



# COVID 19 Update

## June 26, 2020

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## Transmission Routes:

- **Person-to-person** through respiratory droplets in air or on deposited on surfaces, and possibly by the fecal-oral route
- **Vertical transmission** cannot be ruled out
  - No live virus had been detected in breast
- **Shedding in stool** was detected in up to 41% of infected patients
- **Detectable in semen** from men who were acutely ill or in recovery
  - Viability not assessed
  - No reported cases of sexual transmission to date.
- **Has been detected in cats**, their relevance as a reservoir is uncertain

## Viability: remain viable and infectious in

- Aerosols for hours (median half-life 1.1 hours)
- Surfaces up to days.
  - 5.6 hours on stainless steel, 6.8 hours on plastic and cardboard up to 24 hours

# Transmission

## Incubation period:

- Median incubation period to be 5.1 -5.2 days
- 97.5% of those who develop symptoms will do so within 11.5 days (CI, 8.2 to 15.6 days)
- 14 day period for monitoring after potential exposure is generally recommended

## Asymptomatic transmission

- 40-45% of those infected remain asymptomatic
- Infectiousness begins 2.3 days before symptom onset and peaks 0.7 days before symptoms begin
- Pre-symptomatic transmission accounting for 44% of secondary cases.
- An attack rate of 0.7% for exclusive pre-symptomatic exposures has been documented

## The Reproductive Number ( $R_0$ )

- The WHO  $R_0$  for non mitigated reproduction as between 2.0 and 2.5, double that of influenza

# Transmission

### Avoidance of Close Personal Contact

- Respiratory droplets from human respiration, speech, and other routine behaviors generally fall within a couple meters of the person who generates them
- Smaller droplets produced during sneezing or coughing may project 6 to 8 meters away.

### The CDC defines close contact as:

- Being within approximately 6 feet (2 meters), or within the room or care area, of a novel coronavirus case for a prolonged period of time while not wearing recommended personal protective equipment **OR**
- Having direct contact with infectious secretions of a novel coronavirus case (e.g., being coughed on) while not wearing recommended PPE

### Clinical Risk Factors

- As of May 30, 2020, US case surveillance data revealed the most common underlying health conditions were:
  - **cardiovascular disease** (32%)
  - **diabetes** (30%)
  - **Chronic lung disease** (18%).
- Hospitalizations were six times higher and deaths 12 times higher among those with reported underlying conditions compared with those with none reported
- Higher risk has been found associated with **blood group A** and lower risk in blood group O

# Transmission

**Black Race, Latino Ethnicity, increases risk for Covid-19**

**Duration of Viral Shedding**

- The CDC reports negligible risk of recovering replication-competent virus from someone with Covid-19 illness at 10 days after onset of illness and this is based on two studies

**Implications of positive serology**

- Remains uncertain.

**Re-infection Potential**

- Remains uncertain

**Transmission**

# Clinical Manifestations

## Asymptomatic Infection (40-45%)

## Influenza-Like Illness Symptoms (40-45%)

- **Fever** (87-98%) but only 30.7% of patients were febrile at triage. **Cough Shortness of breath myalgias, fatigue, sore throat, and headache**, upper respiratory symptoms and **conjunctivitis**

## Gastrointestinal Symptoms (12%) diarrhea and nausea prior to other symptoms

## Neurological symptoms (36.4%) including headache, AMS, dizziness, and seizure

- **Acute cerebrovascular diseases** can present as initial manifestation

## Anosmia 74%-87%, dysgeusia in 56-69%, and both symptoms in 68%, both occurred on average at day 4

- Consider COVID 19 if Anosmia, hyposmia, and dysgeusia in the absence of allergic rhinitis, acute or chronic rhinosinusitis

## Pediatric Multi-System Inflammatory Syndrome Temporally Associated with SARS-CoV-2")

- **Bilateral bulbar conjunctival injection** was the most common pediatric symptom in a French study.
- **Fever and abdominal/GI symptoms** are prominent, may predate other symptoms
- **Polymorphous rash** may be present, including changes to the **lips and oral cavity**
- **Myocarditis**

# Clinical Manifestations

## Physical Examination

- **Vital signs:** fever, increased respiratory rate, and reduced oxygen saturation
- **Lungs:** relatively benign/quiet auscultation relative to dyspnea and hypoxia

## Laboratory Findings

- Lymphopenia (90% )of patients in a series of persons hospitalized with Covid-19, Thrombocytopenia, LFT elevations, CRP elevation, hypo-albuminemia, LDH elevation, D-dimer elevation, Ferritin elevation

## Prognostic Laboratory Testing associated with mortality:

- **D-dimer:** A level  $>1 \mu\text{g/mL}$  or  $> 2.0 \mu\text{g/mL}$ , **Absolute Neutrophil to lymphocyte ratio** , **Troponin T** and **proBNP**

## Clinical Course

- The acute respiratory disease of Covid-19 may progress to bilateral **pneumonia**, acute respiratory distress syndrome (**ARDS**), or death.
- Diffuse alveolar damage has been identified on postmortem histopathology
- 14-33% of hospitalized patients requiring intensive care with a high mortality for those requiring critical care
- In New York Overall (n=2634)
  - 14.2% were treated in the intensive care unit
  - 12.2% received invasive mechanical ventilation
  - 3.2% were treated with kidney replacement therapy
  - Mortality was 88% for those requiring mechanical ventilation

# Imaging

- **Routine chest radiography -**
  - Chest X-ray does not affect clinical outcomes in persons presenting to a hospital with lower respiratory tract infection
    - 58.3% of plain chest radiographs have been observed to be normal in COVID 19 patients
    - 24.7% of patients in a New York City case series of persons hospitalized with Covid-19 did not demonstrate infiltrates on chest radiography at the time of emergency room presentation
- **Chest CT**
  - A negative chest CT does not rule out Covid-19, and an abnormal CT is not specific
  - Chest CT may be more sensitive for diagnosis than a NP RT-PCR viral test at a single point in time
- **The American College of Radiology**
  - *“A normal chest CT does not mean a person does not have COVID-19 infection - and an abnormal CT is not specific for COVID-19 diagnosis. A normal CT should not dissuade a patient from being quarantined or provided other clinically indicated treatment when otherwise medically appropriate. Clearly, locally constrained resources may be a factor in such decision making.”*

# Chest Imaging Infection Control Guidance

- It is important to note that **chest imaging challenges infection control protocols, uses PPE, and causes disinfection down time for imaging machines**
- The ACR therefore advises use of portable radiography units if possible when chest imaging is considered medically necessary; surfaces of these machines can be more easily cleaned.
- **Recommendations for use of fixed equipment**
  - Use fixed radiology equipment only if necessary for patient care; use portable imaging if available and appropriate.
  - Staff must wear PPE if coming into patient contact.
  - Patients should wear surgical masks.
  - Cover patient mattresses with sheets (reusable).
  - Ventilate the imaging room, waiting time verified for air exchange between patients.
  - Remove all accessories and devices from the exam room
  - If possible, group cases of COVID-19 patients at the end of the day.
  - Clean every surface of the CT scanner or fixed radiology equipment between patients with the manufacturer-specified cleaning protocol; ensure all surfaces remain wet for the contact time specified

# Antiviral Pharmacotherapy

- **Remdesivir Treatment Trials are mixed:**
  - **Some studies report improved time to recovery:** (11 days for those tx with remdesivir vs 15 days for those on placebo)
  - **Survival:** bRemdesivir suggested but did not meet statistical significance
  - **Populations:** significant benefit was most txparentremdesivirized patients with pneumonia requiring oxygen but not intubated treated for 5 days. There also seems to be benefit in those with pneumonia without hypoxemia
- **Famotidine:**
  - Randomized clinical trial on course
- **Dipyridamole:**
  - Dipyridamole binds to a SARS-CoV-2 protease and has been demonstrated to suppress viral replication in vitro. A study involving 31 patients found that dipyridamole was associated with improved clinical outcomes compared to control patients
- **Lopinavir–ritonavir:**
  - Clinical trial did not observe benefit of lopinavir–ritonavir beyond standard care.
- **Ivermectin:**
  - This antiparasitic also has demonstrated inhibition of SARS-CoV-2 replication
- **Hydroxychloroquine/chloroquine guidance statements:**
  - **The American College of Physicians, advises against use of chloroquine or HCQ alone or in combination with azithromycin**

# Convalescent Plasma

- Early data suggest possible benefit of convalescent plasma to shorten viral shedding, reduce disease severity, or shorten the length of Covid-19 illness
- Randomized trial data has not confirmed clinical benefit
- A systematic review of five early descriptive studies and case reports determined that convalescent plasma may reduce mortality in critically ill patients.
- Safety data collected on over 20,000 infused patients found that transfusion reaction occurred in <1%. The Infectious Diseases Society of America clinical treatment guideline recommends that convalescent serum be used for hospitalized patients with COVID-19 in the context of a clinical trial.
- Due to the limitations of clinical trial entry and the volume of patient need while awaiting trial results, the FDA is facilitating access to convalescent plasma for use in individual patients with serious or immediately life-threatening COVID-19 infections.
- **Mayo Clinic is coordinating a national convalescent plasma protocol system ([uscovidplasma.org](https://uscovidplasma.org)), which matches donor plasma with patients**

# Immunomodulation Therapy Presently on Randomized Clinical Trials

- **Dexamethasone**
  - A randomized clinical trial with patients from over 175 British hospitals revealed that low-dose dexamethasone reduce deaths by one-third in ventilated patients and by one fifth in other patients receiving oxygen but not mechanically ventilated.
- **IL-1 Inhibitor (Anakinra)**
- **IL-6 Immunomodulators: Tocilizumab and Sarilumab**
- **Interferon  $\beta$ -1b**
- **Macrophage Signaling Regulation**
- **Acalabrutinib**, (selective BTK inhibitor)
- **Mavrilimumab**, an anti-GM-CSF receptor- $\alpha$  monoclonal antibody.
- **Losmapimod** is an orally available, reversible, competitive, selective inhibitor of p38 $\alpha$ / $\beta$  mitogen activated protein kinase .

# Thromboprophylaxis & Anticoagulation

- Venous and arterial thrombosis are part of the acute illness spectrum of Covid-19, with presumed relationship to inflammatory and pro-thrombotic states
- A CHEST Guideline and Expert Panel has issued.
  - The group endorses either LMWH or fondaparinux thromboprophylaxis for hospitalized patients
  - Favors LMWH for those in critical care, but does not endorse higher dosing
- One practical approach that favors higher doses for critical care includes:
  - Administration of low, prophylactic dose subcutaneous enoxaparin (40 mg daily) for those admitted to general hospital wards and full therapeutic dose (1 mg/kg body weight twice daily) for those requiring mechanical ventilation or other care in the ICU.
- **ACEI/ARBs:**
  - **Guidance statements:** An NIH COVID-19 Treatment Guidelines Panel has recommended against the use of ACEIs or ARBs as a treatment for COVID-19 outside of the setting of a clinical trial, and that persons with COVID-19 who are prescribed ACEIs or ARBs should continue them
- **NSAIDs: Continue Physician-Directed Therapy**