COVID-19 and ARDS for Primary Care

Charlie Strange, MD
Professor of Pulmonary and Critical Care Medicine
Medical University of SC

Disclosures

Consultant: AstraZeneca, CSL Behring, GlaxoSmithKline, Grifols, Inc, Uptake Medical

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Advisory Board: Vertex
Learning Objectives

1. Demonstrate an understanding of mechanisms of oxygenation support in home care and hospitalized patients with COVID-19.

2. Define the options for diagnostic strategies to help define optimal contact tracing and supportive care for populations at risk for COVID-19.

3. Describe the pathophysiology of the acute respiratory distress syndrome due to COVID-19 so that optimal care can be provided.

Corona Viruses and the Lung

- **SARS**- Severe acute respiratory syndrome coronavirus 2003 (SARS-CoV-1)

- **MERS**- Middle East Respiratory Syndrome 2012

- **SARS-CoV-2** -Coronavirus Disease 2019 (COVID-2019)
SARS-CoV-1

Masked Palm Civet

Likely source of SARS

10,000 killed in China as a response to recognition of viruses crossing the xenographic barrier

SARS has since been found in ferrets, raccoon dogs and Chinese bats.

Acquisition

The virus enters the body primarily through the nose. Also, it may get in through eyes and mouth.
After choir practice with one symptomatic person, 87% of group developed COVID-19

- Avoid groups
- Stay at least 6 feet apart
- Wear face coverings

Timeline

Coronavirus incubation

<table>
<thead>
<tr>
<th>Infection</th>
<th>Symptoms appear</th>
<th>Standard 14-day quarantine period</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2</td>
<td>3</td>
<td>8-14</td>
</tr>
<tr>
<td>4-5</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>7-10</td>
<td>12</td>
<td></td>
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</tbody>
</table>

"Viral Shedding" — Ability to infect others until cured
Symptoms

- Fever: 60%
- Cough: 40%
- Sore Throat: 40%
- Anosmia: 30%
- Fatigue: 60%
- Shortness of breath: 30%
- Asymptomatic: 40%

USA Today March 16, 2020

WHO Report

- 80%
- 13.8%
- 6.1%

Mild/Moderate cases: 10%
Severe cases: 20%
Critical cases: 30%

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Case

2/15/2020
42 year old WM in good health
Cough began 1 week ago and has progressed to cause dyspnea with walking 50 feet.
Saw his PCP with fever, myalgias, sore throat, and chest pain. Began on Azithromycin 4 days ago.
   Vital signs Temp 101.8, BP 110/70, HR 110,
       Resp 28
   O2 saturation 91%
In the Emergency Department

Laboratory: Complete Blood Count –
- White Blood Cells =11.2 (High normal)
- Hemoglobin =14.1 (Normal)

Other chemistries normal

Arterial Blood Gas
- pH= 7.48, pCO2= 30, pO2 = 52

Patient is given O2 titrated to keep O2 sats >92%.

Respiratory Virus PCR swab + Influenza A
Patient is begun on oseltamivir (Tamiflu) in the ED and admitted to your care.

The Next AM

He sits in the ER overnight waiting for a bed. On morning rounds you find him on 100% FiO2, O2 sat 92%, with respiratory rate 30.
He is getting tired and did not sleep.

ABG on 100% FiO2 shows:
- pH= 7.32 / pCO2 50 / pO2 64

A chest radiograph is shown.

What is the diagnosis?
Acute Respiratory Distress Syndrome

- International Consensus Conference Definition:
  - Bilateral pulmonary infiltrates
  - Non-cardiogenic cause of <1 week in onset
  - PaO2/ FiO2 ratio depression.
    - P/F <300 mild ARDS
    - P/F <200 moderate ARDS
    - P/F <100 severe ARDS

<table>
<thead>
<tr>
<th>Normal- Room Air</th>
<th>PaO2=90 mmHg</th>
<th>P/F Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Room Air</td>
<td>PaO2 = 52</td>
<td>248</td>
</tr>
<tr>
<td>100% FiO2</td>
<td>PaO2 = 62</td>
<td>62</td>
</tr>
<tr>
<td>100% FiO2 + ETT</td>
<td>PaO2=78</td>
<td>78</td>
</tr>
<tr>
<td>80% FiO2 + 12 cm PEEP</td>
<td>PaO2=92</td>
<td>115</td>
</tr>
</tbody>
</table>

High Flow Nasal Cannula

Continuous High Flow oxygen washes out the upper airways

Reservoir of oxygen in the upper airway available for gas exchange

Avoids rebreathing of CO2 so decreases anatomic dead space

Provides some PEEP to upper airway
ARDS Pathophysiology

Diffuse Alveolar Damage (DAD)
Surfactant deficiency
Lack of patient mobility-
  Gravitational sedimentation of infiltrates

Treatment:
Supportive Care to very fragile lungs
  Avoid O2 toxicity
  Avoid overdistension
  Avoid excess sheer stress
  Prone positioning

Supportive Care for ARDS

Low tidal volume ventilation = 6 ml/kg
Some PEEP
Avoid high peak airway pressures > 30 cm H2O.
ARDS Outcomes

Mortality of Severe ARDS ~ 30 percent
Most Death within the first 2 weeks
Afterwards Gradual Resolution

1 year outcomes:
Normal lung function >90% of patients
Weakness and weight loss average 18 pounds
High frequency of post traumatic distress syndrome

Acute Respiratory Distress Syndrome (ARDS)
The ICU

Viral Replication

1. Virus attaches to cell
2. The virus injects RNA into the cell
3. Cell reproduces virus

USA Today March 16, 2020

USA Today March 13, 2020
# Immune Response

**T lymphocytes**

Memory cells

**B lymphocytes**

White blood cell

Antibody

USA Today March 16, 2020

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# Antibodies

Antibodies attach to antigens killing virus

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The Vaccine

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**NSSP: Percentage of Visits for Influenza-Like Illness (ILI) and COVID-19-Like Illness to Emergency Departments**

Weekly National Summary, September 29, 2019 - April 25, 2020

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**NATIONAL CENTER FOR HEALTH STATISTICS (NCHS) MORTALITY REPORTING SYSTEM**

**U.S. Mortality: Death Certificates Listing Pneumonia, Influenza, and COVID-19**

Data through Week Ending April 24, 2020*

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For more NCHS COVID-19 mortality info, see https://www.cdc.gov/nchs/nvss/vsr/covid19/index.htm

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Age-adjusted COVID-19-associated hospitalization rates by race and ethnicity
COVID-NET, MARCH 1 - MAY 23, 2020

Rates are statistically adjusted to account for differences in age distributions within race and ethnicity strata in the COVID-NET catchment area. Rates are based on available race and ethnicity data which is now complete in 89% of cases from COVID-NET sites. COVID-19-associated hospitalization rates for American Indian and Alaska Natives (AI/AN) may be impacted by recent outbreaks among specific communities within this population and the small numbers of AI/AN cases included in COVID-NET.

CDC.gov/coronavirus

Laboratory-Confirmed COVID-19-Associated Hospitalizations
Preliminary cumulative rates as of May 30, 2020

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**Rates of Hospitalization for COVID-19 Increase with Age**

- 0-4: 0.3 per 100k population
- 5-17: 0.1 per 100k population
- 18-49: 2.5 per 100k population
- 50-64: 7.4 per 100k population
- 65-74: 12.2 per 100k population
- 75-84: 15.8 per 100k population
- 85+: 17.2 per 100k population

Everyone, especially older adults, should: ✔ stay home
✔ use face coverings in public settings
✔ wash hands frequently

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**COVID-19 Laboratory-Confirmed Hospitalizations**

[Chart showing selected underlying medical conditions and their percentages]

- Asthma
- Autoimmune Disease
- Cardiovascular Disease
- Chronic Lung Disease
- Gastrointestinal/Liver Disease
- Hypertension
- Immune Suppression
- Metabolic Disease
- Neurologic Disease
- Obesity
- Pregnancy
- Renal Disease
- Other Disease
- No known Condition

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CellTrials.org
COVID-19 Clinical Trials by Therapy Type

- Vaccine
- Chloroquine
- Anti-Viral
- Cell & Gene Therapy
- Cell Secretome / ESV
- Monoclonal Antibody
- Convalescent Plasma
- Proteins
- Steroid
- Combinations of these
- Other
- Nutritional Supplements
- Traditional Medicine

Celltrials.org accessed 5/12/2020

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Top Candidates for Therapy

Remdesivir - Specific broad spectrum antiviral
  Given IV
  Short supply - rationing
  NIH study shortened recovery time from 15 to 11 days
  Still many deaths in NYC
Convalescent plasma - No good studies yet but many programs active
Mesenchymal stem cells - More than 40 studies ongoing
Vaccines - Full steam ahead

Take Home Messages

SAR-CoV-2 is VERY contagious
It will be a long time before a vaccine is available
The great majority of the population will not die due to COVID-19
  Many at risk populations
But COVID-19 can be a devastating illness
  Clinical trials will be in the news with a new therapy every week
  None of these new therapies will likely be a complete cure
  Testing is increasingly available for viral PCR and for antibodies
We do not know the extent to which antibodies are protective
SARS-Cov2 will be part of our viral illness panel for the foreseeable future