The Situation:
In the world as of August 21, 2020, a total of 22,707,352 cases of Covid-19 and 794,256 deaths have been confirmed. In the United States, there have been 5,576,089 cases, the most in the world followed in order by Brazil, India, Russia and South Africa. China is now 32nd in the world with 89,594 cases. Deaths in the U.S. through August 21 have been estimated at 174,290.¹

From March 10 through August 21, there have been 66,772 confirmed cases of Covid-19 reported from Dallas County with 846 deaths, about 26% of these from long-term facilities.² Of 6,978 hospitalized cases in Dallas County, 70% have been under 65 years of age. Diabetes mellitus has been seen in about one-third of all hospitalized patients. More men than women have died, and 53% of the hospitalized cases have occurred in the Hispanic population. As of 8/18, 839 deaths have been analyzed by race, with 27% occurring in Whites (actual White population 29%), Hispanics 44% (population 41%), Blacks 23% (population 24%), and Asians 3% (population 7%). Specimens submitted for diagnosis of respiratory viruses show continuing positivity rate for SARS-CoV-2 of 14% as of 8/21/20, down from a peak value of 30.5% during the week ending 7/4/20.

References:
1. Covid-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU) (Updated 8/21/20)
2. Dallas County Health and Human Services. Acute Communicable Disease Epidemiology Division 8/21/20

Feature Article
Scarce Evidence of Bacterial Coinfection with SARS-CoV-2
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Bacterial infections occur both concomitantly and subsequent to a variety of viral respiratory illnesses. In the pre-antibiotic era of the 1918 influenza pandemic, bacterial infections complicated a high percentage of influenza-related deaths. More recently during the 2009 influenza A (H1N1) pandemic, bacterial infections were identified in up to 34% of ICU managed patients.¹ In a typical, non-pandemic influenza season, approximately 20% of patients are diagnosed with community-acquired bacterial infections, most commonly caused by Streptococcus pneumoniae or Staphylococcus aureus.¹,² Because COVID-19 has emerged recently, there is limited literature regarding bacterial coinfections in the setting of primary SARS-CoV-2 infection, but a review of 18 studies describing bacterial coinfections in patients with any coronavirus infection was performed by Rawson and colleagues.³ The authors described low rates of bacterial coinfection among the nine studies published for Covid-19 (62/806 [8%]). Since most studies were not specifically evaluating coinfections, they did not report the organisms identified.

At Parkland Memorial Hospital, we found that only 10 of 147 patients admitted with Covid-19 from March 10 to April 21, 2020, had veritable coinfections present at the time of admission (1 bacteremia, 3 UTIs, 1 skin/soft tissue infection, 1 otitis media, and 1 chorioamnionitis).⁴ However, we have yet to take a deeper dive...
into the subsequent secondary infections that we have seen in patients admitted with Covid-19, including hospital-acquired infections. Interestingly, the average time to development of a bacterial superinfection in patients with influenza has been reported to be 7-14 days after the onset of the viral infection.\(^5\) Therefore, the fact that none of the patients in our cohort were found to have definitive evidence of bacterial coinfection on admission is not unusual, as the patients presented a median of five days from symptom onset.\(^6\) Notably, of the patients in our cohort who were tested for influenza or another respiratory virus other than SARS-CoV-2, none was found to have a concurrent viral infection, which is consistent with other studies.\(^3\)

A study done in New York involving 4,267 patients diagnosed with SARS-CoV-2 revealed that bacterial and fungal coinfections and/or secondary bacterial infections occurred in <5% of patients, with the majority of the bacterial infections being nosocomial (51% being central line-associated bacteremias with average time to culture positivity 6-7 days following admission).\(^6\) Subsequently, a study involving a cohort of 836 patients from the United Kingdom (UK) revealed 3.2% of patients having early confirmed bacterial isolates identified (<5 days after admission), though this rose to 6.1% overall throughout admission.\(^7\) As in our study, the UK group concluded that there is a low frequency of bacterial coinfection in early Covid-19 hospitalization.\(^4,7\)

The continued development of antimicrobial resistance globally may be exacerbated in the setting of an infectious pandemic. In light of the rising number of COVID-19 cases worldwide, we believe that it is of utmost importance to continue promoting the judicious use of anti-infective agents and highlight the role of antimicrobial stewardship. Since bacterial coinfection with Covid-19 appears to be infrequent, antibiotics appear unnecessary at presentation in patients with mild symptoms, and there is little role for broad-spectrum antibiotics to empirically treat multidrug resistant organisms in patients initially presenting with COVID-19, regardless of disease severity. As more data emerges regarding the hospital courses of patients who have prolonged admissions with COVID-19, we will likely see patients developing secondary infections (including many nosocomial infections) requiring antibiotic therapy. Thus, for patients initially presenting with SARS-CoV-2 infection it appears prudent to save our antibiotic arsenal for when it is most needed.

References:

Clinical Advance

**T-Cell Responses to SARS-CoV-2 in Pre-Pandemic Persons**

There are seven known human coronaviruses: three of these have appeared in epidemic form (SARS, MERS and SARS-CoV-2) and four (OC-43, 229E, NL63 and HKU1) are endemic, mostly causing mild diseases like the common cold. An essential question with SARS-CoV-2, the cause of the present pandemic, is whether exposure to one or more of the 4 endemic coronaviruses could induce sufficient immunity to modify the clinical manifestations of Covid-19 illness. While it is known that antibodies to the endemic coronaviruses do not
usually cross-react with SARS-CoV-2 sufficiently to be measured or to prevent human disease, an important question is whether T-lymphocyte responses against SARS-CoV-2 occurring after exposure to one or more of the endemic coronaviruses could be detected and whether they can produce an immune response modifying clinical disease. Two recent articles by the same group of investigators summarize evidence for the presence of immune T-cells directed against SARS-CoV-2 in unexposed individuals. In their studies, they cite an absence of antibodies against SARS-CoV-2 in persons previously exposed to OC43 and NL63.

Each coronavirus strain contains multiple proteins that could act as antigens or epitopes capable of being recognized by T-cells and that then could be identified in immune reactions that potentially limit viral infection. Studies to identify these epitopes and measure T-cell responses found that polypeptides containing 15 amino acids (15-mer) are the optimal size for the best epitopes. Each coronavirus strain contains 4 structural proteins: spike (S), nucleocapsid (N), membrane (M) and envelope (E). The S protein can be divided into portions that bind to cells (receptor binding domain, RBD) and portions that do not bind (non-RBD). Other non-structural proteins are present in each virus like RNA polymerase, non-structural proteins, nsp (1-16), and products of open reading frames, ORFs.

The authors screened 474 epitopes derived from SARS-CoV-2 with a size of 15 mer by incubating each epitope for 14 days with peripheral blood mononuclear cells (PBMC) they obtained from a pre-pandemic multi-donor pool and then identifying cells responding to the epitope by detecting interferon gamma in T-cells by immunofluorescence in a FluoroSPOT assay and enumerating positive cells by counting Spot Forming Cells/2 million PBMC. The endpoint they were measuring was the percent of cells that were interferon-gamma-positive. They determined that the responding cells were mostly CD4+ cells and further identified as being primarily effector memory cells. In this initial phase of the studies, they determined that immune responses were occurring commonly in the pooled PBMC cultures and that the best and most frequently positive epitopes were derived from the RBD of the S protein. They actually found the highest frequency of positive epitopes within the S protein outside the binding site of the virus (non-RBD).

The authors then took PBMCs derived from donors obtained prior to the pandemic and reacted them with positive epitopes from SARS-CoV-2 and homologous regions of OC43, 229E, NL63 and HKU1 viruses and found that 10/42 (24%) of the cultures had cross-reactivity between the pandemic virus and one or more of the human endemic coronaviruses. The authors speculate that their study demonstrates the existence of T-cell immunity against SARS-CoV-2 in certain donors prior to the pandemic. This immunity, possibly resulting from previous exposure to one or more of the endemic human coronaviruses, might account for some of the variability encountered in the clinical manifestations of Covid-19. The data from one of their series of experiments is shown in Fig. 4 from their paper (Panels A, B and C. Panels D-L are not shown).

Fig. 4. Cross-reactivity of SARS-CoV-2 and homologous HCoV peptides. Twelve short-term cell lines were generated using specific SARS-CoV-2 epitope/donor combinations selected on the basis of the primary screen. After 14 days of in vitro expansion, each T cell line was tested with the SARS-CoV-2 epitope used for stimulation and peptides corresponding to analogous sequences from other HCoVs at six different concentrations (1μg/mL, 0.1μg/mL, 0.01μg/mL, 0.001μg/mL, 0.0001μg/mL). Spot forming cells per million (SFC/10^6) PBMCs are plotted for T cell lines stimulated with each peptide. N=nucleocapsid, S=spike.
The authors conclude that T-cell reactivity to SARS-CoV-2 epitopes can be detected in non-exposed individuals and that such reactivity may underlie at least some of the extensive heterogeneity observed in Covid-19 patients. These experiments point to epitopes which may be the most immunogenic in humans and which could be considered for inclusion in future vaccine attempts.

References:

Epi Corner

Hundreds of Miscoded Cases Added Show Steeper Recent Decline

Over the past week, the Texas Department of State Health Services discovered a series of coding errors by major Covid-19 testing laboratories, and after correcting the codes, added a large backlog of confirmed Covid-19 cases to the official case count. The most recent epidemic curve of confirmed cases by date the test was collected, generated by Dallas County epidemiologists from the corrected data on 8/18/20 (Fig. 2), shows that the daily case counts in June and early July at the height of the Dallas epidemic increased by an average of approximately 400 cases per day over the curve produced from the uncorrected data the prior week on 8/11/20 (Fig. 1). Consequently, back in late June when we were shocked to see 1,000 to 1,200 cases per day for 2 full weeks, we were really having close to 1,600 per day! We also see that the subsequent decline following the Governor’s orders closing the bars and mandating masking statewide was even steeper than we thought, providing even stronger evidence of the effectiveness of the classic public health control measures of masking and social distancing. The Dallas County graphs are published bi-weekly by the county health department at: https://www.dallascounty.org/departments/dchhs/-2019-novel-coronavirus.php

From the Editors

The editors thank Drs. Wei, Ortwine, Mang and Prokesch for their feature article on bacterial coinfection. The aim of this weekly newsletter is to serve as a source of information for the UT Southwestern community which can lead to better understanding and control of a new disease (COVID-19) caused by the pandemic spread of an emerging viral pathogen (SARS-CoV-2). We welcome questions, comments, and suggestions for topics and authors.