



BULLETIN: UPDATE ON CORONAVIRUS 3/23

March 23, 2020
by Lynne Peterson

Be careful, be safe, and be well.

There was a lot of coronavirus news on Monday, March 23 – enough to justify a new update. Here are the latest developments related to the SARS-CoV-2 virus and the disease it causes, Covid-19. Future updates will be at least weekly but as often as the news flow warrants.

In one day, the U.S. moved up from fourth in the world in terms of the number of Covid-19 cases to third place, and the U.S. is still in the escalation phase. Italy may be getting near the peak of the curve.

Worldwide Covid-19 Statistics									
Country	As of March 18			As of March 22 (just 4 days later)			As of March 23 (one more day later)		
	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate
Worldwide	217,242	8,704	4.0%	335,972	14,632	4.4%	381,293	16,572	4.3%
China	81,137	3,130	3.9%	81,407	3,265	4.0%	81,514	3,274	4.0%
Italy	35,713	2,978	8.3%	59,138	5,476	9.3%	63,927	6,077	9.5%
Spain	13,176	638	4.8%	28,768	1,772	6.2%	35,136	2,311	6.6%
U.S.	9,249	145	1.6%	33,276	417	1.3%	46,332	610	1.3%
Germany	12,327	28	0.2%	24,873	94	0.4%	29,056	123	0.4%
Iran	17,061	1,135	6.7%	21,638	1,685	7.8%	23,049	1,812	7.9%
U.K.	>2,600	104	4.0%	5,741	282	4.9%	6,726	336	5.0%

Source: <https://coronavirus.jhu.edu/map.html>

U.S. Covid-19 Statistics						
State	As of March 22			As of March 23		
	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate
New York	15,168	114	0.8%	21,689	157	0.7%
Washington	1,793	94	5.2%	1,996	95	4.8%
California	1,554	29	1.9%	1,733	27	1.6%
New Jersey	1,914	20	1.0%	2,844	27	0.9%
Michigan	1,035	8	0.8%	1,328	15	1.1%
Florida	830	13	1.6%	1,171	14	1.2%
Louisiana	837	20	2.4%	1,172	34	2.9%
Illinois	1,058	9	0.9%	1,285	12	0.9%
Massachusetts	646	5	0.8%	777	9	1.2%

Source: <https://covidtracking.com/data/>

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Tidbits

■ U.S.

- ~42% of the country is now under a stay-at-home order.
- The **USNS Mercy**, a hospital ship, was sent to Los Angeles instead of Seattle.
- The U.S. Senate failed – twice – to reach agreement on a **stimulus package** as of midnight March 23.
- The October deadline for real ID driver licenses will be extended. The new date has not yet been announced.
- The U.S. Justice Department and the Department of Health and Human Services will crack down on large-scale hoarding and price gouging. It is a crime to stockpile essential items in excessive quantities, and the Attorney General has designed a person in the office of each of the 93 U.S. Attorneys around the country to be in charge of these cases.
- No child less than age 15 has died from Covid-19, and <1% of all deaths are age <50 in the U.S.
- Governors were asked to talk to outpatient surgery centers and hospital operating rooms to identify equipment that, with new FDA guidelines, can be converted to ICU ventilators for Covid-19 patients.

■ **President Trump:** Changed the tone of the Covid-19 response by saying, “America will again and soon be open for business – a lot sooner than 3 or 4 months. We can’t let the cure be worse than the problem...At the end of 15 days [which is March 30]...we will decide which way to go...the timing of the opening of our country...We are going to watch senior citizens very, very carefully...and do that with an open economy...If it were up to the doctors, they might shut down the entire world...You can’t do that...You have 160 million jobs in this country. We can’t turn that off and think it will be wonderful...There will be tremendous death from that...probably more death from that than anything with respect to the virus.”

Asymptomatic patients: Vice President Pence said that on March 24 guidance should be released on when and how someone who has been exposed to the virus but who is asymptomatic may return to work.

■ New York

- New York City – the main hotspot for Covid-19 in the U.S. – saw a 50% one-day increase from Sunday to Monday in Covid-19 deaths (from 66 to 99), a 33% increase in confirmed cases (from 8,115 to 10,764), a 24% increase in overall Covid-19 hospitalizations (from 1,450 to 1,800), and a 22% increase in ICU hospitalizations (from 370 to 450).
 - New York Gov. Andrew Cuomo:
 - ✓ Ordered that hospitals **must** increase their capacity by 50% and should **try** to increase it by 100%.
 - ✓ Asked insurance company nurses to “enlist” to help in the Covid-19 patient surge.
 - ✓ Urged President Trump to use the Defense Production Act despite companies volunteering to produce personal protective equipment (PPE).
 - ✓ 78,000 people have been tested in New York, which is 25% of nationwide testing.
 - ✓ 24% of Covid-19 hospitalizations require an ICU bed (a ventilator bed).
 - ✓ 13% of people testing positive are being hospitalized.
 - ✓ Anyone flying to Florida from the New York City area (New York, New Jersey, Connecticut) is now required by order of the governor of Florida to self-quarantine for 14 days when they arrive in Florida.
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■ Europe

- Britain is on country-wide lockdown, with groups of more than 2 people banned, and it will be enforced by the police. All non-essential shops were ordered to close immediately, and people are only allowed out to buy food or medication, exercise alone once a day, or travel to necessary work.
- German Chancellor Angela Merkel, who was exposed to Covid-19, tested negative.

■ **Blood supply:** A blood bank official said the blood supply is not considered at risk from SARS-CoV-2, explaining that SARS-CoV-2 is a respiratory, not a blood-borne virus (e.g., HIV). Thus, donors are not being treated for Covid-19 and donated blood is not being tested for SARS-CoV-2.

■ Clinical trial interruptions:

- **Bristol-Myers Squibb** said it will not start any new trials of any drugs until at least April 13, 2020.
- **Lilly** said it is delaying the start of most new trials and will pause enrollment in most ongoing trials.

■ **CMS:** In response to the coronavirus crisis, the Centers for Medicare and Medicaid Services (CMS) are easing reporting requirements for Quality Payment Programs and other programs.

■ **Medical supplies:** **Medtronic** said it has increased its production of ventilators by 40%. Draeger, Getinge, and Philips are also boosting ventilator production.

■ **Surfaces** – A new study by the Centers for Disease Control and Prevention (CDC) found that SARS-CoV-2 survived for up to 17 days (yes, 17 *days*) on the Diamond Princess and Grand Princess cruise ships.

■ **Symptoms:** There are new symptoms that could suggest Covid-19 – in addition to fever, cough, shortness of breath, and GI issues. The American Academy of Otolaryngology-Head and Neck Surgery said the loss of smell (anosmia) or taste (dysgeusia) may be useful screening symptoms.

Testing

■ **Home testing** – The FDA is cracking down on companies offering fake coronavirus tests. FDA Commissioner Stephen Hahn, MD, issued an alert to consumers about unauthorized home test kits, noting that the Agency has not authorized any home tests yet for Covid-19 and promising to take action to protect consumers from “bad actors who take advantage of a crisis to deceive the public.”

■ **Laboratory testing** – Commercial labs were ordered to prioritize tests for hospitalized patients.

■ **Self-swabbing tests** – The FDA updated its Covid-19 guidelines to allow self-swab tests. The people taking the test can now do the swab themselves *at a testing site, not at home*.

■ **Investigational tests** – Additional companies keep trying to get into the Covid-19 testing market. The newest added to the list:

- **3D Medicine Science & Technology's SARS-CoV-2** and Influenza A&B RT-qPCR detection kit, which can simultaneously detect influenza A, influenza B, and the coronavirus, was granted a CE Mark.
 - **Bio-Rad Laboratories' QX200 ddPCR system** – The company is collaborating with Biondesix to get emergency use authorization (EUA) from the FDA for this SARS-CoV-2 droplet digital PCR test.
 - **Bioneer's AccuPower SARS-CoV-2 Real-Time RT-PCR Kit** and **AccuPower COVID-19 Real-Time RT-PCR Kit** were granted CE Marks.
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- **Iceni Diagnostics** is developing a fast point-of-care test that uses artificial glycan receptors to detect and differentiate SARS-CoV-2 from common influenza strains.
- **SolGent's DiaPlexQ Novel Coronavirus (2019-nCoV) Detection assay** was granted a CE Mark, emergency use authorization in South Korea, and approval by the Philippines Department of Health Food and Drug Administration.

Treatment

- **AbbVie's Kaletra (lopinavir + ritonavir)** – The company reportedly said it will not enforce its patent rights to this HIV drug for use in Covid-19. It is continuing to be tested in Covid-19 despite one failed trial.
- **AlloVir** expanded its collaboration with Baylor College of Medicine on development of a Covid-19 T cell therapy.
- **Ibuprofen** – The FDA issued a statement saying there is insufficient evidence that using NSAIDs, including ibuprofen, exacerbates the symptoms of Covid-19, advising patients to continue taking prescribed medications as directed.
- **Gilead Sciences' remdesivir**
 - Due to what the company called overwhelming demand, it stopped accepting individual requests for compassionate use of this antiviral for Covid-19, though it will continue to process requests already received. Instead, the company is encouraging patients get into trials but is developing an expanded access program for patients where a trial is not an option. Gilead expects these actions will both accelerate access to remdesivir for severely ill patients and enable the collection of data from all participating patients.
 - The FDA granted remdesivir orphan drug status. *This sets Gilead up to receive additional federal tax credits in the U.S. and seven-year market exclusivity, which Public Citizen called “unconscionable” and potentially “deeply harmful.”* Public Citizen accused Gilead of gaming the system by “rushing through” this application while there are, for this brief moment, fewer than 200,000 Covid-19 U.S. cases.” Public Citizen called this “disingenuous and outrageous,” saying the government “should be urgently concerned with its affordability for citizens. Instead, the FDA has handed Gilead...the ability to charge outrageous prices to consumers.”
- **Head-to-head trial** – The ≥3,200-patient, 5-arm, open-label DISCOVERY trial has started in Europe/U.K., comparing the addition of four investigational therapies to standard of care vs. standard of care alone in hospitalized Covid-19 patients: remdesivir, Kaletra, Kaletra + interferon beta, and hydroxychloroquine.
- **Hydroxychloroquine**
 - Anecdotal reports continue to come in about success in treating Covid-19 with this drug, particularly in combination with azithromycin (Pfizer's Z-Pak) and zinc. New York is officially starting use on March 24.
 - The FDA lifted the ban on **Ipca Laboratories'** imports from its plant in India, imposed after it failed an FDA inspection for, among other things, data manipulation. The move allows Ipca to ship chloroquine sulphate and chloroquine phosphate active pharmaceutical ingredients (APIs) as well as hydroxychloroquine sulphate tablets, to the U.S.
- **REMS** – The FDA issued new guidance on testing required by risk evaluation and mitigation strategy (REMS) programs during the coronavirus pandemic, acknowledging that some required lab testing and imaging studies may be difficult because of quarantines. The FDA said it will work with sponsors to ensure that patients have access to the affected medications and said doctors should “use their best medical judgment” in continuing treatment without the testing. The FDA said it does not intend to take action against companies or doctors for failing to adhere to REMS-required testing during this health emergency.
- **Roche/Genentech's Actemra (tocilizumab)** – The FDA gave the go-ahead for the company's planned Phase III trial of this IV arthritis drug, an anti-IL-6, that is also used to treat cytokine release syndrome (CRS) in cancer patients getting immunotherapy with a PD-1/L1 inhibitor. The double-blind, randomized Phase III COVACTA trial will be conducted in

collaboration with the Biomedical Advanced Research and Development Authority (BARDA). The company also is providing 10,000 doses to the Strategic National Stockpile.

Vaccines

The FDA and the European Medicines Agency (EMA) jointly hosted a *virtual* global regulators meeting to discuss regulatory strategies to facilitate the development of SARS-CoV-2 vaccines. The focus was on the preclinical data needed to demonstrate safety and support proceeding to Phase I trials. The discussions included the need for data evaluating the theoretical risk for vaccine-induced disease enhancement – where vaccinated individuals who subsequently get infected with a virus develop disease that is worse than if they had been unvaccinated. While recognizing the urgency of starting human trials of SARS-CoV-2 candidate vaccines, the regulators stressed the importance of preclinical and clinical risk mitigation strategies so that trial patients are not exposed to unreasonable risk. Additional meetings are planned to continue these discussions.

The Society of Critical Care Medicine (SCCM) concluded there is **insufficient evidence to recommend the use of hydroxychloroquine, chloroquine, Gilead Sciences' remdesivir, or an anti-IL-6** for Covid-19. SCCM convened a panel of 36 experts from 12 countries who agreed on new guidelines with 50 recommendations/suggestions for treating critically ill Covid-19 patients. These include:

- *Recommends:* Against use of hydroxyethyl starches, gelatins, dextrans, albumin for acute resuscitation. Instead, use norepinephrine first-line, or, if not available, vasopressin or epinephrine. Second line, add vasopressin instead of titrating norepinephrine.
- *Recommends:* Titrating vasoactive agents to a target of 60-65 mmHg, not higher.
- *Recommends:* High-flow nasal cannula (HFNC) over conventional oxygen over non-invasive positive-pressure ventilation (NIPPV) – [e.g., CPAP] – for acute hypoxemic respiratory failure despite conventional oxygen therapy.
- *Recommends:* Against use of routine systemic corticosteroids in mechanically ventilated patients with respiratory failure but not ARDS. If ARDS is present, then use corticosteroids.
- *Recommends:* Acetaminophen over no treatment for fever.
- *Recommends:* Against routine use of IVIG or Kaletra, and says there is insufficient evidence to recommend other antiviral agents.

Unanswered questions *(Items will remain on this list until answered. New questions are at the top of the list.)*

- ? Are Covid-19 patients who are put on a ventilator recovering? What percent of patients who get severe Covid-19 are getting discharged from the hospital?
 - ? Will companies that have boosted production of medical supplies, particularly big-ticket items like ventilators get caught at the end of this with products that have no buyers – unsold inventory?
 - ? Can people get Covid-19 more than once?
 - ? Are there long-term effects from getting Covid-19, even mild Covid-19? Will there be long-lasting lung abnormalities or pulmonary fibrosis?
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