Seroprevalence of Antibodies to SARS-CoV-2 in 10 Sites in the United States, March 23-May 12, 2020
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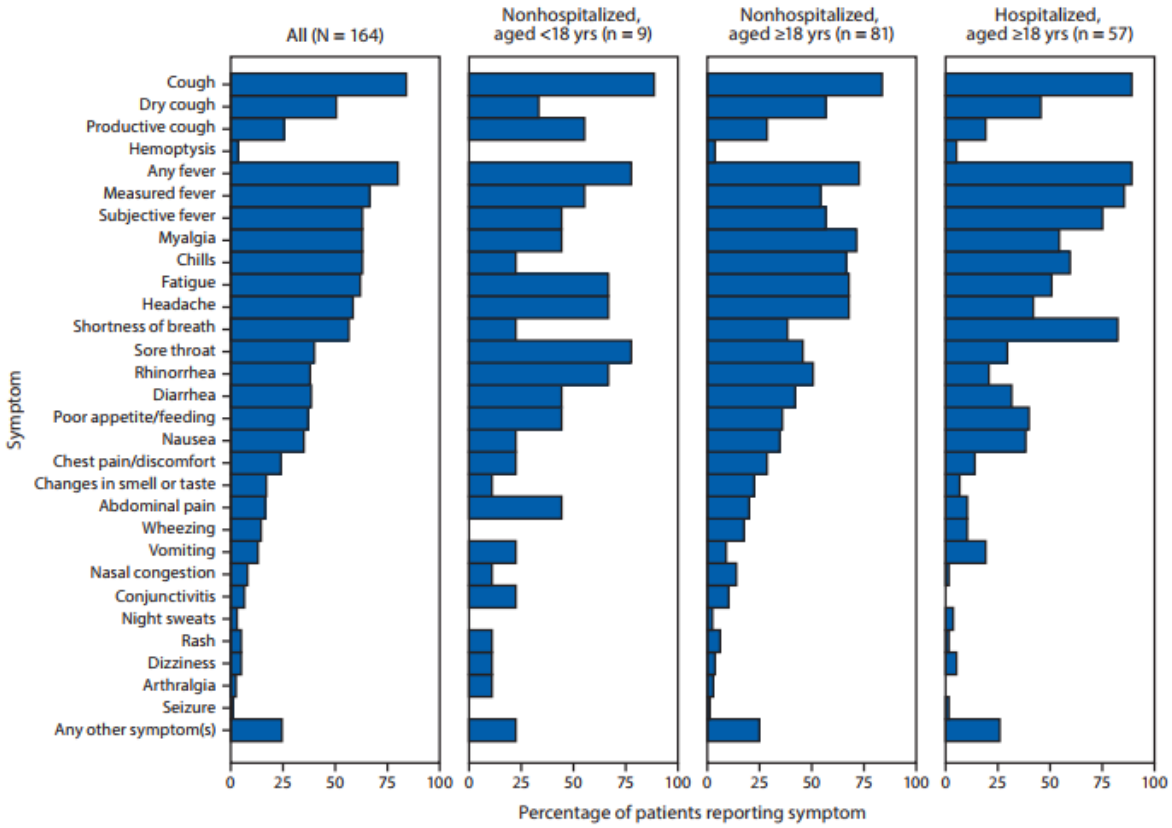
Commercial Laboratory Seroprevalence Survey Data CDC July 21, 2020

This is a cross-sectional study of 16 025 residual clinical specimens, estimates of the proportion of persons with detectable SARS-CoV-2 antibodies ranged from 1.0% in the San Francisco Bay area (collected April 23-27) to 6.9% of persons in New York City (collected March 23-April 1). Six to 24 times more infections were estimated per site with seroprevalence than with coronavirus disease 2019 (COVID-19) case report data. In some regions, the gap between estimated infections and reported cases decreased as testing capacity and reporting improved. South Florida ticked up to 2.9 percent as of April 24 from 1.9 percent just two weeks earlier. Missouri's numbers barely budged from 2.7 percent as of April 26 to 2.8 percent as of May 30. Numbers for both regions are likely to be much higher in the next round of analyses because of the surge of infections in those regions since those dates. New York City showed the biggest leap in its rate, from 6.9 percent as of April 1 to 23.3 percent as of May 6, consistent with its outbreak.

CDC is partnering with commercial laboratories to conduct and publish results from a large-scale geographic seroprevalence survey that has tested de-identified clinical blood specimens from Connecticut, Louisiana, Minnesota, Missouri, New York City, Philadelphia, San Francisco, South Florida, Utah and Western Washington State for SARS-CoV-2 antibodies.

Comment: Not surprisingly the data continue to show that the number of people who have been infected withs Covid-19 far exceeds the number of reported cases. Many of these people likely had no symptoms or mild illness. The United States now tests roughly 700,000 people a day. The new results highlight the need for much more testing to detect infection levels and contain the viral spread in various parts of the country. The studies also did not collect data on race, ethnicity, diagnostic and symptom history or prevention behaviors. Each region also varied on where they were on their own epidemic curve and varied in terms of the amount of testing that they did. Also, the population may not be exactly representative of the population as a whole. Based on recent data CDC now estimated the case fatality rate ~.06%. Diseases such as SARS, MERS, and Ebola have case fatality rates ranging from roughly 10% to 50%.

Symptom Profiles of a Convenience Sample of Patients with COVID-19 — United States, January–April 2020
MMWR 2020; 69:904-908
To better understand symptom profiles of patients with laboratory-confirmed COVID-19 in the United States, CDC used an optional questionnaire to collect detailed information on a convenience sample of COVID-19 patients from participating states. Symptom data were analyzed by age group, sex, hospitalization status, and symptom onset date relative to expansion of testing guidelines on March 8, 2020 . Among 164 symptomatic patients with known onset during January 14–April 4, 2020, a total of 158 (96%) reported fever, cough, or shortness of breath. Among 57 hospitalized adult patients (aged ≥18 years), 39 (68%) reported all three of these symptoms, compared with 25 (31%) of the 81 nonhospitalized adult patients. Gastrointestinal (GI) symptoms and other symptoms, such as chills, myalgia, headache, and fatigue, also were commonly reported.



Nearly all of the 164 symptomatic patients (96%) reported one or more of the typical signs and symptoms of fever, cough, or shortness of breath; 45% of patients reported all three (Table above)). Among all adults, the reported prevalence of all three signs and symptoms increased with increasing age. Among 81 nonhospitalized adult patients, only 25 (31%) reported all three symptoms. As expected shortness of breath was much more common in hospitalized patients. Among 97 patients who reported one or more GI symptoms, 93 (96%) also reported one or more typical symptom.

Comment: This report has several weaknesses. First case investigation forms were occasionally completed by proxy or several weeks after illness onset, some symptoms were unknown or might have been forgotten. Second, sample sizes were small, particularly for children, limiting the ability to draw conclusions about differences by age group. Although COVID-19 can manifest a range of symptoms fever, cough, or shortness of breath predominate especially patients admitted to the hospital. Chills, myalgia, headache, diarrhea or fatigue has been reported. For patients who report less common symptoms such as GI, >90% also reported other symptoms. Loss of taste or smell were not included in this survey.

Prevalence and Mortality of COVID-19 patients with Gastrointestinal Symptoms: A Systematic Review and Meta-analysis

Mayo Clinic Proceeding publish online June 10, 2020

Recent studies have shown the presence of GI manifestations in patients with coronavirus disease 2019 (COVID-19), with 16% to 50% of patients reporting 1 or more GI symptoms at presentation or during the illness. (see above) These investigators conducted a systematic review and meta-analysis evaluating the prevalence of GI symptoms and mortality in individuals diagnosed with COVID-19.

A comprehensive search of several databases was conducted to assess research performed from 2019 to May 7, 2020. Studies measured in this meta-analysis were observational studies that included adults with confirmed COVID-19 infection and reporting GI symptoms The primary outcome assessed weighted pooled prevalence (WPP) of GI symptoms in patients with COVID-19 infection occurring at any time during illness. Secondary outcomes were WPP of mortality in all COVID patients and in patients with GI symptoms.

Overall, 78 studies reporting a total of 12,767 patients were included in the analysis. Among the studies, GI symptoms were reported at onset of illness in 6, at admission in 17, data given separately for both in 3, and data were unavailable in 52 studies. Overall, of the 12,688 patients, the WPP of diarrhea was 12% (95% CI, 8%-17%), *I2*=94%; nausea and/or vomiting was 9.0% (95% CI, 5.5%-12.9%), *I2*=93%; loss of appetite was 22.3% (95% CI, 11.2%-34.6%), *I2*=94%; and abdominal pain was 6.2% (95% CI, 2.6%-10.3%), *I2*=92%. Mortality among patients with GI symptoms was found to be similar to overall mortality (0.4% [95% CI, 0%-1.1%], *I2*=74% and 2.1% [95% CI, 0.2%-4.7%], *I2*=94%, *P* =.15, respectively).

Comment: This was a retrospective design - most of the studies may have a high risk for bias including publication bias, significant heterogeneity, and the overall quality of evidence was judged to be low for all outcomes.

Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial
Lancet published online July 20, 2020

Immunogenicity and safety of a recombinant adenovirus type-5-vectored COVID-19 vaccine in healthy adults aged 18 years or older: a randomised, double-blind, placebo controlled, phase 2 trial
Lancet published online July 20, 2020

In the first paper nearly 1100 adults without a history of SARS-CoV-2 infection were randomized to receive either a chimpanzee adenovirus-vectored vaccine expressing the SARS-CoV-2 spike protein (ChAdOx1 nCoV-19) or a meningococcal conjugate vaccine as a control. With one dose of ChAdOx1 nCoV-19, antibodies to SARS-CoV-2 peaked by day 28 and remained high through day 56. Ten participants who received a booster dose on day 28 achieved higher antibody levels. In addition, neutralizing antibodies against SARS-CoV-2 were detected in over 90% of participants tested. ChAdOx1 nCoV-19 caused more local and systemic reactions (e.g., chills, fever) than did the control vaccine, but no serious reactions occurred. A small non-randomly selected, second-dose boosted subset showed strong neutralizing responses, and few mild adverse events. Importantly, T-cell responses were induced in all participants.

The second trial was conducted in China, with ~ 500 healthy adults were randomized to receive one injection of a non-replicating adenovirus type-5-vectored COVID-19 vaccine (at 1 of 2 concentrations) or a placebo. With the COVID-19 vaccine, antibody responses were noted beginning on day 14, and nearly all participants had seroconverted by day 28. Additionally, both vaccine doses achieved significant neutralizing antibody responses. The most common systemic reactions — fatigue, fever, and headache — occurred more often with the COVID-19 vaccine than with placebo. More than 90% had T-cell responses. People older than 55 years of age had somewhat lower humoral responses.

Comment: The results of both trials argue for starting phase 3 trials, where the vaccines must be tested on much larger populations of participants to assess their efficacy and safety. Overall, the results of both trials are broadly similar and promising. These vaccines plus the Moderna vaccine published and review last week in The Daily Briefing from the N Engl J Med provide cautious optimism that we hopefully with have a vaccine(s) in the next 6-12 months. These vaccines can generate humoral, cellular, and innate responses, have much potential.

Systemic Fibrinolysis for Acute Pulmonary Embolism Complicating Acute Respiratory Distress Syndrome in Severe COVID-19: A Case Series

Eur Heart J published online July 2020

A unique form of coagulopathy develops in patients hospitalized with severe SARS-CoV-2, with elevations in D-dimer levels (parallel with rise in other markers of inflammation), alterations in clotting times and thrombocytopenia. Consequently, a high incidence of venous thromboembolism (VTE) as well as of pulmonary embolism (PE), has been reported, and linked to increased mortality. Clinically, this coagulation imbalance seems different from the classical disseminated intravascular coagulation with a bleeding diathesis but results in a very high incidence of thrombotic and thromboembolic events with, prominently, VTE/PE of variable severity.

This article reports a retrospective case series of four patients needing mechanical ventilation for SARS-CoV-2 infection, who were diagnosed PE and underwent systemic fibrinolysis with full-dose alteplase, with rapid hemodynamic and respiratory success in three. Three cases had been treated with anticoagulants before PE: one case even suffering PE while on sodium heparin, one while on a full dose enoxaparin, and the third one two days after sodium heparin full anticoagulation was downgraded to enoxaparin prophylactic dose.

Comment: The authors I think appropriately believe that ARDS and VTE/PE are, in COVID-19 patients with pulmonary micro- and macrocirculatory thrombosis has a pathogenetic role. It is likely that the prevalence of imaging-evident PE (e.g. thrombi in pulmonary vasculature) is higher than reported. Evidence of right heart strain along with suspected thrombi, might then prompt systemic fibrinolysis. This article along with article from last week suggest there may be a role of alteplase in select patients.

Thrombosis in Hospitalized Patients With COVID-19 in a New York City Health System

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Roughly 16% of patients hospitalized with COVID-19 at a New York hospital had a thrombotic event. All-cause mortality was higher among those who experienced a thrombotic event (43% vs. 21%). Higher D-dimer levels at presentation were predictive of thromboses. Thrombotic events included both DVT and PE] and arterial (myocardial infarction [MI], ischemic stroke, and other systemic thromboembolism). Low-dose (prophylaxis) anticoagulation was used in most patients. Among 829 ICU patients, 29.4% had a thrombotic event (13.6% venous and 18.6% arterial). Among 2505 non-ICU patients, 11.5% had a thrombotic event (3.6% venous and 8.4% arterial).

Comment: Clinical practice changed over the last 2-3 months, with increased awareness of thrombotic events and use of anticoagulation, which has impacted the incidence of thrombosis.