MU Covid Update

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Assistant Professor of Clinical Medicine
Division of Infectious Diseases
8.4.20
MU Updates

<table>
<thead>
<tr>
<th>Current Unit</th>
<th>Detected</th>
<th>Pending Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>EMER CTR C UH</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>FAMILY MEDICINE</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>MED 1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>MICU5</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>MOI ORTHOPAEDICS</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>PROGRESSIVE CARE</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>SURG SPEC</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>WCH EC</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>WCH MATERNAL</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>10</strong></td>
<td><strong>13</strong></td>
</tr>
</tbody>
</table>

**MUHC Volumes**

- Visits Tested: 34.62K
- Positive Visits: 1429
- In-house (+): 10
- In-house (PUI): 13

Unique + Pts: 1291
24 Hr + Rate: 7.1%

**Active Cases per 1,000 Residents: MUHC Market**

- 1.85
- Threshold: 5

**Admitted to Date**

- 116
Boone County Updates

<table>
<thead>
<tr>
<th>Race</th>
<th>Total Boone Co. COVID-19 Cases Per Race</th>
<th>Percent of Total Boone Co. COVID-19 Cases</th>
<th>Percent of Boone Co. General Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>866</td>
<td>68.7%</td>
<td>81.1%</td>
</tr>
<tr>
<td>Black</td>
<td>233</td>
<td>18.5%</td>
<td>8.8%</td>
</tr>
<tr>
<td>Asian</td>
<td>19</td>
<td>1.5%</td>
<td>4.5%</td>
</tr>
<tr>
<td>Two or More Races</td>
<td>6</td>
<td>0.5%</td>
<td>4.2%</td>
</tr>
<tr>
<td>Other / Unknown</td>
<td>137</td>
<td>10.9%</td>
<td>1.4%</td>
</tr>
</tbody>
</table>

Racial disparity in black community
Boone County Updates – Daily Positive Cases

Highest single day: 8/1/20 (61 cases)
Week of 7/24 – 7/30: Case positivity 7.7%
Boone County Updates

Columbia City Manager to authorize COVID-19 aid

- $1.8 million dollars to Boone County [from CARES act – Covid 19 relief bill]
- The money is to be used to “hire contact tracers, data analysts, disease investigators, and health educators to help with public awareness of the virus”
- Also will be put towards payment for Covid testing for the uninsured, much of which has been shouldered by hospitals doing bulk of testing
- Want to hire the new employees and get them trained before classes begin as we expect case rates to increase
  - Young kids and adults with more contacts
Boone County Updates – Schools

• Columbia Public Schools board meeting **today** – to discuss official reopening plan
  • Last updated 6/22/20 on the CPS website

• Possible issues to consider
  • Social distancing will be difficult
  • Older buildings with ? Poor ventilation, smaller classrooms / cafeteria / playgrounds / etc.
  • Children/families of lower economic status may be at higher risk of transmission/infection due to underlying comorbidities, housing issues
  • Enough access to bathrooms / sinks for adequate hygiene ?
  • Virtual learning is not feasible for every child and may put disadvantaged kids at an even bigger disadvantage
  • Parents may not have capability to keep kids at home
  • Among lots of others
Contact Tracing during Coronavirus Disease Outbreak, South Korea, 2020

Young Joon Park¹, Young June Choe¹, Ok Park, Shin Young Park, Young-Man Kim, Jieun Kim, Sanghui Kweon, Yeonhee Woo, Jin Gwack, Seong Sun Kim, Jin Lee, Junghee Hyun, Boyeong Ryu, Yoon Suk Jang, Hwami Kim, Seung Hwan Shin, Seonju Yi, Sangeun Lee, Hee Kyoung Kim, Hyeyoung Lee, Yeowon Jin, Eunmi Park, Seung Woo Choi, Miyoung Kim, Jeongsoo Song, Si Won Choi, Dongwook Kim, Byoung-Hak Jeon, Hyosoon Yoo, Eun Kyeong Jeong, on behalf of the COVID-19 National Emergency Response Center, Epidemiology and Case Management Team

Table 2
Rates of coronavirus disease among household and nonhousehold contacts, South Korea, January 20–March 27, 2020

<table>
<thead>
<tr>
<th>Index patient age, y</th>
<th>No. contacts positive/no. contacts traced</th>
<th>% Positive (95% CI)</th>
<th>No. contact positive/no. contacts traced</th>
<th>% Positive (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Household</td>
<td>Nonhousehold</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>% Positive (95% CI)</td>
<td>% Positive (95% CI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–9</td>
<td>3/57</td>
<td>5.3 (1.3–13.7)</td>
<td>2/180</td>
<td>1.1 (0.2–3.6)</td>
</tr>
<tr>
<td>10–19</td>
<td>43/231</td>
<td>18.6 (14.0–24.0)</td>
<td>2/226</td>
<td>0.9 (0.1–2.9)</td>
</tr>
<tr>
<td>20–29</td>
<td>240/3,417</td>
<td>7.0 (6.2–7.9)</td>
<td>138/12,393</td>
<td>1.1 (0.9–1.3)</td>
</tr>
<tr>
<td>30–39</td>
<td>143/1,229</td>
<td>11.6 (9.9–13.5)</td>
<td>70/7,407</td>
<td>0.9 (0.7–1.2)</td>
</tr>
<tr>
<td>40–49</td>
<td>206/1,749</td>
<td>11.8 (10.3–13.4)</td>
<td>161/7,960</td>
<td>2.0 (1.7–2.3)</td>
</tr>
<tr>
<td>50–59</td>
<td>300/2,045</td>
<td>14.7 (13.2–16.3)</td>
<td>166/9,308</td>
<td>1.8 (1.5–2.1)</td>
</tr>
<tr>
<td>60–69</td>
<td>177/1,039</td>
<td>17.0 (14.8–19.4)</td>
<td>215/7,451</td>
<td>2.9 (2.5–3.3)</td>
</tr>
<tr>
<td>70–79</td>
<td>86/477</td>
<td>18.0 (14.8–21.7)</td>
<td>92/1,912</td>
<td>4.8 (3.9–5.8)</td>
</tr>
<tr>
<td>≥80</td>
<td>50/348</td>
<td>14.4 (11.0–18.4)</td>
<td>75/1,644</td>
<td>4.6 (3.6–5.7)</td>
</tr>
<tr>
<td>Total</td>
<td>1,248/10,592</td>
<td>11.8 (11.2–12.4)</td>
<td>921/48,481</td>
<td>1.9 (1.8–2.0)</td>
</tr>
</tbody>
</table>
Contact tracing during Phase I of the COVID-19 pandemic in the Province of Trento, Italy: key findings and recommendations

Pirous Fateh-Moghadam, Laura Battisti, Silvia Molinaro, Steno Fontanari, Gabriele Dallago, Nancy Binkin, Mariagrazia Zuccali

doi: https://doi.org/10.1101/2020.07.16.20127357

This article is a preprint and has not been peer-reviewed [what does this mean?]. It reports new medical research that has yet to be evaluated and so should not be used to guide clinical practice.

• Contact tracing in Italy
• Pre-print publication
Children 0-14 LEAST likely to become secondarily infected if exposed to positive case

Infected children 0-14 MOST likely to result in secondary infection

Eight of these eleven cases went on to infect others
- Three were < 5 y/o
- Four were ages 5-10
- One was age 11
Reopening Primary Schools during the Pandemic

Meira Levinson, D.Phil., Muge Cevik, M.D., and Marc Lipsitch, D.Phil.

• **Summary of Implications for US policy**
  - Safest way to reopen is to **reduce/eliminate community spread and to ramp up testing and surveillance**
    - “Districts/states refusing to implement the necessary public health measures face the social and moral dilemma of how to weigh risks to students/staff/society vs unknown risks of operating at full capacity when virus is circulating at moderate/high levels”
  - Reduce adult-adult contact at school (digital meetings, PPE, close schools to non-staff adults)
    - Note: **17.5% of teachers are age 55+**
  - Schools should be considered “essential” and teachers/staff should be offered all necessary PPE as well as hazard pay
  - Remote work should be offered if possible for older staff or those with underlying health conditions
  - Students and staff should participate in routine pooled testing
  - Modify social and physical infrastructure to allow for social distancing
“But the fundamental argument that children, families, educators, and society deserve to have safe and reliable primary schools should not be controversial. If we all agree on that principle, then it is inexcusable to open nonessential services for adults this summer if it forces students to remain at home even part-time this fall.”
Hydroxychloroquine – in the news again
Updates on Hydroxychloroquine

- Randomized, double-blind, placebo-controlled trial
- March 22 – May 20
- US and Canada
- 423 patients
  - Symptomatic, non-hospitalized adults with lab confirmed Covid-19 or probable Covid-19 within 4 days of symptom onset
  - “Probable” Covid due to testing shortages in the US (58% of patients in this study had lab-confirmed Covid)
- HCQ 800 mg PO on day 1 followed by 600 mg PO daily for 4 more days versus masked placebo
- Primary endpoint: Change in symptom severity over 14 days
  - Measured at on day 0, 3, 5, 10, 14 using a 10 point scale
Updates on Hydroxychloroquine

- Change in symptoms over 14 days did not differ significantly between groups (p = 0.117)
- Medication adverse effects in 43% of HCQ group vs 22% of placebo group (p = 0.001)
- Placebo: 10 hospitalizations, 1 hospitalized death
- HCQ: 4 hospitalizations, 1 non-hospitalized death (p = 0.29)
- Conclusion: No significant change in symptoms with HCQ vs placebo in outpatients with early, mild Covid-19
Updates on Hydroxychloroquine

- Multicenter, randomized, open label, 3 group controlled trial
- Hospitalized patients with suspected or confirmed Covid receiving 0-4 L O2
- 667 patients (504 with confirmed Covid)
- 1:1:1 ratio randomization
  - Standard care
  - Standard care + HCQ 400 mg PO BID
  - Standard care + HCQ 400 mg PO BID + azithromycin 500 mg PO daily
  - 7 day treatment course
- Primary outcome: Clinical status at 15 days using seven-level ordinal scale
- Also assessed safety
- No significant difference in clinical status between the three groups at 15 days
- Prolongation of QT was more frequent in both treatment groups
- Conclusion: Use of HCQ alone or with azithromycin did not improve clinical status at 15 days compared to standard care
Updates on Hydroxychloroquine

- 1542 patients randomized to HCQ vs 3132 with standard care alone
- Looked at 28 day mortality
  - 25.7% in HCQ group vs 23.5% in standard care group, not significant (p = 0.18)
  - No evidence of beneficial effects on hospital stay duration or other outcomes
- “Convincingly” rules out benefit with HCQ; awaiting full published data from Recovery Trial
- See next slide for prelim results
Updates on Hydroxychloroquine

- RECOVERY Trial prelim data
- No difference in 28 day mortality (HCQ 25% vs standard 23%, p= 0.18)
- Patients on HCQ were less likely to be discharged from the hospital alive within 28 days (60% vs 62%) and were more likely to proceed to mechanical ventilation or death (29% vs 26%) though these are not significant differences
- No excess of new major cardiac arrhythmia
- Conclusion: No mortality benefit, but trend towards long hospital stay and higher risk of mechanical ventilation or death
Updates on Hydroxychloroquine

- Randomized, double-blind, placebo controlled trial in the US and Canada, evaluating HCQ for post-exposure prophylaxis
- 821 asymptomatic patients, 719 of which had high-risk exposure to confirmed Covid-19 contact, remainder with moderate-risk exposure
  - High risk = household or occupational exposure to Covid-19 positive individual, within 6 feet for longer than 10 minutes without a mask or eye shield
  - Moderate risk = same as above, but wearing face mask without eye shield
- Primary outcome was incidence of lab confirmed Covid-19 or Covid-19 compatible illness within 14 days
- HCQ dose (800 mg x 1, 600 mg x 1 eight hours later, then 600 mg daily x 4 more days) started within 4 days after exposure
Updates on Hydroxychloroquine

• New illness in HCQ (11.8%) was not significantly different from placebo group (14.3%), p = 0.35
• Side effects were more common in HCQ group (40% vs 17%)
• No serious adverse effects reported
• Conclusion: After moderate or high risk Covid-19 exposure, HCQ did not prevent Covid-19 (lab confirmed or compatible illness) when used as post-exposure prophylaxis within 4 days after exposure
Updates on Hydroxychloroquine

• Multi-center, retrospective, observational study (all centers were part of Henry Ford health system in Detroit)
• March 10 – May 2, patients hospitalized with Covid-related admission
• 2541 patients included
• Primary outcome: in hospital mortality
• Treatment observed: HCQ + azithromycin, HCQ alone, azithromycin alone, neither drug
Updates on Hydroxychloroquine

- Using Cox regression modeling, found that predictors of mortality were age > 65, Caucasian race, CKD, hypoxia on admission, and mechanical ventilation requirement.
- Hydroxychloroquine provided 66% hazard ratio reduction, and HCQ + azithromycin provided 71% hazard ratio reduction compared to neither treatment (p = < 0.001).
- So, HCQ seems to be the big player in this study.
- Conclusion: HCQ alone or in combination with azithromycin was associated with reduction on Covid-19 associated mortality; prospective trials are needed to examine this impact.
Updates on Hydroxychloroquine

• Important limitations:
  • Retrospective, observation study
  • The clinical guidelines included adjunctive immunomodulatory therapy with tocilizumab and corticosteroids
  • Steroid use:
    • Neither HCQ or azithromycin group: 35% got steroids
    • HCQ alone group: 80% got steroids
    • Azithromycin alone group: 39% got steroids
    • HCQ + Azithromycin group: 74% got steroids
  • This is a major confounding factor given the now recognized mortality benefit with steroids
Updates on Hydroxychloroquine

• Ended live status of this document due to many strong studies showing lack of benefit
• Three large, in-progress, randomized controlled trials ceased enrollment due to lack of efficacy in prelim analysis
• Two literature updates provided no evidence to alter these conclusions
• US FDA recently revoked emergency use authorization due to potential significant harms and lack of benefit
• Annals of Internal Medicine updated evidence review identified 1 new RCT, 5 new cohort studies, and published reports of previously available preprints
  • Insufficient evidence to support efficacy or safety of HCQ/chloroquine +/- azithromycin for Covid-treatment
Coronavirus Vaccine Tracker

By Jonathan Corum, Denise Grady, Sui-Lee Wee and Carl Zimmer  Updated July 30, 2020

- **PRECLINICAL**: 140+ Vaccines not yet in human trials
- **PHASE I**: 18 Vaccines testing safety and dosage
- **PHASE II**: 12 Vaccines in expanded safety trials
- **PHASE III**: 6 Vaccines in large-scale efficacy tests
- **APPROVAL**: 1 Vaccine approved for limited use

*Only for limited use in Chinese Military*
Vaccine Updates

Phase 3 clinical trial of investigational vaccine for COVID-19 begins

Multi-site trial to test candidate developed by Moderna and NIH.

• To evaluate safety of mRNA-1273 and to determine if the vaccine can prevent symptomatic Covid-19 after two doses

• Secondary goals:
  • To evaluate whether the vaccine can prevent severe Covid-19 or laboratory-confirmed asymptomatic Covid-19 infection
  • To evaluate whether the vaccine can prevent death due to Covid-19
  • To evaluate whether a single dose can prevent symptomatic Covid-19
Vaccine Updates

- Participants will receive two IM injections, 28 days apart
- Randomly assigned 1:1 to treatment arm or placebo arm
- Blinded study
- Plan to enroll 30,000 healthy adults without Covid-19
Vaccine Updates

• Five trial sites in the UK
• ChAdOx1 [chimpanzee adenovirus-vectored vaccine] expressing SARS-CoV-2 spike protein, compared with meningococcal conjugate vaccine (MenACWY) as a control
• Prelim data: safe, tolerated, and immunogenic; single dose elicited both humeral and cellular responses against SARS-CoV-2
• Booster dose at day 28 augmented neutralizing antibody titers
Questions?

• As always, feel free to email me at nelsontb@health.missouri.edu

Thanks!