March 18, 2020 COVID-19 Update

Compiled by Katherine Salciccioli MD

Contents include:

Brief summary:

Articles reviewed:
- Epidemiological Characteristics of 2143 Pediatric Patients With 2019 Coronavirus Disease in China (Pediatrics)
- COVID-19 in Children: Initial Characterization of the Pediatric Disease (editorial response, Pediatrics)

ACC-CCA Webinar:

To watch (~2 hours):

General points:
- COVID genome: 79% in common with SARS, 51% with MERS
  - 2.3% mortality vs 9.6% and 34%, respectively
- COVID is spherical with spikes which latch to cells and enter through ACE2
- COVID RNA found in sputum as well as blood and stool
- Respiratory viral particles ARE aerosolized
- Viral particles are found in alveolar cells themselves – true viral PNA, not just ARDS
- Ro = 2.2-2.95 with median incubation 4-5 days (95th percentile 12 days); asymptomatic carriers are important vector for spread
- Chinese protocol: N95 around suspected/confirmed COVID, surgical mask in hospital at all times
- For now, RNA testing appears better than IgM/IgG (especially early in infection)

Cardiology-specific points:
- Given risks of transmission, virtual consults are likely best when at all possible
- Main cardiac complications: acute MI, myocarditis, heart failure
  - Have not been seen in isolation without PNA/sepsis
  - Recovery from
- Critically ill patients with COVID are coagulopathic – microthrombi throughout on autopsy
  - Higher D-dimer independently associated with increased in-hospital mortality
  - Systemic anticoagulation is recommended if no contraindication
- For acute MI, thrombolysis may be preferred over cath
  - Decreased transmission risk to cath lab team – most labs can’t do negative pressure
- For myocarditis, supportive care has led to recovery in some cases
  - Steroids, IVlg, milrinone, diuretics
- Need to watch for long term CV effects in survivors – SARS/MERS had metabolic syndrome issues (HLD, DM) after recovery

Medication issues:
- No solid data outside of WHO recommendations at this time
- Investigations into antiviral, immunomodulating medications ongoing
  - Be wary of interactions with cardiac meds AND direct cardiotoxic effects
- ACE-I/ARB – no data to support stopping chronic meds
- Ibuprofen – no data to support avoidance
Epidemiological Characteristics of 2143 Pediatric Patients With 2019 Coronavirus Disease in China (prepublication release in Pediatrics)
Authors: Yuanyuan Dong, Xi Mo, Yabin Hu, Xin Qi, Fang Jiang, Zhongyi Jiang, Shilu Tong

Key points:
- Study included 731 PCR-proven cases – rest were suspected (fever + (cough or N/V/D or fatigue) + CXR)
- Children of all ages are susceptible to COVID-19, with time course and distribution of infections supporting person-to-person transmission
- Generally well-tolerated
  - 4% asymptomatic, 51% mild, 39% moderate = supportive care at home
  - 6% severe or critical
- Infants appear to have more severe manifestation, with severe/critical disease seen in:
  - Age <1: 10.6%
  - Age 1-5: 7.3%
  - Age 6-10, 11-15, >16: 4.2%, 4.1% and 3.0% respectively
- No gender differences were seen
- One child had died at the time of publication – 14y boy
- Overall, appears less likely to be severe/critical than adults: 5.9% vs 18.5%
  - Why? Speculated to be a combination of pathogen and host factors
    - Children have incompletely functioning ACE2 (lower binding capacity), thought to be the likely mode of cell entry for COVID
    - Children may have partial immunity due to being sick with multiple other viruses during winter respiratory season
    - Inflammatory/immune response once infected likely different than in adults
- Limitations:
  - Included suspected cases which could have been due to other pathogens
  - Didn’t compare severity distribution between suspected and confirmed
  - Exposure data not included, so can’t determine incubation period, risk of infection with exposure

Table 1 Characteristics of Children’ COVID-19 Cases in China

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All cases</th>
<th>Different Category</th>
<th></th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age group</td>
<td>Confirmed</td>
<td>Suspected</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7.00 (11.0)</td>
<td>10.00 (11.0)</td>
<td>6.00 (10.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age group</td>
<td>&lt;1</td>
<td>379 (17.7)</td>
<td>86 (11.8)</td>
<td>293 (20.8)</td>
</tr>
<tr>
<td></td>
<td>1-5</td>
<td>493 (23.0)</td>
<td>137 (18.7)</td>
<td>356 (25.2)</td>
</tr>
<tr>
<td></td>
<td>6-10</td>
<td>523 (24.4)</td>
<td>171 (23.4)</td>
<td>352 (24.9)</td>
</tr>
<tr>
<td></td>
<td>11-15</td>
<td>413 (19.3)</td>
<td>180 (24.6)</td>
<td>233 (16.5)</td>
</tr>
<tr>
<td></td>
<td>&gt;15</td>
<td>335 (15.6)</td>
<td>157 (21.5)</td>
<td>178 (12.6)</td>
</tr>
<tr>
<td>Gender</td>
<td>Boy</td>
<td>1213 (56.6)</td>
<td>420 (57.5)</td>
<td>793 (56.2)</td>
</tr>
<tr>
<td></td>
<td>Girl</td>
<td>930 (43.4)</td>
<td>311 (42.5)</td>
<td>619 (43.8)</td>
</tr>
<tr>
<td>Severity of illness</td>
<td>Asymptomatic</td>
<td>94 (4.4)</td>
<td>94 (12.9)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td></td>
<td>Mild</td>
<td>1091 (50.9)</td>
<td>315 (43.1)</td>
<td>776 (54.9)</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>831 (38.8)</td>
<td>300 (41.0)</td>
<td>531 (37.6)</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>112 (5.2)</td>
<td>18 (2.5)</td>
<td>94 (6.7)</td>
</tr>
<tr>
<td></td>
<td>Critical</td>
<td>130 (6.0)</td>
<td>3 (0.4)</td>
<td>107 (7.0)</td>
</tr>
<tr>
<td></td>
<td>Missing</td>
<td>20 (0.1)</td>
<td>1 (0.1)</td>
<td>19 (0.1)</td>
</tr>
<tr>
<td>Days from symptom onset to diagnosis</td>
<td>2 (4.0)</td>
<td>2 (4.0)</td>
<td>2 (4.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>0-42</td>
<td>0-42</td>
<td>0-36</td>
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<tr>
<td>Province</td>
<td>Hubei</td>
<td>984 (45.9)</td>
<td>229 (31.3)</td>
<td>755 (53.5)</td>
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<tr>
<td></td>
<td>Surrounding areas</td>
<td>397 (18.5)</td>
<td>155 (21.2)</td>
<td>242 (17.1)</td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td>762 (35.6)</td>
<td>347 (47.5)</td>
<td>415 (29.4)</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>2143</td>
<td>731 (34.1)</td>
<td>1412 (65.9)</td>
</tr>
</tbody>
</table>

Table 2 Different Severity of Illness by Age Group

<table>
<thead>
<tr>
<th>Age group*</th>
<th>Asymptomatic</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Critical</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>7(7.4)</td>
<td>205(18.8)</td>
<td>127(15.3)</td>
<td>33(29.5)</td>
<td>7(53.8)</td>
<td>379(17.7)</td>
</tr>
<tr>
<td>1-5</td>
<td>15(16.0)</td>
<td>245(22.5)</td>
<td>197(23.7)</td>
<td>34(30.4)</td>
<td>2(15.4)</td>
<td>493(23.0)</td>
</tr>
<tr>
<td>6-10</td>
<td>30(31.9)</td>
<td>278(25.5)</td>
<td>191(23.0)</td>
<td>22(19.6)</td>
<td>0(0)</td>
<td>521(24.3)</td>
</tr>
<tr>
<td>11-15</td>
<td>27(28.7)</td>
<td>199(18.2)</td>
<td>170(20.5)</td>
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<td>3(23.1)</td>
<td>413(19.3)</td>
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<tr>
<td>&gt;15</td>
<td>15(16.0)</td>
<td>164(15.0)</td>
<td>146(17.5)</td>
<td>9(8.0)</td>
<td>1(7.7)</td>
<td>355(15.7)</td>
</tr>
</tbody>
</table>

Total 94 1091 831 112 13 2141(100)

Data were presented with number and percent (%).*Two cases had missing values.
Key points:

- “suspected” COVID patients overall had more severe disease than PCR/sequencing proven
  - Coinfection? Other viruses? Really hard to know
- Focusing on ONLY those with COVID-proven disease (not suspected):
  - 13% were asymptomatic – so likely even higher given that most asymptomatic kids not tested
  - Only 5% of those with symptoms had dyspnea or hypoxemia
  - Only 0.6% progressed to ARDS or organ failure
- Similar to other viruses and coronaviruses, higher risk populations exist:
  - In this study, infants and younger children
  - In other coronaviruses (and likely this one), underlying lung disease and immune compromise
    - **my input – no comment on CHD, but this is likely true in higher risk CHD as well ie unrepaired, cyanotic, single V, abnormal pulmonary vasculature
- Children likely play a large role in community transmission
  - Higher percentage of upper respiratory involvement
  - Viral particles present in stool and likely shed for weeks
  - Asymptomatic patients make contact tracing and other epi measures much less effective
- Vertical transmission not yet documented
  - **my input – a few new case reports of infected newborns have come up in the last 2 days