SEMC Department of Emergency Medicine

Best Evidence Summary & Guidelines

E. O’Neil MD

**Covid-19**

**3/12/20**

**Hope for the best, but plan for the worst**

***A Note on What Follows***

For nearly 20 years, I have written monthly literature reviews for the staff of the Department of Emergency Medicine at St Elizabeth’s Medical Center in Boston. These literature reviews are typically on clinical topics relevant to our practice in the ER. This one, however, is different. I have adapted this for more broad-based consumption and use. I have tried to explain medical terms within, and tried to paint an accurate picture of the historical background, what we know now, and where this is likely to go, as well as factoring in the ever so important political aspects, which will largely govern our collective response to this looming pandemic. The ideal time to prepare for what is coming was several weeks ago. However, here we are. I encourage you all, should you so choose, to share this with friends and colleagues. It is meant to inform and to bring an accurate read on what is currently in the medical literature about Covid-19 at least as of this date. Should the political aspects offend some, omit it; my goal is to get people of all political persuasions to be prepared. The single most important weapon we have in preparing for Covid-19 is knowledge. I wish for everyone who reads this health and safety as we all move forward into this gathering storm together.

***Uncertainty and Fluidity***

One of the most important initial concepts in understanding Covid-19, its spread, infectivity, lethality, and containment, is just how fluid the information is. In a very short time, this virus has been identified and its structure defined. Yet there has also been distortion and political suppression of information release (mostly early on in China but with US parallels). We are still learning much about it and have a long way to go. What is written here is based on the most current literature (please see the Bibliography at the end for sources used herein). However, by the time someone is reading this, the information will have changed slightly. For example, WHO defines mortality as 3.4%, which is considerably higher than the most frequent 2% mortality estimates for the 1918 “Spanish Flu.” But there has not been enough testing. As more people are tested, most experts think that mortality will drop significantly; the information will adjust. Also, viruses can evolve as they spread, sometimes more lethal, as in HIV, others less so. Our understanding will evolve in the coming weeks. Please read this with the perspective that it is accurate today, but less so tomorrow; you should keep up with reliable sources of information, like the CDC website or [www.worldometers.com](http://www.worldometers.com) websites for accurate, up-to-date information. Please avoid much of social media, and be wary of the spin out of certain media outlets and politicians.

***Background***

Why this virus and why now? To get a good perspective on the history of epidemics, their clinical, economic and political impacts, along with the reasons why they continuously emerge, I recommend two Pulitzer-prize winning authors’ books: Laurie Garrett’s *The Coming Plague*, and Jared Diamond’s *Guns, Germs and Steel*. Here is the brief synopsis of both, relating to this new virus. Human history has been shaped to a large degree by microbes, from the decimation of the Amerindians by imported smallpox to the widespread carnage wrought by HIV. Microbes have long ruled our world. We have just become far too complacent given the illusory “control” we have developed over the past 75 years via hygiene, public health measures, vaccinations, and the knowledge explosion in medical science. But these microbes are out there, and evolution is a force still very much active in our world. Many factors are now forcing us into direct contact with previously unknown pathogens, including population expansion, habitat destruction, the climate crisis, and poverty. HIV emerged from monkeys first in 1935, with isolated epidemics in the 1940s and 1950s before exploding in East Africa in the late 1970s amid considerable political unrest and war. Several other pathogens have emerged amid a multitude of population and environmental interactions: Smallpox, Marburg, Lassa, Legionella, Ebola, Hantavirus, Bolivian Hemorrhagic Fever, Lyme, among others. There have always been and always will be emerging epidemics that shape world orders old and new. Covid-19 is no different. As Hans Zinsser wrote in 1934, “During the first centuries after Christ, disease was unopposed by any barriers. And when it came, as though carried on storm clouds, all other things gave way, and men crouched in terror, abandoning their quarrels, undertakings and ambitions, until the tempest had blown over.” Viewing the footage from China, Iran, and Italy recently, it seems we are not so different from our distant ancestors.

Covid-19 (Coronavirus disease 2019) is the epidemic caused by SARS-Co-V-2, a coronavirus, of the same family that gave us the SARS epidemic in 2002-03 and the MERS epidemic starting in 2012, both quite lethal pathogens with mortality rates of around 10% and 34% respectively. Covid-19 (I’ll use Covid-19 to refer to the virus and epidemic interchangeably here for simplicity’s sake) is nearly identical to a virus found in bats, from whence it likely transmitted to an intermediary species, mostly pangolins, and then on to humans. Pangolins are considered a delicacy in China with traditional healing properties attributed to their scales; the illicit market trading pangolin meat and scales is quite lucrative. Authorities in Hong Kong, Malaysia, and Singapore seized 23 tons of scales and 33 tons of meat in separate raids in in January-April 2019. Epidemiological studies trace the origin of Covid-19 to a wet market in the Chinese city of Wuhan, home to 11 million people. These markets, which are present throughout China, were the likely source of the SARS epidemic. Previous calls to ban such markets in China will soon amplify.

***Incubation Period and Infectivity***

We don’t yet know this for certain. It is hard to accurately read the infectivity, lethality and overall disease severity when we just don’t know how many people are infected or are asymptomatic carriers. This should become clearer once we have larger numbers of people tested, which should be coming in the second half of March into April.

The ***incubation period***, i.e. the period between viral acquisition and disease manifestation, is roughly 5 days. The range is quite broad as of this writing. The listed incubation period range is from 2-14 days, which is why exposed people are now quarantined for 14 days. However, in the Bei et al paper listed in *JAMA* below, one woman had an incubation period of 19 days. The article is quite clear about timeline, symptoms etc. This seems real. Guan et al, in the *NEJM* listed below, listed a patient with an incubation period of 24 days. This raises an even more frightening possibility, that one can be exposed to the disease, and then be re-exposed again before the body has time to develop a sufficient antibody response. This could also explain the high mortality rates seen in the earliest studies. Dr. Li Wenliang, the whistle-blower physician from Wuhan who died from Covid-19 was just 34 years old. But how many times was he and were others exposed to this virus so close to the center of the outbreak?

For now, we should assume that the incubation period is roughly 2-14 days, with an average of around 5-7 days. For comparison, let’s look at several other viral incubation periods.

Covid-19: 2-14 days (average 5-7 days, though case reports up to 24 days)

SARS 2-7 days

Seasonal Flu 1-4 days (average 2 days)

***Infectivity*** is basically how readily a pathogen is transmitted from one person to the next. It is defined by R0 pronounced “R naught.” This number reflects how many people each infected person will likely transmit the virus along to. Most think the R0 value will be like SARS (R0 of 2.0) at somewhere around 2.2, with a range of 1.5 to 3.5. By comparison, the R0 for the seasonal flu is 1.3. Naturally, when the number is less than one, epidemics are more likely to fizzle out. With an R0 of 2.2 and an incubation period of 1-2, and possibly 3 weeks, one can readily understand why this virus is spreading so rapidly.

There is one point from the Huang et al article in *The Lancet* that is worth emphasizing here, even before we cover the specific clinical aspects of this illness. The study authors note that few of the 41 laboratory-confirmed Covid-19 infected patients in their cohort had prominent upper respiratory symptoms (like a common cold). Upper respiratory and lower respiratory infections can overlap but are different. *Upper* respiratory symptoms are just that, symptoms of the mouth, throat, and trachea and include runny nose, sneezing, and sore throat. Covid-19, however, manifests primarily as a *lower* respiratory infection, i.e., an infection of the lungs. The symptoms these authors noted are consistent with what has been reported elsewhere: chiefly fever, dry cough, shortness of breath, and then findings on either chest X-rays (sometimes), and CT scans (virtually always). This does suggest that the primary means of spread is through coughing and getting the virus into your lungs somehow. This can include touching viral-contaminated surfaces, and then touching your face.

***Lethality***

This can be very confusing to understand, and for good reason. Experts in various areas are using the only data we have, which remains incomplete. For example, a quick check of the most current literature on March 10 shows a total of 111,765 cases of Covid-19 with 4,095 deaths. That calculates out to a mortality rate of 3.5%. That is near what the WHO is currently quoting as the overall mortality rate at 3.4%. However, this assumes that we have an accurate understanding of the denominator, i.e. how many true cases there really are. We don’t and likely won’t until we have large scale testing of both clearly infected individuals, and their (particularly young) less ill or completely asymptomatic contacts.

In several of the studies thus far, the mortality rate has been quite different. Guan et al (*NEJM*) found 1.4% mortality when looking at the first 1,099 cases out of Wuhan. In that same study, 5% of patients were admitted to the ICU, and 2.3% were intubated. That represents a whole lot of very ill, highly contagious people that may well exceed the ICU capacity in the US. However, for perspective, Anthony Fauci wrote in *NEJM* on 2/28 the following, “If one assumes that the number of asymptomatic or nominally symptomatic cases is several times as high as the number of reported cases, the case fatality rate may be considerably less than 1%.” I find this reassuring coming from one of the world’s leading infectious disease experts.

To expand on the testing point here, consider the following. South Korea has been testing aggressively for a few weeks now. China, where the pandemic originated, has had 80,761 cases and 3136 deaths, for a mortality rate of 3.9%. South Korea, as of the same date, March 10, has had 7,513 cases and 58 deaths, for a morality rate of 0.77%. Why the difference? There are likely several. First, South Korea is testing many more people; the denominator is simply bigger. This is therefore likely closer to what we will see here. Second, people are now better prepared, take appropriate precautions, and stay home once infected. This should well reduce the occurrence of multiple exposures in the same person, and thereby reduce that person’s mortality. Third, the virus could be changing, which happens in epidemics, though this is the least likely explanation now.

For perspective, let’s look at other disease-associated mortality:

-Seasonal influenza outbreaks in the US: 0.1%

-1918 “Spanish flu”: 2-5% (variable estimates with some over 5%)

-1957 influenza pandemic: 0.6%

-2009-10 SARS 9-10%

-2016 MERS: 34%

-Covid-19: ?

Taking all of the above together, my read is that the mortality rate will ultimately fall somewhere between 0.5-1.0%. However, yet again, we just don’t know enough yet. This is still going to be a quite lethal epidemic, and the South Korea mortality rate of 0.77% is nearly eight times higher than our seasonal flu.

The 1918 H1N1“Spanish flu” originated in Haskell County, Kansas, rapidly spreading east to a large military base, and on to Europe, likely carried by US troops. In 1918, the world population was roughly 1.8 billion, yet this virus killed at least 50 million people, with some estimating as high as 100 million people worldwide (mortality rates 2.8% and 5.6% respectively). In the US, 675,000 people died, much higher than the 10-60K deaths we typically see in recent years from seasonal flu (with a much larger population). Unlike Covid-19, this flu took down young healthy individuals quickly. Author John Barry wrote in *The Great Influenza*, that a doctor in Kansas near the flu’s epicenter, “had never seen influenza like this. This was violent, rapid in its progress through the body… This influenza killed. Soon dozens of his patients—the strongest, the healthiest, the most robust people in the county—were being struck down as suddenly as if they had been shot.” Fortunately for us, Covid-19 does not act like the 1918 flu. Its incubation period is longer, the mortality rate is likely far less, and people who get really sick tend to do so over a longer period, typically a week. They also tend to be older and sicker. So, direct comparisons to the 1918 epidemic are problematic for several reasons. However, that does not mean this will be easy. For most of us, particularly those of us who have not seen Ebola up close, this will likely be the worst epidemic we will see.

To summarize mortality data, here, the bottom line is, we really don’t know yet just how lethal Covid-19 will be. Most experts, including Anthony Fauci, think that the mortality rate will drop to 1% or less. This makes sense. Many are saying that this will likely be just a “bad flu.” Maybe that is accurate; I hope so, but don’t agree. None of us have any immunity to this virus. Most of us get the flu vaccine every year, which is of variable efficacy. We have had variations of influenza in the past and may have partial immunity. We see flu annually, occasionally get it, and are usually fine. This is all new. From the early studies out of Wuhan and the Nursing Home currently in Seattle, this will be considerably worse.

***Clinical presentation/ Course:***

For non-medical readers, this is the one section that may prove a bit more challenging. I have tried to explain medical terms, but there remain testing and procedures that may not be clear. That’s OK, I suggest you read on through this and get to the personal safety, treatment and other sections beyond.

From a US-based perspective, we have just had the first real glimpse of what this virus can do in a Nursing Home in Seattle. (*NYT, 3/8/20*) Life Care had 63 residents cared for by a total of 180 staff when Covid-19 struck. As of 3/7/20, 13 residents and one visitor have died and 70 of the staff have developed symptoms. The home received only 45 testing kits for the 243 people there, not including visitors. One can only assume that while striking down many, the virus is simultaneously spreading by stealth through the surrounding area.

***Wang et al JAMA 2/7/20***

These authors wrote about the clinical characteristics of 138 hospitalized patients at Zhongnan Hospital of Wuhan University from 1/1-1/28/20. They reviewed charts and sent out data collection forms. Testing was done by throat swab RT-PCR samples. Their findings are concerning. The median age of those infected was 56 years (age range 22-92 years) with 54% male. Hospital-associated transmission was responsible for health professionals (29% of patients), and hospitalized patients (17% of patients).

Of the infected health care workers, 78% worked on general medical wards, 7% in the ER, and 5% in the ICU.

*Common symptoms Timing and Course:*

Fever 98.6%

Fatigue 69.6%

Dry cough 59.4%

Other symptoms: anorexia (poor appetite) 40%, myalgia (muscle aches) 35%, dyspnea (shortness of breath) 31%, sore throat 17%; diarrhea 10%, nausea 10%, dizziness 9%, headache 6.5%, vomiting 3.6%, abdominal pain 2%. Keep in mind that 10% of patients initially presented with diarrhea and nausea 1-2 days before development of fever and dyspnea.

Median time from first symptoms to dyspnea (shortness of breath) was 5 days, to hospital admission was 7 days, and to ARDS was 8 days.

26% of patients (36 total) required ICU care, of which 11% (4) received high-flow oxygen therapy, 41.7% (15) received noninvasive ventilation, 47.2% (17) required invasive mechanical ventilation, with 4 of these switched to ECMO (extra corporeal membrane oxygenation, i.e. when the heart or lungs fail).

Patients requiring ICU care were older than those not requiring ICU care (66 years vs 51 years), were more likely to have co-morbidities (i.e. chronic illnesses, 72% vs 37%) and were more likely to have dyspnea (shortness of breath 64% vs 20%). The most common co-morbidities in the ICU were HTN (high blood pressure) 58%, cardiovascular disease 25%, diabetes 22%, and cerebrovascular disease 17%.

The most common serious illness was novel coronavirus-infected pneumonia (NCIP) but very ill patients had myocardial injury, hepatic injury, and kidney injury.

Mortality for all documented cases was 4.3%.

*Diagnostics*: 70.3% had lymphopenia, 58% had prolonged PT, and 40% had elevated LDH. Chest CT scans showed bilateral “patchy shadows” or ground glass opacities in *all* patients.

*Treatment:* All patients received broad-spectrum antibiotics, though no evidence of bacterial growth in most; 90% received oseltamivir and 45% received glucocorticoids. None of them worked. The average length of stay for those who were eventually discharged home was 10 days.

Some important conclusions from this study: This disease carries a significant lethality. It is highly contagious, particularly to health providers, something we are seeing elsewhere. Mortality increases with age and co-morbidities. There is only supportive treatment; none of the antibacterials, antivirals, or glucocorticoids seem to help. Most people come with fever, fatigue and dry cough, but there are many other associated symptoms. This really can look like anything. One patient here (with similar case reports elsewhere) was admitted to a surgical floor with only abdominal pain who then infected 10 staff and 3 other patients on the same ward. The authors noted that the R0 in this study was 2.2 (each patient infected 2.2 other people). They point out that this may well be because many patients presented atypically, with abdominal pain, or with nausea and diarrhea. We need to be highly vigilant! Assume anyone we see could have it. There is not just one presentation. In this study, the number of males and females admitted to ICU was similar. The authors note that other studies have focused on those directly infected at the Wuhan Seafood Wholesale Market, which has mostly male workers.

***Huang et al, The Lancet 2/15/20***

In this study, the authors looked at a cluster of laboratory-confirmed Covid-19 cases in 41 patients admitted to a single designated hospital, Jin Yintan Hospital in Wuhan from 12/16/19 to 1/2/20. Most were men (73%); only 32% had underlying disease, of which diabetes (20%), HTN (15%), and cardiovascular disease (15%) were most common.

66% had been directly exposed at the Huanan seafood market, making this population somewhat unique, perhaps less representative of what is occurring globally. Still, this study offers yet another glimpse and has some valuable lessons, despite the relatively low number of patients (only 41).

49% of patients were age 25-49 years old; 34% were 50-64 years old. The median age was 49 years old. None were adolescents or children.

Common symptoms at the onset of disease in this cohort included the following:

Fever 98%

Cough 76%

Myalgia or fatigue 44%

Less common symptoms were similar to other studies: sputum production (28%), headache (8%), hemoptysis (coughing up blood 5%), and diarrhea (3%).

Shortness of breath developed in 55% on average by day # 8 of illness.

The median time from illness onset to varied events was as follows: time to admission (7 days), shortness of breath (8 days), ARDS (respiratory failure 9 days), ICU admission (10.5 days).

Laboratory abnormalities were like that seen elsewhere, with low lymphocytes, elevated AST, elevated D-dimer and PTT in ICU patients. Procalcitonin levels were low in most and tended to increase in those admitted to the ICU. Of note, troponin assays were elevated in five patients (12%) “in whom the diagnosis of virus-related cardiac injury was made.”

Complications included ARDS in 29%, acute cardiac injury in 12%, and secondary infection in 10%. 32% of patients required ICU admission, 68% were discharged home, and 15% died. 100% of patients had pneumonia. 10% (4 patients) required mechanical ventilation and 5% (2 patients) had refractory hypoxemia requiring ECMO (extra corporeal membrane oxygenation) for salvage therapy.

All patients (100%) received broad-spectrum antibiotics, while 93% received Tamiflu, and 22% received corticosteroids (methylprednisolone 40-120 mg/ day. None of these treatments seemed to work. Naturally, patients with bacterial superinfections should receive antibiotics, and it will be hard not to use them with anyone who appears very ill. As is the case in SARS, steroids don’t work here. As for Tamiflu and other anti-viral medications, the authors write, “No antiviral treatment for coronavirus infection has been proven to be effective,” though many have been studied. Many of these same agents are being tested in ongoing, prospective trials currently. We will know more in the coming weeks to months. However, it is unlikely there will be a magic bullet and a vaccine, again remains months away.

Some things to keep in mind from this study. First there are several cases in this cohort who had direct, repeated exposure to the original source in the market. This may convey some additional virulence. Like elsewhere, the study authors advise close monitoring of health care workers, given the significant risk of infection and subsequent spreading the virus. They add, “Testing of respiratory specimens should be done immediately once a diagnosis is suspected. Serum antibodies should be tested among health-care workers before and after their exposure to [Covid-19] for identification of asymptomatic infections.” Second, and of interest here, 12% of the patients had evidence of myocardial involvement (the virus attacking heart muscle). We don’t know much yet but should closely monitor EKG and troponin (heart muscle testing) in the more severely ill patients. This could all be simply a component of multiple-end organ failure in critically ill and dying patients. But it is worth watching closely as we start to care for these patients soon.

As written above, the authors also point out this this is primarily a lower respiratory infection. Upper respiratory tract infection symptoms such as sore throat, runny nose, sneezing, are far less common.

***Guan et al, NEJM 2/28/20***

The study authors here offer yet another view of the early cases in Wuhan. They studied a larger cohort than above, in this case the first 1,099 patients with laboratory-confirmed Covid-19 cases from 552 hospitals in 30 provinces through the end of January. The endpoint of this study was admission to ICU, use of mechanical ventilation, or death. We briefly discussed this above in the mortality section.

Here are some of this review’s highlights. As previously stated, of the 1,099 patients, 6.1% were admitted to the ICU (5.0%), intubated (2.3%), or died (1.4%) (Numbers don’t add up due to overlap, i.e. one patient could be in all 3 categories). Among all patients, the cumulative risk of reaching one of the study endpoints was 3.6%. Among the 173 patients with severe disease, the risk of the reaching an endpoint was 25%. One can conclude from this that overall risk for most people is low to moderate, but for those who get more severe disease, particularly the elderly or those with significant chronic illness, the risk is fairly high, or a one in four change of ICU admission, intubation, or death.

The study authors were able to get complete information from 1,099 out of a total of 7,736 patients with Covid-19 who had been hospitalized at the 552 sites as of 1/29/20. 3.5% were health care workers, 44% were Wuhan residents; only 2% had direct contact with wildlife. The median incubation period was 4 days (range 2-7), median age was 47 years, and only 0.9% were younger than age 15. 42% were female.

44% had fever on presentation but 89% had fever during hospitalization. (Which is why most recent US national restrictions on testing seem to be resource based, not clinically based.) The second most common symptom was cough (68%), Vomiting (5%) and diarrhea (3.8%) were uncommon. 23.7% had at least one coexisting illness (HTN, COPD, other). Older admitted patients had more severe disease than younger patients.

Only 59% had abnormalities on the initial CXR, though it varied by the severity of presentation with 54% abnormalities in non-severe cases, and 77% in severe cases.

86% of the 975 chest CT scans performed at the time of admission were abnormal, with ground glass opacity (56.4%) and bilateral patchy shadowing (51.8%) being the most common patterns seen (again, findings overlap, so numbers don’t add up). 83% had lymphocytopenia (low lymphocyte counts, a type of blood cell to fight viral infections), 36% had low platelets, and 34% had low overall white blood cell counts. Most patients had elevated CRP, AST, ALT, CK and D-dimer (reflecting varied organ dysfunction). More severe disease correlated with more severe laboratory abnormalities. Of interest, procalcitonin levels were normal in most patients though became elevated in nearly 14% of those with severe presentations, possibly reflecting bacterial superinfections. However, we won’t know from this data set because, as the authors point out, “many patients did not undergo sputum bacteriologic or fungal assessment on admission because, in some hospitals, medical resources were overwhelmed.”

The mean duration of hospitalization was 12 days. 91% were diagnosed with pneumonia, 3.4% with ARDS (respiratory failure), and 1.1% with shock.

Commenting on this study’s overall lower case fatality rate of 1.4% being significantly lower than the reported national official rate of 3.2% as of February 16, the authors note, “Early isolation, early diagnosis, and early management might have collectively contributed to the reduction in mortality in Guangdong.”

***Asymptomatic Carriers***

Of all the unknowns of Covid-19, this may be the most concerning. We just don’t know the number of patients with mild symptoms or asymptomatic carrier states who can infect others. However, there are at least two articles in the current medical literature that raise concerns.

Yan Bei et al in *JAMA* 2/21/20 described a family outbreak of Covid-19 that seems likely to have come from an asymptomatic carrier. The index patient, a 20-year old woman, lives in Wuhan and had traveled to Anyang to visit family on 1/10/20. On 1/13, she met with 5 relatives, who subsequently became ill. None of the other family members traveled to an endemic area or had any known contacts with Covid-19 positive patients. Due to the familial cluster, this patient was isolated and tested. She had no symptoms. No fevers, cough, GI or respiratory symptoms. Her CRP and lymphocyte counts were normal. Her RT-PCR testing (for Covid-19) was negative on 1/26, then positive on 1/28, then again negative on 2/5 and 2/6. Chest CTs on 1/26 and 1/31 were normal. All five family member contacts became ill, two with severe pneumonia, others with moderate infections. All other family members had ground glass opacities on their chest CT scans, a characteristic of Covid-19. The incubation period for this patient was likely 19 days, which is longer than most documented cases. According to the study authors, this case study suggests “an asymptomatic family member who had traveled from the epicenter of Wuhan. The sequence of events suggests that the coronavirus may nave been transmitted by the asymptomatic carrier.” The fact that she had a negative first test is not that unusual, as the authors state, “false-negative results have been observed related to the quality of the kit, the collected sample, or performance of the test.” Her second test was then “unlikely” to have been a false positive and defined her infection with Covid-19.

Chan et al reported in the *Lancet* on 1/24/2020 about a family cluster of 6 patients who flew from Shenzhen to Wuhan on 12/29/29 and then returned home to Shenzhen on 1/4/20. Patient #1 acquired the infection from a Wuhan hospital while visiting a relative, and then most likely transmitted the infection to other family members while there, then to another family member (patient 7) upon their return home. Of note in this cluster, patient #5 was a 10-year-old boy who was completely asymptomatic but was still positive for Covid-19. He subsequently had a CT scan that showed ground glass abnormalities. This study is now relatively older, having come out in January 2020, but it is important. First, the older patients in this family had more serious illness, which has been common in this pandemic. Second, as the authors point out, “These findings suggest that person-to-person transmission and intercity spread of 2019-nCoV (Covid-19) by air travel are possible, supporting reports of infected Chinese travelers from Wuhan being detected in other geographic regions.” Finally, and most relevant here, the 10-year-old boy had no symptoms. None. Other family members exhibited cough, weakness, fever, diarrhea, and two got very ill. Not this 10-year-old boy with a positive test and characteristic findings on his chest CT scan. We can only assume that he returned to school when he returned home to Shenzhen on 1/4, at least until the authorities instituted quarantines in the region. How many did he infect back at home while he had absolutely no symptoms? And what does this mean for us moving forward?

The final consideration in the asymptomatic carriers’ piece is the timing of the illness itself. There are descriptions in John Barry’s book of the 1918 Spanish flu in which patients would start coughing at noon, turn cyanotic hours later and be dead by 6 PM. That had to do with the intensity of the immune response to the virus and the immune system punching holes in the alveoli of the lung and causing the lungs to then fill up with fluid. This virus is different and seems to act more slowly. As such, in the early stages, even those who may eventually die from it may only have a cough, or flu-like symptoms. There is no way other than PCR testing (a nasal swab) to differentiate Covid-19 from many other viruses. Some will remain asymptomatic or only mildly ill with this virus, certainly during the incubation period, but even during the early clinical manifestations, which could be up to several days in some people.

All of this means that we must be exceedingly careful right now.

***Testing***

This is an area that is rapidly evolving and is subjective to state and regional regulations. Widely available testing should be here soon. Check with local authorities for details. We might consider looking toward South Korea for some guidance when we expand our testing capacity. As of March 10, South Korea has noted decreases in its daily number of new cases. The Korean Centers for Control & Prevention (KCDC) reported 131 new cases on March 8, which was its lowest figure since its peak of 909 new cases on February 29. The South Korean epidemic really centered on a religious sect (Schincheonji), who transported the virus back from Wuhan, and spread it rapidly in one city, Daegu. In response, the south Korean government rapidly expanded testing, free to anyone (including undocumented immigrants—viruses don’t recognize borders). Ingeniously, they offered testing via 10-minute drive-through clinics. Those who test positive self-quarantine. Schools closed, and the government shares accurate, non-partisan information daily. There are lessons available to us from South Korea. Imagine people getting test results from testing sites separated from hospitals, where the sickest and most contagious patients will be. Again, we will have to see how local and national government agencies in the US respond.

***Personal Safety***

We do know that this illness is transmitted through small respiratory droplets. As such, health providers should properly protect themselves when examining patients. N-95 masks that properly fit are preferred. Once in the outside world, these droplets dissipate and are scattered by the wind quickly, so masks likely don’t help. But in areas of close contact, such as public transportation, airline travel, etc. they may offer some help.

We should keep in mind that health providers are at significant risk. To reiterate, in the Wang et al article published in *JAMA* on 2/20/20, about 138 hospitalized patients in Wuhan, China the authors noted, “hospital associated transmission was suspected as the presumed mechanism of infection for affected health professions (29%) and hospitalized patients (12.3%).” While this is likely before health personnel had sufficient understanding as to appropriate personal precautions, that percentage is still alarming.

Of particularly concern in the ED and ICU is the risk during intubation. Studies have shown that the infectivity correlates with illness severity. Those who are on the high end of the illness scale are likely the most infective. They will also be coughing up a lot of sputum, droplets containing virus during airway management. We really should be preparing to have gowns, hoods, and complete coverage for this critically ill subset of patients. Since so many medical supplies are now manufactured in Asia (many in China) and supply lines have been greatly disrupted by Covid-19, this could be a huge problem. We will have to improvise but should really start preparations now. Realistically, preparations should have begun nationally weeks ago.

Covid-19 is likely transmitted by fomites (surfaces, clothing, stethoscopes, etc.). Other strains of coronaviruses have been able to live outside the host for several days. As such, frequent handwashing is key, but for 20 seconds, not a quick once over. Hand sanitizers work if there it at least 60% alcohol. If it is transmitted by contact, it will be only by directly touching your face afterwards. This is a difficult habit to get out of. But everyone should do their best to try to not touch their eyes, nose, mouth, after contacting a potentially infected patient or area surfaces. Always wipe down areas and be aware when you are around anyone potentially infected, which soon will be many. For those who want to learn more here, the best single article I saw was from the CDC. “Interim Infection Prevention and Control Recommendations for Patients with Confirmed Coronavirus Disease 2019 (Covid-19) or Persons Under Investigation for Covid-19 in Health Care Settings.” This article is available on the CDC website [www.cdc.gov](http://www.cdc.gov) or simply by entering this title into Google.

All unnecessary travel should be stopped. That includes students traveling abroad for study or service. Since young people do very well with Covid-19 and are more likely to be asymptomatic carriers or have few symptoms, is it worth potentially introducing a lethal virus to a vulnerable population for a few weeks of study or volunteering? It is a moral question. As director of an NGO myself ([www.omnimed.org](http://www.omnimed.org)), on Monday March 2, we canceled 25 nursing, medical and undergraduate students planning to visit our site in Uganda during March and April. We have suspended further site visits indefinitely, likely until we can have antibody testing or other evidence of immunity. These were not easy decisions, but they were the right decisions from a moral standpoint. Large gatherings should be postponed (as evidenced by the fallout from the recent Biogen meeting). People should work from home if possible. Keep in mind the H.L. Mencken aphorism as we move forward. “It is difficult to get a man to understand something when his salary depends on his not understanding it.” This pandemic will present many people with some very difficult choices.

***Treatment***

The reality is that we have no effective treatments right now. Studies are ongoing for several agents, including alpha interferon, lopinavir/ ritonavir, oseltamivir (Tamiflu), remdesivir, chloroquine, among others. It is very clear that glucocorticoids do not work and should not be given. But we really don’t have effective treatment for seasonal flu either. Tamiflu is worthwhile in higher risk or pregnant patients, but it doesn’t really change the disease course all that much, and it has many side effects. The best advice for people to follow is to stay home. Most people, particularly young and healthy people, will do fine with this illness. And we will only be able to offer supportive care for them anyway. In the coming weeks, we should have the ability to test, but we don’t as of this writing. When we have patients in the ER whom we suspect may have Covid-19, we have to call Mass DPH and get permission to test. I have called three times in the past week and been told no each time. The test, as of this writing, is a send out and takes a day to return. That will soon change, again, maybe by this week or next. It will be helpful to track cases, but there is little we can offer unless patients have significant respiratory symptoms or become very ill.

When people develop respiratory symptoms like shortness of breath or any difficulty breathing, they should seek care. These people will pose the most significant challenges to us, particularly if the epidemic crests with a lot of sick people at the same time. Isolation will be important, as will be personal protection.

We have now been seeing people coming to the ER with concerns of Covid-19. Here is what I have been telling them, based on the above. First, right now there is really no reason to come. We can’t test most people, and even if positive, we have nothing to offer them for treatment. In fact, the paradox of coming to the ER now is that you are increasing your likelihood of becoming exposed. The ER is the last place anyone should go now for minor ailments since it is where the sickest and most contagious patients will gather. The true value in the ER right now is for those who become more severely sick with Covid-19 with difficulty breathing or overwhelming sepsis. We can apply positive pressure ventilation, mechanical ventilation, and admit to ICU (until we become overwhelmed.) for everyone else, the risk of sitting in the ED waiting room and coming into direct contact with sick patients simply outweighs the potential benefits of our evaluation. Stay home, minimize social interactions, maximize personal protections, and come to see the doctor or ER only if you become sick with breathing or other more severe complications. Once testing is widely available, there should be many sites for testing; that really is the role of good governance to direct people to safe testing sites. South Korea seems to have done so very well. We will see how this aspect plays out in the US.

***The Political and Big Picture***

This epidemic has been characterized by political failures right from its outset. Chinese authorities had the opportunity to contain it early on, but instead silenced those who tried to speak out. Dr Li Wenliang, the 34-year old ophthalmologist whistle-blower from Wuhan, was forced by authorities to sign a document that he was “making false comments” about Covid-19 after he wrote to medical school classmates, “If the officials had disclosed information about the epidemic earlier, I think it would have been a lot better. There should be more openness and transparency.” He subsequently died, leaving his wife and young child behind. He has since become a national hero in China for standing up to authorities.

Unfortunately, the US was poorly prepared for the arrival of Covid-19 when it first struck here in late January. Much of the personal protective equipment (PPE) required for health care providers is woefully understocked, at least in part since so much of it is now manufactured in Asia. And the initial testing rolled out by the CDC has been disastrous. Testing in a pandemic like this one is critically important. According to *The Economist* magazine, “By March 1st, when South Korea had run 100,000 tests for the virus, America—which saw its first case on January 23rd—had run fewer than 500.” As a WHO Team member recently stated, “You either test and find it early, and do something about it, or the body bags are going to pile up.”

It will be important for all of us now to take a break from our partisan worldviews and listen to the scientists and health professionals. Research from the Swine Flu epidemic of 2009-2010 has shown that those who don’t trust information from health experts were less likely to receive protective vaccinations and therefore more likely to die. Unfortunately, we are not all listening to the health experts now. Again, according to *The* *Economist*, “in countries where there is a high level of trust in government, some strong measures [like mandatory quarantines] will be supported. June 2019 polling found that people in different countries have variable degrees of trusting government health information, including 78% of Canadiens, 80% of Germans, 80% of Brits, and 86% of South Koreans. However, only 59% of Americans do. In a pandemic with a virus that carries such lethality as this one, such views can cost lives. Now is the time to pull together. While we may disagree politically, we should remember Lincoln’s call to the “better angels” of our nature. We have been divided as a country before, and we will come together again both as a nation and as a people. We should all do what we can to get accurate information into all hands; peoples’ lives depend on it.

**Summary:**

This information is fluid and will change daily. Follow daily updates on the <https://www.worldometers.info/coronavirus/>, or on [www.cdc.gov](http://www.cdc.gov).

Stay home and minimize contacts as much as possible. Limit travel, attendance at conferences, public gatherings, etc. In the coming weeks we will increasingly see closure of schools, sporting events, other public gatherings. Many industries will be hit hard like airlines, restaurants, tourism, etc. The Boston Bruins are on track for the President’s Cup this year. The NHL season, along with that of the NBA, may not be able to finish.

This virus is not coming; it is already here. News reports lag behind the incubation period and early symptomatic phase in many people by at least a week. Once you are reading about it, assume the pandemic has spread far more. And please stay away from the political spin on this. Avoid Fox News as well as statements out of the Trump White House.

Take personal precautions. Wash your hands frequently. Avoid touching your face. Wear a facemask when in direct contact with anyone coughing or sick; though it won’t necessarily help you outside.

Seek health care only if you become very ill. As of this writing, we cannot treat Covid-19 directly. We can help those with difficulty breathing or who become very ill. But keep in mind that the very locations that will provide aid to the sickest, will also likely prove to have the highest risk for viral transmission. For well over 80% of those infected, this will prove just another flu-like illness. For a smaller percentage, it will require the best in our emergency and critical care. Try to stay home but come in if you need us.

***A Closing Thought***

I hope what is coming, in fact what is already here, will not hit us all as hard as what we’ve seen elsewhere. As of this writing, we are actively gearing up at St Elizabeth’s, which reflects a practice happening in hospitals and medical facilities throughout the US. Please remember that despite the observations above, we are all in this together. We will get through this best if we help each other. Avoid contacting others if you become ill. Stay away from vulnerable people and keep close tabs, preferably by phone, on elderly or infirm neighbors and relatives. Follow directives from local governments. I know many people don’t get paid if they don’t work. But this will pass, likely in weeks to months if we all work together. Try to work from home or avoid work if you can—just for a little while. Let me leave you with some words from one of my heroes, Albert Schweitzer, who wrote over a century ago, “Just as the wave cannot exist for itself but is ever a part of the heaving surface of the ocean, so must I never live my life for itself, but always in the experience which is going on around me.” Let’s all work together on this.

**Bibliography:**

Guan et al, “Clinical Characteristics of Coronavirus Disease 2019 in China,” *NEJM* published on-line 2/28/20 and updated 3/3/20 at NEJM,.org.

Wang et al, “Clinical Characteristics of 138 Hospitalized Patients with 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China, *JAMA* published on-line 2/7/20, corrected on 2/20/20. JAMA.org

Al Giwa and Akash Desai, “Novel Coronavirus Covid-19: An Overview for Emergency Clinicians,” *Emergency Medicine Practice,* February 2020

Fleisher, Jorge, Chief, Infectious Disease at SEMC, “Coronavirus,” Resident Rounds at SEMC Seton Auditorium, 3/3/20.

Jasper Fuk-Woo Chan et al, “A Familial Cluster of Pneumonia Associated with the 2019 Novel Coronavirus Indicating Person-to-Person Transmission: A Study of a Family Cluster, *The Lancet*, February 15, 2020, 395: 514-523.

Stanley Perlman, “Another Decade, Another Coronavirus,” *NEJM*, 382: 760-762, February 20, 2020.

Yan Bei, et al, “Presumed Asymptomatic Carrier Transmission of COVID-19,” *JAMA* published online 2/21/20.

Chaolin Huang et al, “Clinical Features of Patients Infected with 2019 Novel Coronavirus in Wuhan, China,” *The Lancet,* 395: 497-506, February 15, 2020

Chen Wang et al, “A Novel Coronavirus Outbreak of Global Health Concern,” *The Lancet*, 396: 470-473, February 15, 2020

Carlos del Rio and Preeti Malani, “Covid-19- New Insights on a Rapidly Changing Epidemic,” *JAMA* on-line 2/28/20

Bill Gates, “Responding to Covid-19—A Once-in-a-Century Pandemic?” *NEJM* February 28,2020, online at NEJM.org

<https://www.worldometers.info/coronavirus/> (This is a nice website that is updated many times daily. It has sections on infectivity, lethality, new insights, as well as a trove of basic explanations about this particularly epidemic. It is very good and reliable.)

Randy Shilts, *And the Band Played On: Politics, People and the AIDS Epidemic*, St Martin’s Press, New York, 1987.

O’Neil, Edward Jr, *Awakening Hippocrates: A Primer on Health, Poverty, and Global Service*, American Medical Association Press, Chicago, 2006.

Lena H. Sun, “CDC to cut by 80% efforts to prevent global disease outbreak, *The Washington Post*, February 1, 2018

Paul Krugman, “When a Pandemic Meets a Personality Cult,” *The New York Times*, February 28, 2020

Michael Shear and Maggie Haberman, “Pence Will Control All Health Messaging from Health Officials,” *The New York Times*, February 28, 2020.

Paul Krugman, “Paranoid Politics Goes Viral,” *The New York Times*, March 2. 2020

Michelle Goldberg, “Trump’s Calamitous Coronavirus Response,” *The New York Times*, March 6, 2020

Barry, John, *The Great Influenza, The Epic Story of the Deadliest Plague in History*, Penguin Books, New York 2004 (This is a classic book that goes into painful detail of the Spanish flu that killed upwards of 50 million people.

Hans Zinsser, *Rats, Lice and History, The Biography of a Bacillus*, Little, Brown and Company, Boston 1934

Paul Farmer, Margaret Connors, Janie Simmons, Editors; *Women, Poverty and AIDS, Sex, Drugs, and Structural Violence*, Common Courage Press, Cambridge, 1996

Paul Farmer, *The Uses of Haiti*, Common Courage Press, Cambridge, 1994

Garrett, Laurie, *The Coming Plague, Newly Emerging Diseases in a World out of Balance*, Penguin Books, New York, 1994

Diamond, Jared, *Guns, Germs and Steel, The Fates of Human Societies*, Norton Press, New York, 1999.

Wufel Yu, “Coronavirus: Revenge of the Pangolins,” *The New York Times*, March 5, 2020

Michael D Shear, Sheri Fink, and Noah Weiland, “Behind Coronavirus Chaos at the White House: Fears, Confusion and Miscommunication Mar a Response,” *The New York Times*, March 8, 2020

Nicholas Kristof, “Beware the Contagion Spread by Blowhards,” *The New York Times*, March 8, 2020

Washington Post Fact Checker, “In 1,095 days, President Trump has made 16,241 False or Misleading Claims, *The Washington Post,* January 19,2020

“Briefing Covid-19, New World Curriculum,” *The Economist Magazine*, March 7, 2020

Mike Baker, “Group Home Near Seattle Has Shortage of Test Kits,” *The New York Times,* March 8, 2020

Adam Beckman et al, “Covid-19: Lessons from South Korea,” The Bulwark.com March 10, 2020

Aylin Woodward and Ryan Pickrell, “Whistleblower doctor Li Wenliang, who was Censored after Sounding the Alarm about the Coronavirus, has Died in Wuhan,” *Business Insider*, February 6, 2020

Centers for Disease Control and Prevention (CDC), “Interim Infection Prevention and Control Recommendations for Patients with Confirmed Coronavirus Disease 2019 (Covid-19) or Persons Under Investigation for Covid-19 in Health Care Settings,” February 21, 2020, from [www.cdc.gov](http://www.cdc.gov)

Edward O’Neil Jr, M.D.

[ejoneil@omnimed.org](mailto:ejoneil@omnimed.org)

[www.omnimed.org](http://www.omnimed.org)

Staff Physician, Steward St Elizabeth’s Medical Center, Boston

Associate Prof., Tufts Univ. School of Medicine