85% vs 15%). The majority of the patients had no significant history of COVID-19 infection or any other.

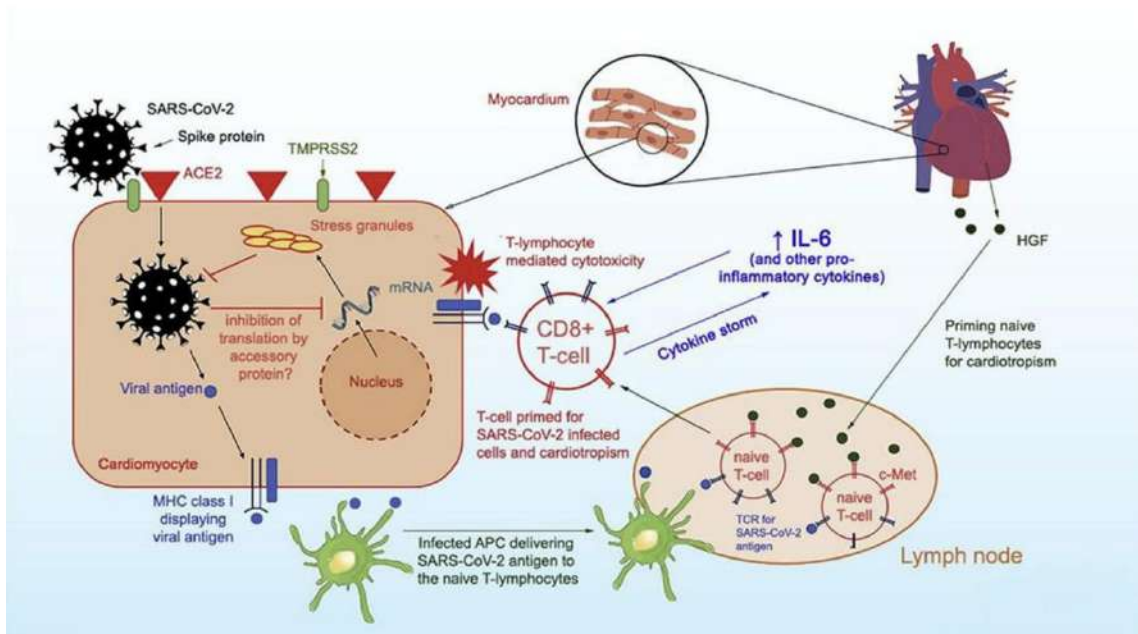
Myocarditis is the inflammation of the myocardium that occurs most commonly due to viral illnesses although non-infectious etiologies have also been reported. It is believed that myocarditis and its complications are largely immune mediated. Myocarditis usually presents with chest pain, which can result from associated pericarditis, or occasionally, from coronary artery spasm. Acute myocarditis is frequently first diagnosed as nonischemic dilated cardiomyopathy in a symptomatic patient. The prevalence of myocarditis and pericarditis was more among the patients who received Pfizer-BioNTech (BNT162b2) than those who received other vaccines, but this may be due to the fact that more patients included in this review had received the aforementioned vaccine.

Similarly, a greater percentage of patients who developed the symptoms received two doses of vaccine (compared to one). Chest pain, fever, myalgias, and dyspnea were the most common presentations. The majority of the patients who presented with myocarditis and pericarditis had a good recovery and were discharged.

Several hypotheses have been put forward to explain the factors that might cause these complications of the COVID-19 vaccine. However, the exact pathophysiology is yet to be elaborated. One of the proposed mechanisms is the interaction between components of the vaccine and the susceptibility of the subject known as molecular mimicry. Due to the similarity between the pathogenic component of the vaccine and specific human proteins, there is immune cross reactivity resulting in autoimmune disease. Among other vaccines for which myocarditis has been reported as an adverse effect, only the smallpox vaccine has demonstrated a significantly high risk.

The higher prevalence of this condition among males can be explained based on the role played by variations in hormone signaling. Testosterone has the ability to suppress anti-inflammatory immune cells while promoting a more aggressive T-helper-1 cell immunological response. Estrogen, on the other hand, inhibits pro

inflammatory T cells, resulting in a reduction in cell-mediated immune responses. However, further research is required to explore the exact phenomenon.



Pic. 2 Possible mechanisms of COVID-19-induced myocarditis

The institutional ethics commission approved this prospective study. All participants gave written informed consent. Participants with COVID-19 without structural heart disease and mechanical ventilatory support were included consecutively during the recruitment period from April 2020 to December 2020. Participants had a clinical suspicion for COVID-19-associated myocarditis with signs of acute myocardial injury (elevated troponin levels with or without electrocardiographic changes). Acute coronary syndromes were excluded with cardiac catheterization. The control groups consisted of healthy volunteers and participants with suspected acute non-COVID-19 myocarditis.

Myocarditis and pericarditis after the COVID-19 vaccine occur most commonly in adult males after the second dose of mRNA vaccines (Pfizer and Moderna). The presentation is usually mild, and the majority of patients have a good recovery. Cell-mediated immune responses generated by the body against the vaccine components cross-react with cardiac cells to cause myocardial and pericardial inflammation. It follows that the most effective treatment for this clinical entity are immunosuppressants and anti-inflammatory agents (e.g., colchicine, NSAIDs and

steroids). Physicians should consider myocarditis and pericarditis as a probable diagnosis in patients who have received COVID-19 vaccines, especially in males who develop suggestive symptoms after a second dose of Pfizer and Moderna. Viral vector vaccines may be a better alternative for patients with a history of cardiac diseases.

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