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## In the Limelight: November 2020



This month's feature highlights four articles, three of which focus on COVID-19 that appear in the current print and online issue of *Mayo Clinic Proceedings*. These articles are also featured on the *Mayo Clinic Proceedings*' YouTube Channel ([https://youtu.be/85\\_u31VOR8Q](https://youtu.be/85_u31VOR8Q)).

### COAGULOPATHY, CLOTTING, AND COVID-19

Shortly after the spread of COVID-19, it became apparent that patients with this disease were at an increased risk for a coagulopathy and thrombosis, the latter occurring, as described in some patients, despite seemingly appropriate anticoagulant prophylaxis. In the present issue of *Mayo Clinic Proceedings*, McBane et al provide a systematic review and meta-analysis of relevant literature that address these considerations. Beginning with more than 4000 citations, these authors culled 37 studies based on such predetermined criteria as number of participants, assessment of coagulation profile, the effect of anticoagulation strategies, and documentation of relevant outcomes; where possible, meta-analyses were undertaken. The findings indicate that in COVID-19 there is a propensity to such abnormalities as elevated levels of fibrinogen and elevated D-dimer levels, prolongation of the prothrombin time (PT) or activated thromboplastin time, and thrombocytopenia. As pointed out by McBane et al, COVID-19-associated coagulopathy (CAC) differs from disseminated intravascular coagulation (DIC) because in CAC fibrinogen levels are elevated (not decreased as in DIC) and the PT and platelet count are only mildly prolonged or decreased respectively. Patients with severe COVID-19, as compared with those with milder manifestations, are more likely to exhibit elevated D-dimer levels and thrombocytopenia. The occurrence of thrombosis varied substantially (2% to 69%), with a lower rate occurring in a study in which clinical assessment led to imaging studies, whereas the higher rate was

described in one study employing mandatory surveillance ultrasound imaging. For those studies reporting a higher incidence of thrombosis in patients in the ICU with COVID-19, such incidence is substantially greater than is generally expected for similarly ill patients without COVID-19. McBane et al summarize findings from available studies regarding the rates of venous thromboembolic disease (VTE) and outcomes in patients receiving prophylaxis-dosed and therapeutically dosed anticoagulation therapy. Based on such analyses of the literature and the input from experts in thrombosis, hematology, cardiovascular medicine, and pulmonary and critical care medicine at Mayo Clinic, McBane et al provide a consensus approach that addresses the prevention of thrombosis, including such considerations as whether the patient is already on anticoagulation therapy for a specific indication; how prophylaxis is preferably achieved such that the risks of bleeding are minimized; the need for daily clinical evaluation for VTE and, where indicated, imaging studies; laboratory evaluation; assessing the risk for VTE and how increased risk lowers the threshold for imaging studies and tailors the type of prophylaxis; and, finally, whether prophylaxis should be continued following dismissal to the outpatient setting. In their consensus approach to treatment of thrombosis, McBane et al underscore that in patients in whom VTE is confirmed, the therapeutic approach should generally follow practice guidelines for VTE in patients without COVID-19; they discuss the uncommon instances when thrombophilia testing (such as lupus anticoagulant) may be indicated; and they delineate key considerations underlying the assessment and management of patients who have failed to respond to anticoagulation therapy. The authors emphasize that the certainty of evidence in the literature is, broadly speaking, quite low, and in this regard, they point out the



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unaddressed and unresolved questions in this field. Finally, they outline mechanisms that promote a thrombogenic state in COVID-19, several of which involve the endothelium being transformed into a pro-thrombotic surface because of endothelial activation/injury caused by SARS-CoV-2 infection, complement, cytokines, hypoxia, or angiotensin II. McBane et al are to be commended for undertaking this timely and important analysis and providing these needed consensus recommendations based on the currently available literature.

McBane RD II, Torres Roldan VD, Niven AS, et al. Anticoagulation in COVID-19: A systematic review, meta-analysis, and rapid guidance from Mayo Clinic. *Mayo Clin Proc.* 2020;95(11):2465-2484.

#### INFODEMIOLOGY, INFOVEILLANCE, AND IDENTIFYING COVID-19 CASES

In the present issue of *Mayo Clinic Proceedings*, and in introducing their novel observations regarding the COVID-19 pandemic, Kurian et al provide the backdrop of “Infodemiology” and “Infoveillance,” terms that describe the analysis of data available on the Internet that are relevant to public health and health care policy (please see reference #4 in this article by Kurian et al). These authors applied these analytical approaches to assess the occurrence of cases of COVID-19 state by state as well as collectively for the United States; to this end, they employed Web-based data available in Google Trends. Google Trends is a vast repository of data based on specific Internet searches that can be analyzed either in real time (over the past week) or in non-real time (data that go back as far as 2004 to almost the present). Kurian drew upon data obtained from 1/22/20 to 4/6/20 and selected 10 keywords that relate to COVID-19 including those pertaining to the main symptoms of the disease, diagnosing the disease, and how spread of the disease may be minimized or prevented. These authors employed the database from Johns Hopkins University Center for Systems Science and Engineering that provides not only the total

number of COVID-19 cases and deaths, but also those that occur on a daily basis; these data are gathered on a county-specific and state-specific basis in the United States. Among the salient findings in this study by Kurian et al are the following. First, certain key words tended to have their own temporal profiles of usage, as for example, “face mask” steadily rose over the time frame studied while others did not; specific keywords were more commonly used when COVID-19 cases were lower, and others when COVID-19 cases were higher. Second, when analyses were undertaken for the entire United States, 6 keywords had moderate correlations, and 3 keywords (face masks, Lysol, and COVID stimulus check) had strong correlations with daily new cases; four keywords exhibited significant correlations when analyzed for individual states. Third, additional analyses were undertaken by Kurian et al to determine lag correlations (over a time frame of 16 days prior to the appearance of the first case) and lead correlations (over a time frame of 16 days following the appearance of the first case). Most of the keywords had moderate to strong correlations in the days preceding the appearance of the first case, with declining correlations thereafter. Such correlations tended to vary by state; in Florida, for example, strong correlations were exhibited by virtually all of the 10 keywords prior to the appearance of the index case of COVID-19. The importance of the study by Kurian et al is that it shows how certain keywords used in Internet-based searches not only correlate with cases of COVID-19 in the United States, but also antedate the emergence of such cases in specific geographic states. Because these data can be gathered in real-time, they may possess an immediacy and timeliness otherwise lacking in traditional methods for disease surveillance. Such data may thus aid strategies that seek to forecast and restrain the spread of the disease and to judiciously apportion resources in caring for patients with COVID-19. Finally, the study by Kurian et al provides a persuasive example of the power and scope

of Infodemiology and Inveillance in the service of health care policy and public health.

Kurian SJ, Bhatti AuR, Alvi MA, et al. Correlations between COVID-19 cases and Google Trends data in the United States: A state-by-state analysis. *Mayo Clin Proc.* 2020;95(11):2370-2381.

### CARING FOR CRITICALLY ILL COVID-19 PATIENTS AMIDST COVID-19-INDUCED STRESS

In a recent issue of *Mayo Clinic Proceedings*, Vance and Howell discussed the functional compromise and sequelae caused by posttraumatic stress disorder (PTSD) and traced the original recognition of a type of PTSD to shell shock incurred during World War I. The current global crisis caused by the COVID-19 pandemic imposes its own unique shock and stress to patients with the disease, to the family and loved ones of these patients, and to physicians, other providers, and health care workers caring for patients with suspected or confirmed COVID-19; indeed, in the COVID-19 pandemic, PTSD may occur in individuals belonging to all such subgroups. In the present issue of *Mayo Clinic Proceedings*, Karnatovskaia et al broadly discuss the emotional and psychological burden mightily imposed by the COVID-19 crisis on providers and patients, and they suggest approaches that may reduce the impact and adverse outcomes caused by such burdens. These authors begin by delineating the reasons why health care workers may be inordinately exposed to such stress — the rapid and at times overwhelming surge in patient volumes, the witnessing of patient suffering and demise, insufficient medical supplies and resources and the need for rationing, the fear of infection and causing the spread of infection among others. Karnatovskaia et al discuss the physiological effects of stress

and how such effects become pathobiologic and disease-provoking when imposed stress is either precipitate, inordinate, or unremitting; notably, the adverse immune effects of sustained stress can itself predispose to infection with SARS-CoV-2. The authors then discuss the physiological and pathophysiologic effects of emotion and attitude, emphasizing the generally salutary effects of a positive outlook on the one hand and, on the other, the unhealthy (including nocebo) effects and the propensity for errors in judgment of a largely fearful and negative mindset. All these considerations are then brought back to the care of the critically ill patient as the authors discuss how such considerations can affect both the provider and patient and may influence patient outcomes. Karnatovskaia et al conclude with strategies for staff that may promote resilience, a positive attitude, and the practicing of the Golden Rule, as well as those that may optimize patient-provider interaction and patient care. Responses to stress are categorized, biologically and broadly, into those that are adaptive because they mitigate the adverse effects of stress, and those that are maladaptive as they exaggerate the perturbing effects of stress. Karnatovskaia et al provide a number of important adaptive approaches that can safeguard the health care team from the stress and fear imposed by the COVID-19 pandemic and, in so doing, may improve outcomes for patients under their care.

Vance MC, Howell JD. Shell shock and PTSD: A tale of two diagnoses. *Mayo Clin Proc.* 2020;95(9):1827-1830.

Karnatovskaia LV, Johnson MM, Varga K, et al. Stress and fear: Clinical implications for providers and patients (in the time of COVID and beyond). *Mayo Clin Proc.* 2020;95(11):2485-2496.

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