

COVID-19 Action Newsletter

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The Situation: Confirmed U.S. Deaths Top 220,000

In the world as of October 19, 2020, 40,122,835 cases and 1,114,857 deaths have been confirmed. In the United States, there have been 8,157,704 cases, the most in the world followed in order by India, Brazil, Russia and Argentina. China is now 49th in the world with 90,989 cases. Deaths in the U.S. through October 5 have been estimated at 220,020.¹

From March 10 through October 18, there have been 89,987 confirmed cases of Covid-19 reported from Dallas County with 1,085 deaths, about 25% of these from long-term care facilities.² Seventy percent of hospitalized cases in Dallas County 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 52% of the hospitalized cases have occurred in the Hispanic population. As of 10/13, 1,057 deaths have been analyzed by race with 26% occurring in Whites (actual White population 29%), Hispanics 46% (population 41%), Blacks 24% (population 24%), and Asians 3% (population 7%). Specimens submitted for diagnosis of respiratory viruses show continuing positivity for SARS-CoV-2 with the latest result on 10/3 being 10.0%, down from a peak value of 30.5% obtained during the week ending 7/4/20. Influenza A and B antigen tests in specimens from the respiratory tract from 8/1 through 10/3 have been negative.

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Feature Article

Covid-19 in Pregnancy

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As the Covid-19 pandemic continues into the winter months in North America, we have learned much about how the SARS-CoV-2 virus behaves in nonpregnant individuals. Information has lagged about how the virus behaves in pregnancy and what maternal and neonatal consequences may result. Several recent studies have been published that lend insight to current understanding of the risks of SARS-CoV-2 infection and pregnancy, although significant limitations to these studies should be acknowledged. Comprehensive, population-based studies on the outcomes of pregnant women and their neonates are still needed. Some common questions about pregnancy and Covid-19 are addressed in this article.

Are pregnant women more likely to acquire Covid-19 than nonpregnant women?

There is no evidence that pregnant women are more susceptible to SARS-CoV-2 infection than non-pregnant women of comparable age. Risk factors for infection, such as close contact with symptomatic individuals and lack of masking or improper personal protective equipment use, appear to be similar for both pregnant and nonpregnant individuals.

Is Covid-19 in pregnancy more severe than in nonpregnant women?

Physiologic changes in the pulmonary function of a late trimester pregnant woman decrease functional residual capacity by approximately 20 to 30 percent and increased oxygen consumption by 20 percent, making respiratory infections potentially more serious. A compensated respiratory alkalosis is expected in the third trimester of pregnancy, and normal or elevated pCO₂ levels warn of impending respiratory failure.

Generally, pregnant women with symptoms of Covid-19 appear to present with similar symptoms as nonpregnant individuals. In most studies of outcomes in pregnancy, however, two groups of pregnant women predominate. The first group includes women with asymptomatic or mild illness diagnosed after admission for obstetric reasons via universal SARS-CoV-2 screening instituted in many maternity centers after early reports of exposures among healthcare workers. The second group includes hospitalized pregnant women with severe or critical Covid-19 pneumonia.¹⁻³ These studies demonstrate higher rates of ICU admission and the need for supplemental oxygen in pregnant compared with nonpregnant women. The authors concede that the "threshold for diagnostic evaluation, hospitalization, and certain treatments may in fact be lower for pregnant women than for others, which may have biased our finding of increased disease severity in this group."¹

Likewise, in a September issue of MMWR, the CDC reported that based on surveillance of hospitalizations among pregnant women with a Covid-19 diagnosis, 18.8% of 324 women for whom the reason for hospitalization was known were hospitalized for a Covid-19-related illness.⁴ They also report that over half of their sample was asymptomatic, which is reflective of universal screening practices common to Labor and Delivery units now. Of symptomatic women, hospitalization (26%), ICU admission (16%), mechanical ventilation (8%), and adverse pregnancy outcomes such as preterm birth (23%) rates were high. In another surveillance report, diabetes and obesity appear to be more common in those hospitalized.⁵ However, the surveillance sampling appears "bimodal," comprised of hospitalized asymptomatic or severely symptomatic women, and seems to miss the bulk of mildly symptomatic women who are diagnosed as outpatients, isolate and recover at home, and are never hospitalized. Population-based studies that include inpatient and outpatient tests from a single population of pregnant women are needed to clarify the risks of severe illness and clinical outcomes.

Does SARS-CoV-2 infection cause adverse pregnancy outcomes?

A large case series of delivered pregnant women from several hospitals in New York describe relatively high risk of cesarean delivery and preterm delivery, particularly among women with severe and critical illness.² There is no strong evidence of increased risk for preeclampsia and stillbirth, and studies are generally limited by small numbers and sampling limitations.

For women who develop severe or critical illness in the third trimester, considerations for respiratory support include concerns over whether adequate fetal monitoring is possible if maternal prone positioning is necessary. Thus, iatrogenic preterm delivery may be considered with worsening maternal respiratory status, particularly when noninvasive modes of respiratory support are unsuccessful and intubation is anticipated. Noninvasive modes of respiratory support such as high flow nasal cannula can be used in pregnancy to avoid intubation, although frequent reassessment is needed to determine whether the support is adequate to reduce tachypnea and dyspnea while maintaining oxygen saturation above 94%, which is the goal for pregnant women.⁶ Fetal monitoring in this scenario can be challenging. The need to maintain higher oxygen saturation in pregnancy may be one reason that ICU admission and iatrogenic delivery are more frequent in pregnant women with severe or critical Covid-19.

What is the risk for vertical transmission of SARS-CoV-2 to the fetus?

Case reports of vertical transmission of SARS-CoV-2 to the fetus have been published, although the risk appears to be low, and factors increasing this risk are unknown. Intrauterine transmission appears to be biologically plausible, due to presence of the ACE2 receptor in human trophoblastic tissues.⁷ In cases where early neonatal SARS-CoV-2 transmission occurs, most infants are either asymptomatic or have a mild, self-limited febrile illness. Long-term effects among infants with early neonatal SARS-CoV-2 infection are still unknown.

As the pandemic evolves, population-level data are needed to determine risks for severe maternal illness and vertical transmission among pregnant women with Covid-19.

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<u>Clinical Advance</u> Multisystem Inflammatory Syndrome in Adults (MIS-A)

The May 8 issue of *C.A.N.* (Vol. 1 No. 4) covered the breaking clinical news of a new Covid-19-related inflammatory disease of children termed "multisystem inflammatory syndrome in children (MIS-C)," first described in a letter to *The Lancet* and simultaneously in the *New York Times*. And in the September 18 issue (*C.A.N.* Vol. 1, No. 21) Drs. Most and Kahn provided an in-depth discussion of it. The presentation included high fever, abdominal pain, myalgia, rash including palms and soles, lymphadenopathy, sometimes hypotension and shock refractory to volume resuscitation, but the absence of cough and shortness of breath. Some also developed small pleural, pericardial and ascitic effusions. Laboratory testing often revealed either PCR or antibody evidence of recent Covid-19 infection as well as markers of severe systemic inflammation. The condition usually responds to therapy with corticosteroids, intravenous immune globulin, high dose aspirin, and oxygen supplementation. As of October 1, CDC has received reports of 1,027 cases.

Since June, three small cases series appearing in peer-reviewed journals have reported similar cases in adults, and recently CDC described the clinical presentation of 27 cases including the previously reported 11. The case definition of the illness, referred to as "multisystem inflammatory syndrome in adults (MIS-A)," includes the following features:

- 1. A severe illness requiring hospitalization in a person aged \geq 21 years;
- 2. A positive test result for current or previous SARS-CoV-2 infection (nucleic acid, antigen, or antibody) during admission or in the previous 12 weeks;
- 3. Severe dysfunction of one or more extrapulmonary organ systems (e.g., hypotension or shock, cardiac dysfunction, arterial or venous thrombosis or thromboembolism, or acute liver injury);
- 4. Laboratory evidence of severe inflammation (e.g., elevated CRP, ferritin, D-dimer, or interleukin-6);
- 5. Absence of severe respiratory illness (to exclude patients in which inflammation and organ dysfunction might be attributable simply to tissue hypoxia). Patients with mild respiratory symptoms who met these criteria were included. Patients were excluded if alternative diagnoses such as bacterial sepsis were identified.

In these patients, cardiac involvement has included chest pain and palpitations, electrocardiogram abnormalities such as arrhythmias, elevated troponin levels, or echocardiographic evidence of left or right ventricular dysfunction (see *C.A.N.* Vol. 1, No. 21). Dermatologic manifestations have included skin rash as well as

mucositis. Despite minimal or no pulmonary symptoms, some patients have had pleural effusions or ground glass pulmonary infiltrates.

Treatment with intravenous immunoglobulin, corticosteroids or the interleukin-6 inhibitor tocilizumab have generally been effective, although a third required intensive care for circulatory and respiratory support and two died. Since treatment can be life-saving, it is important to recognize the MIS-A syndrome.

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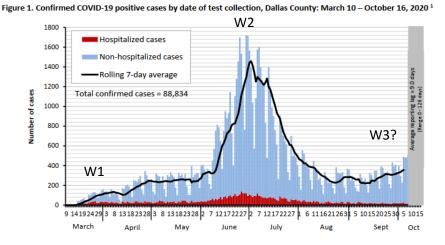
Epi Corner A "Third Wave" May Be Just Around the Corner

From the beginning of the Covid-19 pandemic in the U.S., epidemiologists have been anticipating a "Second Wave" in the fall following an expected summer pause. This expectation was based on analogy to the 1918 influenza pandemic, but due to the many fundamental differences between Covid-19 and influenza, the actual course has been full of surprises. Following the First Wave in March of this year, we saw a two-month plateau. The three-phase opening of the Texas economy then set off a spectacular summer explosion throughout the state, constituting a premature Second Wave (Figure).

At its apex in late June, the state-ordered bar closures and mask mandate precipitated an immediate plunge of cases approximately back to the April-May plateau stretching through August and September. Apparently with the public tiring of masking and social distancing, the mobility index from cell phone signal

analysis has grown, Covid-19 case counts as well as hospitalizations have started to creep up, and a Third Wave appears imminent.

With hospital ward and ICU teams starting to put together systems to meet an onslaught of critical Covid-19 cases, it is time for the public to remember the connection between their social behaviors and the harm expected from another wave.



From the Editors

The editors thank Dr. Adhikari for her feature article on Covid-19 in pregnancy.

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.