COVID-19: *Updates*

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University of Chicago
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Disclosures

- I have no relevant financial interests to disclose.
Hard not to start here...
Local Epidemiology

**CHICAGO COVID-19 Citywide Positivity Rate**

Current Positivity Rate
Based on a 7 day rolling average

4.4% ▲
Prior wk.: 4.3%

Tests performed (3/1/2020 - 10/12/2020)

Cumulative tests
1,235,809

Daily tests (7 day rolling average)
10,243 ▲
Prior wk.: 9,164 (12%)

Confirmed cases (3/1/2020 - 10/13/2020)

Cumulative cases
85,602

Daily cases (7 day rolling average)
399 ▲
Prior wk.: 332 (20%)

Positivity rate and positivity target (7 day rolling average)
Target positivity < 5.0%

Tests performed and testing target (7 day rolling average)
Daily testing target > 4,500

Built by slalom

Last updated October 12, 2020
Data for this dashboard is updated daily.
And Elsewhere...

New Confirmed COVID-19 Cases per Day by US States/Territories, normalized by population.
Chicago’s Quarantine List Grows...

- Now includes **Indiana** in addition to the previous Wisconsin, Iowa, Missouri.
- 26 states are now listed
- While numbers remain relatively stable in Chicago, fear of a resurgence persist...
SARS-CoV-2 Vaccine Candidates:

**VIRUS VACCINES**
At least seven teams are developing vaccines using the virus itself in a weakened or inactivated form. Many existing vaccines are made in this way, such as those against measles and polio, but they require extensive safety testing. Sinovac Biotech in Beijing has started to test an inactivated version of SARS-CoV-2 in humans.

- **Weakened virus**
  - A virus is conventionally weakened for a vaccine by being passed through animals or human cells until it picks up mutations that make it less able to cause disease. Oxitec Ltd., in Farnham, New York, is working with the Serum Institute of India, a vaccine manufacturer in Pune, to weaken SARS-CoV-2 by altering its genetic code so that viral proteins are produced less efficiently.

- **Inactivated virus**
  - In these vaccines, the virus is rendered uninjectable by chemicals, such as formaldehyde, or heat. Reducing them, however, requires starting with large quantities of infectious virus.

**NUCLEIC-ACID VACCINES**
At least 30 teams are aiming to use genetic instructions in the form of DNA or RNA for a coronavirus protein that prompts an immune response. The nucleic acid is injected into human cells, which then churn out copies of the virus protein. Most of these vaccines encode the virus’s spike protein.

- **DNA vaccine**
  - DNA is often encased in a lipid coat so it can enter cells.

- **RNA vaccine**
  - RNA and DNA-based vaccines are safe and easy to develop, to produce them involves making genetic material, and the virus, but they are problematic. No licensed vaccines use this technology.

**VIRAL-VECTOR VACCINES**
Around 25 groups say they are working on viral vector vaccines. A virus such as measles or adenovirus is genetically engineered so that it can produce coronavirus protein in the body. These vaccines are weakened so they cannot cause disease. There are two types: those that can still replicate within cells and those that cannot because key genes have been disabled.

- **Replicating viral vector** (such as weakened measles)
  - The newly approved Chiron vaccine is an example of a viral vector vaccine that replicates within cells. Such vaccines tend to be safer and provide a stronger immune response, existing immunity to the vector could limit the vaccine's effectiveness.

- **Non-replicating viral vector** (such as adenovirus)
  - Non-licensed vaccines use this method, but they have a long history in gene therapy. Further shots can be needed to induce long-lasting immunity. US-based drug giant Johnson & Johnson is working on this approach.

**PROTEIN-BASED VACCINES**
Many scientists want to target coronavirus proteins directly into the body. Variants of proteins or protein shells that mimic the coronavirus's outer coat can also be used.

- **Protein subunits**
  - Twenty-eight teams are working on vaccines with viral protein subunits—most of these are focusing on the virus's spike protein or a key part of it called the receptor binding domain. Similar vaccines against the SARS virus protected monkeys against infection but haven’t been tested in people. To work, these vaccines might require adjuvants—immune-stimulating molecules delivered alongside the vaccine—as well as multiple doses.

- **Virus-like particles**
  - Empty virus shells mimic the coronavirus structure, but aren't infectious because they lack genetic material. Many teams are working on Virus-like particle (VLP) vaccines, which can trigger a strong immune response, but can be difficult to manufacture.
Traditional Vaccine Development vs. Development Using a Pandemic Paradigm

Traditional Paradigm — Multiple Years
- Target ID, development partner selection, and preclinical trial
- Phase 1
- Phase 2a
- Phase 3
- Licensure
- Go or no-go decision to invest in candidate
- First trial in humans
- Efficacy trial in humans
- Evaluation trial in humans

Outbreak Paradigm — Overlapping Phases Shorten Development Time
- Target ID, development partner selection, and preclinical trial
- Clinical development
  - Safety/dose selection
  - Safety/efficacy
- First in humans (safety)
- Efficacy trial
- Regulatory pathway for emergency authorization
- Manufacturing development, scale-up, clinical trial material, commercial scale, validation of process
- Large-scale manufacturing

5-10 years; 0.5-1.5 billion dollars

1 in 10 candidates make it to registration
93% fail

6-18 months

Safety

Immunogenicity
# WHO Target Product Profile

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Preferred (wish list)</th>
<th>Critical / Minimal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target population</td>
<td>All ages, pregnant women</td>
<td>Adults, elderly</td>
</tr>
<tr>
<td>Safety / Reactigenicity</td>
<td>No serious Aes, transient AE, favorable fisk / benefit ratio context of known efficacy</td>
<td>Safety and reactogenicity outweighs risk; Long-term safety and reactogenicity</td>
</tr>
<tr>
<td>Measure of Efficacy</td>
<td>70% efficacy (on population basis with consistent results in the elderly)</td>
<td>~50% point estimate (vaccine efficacy)</td>
</tr>
<tr>
<td></td>
<td>Endpoint may be assessed vs. disease; severe disease; and/or shedding/transmission**</td>
<td>Endpoint may be assessed vs disease; severe disease; and/or shedding / transmission</td>
</tr>
<tr>
<td>Schedule</td>
<td>1 dose</td>
<td>2 doses</td>
</tr>
</tbody>
</table>

** Measurable endpoints will be defined as symptoms consistent with COVID infection and a positive RT-PCR (given multiple comparable trials)
Vaccines updates as of 10/13...

- **Johnson & Johnson (Janssen)** vaccine study placed on hold due to SAE in participant
  - The company did not disclose what the illness was, citing the participant’s privacy. The illness is still under investigation
- **AstraZeneca** study still on hold in US
- **Pfizer** announced this week that it has received FDA approval to enroll children as young as 12 years old in its COVID-19 vaccine trial
- Moderna’s chief executive officer, Stephane Bancel, said this week that he expects the company to submit the data to the U.S. Food and Drug Administration (FDA) for emergency use authorization (EUA) on November 25
- In terms of more broad availability, Bancel indicated late March or early 2021
- More than 28,000 of the planned 30,000 people have enrolled in the **Moderna** study
First, a Vaccine Approval. Then ‘Chaos and Confusion.’

Come spring, Americans may have their choice of several so-so coronavirus vaccines — with no way of knowing which one is best.

C. Zimmer, New York Times 10/12/2020
Recent case...

- 60 y/o male with PMHx HTN, asthma, and bladder cancer (s/p BCG 2005) who presented on 10/5 w/ SOB, peripheral edema, weight gain, and found to have newly significantly reduced LVEF w/ concern for non-ischemic etiologies.

- Work up significant for BNP on admission 4513, echo with LVEF 28%, and SARS-COV2 antibody positive. Cardiac catheterization 10/6 with nonobstructive CAD and elevated filling pressures consistent with Group 2 pulmonary hypertension.

- Cardiac MRI 10/8 with nonischemic pattern and small areas of LGE which may be consistent with prior viral illness as etiology.

- Interestingly, Covid PCR found to be positive as well.
Outcomes of Cardiovascular Magnetic Resonance Imaging in Patients Recently Recovered From Coronavirus Disease 2019 (COVID-19)

Valentina O. Puntmann, MD, PhD; M. Ludovica Carerj, MD; Imke Wieters, MD; Masia Fahim; Christophe Arendt, MD; Jedrzej Hoffmann, MD; Anastasia Shchendrygina, MD, PhD; Felicitas Escher, MD; Mariuca Vasa-Nicotera, MD; Andreas M. Zeiher, MD; Maria Vehreschild, MD; Eike Nagel, MD

RESULTS Of the 100 included patients, 53 (53%) were male, and the mean (SD) age was 49 (14) years. The median (IQR) time interval between COVID-19 diagnosis and CMR was 71 (64-92) days. Of the 100 patients recently recovered from COVID-19, 67 (67%) recovered at home, while 33 (33%) required hospitalization. At the time of CMR, high-sensitivity troponin T (hsTnT) was detectable (greater than 3 pg/mL) in 71 patients recently recovered from COVID-19 (71%) and significantly elevated (greater than 13.9 pg/mL) in 5 patients (5%). Compared with healthy controls and risk factor–matched controls, patients recently recovered from COVID-19 had lower left ventricular ejection fraction, higher left ventricle volumes, and raised native T1 and T2. A total of 78 patients recently recovered from COVID-19 (78%) had abnormal CMR findings, including raised myocardial native T1 (n = 73), raised myocardial native T2 (n = 60), myocardial late gadolinium enhancement (n = 32), or pericardial enhancement (n = 22). There was a small but significant difference between patients who recovered at home vs in the hospital for native T1 mapping (median [IQR], 1119 [1092-1150] ms vs 1141 [1121-1175] ms; P = .008) and hsTnT (4.2 [3.0-5.9] pg/dL vs 6.3 [3.4-7.9] pg/dL; P = .002) but not for native T2 mapping. None of these measures were correlated with time from COVID-19 diagnosis (native T1: r = 0.07; P = .47; native T2: r = 0.14; P = .15; hsTnT: r = −0.07; P = .50). High-sensitivity troponin T was significantly correlated with native T1 mapping (r = 0.33; P < .001) and native T2 mapping (r = 0.18; P = .01). Endomyocardial biopsy in patients with severe findings revealed active lymphocytic inflammation. Native T1 and T2 were the measures with the best discriminatory ability to detect COVID-19–related myocardial pathology.

CONCLUSIONS AND RELEVANCE In this study of a cohort of German patients recently recovered from COVID-19 infection, CMR revealed cardiac involvement in 78 patients (78%) and ongoing myocardial inflammation in 60 patients (60%), independent of preexisting conditions, severity and overall course of the acute illness, and time from the original diagnosis. These findings indicate the need for ongoing investigation of the long-term cardiovascular consequences of COVID-19.
Long-term Health Consequences of COVID-19

• Definitions:
  • Post-acute COVID-19 = extends beyond 3 weeks
  • Chronic COVID-19 = extends beyond 12 weeks

• Pathogenesis
  • Direct tissue invasion
  • Profound inflammation/cytokine storm
  • Immune system damage
  • Hypercoagulable state
  • Combination of factors
Persistent Symptoms in Patients After Acute COVID-19

Angelo Carfi, MD; Roberto Bernabei, MD; Francesco Landi, MD, PhD; et al

- Post-hospital discharge outpatient service for COVID-19 patients in Italy
- **143 patients total, mean age 56y (19-84y)**
- 72% of patients had interstitial pneumonia in the hospital
- Mean LOS 13.5 days, 15% NIV, 5% invasive ventilation
- Assessed **mean of 60d** after onset of first symptom
- **32% had 1-2 symptoms and 55% had 3+**
- Worsened quality of life in 44%

The figure shows percentages of patients presenting with specific coronavirus disease 2019 (COVID-19)-related symptoms during the acute phase of the disease (left) and at the time of the follow-up visit (right).

• 150 patients with non-critical COVID-19
• 68% (n=103/150) reported at least one symptom at day 30
• 66% (86/130) at day 60

Table I. Patient symptoms at COVID-19 onset and at day 30 (D30) and 60 (D60).

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Onset n=150</th>
<th>D30 n=150</th>
<th>D60 n=130</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever (&gt;38°C temperature)</td>
<td>76 (51.4)</td>
<td>5 (3.6)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Dyspnea/shortness of breath¹</td>
<td>49 (42.2)</td>
<td>16 (10.7)</td>
<td>10 (7.7)</td>
</tr>
<tr>
<td>Chest pain</td>
<td>15 (14.0)</td>
<td>27 (18.0)</td>
<td>17 (13.1)</td>
</tr>
<tr>
<td>Abnormal auscultation</td>
<td>46 (39.3)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Flu-like symptoms²</td>
<td>129 (87.2)</td>
<td>54 (36.0)</td>
<td>28 (21.5)</td>
</tr>
<tr>
<td>Digestive disorders³</td>
<td>48 (33.1)</td>
<td>26 (17.3)</td>
<td>15 (11.5)</td>
</tr>
<tr>
<td>Including diarrhea⁴</td>
<td>44 (91.7)</td>
<td>13 (50.0)</td>
<td>5 (33.3)</td>
</tr>
<tr>
<td>Weight, mean ± SD</td>
<td>78.0 ± 19.4</td>
<td>77.2 ± 20.2</td>
<td>75.6 ± 18.0</td>
</tr>
<tr>
<td>Weightloss ≥ 5%</td>
<td>-</td>
<td>13 (15.9)</td>
<td>15 (17.2)</td>
</tr>
<tr>
<td>Anosmia/ageusia</td>
<td>89 (59.3)</td>
<td>40 (27.8)</td>
<td>29 (22.7)</td>
</tr>
<tr>
<td>Palpitations</td>
<td>-</td>
<td>9 (6.5)</td>
<td>14 (10.9)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>-</td>
<td>13 (9.8)</td>
<td>21 (16.3)</td>
</tr>
<tr>
<td>Cutaneous signs</td>
<td>-</td>
<td>21 (15.4)</td>
<td>15 (11.5)</td>
</tr>
<tr>
<td>Initial hospitalization</td>
<td>53 (35.3)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Initial clinical presentation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild/moderate COVID</td>
<td>116 (77.3)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Severe COVID</td>
<td>34 (22.7)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Sickleave</td>
<td>-</td>
<td>26 (19.7)</td>
<td>14 (11.2)</td>
</tr>
</tbody>
</table>

Data are n (%) unless indicated.
1: grade 2-4 dyspnea according the modified Medical Research Council scale
2: myalgia, headache and/or asthena
3: digestive disorders (i.e., diarrhea, vomiting)
4: denominator is digestive disorders
Persistent symptoms at D60 were significantly associated with age 40-60y, hospital admission, and abnormal auscultation at symptom onset.
COVID-19 cardiac injury: Implications for long-term surveillance and outcomes in survivors

Raul D. Mitrani, MD, Nitika Dabas, MD, MPH, Jeffrey J. Goldberger, MD, MBA

From the Cardiovascular Division, Department of Medicine, University of Miami Miller School of Medicine, Miami, Florida.

Outcomes of Cardiovascular Magnetic Resonance Imaging in Patients Recently Recovered From Coronavirus Disease 2019 (COVID-19)

Valentina G. Puntmann, MD, PhD; M. Ludovica Carejo, MD; Imke Wieters, MD; Masia Fahim; Christophe Arendt, MD; Jedrej Hoffmann, MD; Anastasia Schendryk, MD; F. Kalkofen Escher, MD; Mariusca Vasa-Nicola, MD; Andreas M. Zeiher, MD; Maria Wehreschild, MD; Elke Nagel, MD

- Up to 20-30% of patients hospitalized have increased troponins -> evidence of myocardial involvement
  - Worse prognosis, greater need for mechanical ventilation, higher mortality
- Post-COVID19 monitoring may be appropriate for some patients
- 100 patients received cardiac MRI after recovery from COVID-19 infection
- Cardiac involvement in 78%; ongoing myocardial inflammation in 60% patients
- Independent of preexisting conditions, severity and overall course of the acute illness and time from the original diagnosis

**CONVALESCENT PHASE 2-6 MONTHS**

- ECG and ECHO
- Cardiac Monitor depending on symptoms
- Consider patient specific cardiac risk factors

Consider Advanced Imaging
- ECHO with Strain
- LGE MRI scan
Treat as clinically indicated

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**Flowchart demonstrating the pathophysiology and various mechanisms of cardiac injury during acute coronavirus disease 2019 infection.** Possible sequelae after recovery are then demonstrated. EAT = epicardial adipose tissue; MI = myocardial infarction; PVC = VT; SCD = sudden cardiac disease; STEMI = ST-segment elevation myocardial infarction; VT = ventricular tachycardia.
MRI was performed in 60 recovered COVID-19 patients and 39 age- and sex-matched non-COVID-19 controls.

At 3 months, neurological symptoms were present in 55%.

Most common - myalgia, memory loss, mood change, headache.

COVID-19 patients had significantly higher bilateral gray matter volume changes compared to controls.

Interpretation: Possible disruption to micro-structural and functional brain integrity in the recovery stages of COVID-19, suggesting the long-term consequences of SARS-CoV-2.
Follow-up study of the pulmonary function and related physiological characteristics of COVID-19 survivors three months after recovery

Yu-miao Zhao1,2,*, Yao-min Shang3,*, Wen-bin Song4,*, Qing-quan Li5, Hua Xie5, Qin-fu Xu1, Jun-lj Jia1, Li-ming Li1, Hong-li Mao6, Xiu-man Zhou1, Hong Luo1,2,***, Yan-feng Gao1,2,**, Ai-guo Xu1,2,*

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• 55 recovered patients
• 3 months after discharge
  • SARS-CoV-2 infection related symptoms were detected 35/55
• Radiologic abnormalities in 39/55
• Lung function abnormalities 14/55
  • Impaired DLCO was associated with D-dimer levels at admission (P=0.031)
27 cases from the US and UK
Patients 21-50 years old
21/22 patients with ethnicity data available belonged to minority groups
Of cases reported to CDC and single cases (n=16)
  • 8 had documented respiratory illness before developing symptoms of MIS-A 2-5 weeks later
  • 8 without any preceding respiratory symptoms
Case series (n=11)
  • 7 patients 20-42 years presenting with mixed cardiovascular and vasoplegic shock with hyperinflammation
  • 2 patients p/w large vessel strokes
  • 2 patients with cardiac dysfunction, abdominal signs/sx and rash

Presenting symptoms
  • Fever (12/16)
  • Cardiac symptoms/evidence of cardiac effects (16/16)
  • GI symptoms (13/16)
  • Dermatologic symptoms (5/16)

Diagnosis
  • Recommend both PCR and AB testing to diagnose

Treatment
  • IVIG, corticosteroids, tocilizumab

Outcomes
  • 10/16 required ICU level care
  • 2 patients died
MIS-A Case Definition

1) A severe illness requiring hospitalization in a person aged >21 years
2) 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 or organ dysfunction might be attributable simply to tissue hypoxia.

**Patients with mild respiratory symptoms who met these criteria were included, but those with suspected alternative diagnoses (e.g., bacterial sepsis), were identified.
Surgical masks vs. N95s

4. Put on NIOSH-approved N95 filtering facepiece respirator or higher (use a facemask if a respirator is not available). If the respirator has a nosepiece, it should be fitted to the nose with both hands, not bent or tented. Do not pinch the nosepiece with one hand. Respirator/facemask should be extended under chin. Both your mouth and nose should be protected. Do not wear respirator/facemask under your chin or store in scrubs pocket between patients. *
   - **Respirator**: Respirator straps should be placed on crown of head (top strap) and base of neck (bottom strap). Perform a user seal check each time you put on the respirator.
   - **Facemask**: Mask ties should be secured on crown of head (top tie) and base of neck (bottom tie). If mask has loops, hook them appropriately around your ears.

- Indirect data from SARS and other respiratory viral infections
- Wearing ANY mask (surgical or N95) reduces risk of developing infection
- Studies comparing N05 respirators with surgical masks fail to show or exclude a beneficial effect on rates of SARS infections (OR 0.86; 95% CI:0.22, 3.33)

Use reprocessed or surgical masks if N95 not available.
Avoid re-using masks if at all possible.