From the beginning of the coronavirus disease-2019 (COVID-19) pandemic, both journals of the Israel Medical Association, Israel Medical Association Journal (IMAJ) and Harefuah, followed development in research and medical care for patients regarding the virus. During 2020, more than 20 papers were published in IMAJ and Harefuah that dealt with the virus, the pandemic, public health, vaccine development, old and new drugs and care modalities, and more. All of these manuscripts were selected and published in an electronic edition of IMAJ. The highlights are presented here.

Sheba Medical Center, Tel Hashomer, is a tertiary hospital located in the center of Israel. It is the largest hospital in Israel and was the first to face coronavirus disease-2019 (COVID-19) patients in the country at the beginning of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic. Levy and colleagues [1] described the experience with the COVID-19 pandemic, focusing on triage methods in the emergency department (ED). The goal of the ED staff was to keep the main hospital buildings clean of infection by separating COVID-19 positive patients from COVID-19 negative patients. It turned out that the triage method was successful in separating COVID-19 positive patients and kept the regular hospital clean of COVID-19 allowing treatment continuation of regular non-COVID-19 patients.

Analysis by Itelman and colleagues [2] included all COVID-19 patients treated at Sheba Medical Center from February 2020 to April 2020. Clinical, laboratory, and epidemiological data gathered during the patients’ hospitalization were presented.

The cohort of 162 patients included mostly adult (mean age 52 ± 20 years) males (65%). Patients classified as severe COVID-19 were significantly older and had higher prevalence of arterial hypertension and diabetes. They also had significantly higher white blood cell counts, absolute neutrophil counts, and lactate dehydrogenase. Low folic acid blood levels were more common among severe patients (18.2 vs. 12.9 vs. 9.8, \( P = 0.014 \)). The rate of immune compromised patients (12%) in this cohort was also higher than in the general population. The rate of deterioration from moderate to severe disease was high: 9% necessitated non-invasive oxygenation and 15% were intubated and mechanically ventilated. The mortality rate was 3.1%.

**CYTOKINE STORM AND TREATMENT**

In the absence of definitive anti-viral therapy, there is considerable interest in mitigating against severe inflammatory reactions in COVID-19 pneumonia to improve survival. These reactions are sometimes termed cytokine storm. PDE4 inhibitors (PDE4i) have anti-inflammatory properties with approved indications in inflammatory skin and joint diseases as well as chronic obstructive pulmonary disease (COPD). Furthermore, multiple animal models demonstrated strong anti-inflammatory effects of PDE4i in respiratory models of viral and bacterial infection and also after chemically mediated lung injury. The rationale for PDE4i use in COVID-19 patients comes from the multimodal mechanism of action with cytokine, chemokine, and other key pathway inhibition all achieved with an excellent safety profile. Bridgewood et al. [3] highlighted how PDE4i could be an overlooked treatment from the rheumatologic and respiratory armamentarium, which has potential beneficial immune-modulation for treating severe COVID-19 pneumonia associated with cytokine storms. The proposed use of PDE4i is also supported by age-related immune changes in inflammation severity in PDE4i modifiable pathways in primate coronavirus disease. Over-exuberant anti-viral immune responses in older patients with COVID-19 may pose a substantial risk to patient survival and mitigation against such hyper-inflammatory with PDE4i, especially with anti-viral agents, is a strategy that needs to be pursed, especially in older patients.

**DIAGNOSIS: SMELL EFFECT**

There is a high prevalence of olfaction changes, especially in the early presentation, in COVID-19 patients. The mechanisms through which the virus leads to anosmia/hyposmia is still not fully understood. However, olfaction changes could be used as an indication for testing or quarantine. Screening for infections and other diseases by recognizing volatile organic compounds
(VOCs) has been previously conducted. Hence, if the coronavirus infection also results in VOCs excretion, physicians could “smell” the virus by using electronic noses. The authors conducted a literature review on olfaction changes and COVID-19. These results suggest that these changes could be used an indication for early testing, even as an isolated symptom. David and Shoenfeld [4] proposed that the electronic nose be used as a future screening tool, especially in agglomeration spaces such as airports, for screening for the COVID-19 infection.

**DIAGNOSIS AND PROGNOSIS**

Ferritin, the cellular protein storage for iron, has emerged as a key molecule in the immune system by orchestrating the cellular defense against inflammation. A significant increase in ferritin levels was demonstrated by Dahan and co-authors [5] in patients with moderate and severe disease, compared with patients with a mild disease ($P = 0.006$ and $0.005$, respectively). Severe patients had significantly higher levels of ferritin (2817.6 ng/ml) than non-severe patients (708.6 ng/ml) $P = 0.02$. In this preliminary cross-sectional study, elevated ferritin levels were shown to correlate with disease severity in 39 patients from Israel with confirmed COVID-19 infection. These results further strengthened the hypothesis that severe COVID-19 disease might be due to an underlying dysregulated hyperimmune response.

**OBSTETRICS AND NEONATALICS**

Justman et al. [6] evaluated whether the pandemic changed the prenatal care and pregnancy outcome in pregnant women without COVID-19. The authors conducted a cross-sectional study to describe changes in outpatient clinic visits and compared the rates of cesarean and instrumental deliveries between two periods of time: March–April 2020 (during the COVID-19 outbreak) with March–April of the preceding year: 2019. The medical facility experienced a major decline in all aspects of the routine obstetrics activities during the time of the pandemic. The higher rate of operative vaginal deliveries among nulliparous may be associated with the pandemic effect on the rate of high-risk patients.

**ANESTHESIA AND COVID-19**

Droplets from the upper airway of COVID-19 patients may infect the inhalation sedation mask and tubing. Yanko and colleagues [7] determined the adequate measures needed to prevent the transmission of COVID-19 by nitrous-oxide ($N_2O$) systems during inhalation sedation in dentistry and provided evidence on mask and tubing sterilization. Additional measures to protect patients and healthcare workers from COVID-19 that may be transmitted by the inhalation sedation system were discussed. The authors recommended minimal use of a $N_2O$ system during inhalation sedation in dentistry. In case of need, the practitioners should have more than one scavenger kit and nasal masks for each $N_2O/O_2$ mixer. Biological barriers should be mounted between the scavenger's tubing and the central evacuation system. Strict cleansing and sterilization should be performed for all parts of the $N_2O$ system. The use a disposable scavenger system and nasal mask should be considered as a viable option.

**DIAGNOSIS**

Elhadad et al. [8] conducted a single-center, retrospective study of 58 consecutive laboratory-confirmed COVID-19 patients admitted to Laniado Hospital, Israel, between 14 March 2020 and 14 May 2020. Demographic, clinical, and laboratory data on admission were collected and analyzed, and the association to subsequent respiratory failure was assessed. The results showed that C-reactive protein, creatine kinase, and absolute lymphocyte count levels on admission could possibly be used to detect high-risk patients prone to develop respiratory failure.

**ADMISSIONS OF SURGICAL PATIENTS DURING THE EPIDEMIC**

As part of the effort to control the coronavirus disease-19 (COVID-19) outbreak, strict emergency measures, including prolonged national curfews, have been imposed. Even in countries where healthcare systems still functioned, patients avoided visiting emergency departments (EDs) because of fears of exposure to COVID-19. Aviram and co-authors [9] described the effects of the COVID-19 outbreak on admissions of surgical patients from the ED and characteristics of urgent operations performed. It turned out that during the COVID-19 epidemic, fewer patients presented to the ED requiring acute surgical care. Those who did often did so in a delayed fashion and in worse clinical condition. More patients required urgent surgical interventions compared to the control period. Governments and healthcare systems should emphasize to the public not to delay seeking medical attention, even in times of crises.

**NEUROLOGY AND COVID-19**

COVID-19 and its management in patients with epilepsy can be complex. Prescribers should consider potential effects of investigational anti-COVID-19 drugs on seizures, immunomodulation by anti-seizure medications (ASMs), changes in ASM pharmacokinetics, and the potential for drug-drug interactions (DDIs). The goal of the Board of the Israeli League Against Epilepsy (the Israeli Chapter of the International League Against Epilepsy, ILAE) was to summarize the main principles of the pharmacological treatment of COVID-19 in patients with epilepsy. This guide, as reported by Ekstein and associates [10], was based on current literature, drug labels, and drug interaction resources.

**DRUGS AND PRESCRIPTIONS DURING COVID-19**

Ekstein et al. [10] summarized the available data related to the potential implications of anti-COVID-19 co-medication in patients treated with anti-seizure medications (ASMs). The recommendations refer to drug selection, dosing, and patient...
monitoring. Given the limited availability of data, some recommendations were based on general pharmacokinetic or pharmacodynamic principles and might apply to additional future drug combinations as novel treatments emerge. The guidelines that were reported would not replace evidence-based guidelines, should those become available. Awareness to drug characteristics that increase the risk of interactions can help adjust anti-COVID-19 and ASM treatment for patients with epilepsy.

COVID-19 PATIENTS: WEANING FROM VENTILATORS

Patients diagnosed with COVID-19 who deteriorate to respiratory failure and require mechanical ventilation may later need to be weaned from the ventilator and undergo a rehabilitation process. Ovadya et al. [11] presented experience with ventilator weaning of COVID-19 patients in a dedicated facility. Eighteen patients were hospitalized in the dedicated unit between 6 April and 19 May 2020. Despite the high mortality of COVID-19 patients who require mechanical ventilation, most of the patients in the cohort were weaned in a relatively short period of time.

CONCLUSIONS

The previously cited articles, in addition to nine others [12-20] from IMAJ and more than 20 published in Harefuah (not cited), follow medical advances developed in Israel and lead the scientific and medical community by publishing up-to-date reviews and research on urgent medical and health matters, keeping pace with first-line scientific journals worldwide.

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References


