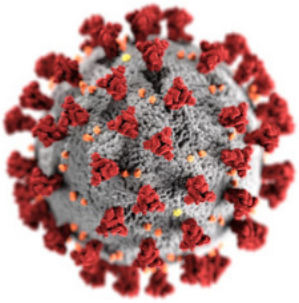


COVID-19 Action Newsletter

UT Southwestern Department of Internal Medicine
James Luby, M.D., and Robert Haley, M.D., editors

The Situation: U.S. Confirmed Cases Exceed 1.5 Million

In the world as of May 22, 2020, 5,128,492 cases of Covid-19 have been confirmed, including 651,141 with onset in the past 7 days, and 333,489 deaths. In the United States, there have been 1,577,758 cases, the most in the world followed in order by Brazil, Russia, the United Kingdom, Spain, Italy, France, Germany, Turkey, Iran, India, Peru, Canada and China.[1] Deaths in the U.S. through May 22 have been estimated at 94,729.[2]

From March 10 through May 19, there have been 7,904 confirmed cases of Covid-19 reported from Dallas County with 191 confirmed deaths, 38% of these from long-term care facilities.[3] Of the 1,335 hospitalized cases in Dallas County, two-thirds were under 65 years of age and about half did not have any chronic health conditions. Diabetes mellitus was seen in about one-third of all hospitalized patients. More men than women have died. Of the deaths in Dallas County, the distribution of cases by race/ethnicity did not differ significantly from that of the Dallas population. Differences have been seen in other cities.

References:

1. Covid-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU) (Updated 5/22/20)
2. Worldometer. Coronavirus update 5/22/20
3. Dallas County Health and Human Services. Acute Communicable Disease Epidemiology Division 5/22/20

Feature Article

Does SARS CoV-2 affect the gastrointestinal tract and the liver?

William M. Lee, MD

Until now, most of the efforts to understand this novel coronavirus have concentrated on the obvious severe respiratory distress, the cardiovascular failure, and the coagulopathy. As a hepatologist, I am asked, "What is happening to 'our' organ, surely it is not totally spared?" Indeed not, but fortunately, it is not often severely injured either.

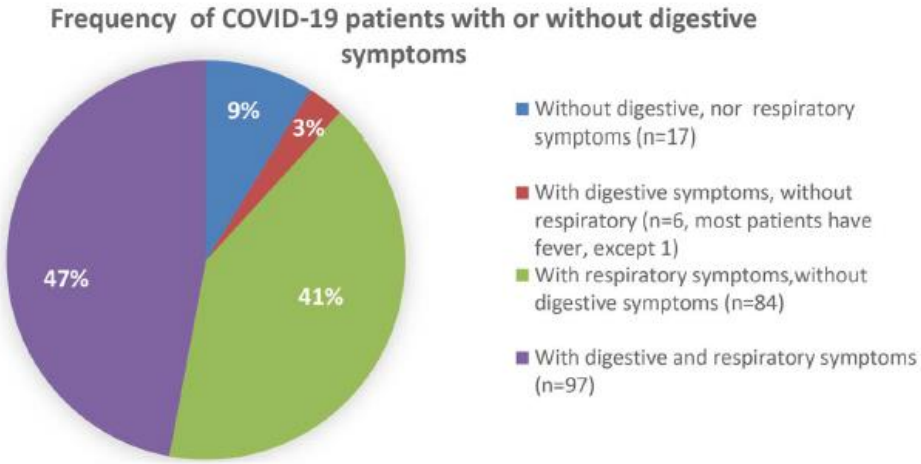
Gastrointestinal disease related to COVID-19

Although primarily spread via respiratory droplet transmission, SARS-CoV-2 can also be recovered from stool samples. In an early study from Wuhan, where nasopharyngeal swabs were positive by PCR for a mean of 16.9 days from initial sampling, stool samples remained positive for a mean of *27.9 days*.[1] This could be a long-term infection!

The significance of this finding, however, is unclear: are these noninfectious PCR fragments or viable viruses? Can SARS-CoV-2 be spread by the fecal-oral route? This has not been documented but seems likely. Fecal-oral transmission might not matter within the hospital where PPE and handwashing are routine but might be very relevant in enclosed facilities like prisons or nursing homes. The fact that shedding in stool outlasts nasopharyngeal shedding should be a caution about allowing recovering patients out of quarantine as soon as

the nasopharynx becomes PCR negative. Evidence from China indicates that ACE2 receptors and SARS-CoV-2 virus are present in biopsy material from stomach, duodenum and colon, but their significance is uncertain.[2] The major unanswered question is, can the GI tract serve as a source of entry to systemic infection?

In one Chinese study, GI symptoms, mostly diarrhea, were detected in 26% of Covid-19 patients, but they did not correlate with degree of illness or the outcome.[3] In another, only 3% were recorded as having diarrhea.[4] In a third study, up to 56% had some gastrointestinal symptoms, broadly defined, most commonly loss of appetite and diarrhea (see pie chart).[5] GI symptoms were associated with longer time from first symptoms to presentation perhaps because the respiratory symptoms were less evident. Elevated liver enzymes were more likely to be observed in cases with GI symptoms, but significant aminotransferase abnormalities have been uncommon (see below). A small number had all GI symptoms and essentially none from the respiratory tract.



Covid-19 in Patients with underlying GI disease?

Patients with inflammatory bowel disease (IBD) are often on immunosuppressive therapy including both steroids, azathioprine and biologics. Guidance from the American Gastrointestinal Association (AGA) suggests there seems to be no need to discontinue immunosuppression in this setting just because of the pandemic.[6] Such patients are not at increased risk for acquiring Covid-19 and should not have their dose of therapy altered but should follow strict guidelines. Those needing biologic infusions should still be able to receive treatment; however, strict local rules should be adhered to for the safety of the patient and staff as well. In general, if Covid-19 infection occurs, dosing of immunosuppression should be lowered, all other things being equal, but taking into account the state of disease, whether active or totally inactive at the time of initial evaluation.

Liver Disease in Covid-19 patients

The overall impact of SARS-CoV-2 on the liver has been limited in comparison to the heart and lungs. Nonetheless, about a third of patients with typical Covid-19 infection will have aminotransferase elevations in the 50-200 IU/L range.[7] For the most part, patients are not jaundiced, and life-threatening acute liver failure, absent severe multi-system failure, has not been identified. Having abnormal liver tests on admission in one study was associated with longer hospital stays; whereas, developing enzyme elevations following admission was not. It is uncertain whether worse outcomes are observed in those with liver changes.

Alkaline phosphatase levels are even less elevated. This is of interest since the ACE2 receptor is present on bile duct cells but not on hepatocytes.[7] Low albumin levels are a marker of disease severity. In most instances, it is important to look elsewhere besides the SARS-CoV-2 infection for the liver test abnormalities if more than minimal. Since many medications, including lopinavir/ritonavir, remdesivir and azithromycin, are associated with drug-induced liver injury, we must be careful not to implicate the virus in every instance, and stop medications where feasible.

In general, imaging is not helpful nor does liver biopsy show unique features, although micro-vesicular fat has been observed in some biopsy specimens. Unless a thrombotic event is suspected, there are few indications for imaging, which only cause more viral exposure for patient and personnel in the radiology suite. Again, to manage the Covid-19 patient with hepatitis, it is wise to review medications, consider sepsis or a role

for heart failure, and do little about the findings unless an hepatotoxic agent needs to be stopped or evidence for vascular thrombosis such as Budd-Chiari syndrome is present.

Patients with hepatitis A, B or C may be at somewhat increased risk of bad outcomes with Covid-19, but the evidence is inconclusive. Certainly, those with NAFLD and other forms of cirrhosis are likely to experience worse outcomes. Sensible rules must be in place for managing the Covid-19 in post-transplant patients. In general, immunosuppression cannot and need not be discontinued, particularly in the first year after transplantation. Anti-metabolite agents (azathioprine, seldom used) should be discontinued. After one year, it may be prudent (and safe) to lower immunosuppression with calcineurin inhibitors in the infected patient. Most transplant programs have continued to function and provide transplants to suitable recipients with the proper viral screening precautions for donor and recipient. No living related donations/transplants are being performed since these tend to be more elective in nature.

References:

1. Wu Y, Guo C, Tang L, et al. Prolonged presence of SARS-CoV-2 viral RNA in faecal samples. *Lancet Gastroenterol Hepatol* 2020;5:434-435.
2. Xiao F, Tang M, Zheng X, Liu Y, Li X, Shan H. Evidence for gastrointestinal infection of SARSCoV-2. *Gastroenterology*. 2020 May;158(6):1831-1833
3. Zhou Z, Zhao N, Shu Y et al. Effect of gastrointestinal symptoms on patients infected with coronavirus disease 2019. Gastroenterology 2020; epub May7
4. Huang C, Wang Y, Li W, et al. Clinical features of patients infected with novel coronavirus in Wuhan, China. *Lancet* 2020 395:497-506.
5. Pan L, Mu M, Yang P, et al. Clinical characteristics of COVID-19 patients with digestive symptoms in Hubei, China: a descriptive, cross-sectional, multicenter study. *Am J Gastroenterol* 2020.
6. Rubin DT, Feuerstein JD, Wang AY et al., AGA Clinical Practice Update on Management of Inflammatory Bowel Disease During the COVID-19 Pandemic: Expert Commentary. *Gastroenterology* 2020, epub ahead of print.
7. Fann Z, Chen L, Cheng JL, et al., Clinical features of COVID-19-related liver damage. *Clin Gastroenterol Hepatol* 2020; epub ahead of print.
8. *Clinical Best Practice Advice for Hepatology and Liver Transplant Providers during the Covid-19 Pandemic: AASLD Expert Panel Consensus Statement. Accessed on AASLD website*, AASLD.org May 13, 2020.

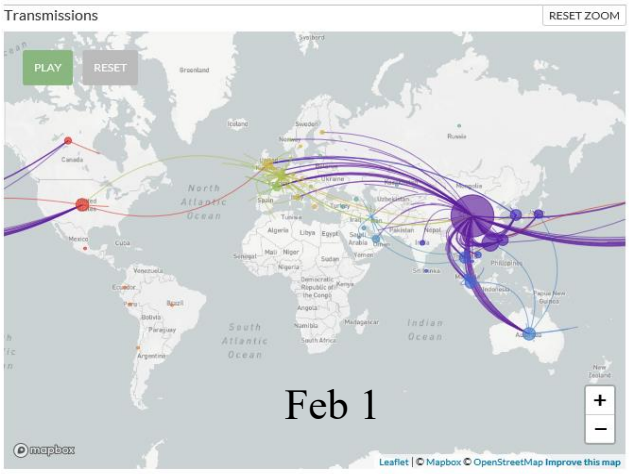
Epi Corner

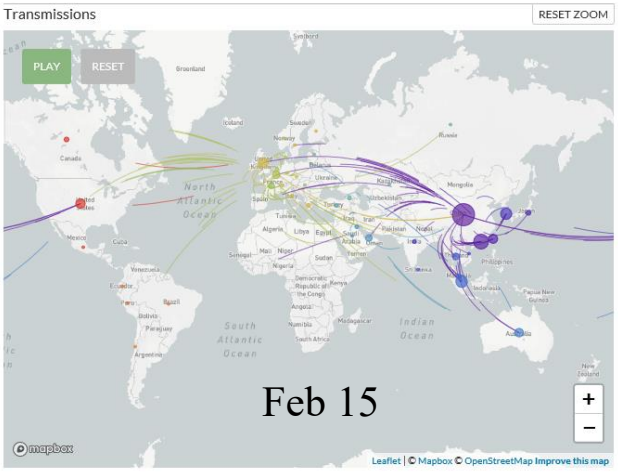
Follow the International Spread of the Pandemic over Time

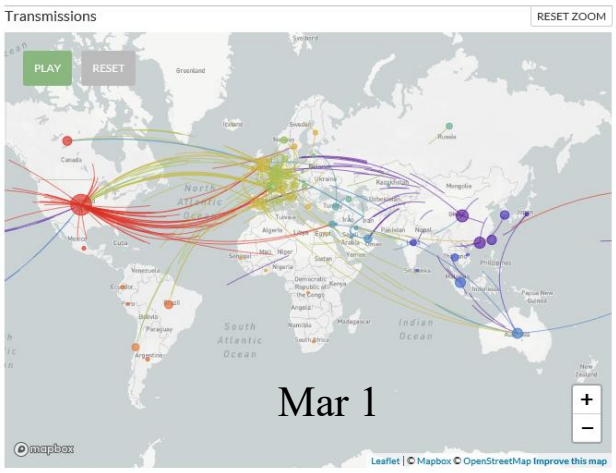
The maps below are every-two-week snapshots of the size of each country's epidemic and export of cases to other countries, color coded by country, from https://nextstrain. Notice that the earliest spread to the U.S. (January 15) came from China but that this was soon eclipsed by spread from Europe. Importantly, spread to and within the U.S. was negligible until late February, but by March 1 the U.S. epidemic was growing rapidly and beginning to export cases to China and Europe, while the Chinese epidemic had been effectively suppressed. Between March 1 and 15, the epidemics in the U.S. and Europe exploded simultaneously. Within 2-3 weeks after shelter-at-home control measures were instituted in the U.S. and Europe in mid to late March (March 23 in Dallas), between April 1 and 15 transcontinental transmission all but ceased and by early May ended.

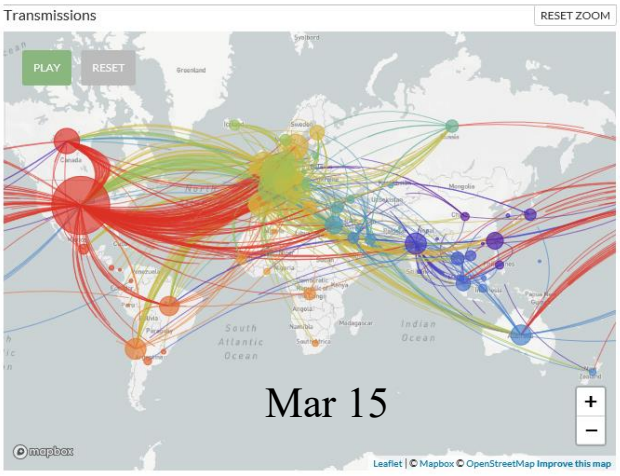

Transmissions
RESET ZOOM
PAUSE
RESET
Jan 1
Leaflet | © Mapbox © OpenStreetMap Improve this map

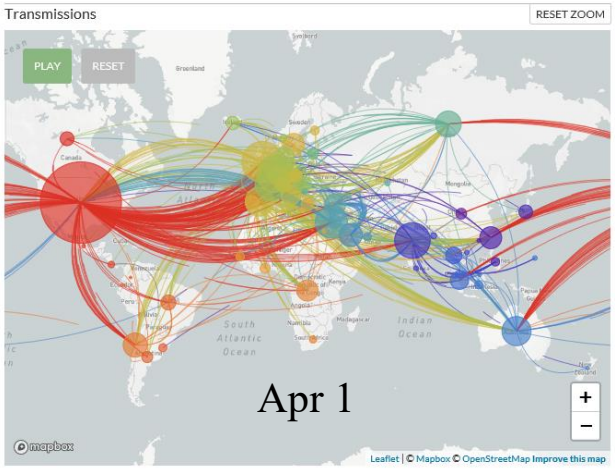

Transmissions
RESET ZOOM
PAUSE
RESET
Jan 15
Leaflet | © Mapbox © OpenStreetMap Improve this map

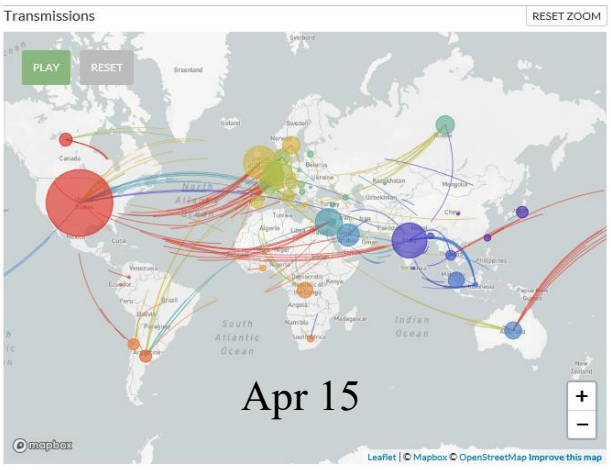

Transmissions
RESET ZOOM
PLAY
RESET
Feb 1
Leaflet | © Mapbox © OpenStreetMap Improve this map

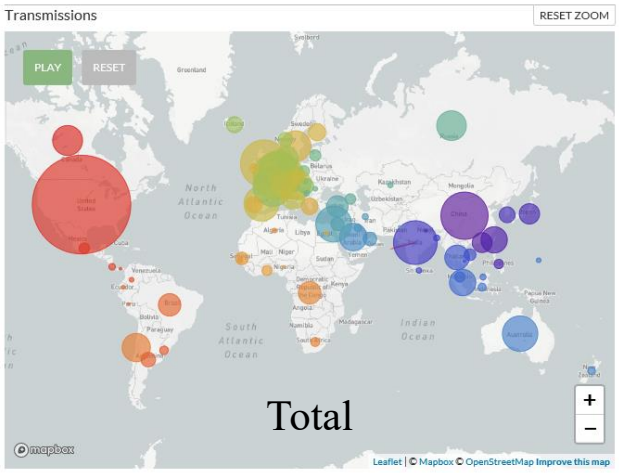

Transmissions
RESET ZOOM
PLAY
RESET
Feb 15
Leaflet | © Mapbox © OpenStreetMap Improve this map


Transmissions
RESET ZOOM
PLAY
RESET
Mar 1
Leaflet | © Mapbox © OpenStreetMap Improve this map


Transmissions
RESET ZOOM
PLAY
RESET
Mar 15
Leaflet | © Mapbox © OpenStreetMap Improve this map







From the Editors

The editors thank Dr. Will Lee for contributing his feature article on involvement of the GI tract in Covid-19.

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.