Today's Agenda

Time (MT)	Presentation	Presenter(s)
Noon – 12:05 pm	Welcome, Announcements, Introductions	Lachelle Smith, Director, ECHO Idaho
12:05 – 12:10 pm	Idaho Epidemiology Curves and Public Health Updates	Carolyn Buxton Bridges, MD FACP
12:10 – 12:15 pm	Update on Medications for COVID-19	Cathy Oliphant, PharmD
12:15 – 12:55 pm	Inpatient and Critical Care COVID-19 Case Conversations and Q&A	Saadia Akhtar, MD MSc Sky Blue, MD Mark McConnell, MD Cathy Oliphant, PharmD Andrea Christopher, MD MPH Megan Dunay, MD MPH
12:55 – 1:00 pm	Closing, Announcements, Call to Action	Megan Dunay, MD MPH Lachelle Smith, Director, ECHO Idaho

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COVID-19 Case Conversation: Inpatient and Critical Care

April 21, 2020

Saadia Akhtar, MD MSc

Sky Blue, MD

Mark McConnell, MD

Cathy Oliphant, PharmD

Carolyn Buxton Bridges, MD FACP

Andrea Christopher, MD MPH

Megan Dunay, MD MPH

Idaho Epidemiology Curves and Public Health Updates

Carolyn Buxton Bridges, MD, FACP
Governor's Coronavirus Working Group, Former CDC Public Health Physician and Researcher

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Case Counts and SARS-CoV-2 PCR Testing in Idaho

- Total lab-confirmed and probable cases: **1,736**
- Deaths: 48 (2.8%)
- At least 157 (9.0%) hospitalized
- At least 58 (3.3%) ICU, ~ 36.9% of hospitalized in ICU
- At least 209 (12.0%) HCP
- Number of people tested: 17,562

https://coronavirus.idaho.gov.

Cumulative number of people tested through the Idaho Bureau of Laboratories (IBL)*	3/30: 1,567 4/2: 1,851 4/6: 2,263 4/9: 2,571 4/13: 2,828 4/16: 3,041 4/20: 3,211
Cumulative number of people tested through commercial laboratories**	3/30: 4,145 4/2: 6,094 4/6: 8,983 4/9: 10,523 4/13: 12,284 4/16: 13,142 4/20: 14,351

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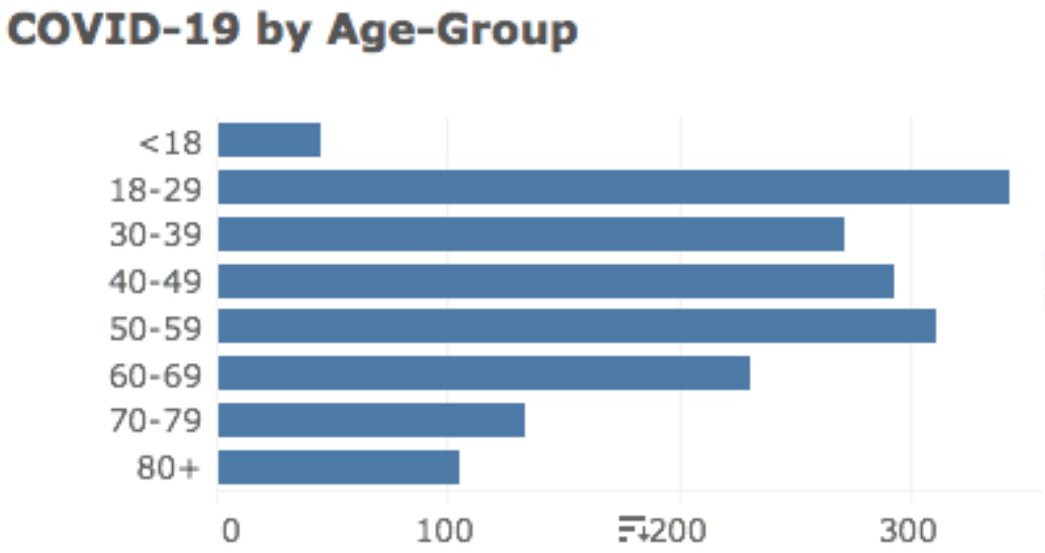
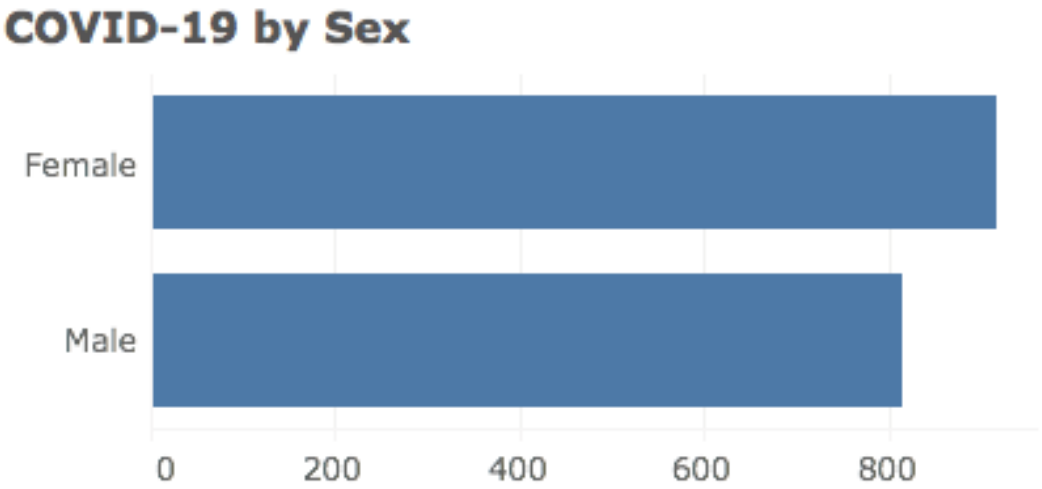
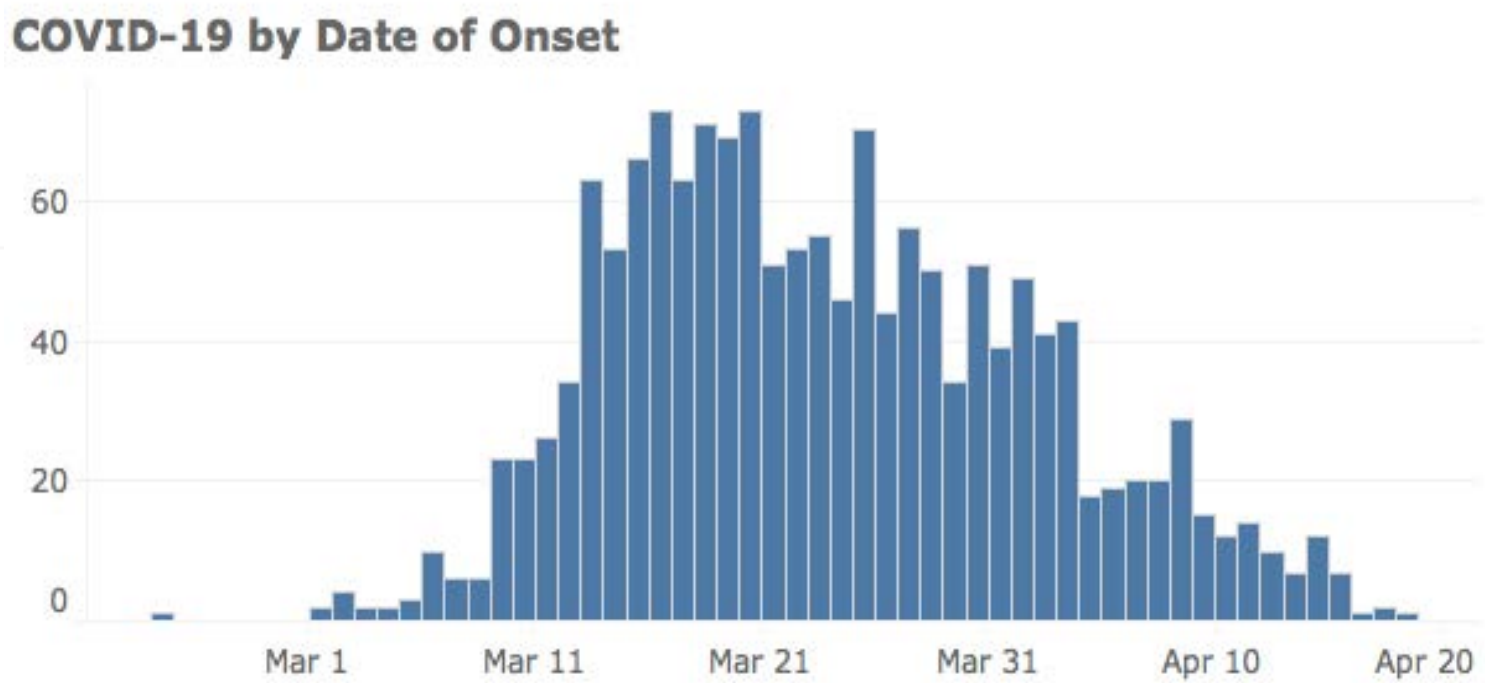
Cases in Idaho, and by Date, Age Group and Sex







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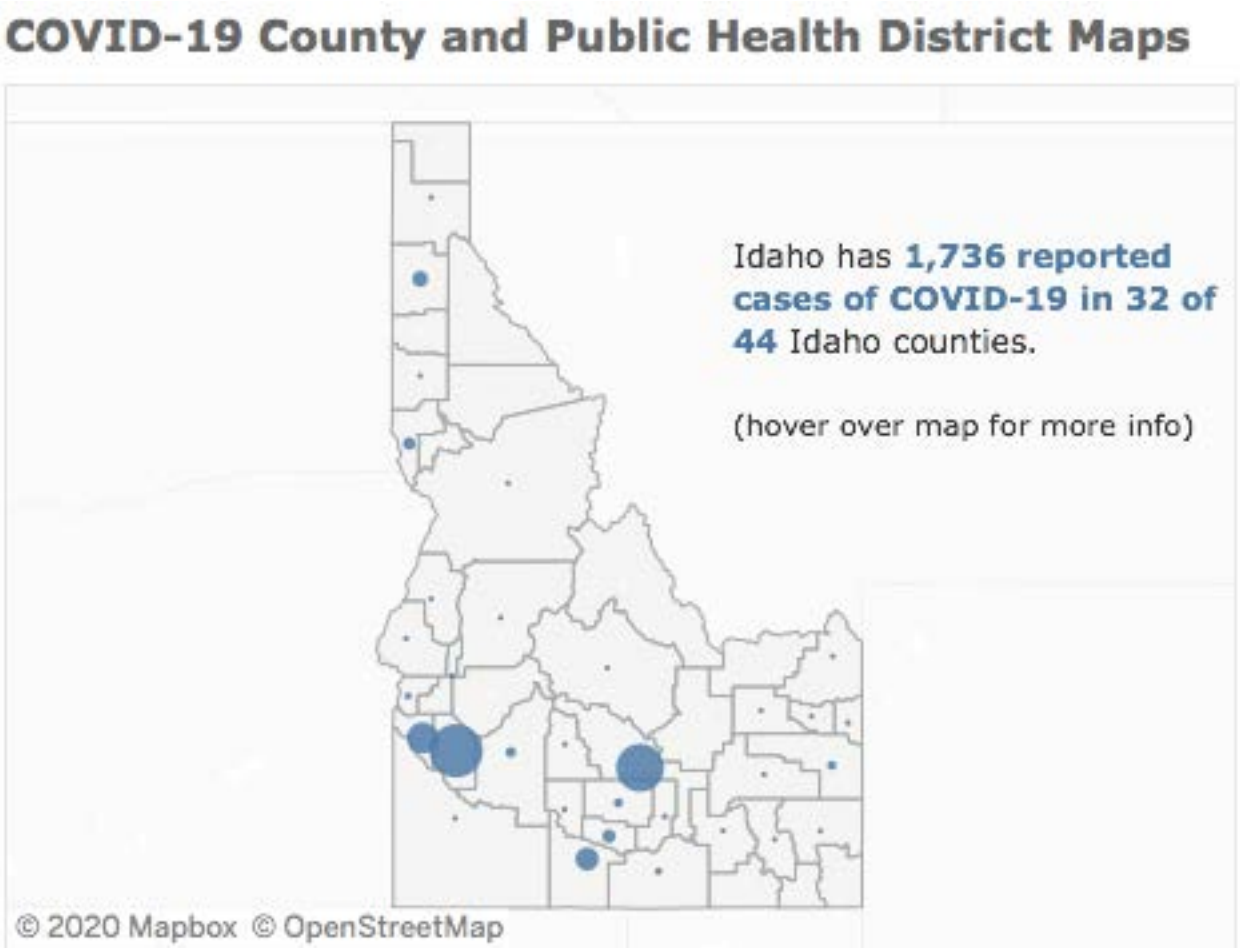
https://coronavirus.idaho.gov.

Variation by County

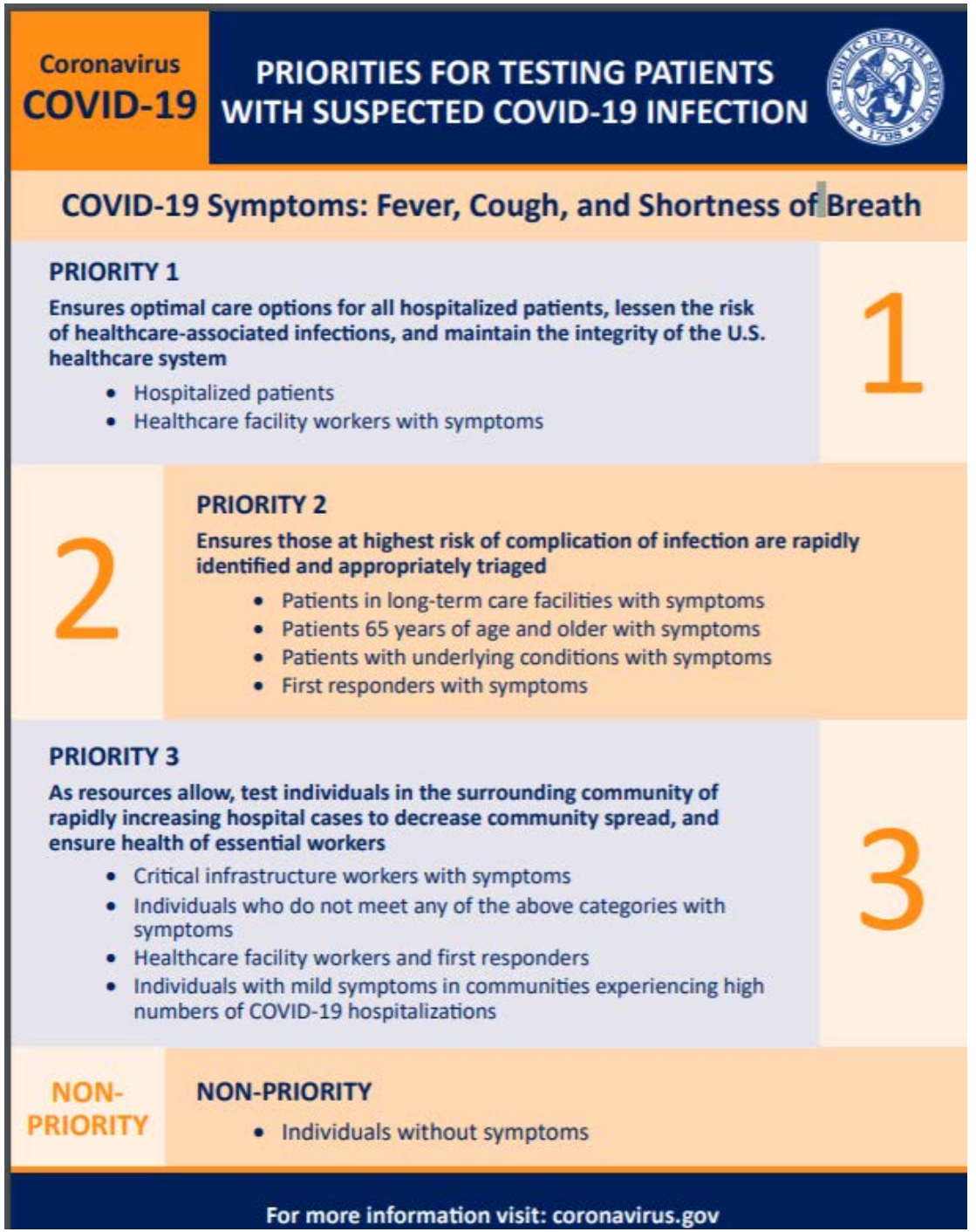
- 32 of 44 counties have reported cases
- # PCR-positive cases/population vary widely (deaths)
- Blaine – 2 per 100 (5)
- Jerome – 1.5/1,000 (2)
- Twin Falls – 1.28/1,000 (10)
- Ada – 1.25/1,000 (12)
- Canyon – 0.9/1,000 (5)
- Nez Perce – 0.8/1,000 (11)
- Kootenai – 0.3/1,000 (0)



CDC Testing Priority Guidance - March 24, 2020

- Can be modified based on state/local situations
- Idaho currently about 10% positive among PCR-tested
- Decreasing numbers of persons seeking testing for acute illness

- Many questions remain – what % positive range is ideal? What is testing capacity, including reagents and swabs? Where does serologic testing fit in?



Serology Testing Guidance and Q&A's

- Both FDA and CDC state:
  - Results should not be used as the sole basis for diagnosis
- New Q&A's on Idaho coronavirus website at: https://coronavirus.idaho.gov/wp-content/uploads/sites/127/2020/04/COVID-19-Serological-Testing-FAQs-Apr-17-2020.pdf.
- Guidelines, Statements and Q&A's from FDA, CDC, and IDSA:
  - "IDSA COVID-19 Antibody Testing Primer" at www.idsociety.org/news
    "Important Information on the Use of Serological (Antibody) Tests for COVID-19 - Letter to Health Care Providers" www.fda.gov/medical-devices/letters-health-care-providers/important-information-use-serological-antibody-tests-covid-19-letter-health-care-providers
  - "FDA Fact Sheet: Serological testing for antibodies to SARS-CoV-2 infection," www.fda.gov/media/137111/download
  - Serology/Antibody Test FAQs, www.fda.gov/medical-devices/emergency-situations-medical-devices/faqs-diagnostic-testing-sars-cov-2#serology
  - "CDC Serology Testing for COVID-19" www.cdc.gov/coronavirus/2019-ncov/lab/serology-testing.html.

Characteristics of Health Care Personnel (HCP) with COVID-19 — United States, February 12–April 9, 2020. MMWR. 4/14/2020

- Of 315,531 U.S. COVID-19 cases reported to CDC
  - 49,370 (16%) included data on HCP status
    - 9,282 (19%) were identified as HCP

TABLE 2. Hospitalizations,* intensive care unit (ICU) admissions,† and deaths,§ by age group among health care personnel with COVID-19 — United States, February 12–April 9, 2020

Age group¶ (yrs) (no. of cases)	Outcome, no. (%)**		
	Hospitalization††	ICU admission	Death
16–44 (4,898)	260 (5.3–6.4)	44 (0.9–2.2)	6 (0.1–0.3)
45–54 (1,919)	178 (9.3–11.1)	51 (2.7–6.3)	3 (0.2–0.3)
55–64 (1,620)	188 (11.6–13.8)	54 (3.3–7.5)	8 (0.5–1.0)
≥65 (508)	97 (19.1–22.3)	35 (6.9–16.0)	10 (2.0–4.2)
Total (8,945)	**723 (8.1–9.7)**	**184 (2.1–4.9)**	**27 (0.3–0.6)**

Abbreviation: COVID-19 = coronavirus disease 2019.
* Hospitalization status known for 7,483 (84%) patients.
† ICU status known for 3,739 (42%) patients.
§ Death outcomes known for 4,407 (49%) patients.
¶ Age status known for 8,945 (96%) patients.
** Lower bound of range = number of persons hospitalized, admitted to ICU, or who died among total in age group; upper bound of range = number of persons hospitalized, admitted to ICU, or who died among total in age group with known hospitalization status, ICU admission status, or death.
†† Hospitalization status includes hospitalization with or without ICU admission.

Exposures†,§ (1,423)	
Only health care exposure	780 (55)
Only household exposure	384 (27)
Only community exposure	187(13)
Multiple exposure settings¶	72 (5)
Symptoms reported§, (4,707)**	
Fever, cough, or shortness of breath††	4,336 (92)
Cough	3,694 (78)
Fever§§	3,196 (68)
Muscle aches	3,122 (66)
Headache	3,048 (65)
Shortness of breath	1,930 (41)
Sore throat	1,790 (38)
Diarrhea	1,507 (32)
Nausea or vomiting	923 (20)
Loss of smell or taste¶¶	750 (16)
Abdominal pain	612 (13)
Runny nose	583 (12)
Any underlying health condition§,* (4,733)**	1,779 (38)

https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm6915e6H.pdf

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Question from the Field

Currently, the antibody test from U of Washington Virology Department is being offered by Crush the Curve Idaho. They report that this is a very sensitive and specific test and that they are offering it to all people in the Treasure Valley.

- Can you tell us more about the reliability of this test?
- Is there a difference in reliability between different PCR tests, specifically those that take days for results and those that take 10-15 minutes?
- Could you speak to the false negative and false positive rates for all of these tests?

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Update on Medications for COVID-19

Cathy Oliphant, PharmD
Infectious Disease, Professor and Interim Chair, ISU College of Pharmacy

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Investigational Therapies for COVID-19

- **Hydroxychloroquine (or chloroquine) +/- azithromycin**
- **Remdesivir**
- Lopinavir/ritonavir (Kaletra) +/- interferon-beta +/- ribavirin
- Favipiravir
- Ivermectin

- Convalescent plasma
  - Collected from COVID-19 survivors
- **Interleukin-6 Inhibitors**
  - Tocilizumab (Actemra)
  - Sarilumab (Kevzara)
  - Cytokine release (IL, TNFα and other inflammatory mediators) causes severe lung damage in serious COVID-19 infections

Hydroxychloroquine/Chloroquine - Update

China Study

- Randomized controlled trial
  - HCQ 1200 mg daily x 3 days then 800 mg daily for 2-3 weeks
- No difference in resolution of s/s
  - 28 day negative conversion rate
    - HCQ 85.4% vs 81.3% in Std of care
- Groups not equivalent
- Adverse effects more common in HCQ vs std of care group

France Study

- 181 patients (84 received HCQ)
- No difference in outcomes
  - Transfer to ICU or death w/in 7d
    - HCQ 20.2% vs 22.1% no-HCQ
  - ARDS w/in 7 days
    - HCQ 27.4% vs 24.1% no=HCQ
- Increased adverse events in HCQ group

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Hydroxychloroquine/Chloroquine: IDSA Guidelines on Treatment Recommendations

- For inpatients, the panel recommends HCQ/CQ use in the context of a clinical trial
- For inpatients, they recommended HCQ/CQ plus azithro only through a clinical trial
- Avoid HCQ/CQ + azithro in the outpatient setting due to lack of adequate monitoring for QT prolongation
- All therapies are recommended in the context of a clinical trial
- Recommend that patients be enrolled into ongoing trials, which will provide much needed evidence on safety and efficacy
- Current data has failed to demonstrate or to exclude a beneficial effect of HCQ/CQ on clinical progression or on viral clearance by PCR
- Harms: QT prolongation, GI

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Ongoing Clinical Trials – Hydroxychloroquine/Chloroquine

- Websites
  - NIH
  - Clinicaltrials.gov
- COVID patients
  - Mild
  - Moderate
  - Severe
  - Hospitalized
- Pre-exposure prophylaxis
- Post-exposure prophylaxis or preemptive treatment

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Remdesivir

Compassionate Use of Remdesivir (NEJM 4/10/2020)

- Data suggest clinical improvement in 36/53 patients
- Not randomized, lack of a control group

Ongoing Clinical Trials

- University of Chicago
  - 'Preliminary' evidence promising
    - 125 pts (113 w/severe dz)
    - 2 died
    - Many D/C from hospital < 7 days
  - No control group
- NIH sponsored studies

Interleukin-6 Receptor Antagonists: Tocilizumab & Sarilumab

- Monoclonal antibody specific for the interleukin-6 receptor
- IL-6 is an inflammatory cytokine and mediator for fever and inflammation
- Studies have identified elevated IL-6 as a predictor of mortality in COVID
  - Elevated IL-6 associated with hyperinflammation in the lungs of severe COVID patients
- IL-6 receptor antagonists prevent IL-6 binding to soluble and cell associated IL-6 receptors, inhibiting cascade signaling
- Used for reversal of cytokine release syndrome
  - Cytokine release syndrome is thought to be associated with severe COVID disease and pulmonary symptoms

IL-6 Inhibitors

Tocilizumab (Actemra)

- Non-randomized trials/case reports have demonstrated rapid reduction in fever and a reduction in the need for supplemental O2 w/in days after infusion
- Randomized, double-blind, placebo-controlled trials in progress or planned
- Single dose with an additional dose if s/s worsen or fail to show improvement

Sarilumab (Kevzara)

- Compassionate use and investigator-sponsored clinical trials
- Randomized, double-blind, placebo-controlled trials assessing the safety and efficacy
  - https://clinicaltrials.gov
- Single dose

Cases/Questions From the Field

Saadia Akhtar, MD MSc, General Pulmonary Medicine and Critical Care
Sky Blue, MD, Infectious Disease Medicine
Mark McConnell, MD, Pediatrics, Internal Medicine, Pediatric Critical Care, and Adult Critical Care Medicine
Cathy Oliphant, PharmD, Infectious Disease, Professor & Interim Chair, ISU College of Pharmacy

Andrea Christopher, MD MPH, Internist, Boise VA; Associate Program Director for UW Boise Internal Medicine Residency
Megan Dunay, MD MPH, Geriatrician, Boise VA and Medical Director for Geriatrics and Extended Care for VA Pacific Northwest Region

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Case 1

An overweight 60-year-old man with hx HTN, HLD and BPH presented to ED with fever that started ten days ago.

- Temp 38.5 °C, SpO2 99%, HR 97, RR 14
- Lungs: fine crackles, slightly increase work of breathing
- CV: rapid, regular, no murmur. No JVD. No BLE edema, good perfusion

- WBC 5,000; Elevated Lactate 100 U/L; Elevated CRP 27 mg/dL
- CXR: patchy bilateral groundglass opacities

→ Admitted to acute care for observation

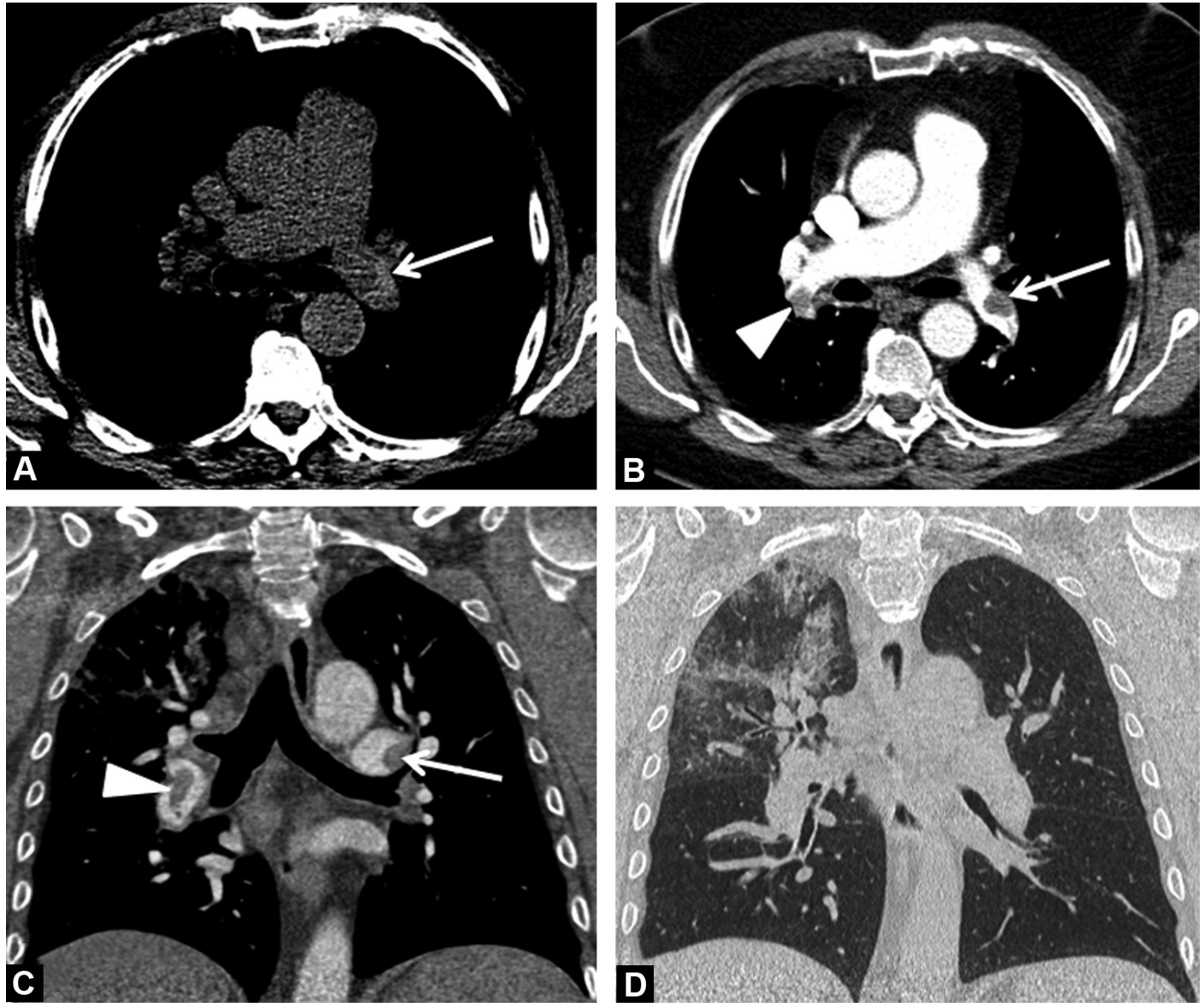
- SARS-CoV2 + on RT-PCR (nasopharyngeal swab) 48hrs later

Case 1

- Returns on Day 3, with dyspnea; SpO2 90% on room air
- D-Dimer elevated 5411 ng/mL
- CT chest: acute bilateral pulmonary emboli and findings consistent with COVID-19 pneumonia

→Admitted to medical step-down unit

Case 1



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Case 1

- Treatment considerations:
  - Respiratory support
  - Antiviral regimen
  - Anticoagulant regimen
  - Mobilization

- What if this patient is unable to tolerate high flow oxygen, venti-mask?
- What if this patient develops cardiogenic shock?

1. J. Chen, X. Wang, S. Zhang, *et al.*Findings of acute pulmonary embolism in COVID-19 patients. Lancet Infect Dis (2020), 10.2139/ssrn.3548771
2. Cellina M, Oliva G. Acute pulmonary embolism in a patient with COVID-19 pneumonia. Diagnosticand Interventional Imaging (2020), https://doi.org/10.1016/j.diii.2020.04.001ARTICLE IN PRESSG ModelDIII-1302; No. of Pages 22 M.

Case 2

- Patient has been on a ventilator for about 22 days (symptoms began ~3/16)
- ABG and O2 sats excellent on 30% FIO2 and PEEP of 5
- CPAP trials are going well - is able to tolerate CPAP for 5-6 hours at a time with respirations of 12-18 and TV of about 500
- Is physically weak (good hand/arm strength, but neck and legs weak) - no PT/OT is allowed in the ICU room
- Tracheostomy is being advised to give him time to regain the strength to breathe on his own rather than attempting extubation at this point
- Initial rapid PCR test (prior to tracheostomy) was negative and 2 subsequent tests the following day were positive

Case 2 Questions

- Does anyone have information on performing tracheostomies on patients with COVID-19 since they are often on the ventilators for 2 weeks or more?
- Have standards been adopted prior to tracheostomy (i.e. 2 negative PCR tests etc.).
- If a patient who is being considered for tracheostomy has a negative rapid PCR followed by 2 positive rapid PCRs, is it most likely that the first test is a false negative or the second tests are false positives?

Case 3

- 31yo M with no known PMHx presents with cough, shortness of breath and subjective fevers x 7 days.
- On exam: Temp 38.5, BP 127/56, RR 20, HR 121, SpO2 88% RA
  - Markedly tachypneic
  - Lungs with coarse crackles, diminished breath sounds right base
  - CV rapid, regular
- WCB 14.6 (6.1% lymphs); PLT 309K
- PAO2/FiO2: 230
- LDH 1149, CRP 40, Ferritin 866
- CXR: right basilar pneumonia with pleural effusion

→ Admitted to ICU

Case 3

On further hx, patient transgender M → F, sex worker

- HIV + but not aware of dx prior to admit
  - CD4 13
  - HIV viral load 45,000 on no antiretroviral treatment
- SARS-CoV2 +, 24hrs after admit
- Pneumocystis jiroveci +
- Presumed secondary bacterial PNA/?staph

www.thelancet.com/hiv; Published online April 15, 2020 https://doi.org/10.1016/S2352-3018(20)30111-9

Case 3

Treatment Considerations

- Respiratory support
  - Able to tolerate non-invasive mechanical ventilation
  - Systemic corticosteroids added
- Venous thromboembolism prophylaxis
- Cured by hospital day #12
- Disposition post-hospitalization?

Anti-microbials

- HIV ART:
  - Tenofovir
  - Emtricitabine
  - Darunavir-boosted Cobicistat
- Other antiviral:
  - Interferon Beta-1b x 4 days
  - Hydroxycholorquine x 5 days
- Other antibiotics:
  - Azithromycin x 5 days
  - Ceftaroline x 7 days
  - Co-trimoxazole x 21 days, then prophylactic

More to come…

Friday, April 24 – answering COVID-19 questions, especially those related to **Outpatient/ED.**

Submit your Questions
https://www.uidaho.edu/academics/wwami/echo/covid-19/clinical-question-form

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