COVID-19: Implications for Pharmacists - Round 3
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Objectives

1. Summarize the NIH/HHS recommendations regarding treatment of COVID-19
2. Describe the data regarding supplement use for treatment or prevention of COVID-19
3. Review the available tests to detect for presence of or immunity from COVID-19
4. State the potential role of pharmacists in testing for COVID-19
Hierarchy of Evidence

- Systematic Reviews and Meta-Analyses
- Randomized controlled trials with definitive results
- Randomized controlled trials with non-definitive results
- Cohort Studies
- Case-Control Studies
- Cross Sectional Surveys
- Case Reports

The Current Norm…

- Rapid release of information
- Hypotheses and loose associations turn into potential treatments
- Pre-publication before completion of peer review
- Recommendations from non-healthcare professionals
Coronavirus Disease 2019 (COVID-19) Treatment Guidelines

Available at [https://covid19treatmentguidelines.nih.gov](https://covid19treatmentguidelines.nih.gov)

Developed by panel representing:

- American College of Chest Physicians
- American College of Emergency Physicians
- American Thoracic Society
- Biomedical Advanced Research and Development Authority
- Centers for Disease Control and Prevention
- Department of Defense
- Department of Veterans Affairs
- Food and Drug Administration
- Infectious Diseases Society of America
- National Institutes of Health
- Pediatric Infectious Diseases Society
- Society of Critical Care Medicine
- Society of Infectious Diseases Pharmacists
The COVID-19 Treatment Guidelines Panel does not recommend the use of any agents for pre-exposure prophylaxis against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (A III).

The Panel does not recommend the use of any agents for post-exposure prophylaxis against SARS-CoV-2 infection (A III).

At present, no drug has been proven to be safe and effective for treating COVID-19. There are insufficient data to recommend either for or against the use of any antiviral or immunomodulatory therapy in patients with COVID-19 who have mild, moderate, severe, or critical illness (A III).
Purported Pharmacotherapy for COVID-19

Hydroxychloroquine (HCQ) in COVID-19

▶ Retrospective analysis; 368 hospitalized US Veterans
  ▪ Death: 27.8% with HCQ; 22.1% with HCQ/AZ; 11.4%, neither
  ▪ Ventilation: 13.3% with HCQ; 6.9% with HCQ/AZ; 14.1%, neither

▶ Open-label, randomized controlled trial; 150 patients from China
  ▪ 28-day negative seroconversion:
    • 85.4% with HCQ vs 81.3% without (P=0.34)
  ▪ Symptoms resolved quicker with HCQ

Tang W, et al. doi: https://doi.org/10.1101/2020.04.10.20060558
HCQ with Azithromycin

<table>
<thead>
<tr>
<th>Drugs:</th>
<th>Severity:</th>
<th>Documentation:</th>
<th>Summary:</th>
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<tr>
<td>AZITHROMYCIN – HYDROXYCHLOROQUINE SULFATE</td>
<td>S</td>
<td>Good</td>
<td>Concurrent use of HYDROXYCHLOROQUINE and QT PROLONGING AGENTS may result in increased risk of QT-interval prolongation.</td>
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<td>Major</td>
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Coadministration is not recommended (Prod Info PLAQUENIL® oral tablets, 2017) as life-threatening additive effects on the QT interval, including torsades de pointes, may occur.

University of Liverpool COVID-19 drug-interactions (http://www.covid19-druginteractions.org/)
Drug Interactions on QTc in Exploratory COVID-19 Treatment

Recommendations to minimize arrhythmia risk:

1. ECG/QT interval monitoring
   - Withhold medications if baseline QT ≥500 msec, or known congenital long QT
   - Stop medications if QT becomes ≥500 msec
2. Correct electrolyte abnormalities
   - Hypokalemia to >4 mEq/L
   - Hypomagnesemia to >2 mg/dL
3. Avoid other QTc prolonging medications whenever feasible

Roden et al. 10.1161/CIRCULATIONAHA.120.047521
Chloroquine (CQ)

- Double-blind trial in hospitalized with severe COVID-19 randomized to
  - High-dose CQ: 600 mg twice daily x 10 days
  - Low-dose CQ: 450 mg twice daily day 1 then once daily x 4 days

- Results:
  - Death at day 13: 39.0%, high-dose vs 15.0%, low-dose
  - QTc prolongation: 18.9%, high-dose vs. 11.1%, low-dose

FDA Drug Safety Communication

FDA cautions against use of hydroxychloroquine or chloroquine for COVID-19 outside of the hospital setting or a clinical trial due to risk of heart rhythm problems

Close supervision is strongly recommended

Safety Announcement [04-24-2020]
Persons with COVID-19 who are prescribed an **ACEi or ARB** for cardiovascular disease (or other indications) should **continue** these medications (A III)
SARS-CoV-2 and the RAAS are Related

- ACEi or ARB therapy can upregulate ACE2 expression in animal models.
- ACEi or ARB therapy might increase SARS-CoV-2 attachment and COVID-19.
- Observational data suggest COVID-19 patients with CVD/risk factors have worse outcomes.

ACEi/ARB use in COVID-19 from China

- Retrospective case series; 1178 hospitalized patients
  - 32.9% ACEi/ARB users had severe disease, 30.7% in non-users (P=.65)
  - 27.3% non-survivors used ACEi/ARB vs 33.0% in survivors (P=.34)

- Retrospective study; 1128 hospitalized patients with hypertension
  - ACEi/ARB users (n=188) compared to non-users (n=940)
    - Mortality rate lower in the ACEi/ARB group (3.7% vs. 9.8%; P = 0.01)
      - Adjusted for variables HR, 0.37 (95% CI, 0.15-0.89; p=0.03)
      - Compared to other antihypertensives HR, 0.30 (95% CI, 0.12-0.70; p=0.01)
Persons with COVID-19 who are prescribed statin therapy for the treatment or prevention of cardiovascular disease should continue these medications (A III)
Coronavirus Disease 2019 (COVID-19)
Treatment Guidelines

- **Oral corticosteroid therapy** used prior to COVID-19 diagnosis for another underlying condition (e.g., primary or secondary adrenal insufficiency, rheumatological diseases) should not be discontinued (A III).

- **Inhaled corticosteroids** used daily for patients with asthma and chronic obstructive pulmonary disease for control of airway inflammation should not be discontinued in patients with COVID-19 (A III).

- Persons with COVID-19 who are taking **NSAIDs** for a co-morbid condition should continue therapy as previously directed by their physician (A III).

- The Panel recommends that there be no difference in the use of **antipyretic strategies** (e.g., with acetaminophen or NSAIDs) between patients with or without COVID-19 (A III).

https://covid19treatmentguidelines.nih.gov
Purported Pharmacotherapy for COVID-19

Emerging Treatments: Possibly Effective

» Remdesivir
  ▪ 61 hospitalized patients requiring oxygen support
  ▪ Compassionate use provided for 10 days
    • 36 of 53 (68%) had clinical improvement in oxygen support
    • 25 of 53 (47%) were discharged
    • 7 of 53 (13%) died
    • No placebo group

» Convalescent Plasma
  ▪ Case series of five critically ill patients with COVID-19 and ARDS
  ▪ Treatment provided between days 10 and 22
  ▪ All five patients clinically improved
    • 3 were discharged
    • 2 in stable condition 37 days post treatment

Want Ongoing COVID Updates?

➤ Ongoing ECHO sessions held virtually Mon/Wed/Fri 7:00 - 8:00 AM MST
  ▪ Featured topic by local experts,
  ▪ CO epidemiology updates
  ▪ Medication updates

➤ Sign up:
  ▪ https://projectcore.echocolorado.org/Series/Registration/258
Supplements: Should we recommend them?
Vitamin C: Does it help?

- Observational data suggests high-dose Vitamin C may benefit patients with sepsis and ARDS
- Upregulates protein channels regulating alveolar clearance
- RCT in China evaluating IV Vitamin C in patients with SARS CoV-2: 12g every 12 hours for 7 days
  - Primary outcome measure: # of ventilator free days
  - Expected completion date: September 2020

Vitamin C: Does it help?

BOTTOM LINE:
- There is only observational data with high-dose IV vitamin C in ARDS
- No evidence to support oral vitamin C can prevent or treat COVID-19
What about Vitamin D?

- Metanalysis of 25 trials of patients with acute respiratory tract infections
  - NOT COVID-19 patients
  - Daily or weekly dosing of vitamin D decreased the risk of respiratory track infection
    - Most benefit seen in patients that had significant vitamin D deficiencies
  - The pandemic started during the winter when vitamin D levels are low

Surely, elderberry can help, can’t it?

- One relatively small (n=312) study claimed elderberry extract decreased the incidence and duration of cold symptoms.
- Another small study (n=60) claimed elderberry syrup, started within 48 hours of flu symptoms, decreased symptoms four days earlier than those patients who received placebo.

BOTTOM LINE:
- NO evidence that elderberry can prevent or treat COVID-19.
Emerging Treatments: Hope and Hype

♦ Bacille Calmette-Guérin (BCG) vaccine:
  ▪ Ongoing trials
  ▪ Unpublished study shows COVID-19 mortality lower among BCG-using countries

♦ Zinc lozenges
  ▪ May shorten duration of the common cold.
  ▪ Speculation that hydroxychloroquine helps the zinc enter SARS-CoV-2 infected cells and might then exert antiviral effects

https://www.medrxiv.org/content/10.1101/2020.04.01.20049478v1
And more hype.....

Missouri Sues Televangelist Jim Bakker For Selling Fake Coronavirus Cure

Silver Solution "has been proven by the government that it has the ability to kill every pathogen it has ever been tested on, including SARS and HIV," Sellman continued. Four 4-ounce bottles could be yours, a message on the screen said, for just $80.
Testing
Emergency Use Authorization (EUA)

- Allows unapproved products or unapproved uses of an approved product
- Public health emergency
- No adequate, approved or available alternatives
- Includes labs, PPE, ventilators
Testing: What we know

- Pharmacists may administer CLIA-waived tests, provided they have a CLIA waiver.

- All current CLIA-waived tests (as of 4/29/20 at noon) are for detecting the presence of virus:
  - AKA, “molecular” or “PCR”
  - Variable approaches:
    - Collection only (in partnership with a lab)
    - Collection and testing
    - Home testing
  - CLIA waiver only needed if the pharmacy runs the test.
Testing: What we know

- Antibody testing
  - AKA, serology tests
- There are no CLIA-waived tests for antibodies
  - Questionable sensitivity and specificity
  - Important from a public health perspective to detect viral prevalence in a community
  - Does NOT indicate an individual is immune
# CLIA-waived tests

<table>
<thead>
<tr>
<th>Company</th>
<th>Test Name</th>
<th>Collection method</th>
<th>Timing of results</th>
<th>Product image</th>
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<tbody>
<tr>
<td>Abbott Diagnostics</td>
<td>ID Now COVID-19</td>
<td>Nasal, nasopharyngeal, or throat</td>
<td>5-13 mins</td>
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<tr>
<td>Mesa Biotech Inc</td>
<td>Accula SARS-CoV-2 Test</td>
<td>Nasal or throat</td>
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<tr>
<td>Cepheid</td>
<td>Xpert Xpress SARS-CoV-2 Test</td>
<td>Nasal, mid-turbinate, nasopharyngeal</td>
<td>45 mins</td>
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Other considerations

➤ DORA/Governor’s Communication (4/28/20)
  ▪ Make sure to include appropriate patient identifiers on all specimens
  ▪ State contacts:
    ▪ Ben Henderson, Director of Operations (Benjamin.s.henderson@state.co.us)
    ▪ Alicia Cronquist, Chief of the Public Health Informatics, Reporting, and Refugee Branch (alicia.cronquist@state.co.us)

➤ Reimbursement
Resources

- HHS Pharmacist Guidance

- COVID-19 Tests

- Antibody Tests

- FDA
  - https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations#ivdnote1
Continuing Education

How to claim credit (pharmacists & pharmacy technicians)

1. Navigate to UCDenver.edu/pharmacy/continuingeducation
2. Select Online CE
3. Select Today’s Webinar

Questions: sop.continuingeducation@cuanschutz.edu

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