COVID-19: Implications for Pharmacists

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Learning Objectives

➧ Identify the unique clinical and epidemiological characteristics of Coronavirus (COVID-19) in the spectrum of viral clinical illnesses and previous Coronavirus (SARS, MERS) and non-Coronavirus (influenza, common cold) related illnesses
➧ Describe the epidemiological impact of interventions to reduce spread of disease in the setting of limited healthcare resources
➧ Summarize common clinical presentations of COVID-19 compared to other cold and influenza related illnesses and describe who should receive referral for testing
➧ Analyze emerging literature regarding potential treatment modalities for COVID-19
➧ Devise potential roles for pharmacists and technicians in a variety of healthcare settings for the management of a COVID-19 pandemic
➧ List the steps the Colorado Pharmacists Society (CPS) is taking to address COVID-19.
➧ Describe how CPS is collaborating with other professional pharmacy organizations and state and federal agencies.

Before Our Talk…

• Information regarding COVID-19 is rapidly evolving
• Quality of data in a pandemic is limited (especially early)
  ➥ Case Series
  ➥ Case Reports
  ➥ Important to separate preliminary information from fact
  ➥ Experimental conditions vs real world data
• Pharmacist’s role:
  ➥ Trusted
  ➥ Source of truth
  ➥ Separate science from theory and opinion

Introduction and Nomenclature

Coronavirus as a Family of Viruses

• Positive sense RNA viruses
• Largest genome of RNA viruses
• Beta-Coronaviruses most common to infect humans
  ➥ HCoV variants – the common cold (infecting humans for 800 plus years)
  ➥ Mutant variants – SARS-CoV, MERS, SARS-CoV-2/COVID19

COVID-2019

• Also known as “coronavirus” or SAR-Cov-2
• Originates in China (patient zero likely November or December 2019)
• 76% identical genome to SARS
• 96% identical genome to Cave Bat CoV

Original Mode of Transmission
COVID-19 Myth 1: ACE/ARB Treated Patients Do Worse Because of Viral Entry ACE Protein

Answer: Could Happen But No Data

ACCF/AHA/ESC say do not discontinue to prevent COVID-19

Few differences in hypertension patients with mild vs severe disease

COVID-19 Myth 2: COVID-19 Can Live on Surfaces for Days

Answer 1: Partially False

Determined by inoculum size and half life on object

Steel: 5-6 hours
Plastic: 6-8 hours

Very low inoculum at 72 hours but still there (same as SARS)

Answer 2: Droplets are primary mode of transmission

(Aerosol Half Life - 1 hour)

Asymptomatic patients with a high viral load can transmit (2 days before symptoms)

Why Is COVID-19 So Clinically Relevant?

COVID-19 Has a Basic Reproduction (Ro) number of 2-3

Journal of Travel Medicine, 2020, 1–4

Why Is COVID-19 So Clinically Relevant?

Source: CDC
Source: Baud et al Lancet Infectious disease 2020

Differentiating Symptoms

<table>
<thead>
<tr>
<th>Symptom/Sub</th>
<th>COVID-19</th>
<th>Influenza</th>
<th>Common Cold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>&gt;39-40% – careful sometimes delayed!</td>
<td>&gt;39-40%</td>
<td>Very Rare</td>
</tr>
<tr>
<td>Cough</td>
<td>70% of which majority is dry cough (50% sputum productive)</td>
<td>Dry Mucus</td>
<td>Common – dry or wet</td>
</tr>
<tr>
<td>Myalgia/Fatigue</td>
<td>11-50%</td>
<td>Common</td>
<td>Rare</td>
</tr>
<tr>
<td>Immune effects</td>
<td>Leucopenia (80-60%) – T cell Depression</td>
<td>Rare</td>
<td>Never</td>
</tr>
<tr>
<td>Phlebitis</td>
<td>Thrombophlebitis (40-60%)</td>
<td>Rare</td>
<td>Never</td>
</tr>
<tr>
<td>Sneeze</td>
<td>No</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>Congestion</td>
<td>No</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>Sore Throat</td>
<td>No</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>Hospitalization Rate</td>
<td>6-16% (ICU)</td>
<td>0.03%</td>
<td>Rare</td>
</tr>
<tr>
<td>Cause of Death</td>
<td>Acute Respiratory Distress Syndrome (ARDS)</td>
<td>ARDS</td>
<td>Rare</td>
</tr>
</tbody>
</table>

Source: https://special.croi.capitalreach.com/
Testing for COVID-19

- What tests are available?
  - Standard of care: Real time rRT-PCR (Nasopharyngeal, oropharyngeal, bronchoalveolar lavage, aspirates, sputum)
  - Alternative testing (in development): IgM ELISA, Point of care testing

- Who to test?
  - At risk individuals with symptoms compatible with COVID-19
  - Hospitalized patients with symptoms compatible with COVID-19
  - Any persons (esp healthcare workers) within 14 days of close contact (from sx onset) of a confirmed COVID-19 patient

- Colorado: Mitigation strategies may go into effect

The Reason for Separation

Source: Medium.com

The Compliance and Spread

No Distancing

USA Has:
- 95,000 ICU beds
- 62,000 ventilators (60% of which for adults) – may be able to get to 200,000 with old ventilators and emergency supplies (130,000 to start)
- 903,000 will require ventilation

More information can be found [here](https://towardsdatascience.com/social-distancing-to-slow-the-coronavirus-768292f04296)
Therapeutics for COVID-19

No antiviral therapy has proven effects against COVID-19, and none of the following agents have any approved indications for COVID-19.

- Chloroquine
- Hydroxychloroquine
- Lopinavir/ritonavir
- Remdesivir
- +/− favipiravir

Clinical Evidence – Chloroquine/hydroxychloroquine

- In vitro data only published
  - Hydroxychloroquine 400mg PO BID x 1 day, then 200mg PO BID x 4 days
  - Chloroquine 500mg PO BID x 5 days
- No published clinical experience to date
- Reports from China (not actual data presented/published)
  - Reduces pneumonia exacerbation
  - Reduces duration of symptoms
  - Improves viral clearance
- Well-tolerated
- Monitoring – QTc prolongation, GI side effects, retinopathy

Clinical Evidence – Hydroxychloroquine

- Prospective, non-randomized, open-label study
  - Hospitalized with confirmed COVID-19
  - All patients offered hydroxychloroquine (HCQ) 200mg PO TID
  - Those refusing treatment or who met exclusion (allergic to HCQ, retinopathy, QT prolongation, G6PD deficiency) served as untreated controls
  - Antibiotics could be given for treatment/prevention of bacterial infection
  - Primary endpoint = virologic clearance at day 6

Results excluded 6 HCQ treated patients
  - 3 ICU transfers
  - 1 died
  - 1 left hospital
  - 1 stopped HCQ for GI upset

Limited data for clinical outcomes
- Unclear role of azithromycin
Clinical Evidence – Hydroxychloroquine

Post-exposure prophylaxis study - HCWs:

- Chu et al. 2004: ARDS or death lower with lopinavir/ritonavir vs. ribavirin alone (2.4% vs. 29%)
- Retrospective, imbalance in baseline characteristics between groups. lopinavir/ritonavir patients received concomitant ribavirin
- Rapid viral load decline in lopinavir/ritonavir recipients from nasopharyngeal specimens

- Chan et al. 2003: lopinavir/ritonavir plus ribavirin decreased mortality compared to ribavirin alone (2.3% vs. 11%, p < 0.05)
- Matched, retrospective study. All patients received concomitant corticosteroids as well
- Rescue therapy with lopinavir/ritonavir not different from matched controls

- Park et al. 2019: lopinavir/ritonavir plus ribavirin effective as post-exposure prophylaxis against MERS-CoV

Clinical Evidence – Lopinavir/ritonavir

SARS-CoV-1

- Chu et al. 2004: ARDS or death lower with lopinavir/ritonavir vs. ribavirin alone (2.4% vs. 29%)
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Clinical Evidence

Open label RCT, published 3/19/2020

- Inclusion: adults with confirmed COVID-19 with radiographic pneumonia and hypoxia (SaO2 < 94% on RA or PaO2/FiO2 < 300)
- Exclusion: severe liver dysfunction, HIV, pregnancy, significant interactions
- Outcomes:
  - Primary: time to clinical improvement
  - Secondary: clinical status, 28-day mortality, duration of mechanical ventilation, hospital and virologic measures

Clinical Evidence - Remdesivir

- Appears effective against Ebola
- Clinical studies lacking for SARS-CoV-2
- Ongoing clinical trials
  - U.S. = 3 studies (1 NIAD and 2 Gilead sponsored)
  - China = 2 studies
- Dosing – 200mg IV load, then 100mg IV daily x 5-10 days
- Safety: mostly GI and liver-related effects to date reported
  - IV contains cyclodextrin (SBECD)
**Remdesivir**

- Compassionate use available ([https://rdvcu.gilead.com/](https://rdvcu.gilead.com/))

**Key Inclusion criteria:**
- Moderate to severe COVID-19 infection
- Oxygen therapy needed
- Not pregnant

**Key Exclusion criteria:**
- Contraindication to Remdesivir
- Known hypersensitivity to Remdesivir

**Clinical Evidence – Tocilizumab**

- Observational study from China, n=21
- Standard of care + Tocilizumab 400mg IV single dose
  - n=3 had repeat dose within 12 hours
- Severe (81%) and critical disease (19%) at time of treatment
  - Severe – RR ≥ 30, SpO2 < 94% on RA, or PaO2/FiO2 ≤ 300
  - Critical – mechanically ventilated, shock, other organ failure
- All 21 survived, 91% discharged
- Only 10% were mechanically ventilated

**Hyperinflammation**

- Subset of COVID-19 progress to hyperinflammatory state
  - High, persistent fever
  - Cytopenias
  - Hyperferritinemia
  - Increased IL-6, CRP, and d-dimer

**Screening – Hscore for probability of secondary HLH**

**Immunosuppression - tocilizumab**

**Clinical Evidence - Others**

- Nitazoxanide – in vitro only to date
- Interferon – in vitro and limited clinical experience from SARS-CoV-1 and MERS-CoV (combined with other agents)
- Statins – anti-inflammatory mechanism – theoretical presently and no published evidence of direct benefit for COVID-19
- IVIG – not expected to be effective, pooled sources unlikely to have any sufficient anti-SARS-CoV-2 neutralizing antibodies
- Corticosteroids – unclear role, likely beneficial during later stages of infection where inflammatory response increased

**Tocilizumab and Sarilumab**

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Clinical Evidence – Vaccine

Trials to begin on Covid-19 vaccine in UK next month

No approved or proven treatment of COVID-19 to date

Limited evidence may support trial of off-label agents with possible anti-viral activity (rapidly evolving, keep up to date)

Challenges – diagnostic delays, shortages, and low quality evidence to date

Pharmacist Involvement

- Strategies to limit healthcare exposure of patients not suffering from COVID-19
- Inventory control and resource conservation
- Treatment pathway development and resource for critical evaluation of related evidence for novel therapies to manage COVID-19
- Navigation of clinical trials/compassionate use of investigational therapies
- Problem solving around supportive care measures

EIND Process

- Step 1: contact company with investigational product to obtain approval for compassionate use
- Step 2: contact FDA for approval to use investigational product
- Step 3: if FDA approves, reach back out to company and coordinate with pharmacy and local IRB

Social Media and Misinformation

Letter to the governor asking for emergency measures (sent March 13th)
- Remote pharmacy practice – remove requirements for prior board approval
- Allow 90 day supplies of chronic medications
- Extend technician certification deadlines
- Allow the CMO of CDPHE to allow pharmacists to provide designated services for:
  - Testing
  - Screening
  - Prescribing (standing order or CPA)
What is CPS doing?

- Community forum for COVID-19
  - Childcare options for healthcare workers
  - Clinical trial information (post-COVID exposure prophylaxis)
- Dedicated web page
- Social media posts (follow us!)

National professional organizations

- NACDS policy requests (partial list)
  - In anticipation of a COVID-19 vaccine, making sure pharmacists may access and immunize without barriers
  - Allowing pharmacists and techs to work across state lines
  - Broader prescriptive authority for mild ailments
  - Allowing remote verification of prescriptions
- NASPA
  - Regular communication regarding activities in other states

Questions and Answers