WELCOME to the

Learning Together About COVID-19

Session will start in less than 15 minutes
COVID-19: Clinical Presentation
Conflict of Interest Disclosure Statement

Dr. Parsonnet has no conflicts of interest.
COVID-19: Wide spectrum of illness

<table>
<thead>
<tr>
<th>Severity of Illness</th>
<th>Symptom Complex</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td></td>
<td>Uncertain, estimated to be 25%</td>
</tr>
<tr>
<td>Mild illness</td>
<td>Uncomplicated upper respiratory tract viral infection</td>
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<tr>
<td>Moderate pneumonia</td>
<td>Pneumonia without the need for supplemental oxygen</td>
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<tr>
<td>Severe pneumonia</td>
<td>Pneumonia with dyspnea, respiratory distress, SpO2 ≤93% on RA</td>
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<tr>
<td>Critical illness</td>
<td>Respiratory failure, septic shock, multiple organ dysfunction/</td>
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</table>
Clinical presentation of SARS-CoV-2 infection

- Fever. Upon admission to hospital, 50%; during hospitalization: 90%
- Cough: 70% (usually nonproductive)
- Fatigue: 39%
- Dyspnea: 20-40%
- Headache: 15%
- Myalgia/arthralgia: 15%
- Sore throat: 14%
- GI symptoms: 5%?
Clinical presentation of SARS-CoV-2 infection

- Typically *gradual onset* of fever, fatigue, myalgia, cough (vs. influenza)
- Anosmia and ageusia: increasingly recognized as an early symptoms
  - Genes required for SARS-CoV-2 cell entry are expressed by olfactory epithelial and stem cells
- GI presentations are being increasingly recognized, especially diarrhea
- More reports of prodrome that includes upper respiratory tract symptoms (does not exclude the possibility of COVID-19)
Risk factors for severe disease

• Age ≥ 65
• Residence in nursing home or long-term care facility
• Underlying medical conditions, especially if not well controlled
  • Cancer treatment
  • Chronic lung disease or moderate to severe asthma
  • Serious heart conditions
  • Immunocompromised: e.g., poorly controlled HIV, BM or organ transplant, chronic steroid use
• Obesity: BMI ≥ 40
• Diabetes
• Renal disease on dialysis
Underlying illnesses among patients with severe COVID-19

- US data through March 29
- 71% of patients requiring hospitalization have at least 1 underlying health condition or risk factor (78% of ICU patients)
  - Diabetes: 24% (prevalence in US population 10%)
  - Chronic lung disease (asthma, COPD): 15% (vs.~6%)
  - Cardiovascular disease: 23% (vs.~11%)
  - Chronic renal disease: 9%
Laboratory findings at hospital admission

- Median WBC: 4700
  - Lymphopenia: 83% (96% in severe)
- C-reactive protein $\geq$10 mg/L: 60%
- D-Dimer elevation: 46% (60% in severe)
- Thrombocytopenia (36%)
- Elevated transaminases (20-39%), higher with severe disease
- Procalcitonin is usually normal
- Initial creatinine is usually normal
Laboratory abnormalities in severe disease

- Severe lymphopenia, neutrophilia
- High transaminases (>5 x normal)
- Very high ferritin, CRP, LDH
- When measured: increased levels of pro-inflammatory cytokines
  - High plasma levels of TNFα, IL-1, IL-6
Radiographic findings at hospital admission

- Abnormalities on CXR: 59% (77% in severe cases)
  - Patchy or ground glass opacities
- Abnormalities on chest CT: 86% (95% in severe cases)
Case-fatality is disproportionately higher among older adults
COVID-19 - United States, February 12–March 16, 2020 (N = 4,226)

Links: MMWR 2020
COVID-19 Case Fatality is highest among persons with underlying medical conditions
COVID-19 - China through 11-Feb-2020

- Cardiovascular Disease: 10.5%
- Diabetes: 7.3%
- Chronic Respiratory Disease: 6.0%
- Cancer: 5.6%

Link: China COVID-19 Epi Team 2020
Complications of SARS-CoV-2 infection

- Pneumonia (91%)
- Among critically ill patients
  - ARDS (61%)
  - Hypotension (31-67%)
  - Acute renal insufficiency (5-29%)?
  - Acute hepatic injury (14%)
  - Cardiac abnormalities
    - Acute cardiac injury (12-23%)
    - Cardiomyopathy (33%)
    - Arrhythmia (44%)
  - Hospital-acquired infection/VAP (not common)
Using Hydroxychloroquine (Plaquenil)

• Dosing
  • Adult 400mg po bid for 1 day, then 200mg po BID for 4 days
  • Pediatric: 10 mg/kg (max of 600 mg/dose) PO BID x2 followed by 3 mg/kg PO TID (max of 200 mg/dose) for 5 days

• Can compound for pediatric use and for use in tube feeds

• Side effects
  • Common: diarrhea, nausea, QTc prolongation
  • Less common: retinopathy, SJS/TENS, pancytopenias, myopathies

• No dosage adjustment in renal impairment (use with caution)
• No dosage adjustment in hepatic dysfunction (use with caution)
• Contraindications: Porphyria (relative), G6PD deficiency
  • G6PD testing not necessary before use
HCQ in vivo – lack of high-quality evidence

- Several uncontrolled case series from China
- At least 10 ongoing controlled trials
- Controversial French study showed faster viral clearance with HCQ and azithromycin
- Small Chinese controlled trial showed no benefit
- Several papers on pre-publication servers, not peer reviewed
Remdesivir

• 2014: IV prodrug of a nucleoside analogue with broad spectrum antiviral activity.
• Developed by Gilead, CDC, U.S. AMRIID
• Blocks RNA polymerase → chain termination
• Safe in animal and human studies
  • Minor LFT abnormalities
• NIH dropped from Ebola trial
  • Compared to MAb’s which were more efficacious
  • Has been some compassionate use
• China filed patent against Gilead Sciences’ 2016 patent
• WHO – most promising agent
### Gilead Remdesivir (RDV) Clinical Trials (DHMC site)

#### Criteria for Both Trials

<table>
<thead>
<tr>
<th>INCLUSION</th>
<th>EXCLUSION</th>
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<tbody>
<tr>
<td>Hospitalized</td>
<td>COVID med within 24 hrs</td>
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<tr>
<td>Age ≥12 (&gt; 40kg)</td>
<td>Liver and renal failure</td>
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<tr>
<td>SARS-CoV+ within 4 days</td>
<td>Pregnancy, breastfeeding</td>
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<td>Radiographic infiltrate</td>
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<td>Must use birth control</td>
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#### Moderate COVID-19 (F20078) vs Severe COVID-19 (F20079)

<table>
<thead>
<tr>
<th>Moderate COVID-19 (F20078)</th>
<th>Severe COVID-19 (F20079)</th>
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<tr>
<td>RA Sat &gt;94%</td>
<td>RA Sat ≤94%</td>
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<tr>
<td></td>
<td>Mechanically ventilated &lt;5 days</td>
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<td>Excludes: any duration of V-A ECMO</td>
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**Part A** - Randomized (n=600) | **Part A** – Randomized (n=400) FILLED 3/27
1) Standard of Care            1) RDV for 5 days
2) RDV for 5 days               2) RDV for 10 days
3) RDV for 10 days              Part B – Enrollment (n=2000) **Enrolling**
Part B – (n=1000)               1) RDV for 10 days
1° Outcome: Average hospital stay 1° Outcome: fever and oxygen improvement