Pulmonary and Critical Care Medicine

Covid-19 Bootcamp #2

Jasleen Minhas, Katie Auriemma, Roger Kim

March 31, 2020
Presentation Slides and Tip sheets
Penn Medicine Tip Sheet: Personal Protective Equipment
Updated 3/5/2020 – newest version here

DONNING PPE
HAND HYGIENE

HIGH-RISK PROCEDURES & ALTERNATIVES
Nebulized bronchodilators
Inhaled epoprostenol (Prostacyclin)
BIPAP or HFNC
Mask ventilation
Ventilator disconnect
Open suctioning
Also includes: Intubation, CPR, bronchoscopy

PPE GUIDELINES

Workspaces
Non-PUI
PUI
Confirmed COVID-19 +
Aerosol Generating Procedures (PUI or COVID-19+)

RRT CODE

DOFFING PPE
SANITIZE GLOVES

HAND HYGIENE
Exit room

HAND GLOVES
Put on clean gloves

SANITIZE GLOVES

CONSERVING PPE

CHECK SHAREPOINT FOR UPDATES

Penn Medicine
Intranet

A quick reference guide created for the Division of Pulmonary and Critical Care Medicine. Contents may change as situation demands. Email Jeff Min & Jennifer Griemstine for corrections.
Please reach out to the following fellows for questions:

- Jeff Min: jeff.min@pennmedicine.upenn.edu
- Jen Ginestra: Jennifer.ginestra@pennmedicine.upenn.edu
- Jasleen Minhas: jasleen.minhas@pennmedicine.upenn.edu
Screening and Diagnosis
HUP COVID-19 Testing - Logistics

- Rapid Cartridge PCR with run time of < 45 minutes

- Specimens: obtained by MDs
  - Non intubated: NP or OP swab
  - Intubated: NP swab only

- Can be added on to RPP if sent in ED

- In house testing: currently only by approval from ID

Key Contact Information

HUP ID APPROVAL PAGER: (215)-614-0895 → contact 24/7 for in-house test approval
### HUP COVID-19 Testing - Logistics

<table>
<thead>
<tr>
<th>Daily Volume</th>
<th>Result time</th>
<th>Population targeted</th>
<th>Order</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urgent</td>
<td>120 tests/day</td>
<td>&lt;4 hours</td>
<td>Golden Ticket</td>
</tr>
<tr>
<td>Less Urgent</td>
<td>200 tests/day</td>
<td>4-12 hours</td>
<td>Blue Ticket</td>
</tr>
</tbody>
</table>

- As of 3/30 testing is being offered 24 hours a day
HUP COVID19 – Inpatient Protocol

Has patient had a recent RPP or rapid flu/RSV sample that is still in HUP lab

1. Call ID approval pager
2. Infection control completes COVID-19 Requisition form aka “Golden Ticket”. No order entry in EPIC
3. Deliver / tube form to Central Receiving (Founders 7)

1. Call ID approval pager
2. Infection control completes COVID-19 Requisition form aka “Golden Ticket” – form emailed/delivered in person
3. Collect Specimen
4. Deliver / tube form to Central Receiving (Founders 7)
### Table 4. Common respiratory pathogens detected in COVID-19 patients and healthy controls

<table>
<thead>
<tr>
<th>Pathogens detected</th>
<th>COVID-19 patients (n=30)</th>
<th>Healthy controls (n=30)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>No. (%)</td>
<td></td>
</tr>
<tr>
<td>IFV-A</td>
<td>18 (60.00)</td>
<td>0 (0.00)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IFV-B</td>
<td>16 (53.33)</td>
<td>4 (13.33)</td>
<td>0.0018</td>
</tr>
<tr>
<td>MP</td>
<td>7 (23.33)</td>
<td>0 (0.00)</td>
<td>0.0105</td>
</tr>
<tr>
<td>LP</td>
<td>6 (20.00)</td>
<td>0 (0.00)</td>
<td>0.0237</td>
</tr>
<tr>
<td>RSV</td>
<td>0 (0.00)</td>
<td>0 (0.00)</td>
<td>NA</td>
</tr>
</tbody>
</table>
Nasopharyngeal Swabs

- PPE: surgical mask + eye protection + gown + gloves

- Procedure:
  - Tilt head back & insert swab parallel to palate
  - Stop when resistance met
  - Leave in place for 2 – 3 seconds
  - Rotate 10 – 15 sec
  - Repeat on other side

- OP swab: larger swab
- Immediately place both into sterile viral transport media vial
- Double bag specimen
- Include “golden ticket”
- Deliver to central receiving (Founders 7)
Correlation of Chest CT and RT-PCR

1049 patients suspected of COVID-19 underwent both chest CT and RT-PCR assays from January 6 to February 6, 2020.

Excluded 35 patients: Time-interval of CT and RT-PCR was longer than 7 days.

Included patients (n=1014)

- 580 patients with positive RT-PCR and positive CT
- 308 patients with negative RT-PCR and positive CT
- 21 patients with positive RT-PCR and negative CT
- 105 patients with negative RT-PCR and negative CT

Graph showing correlation between initial and follow-up chest CT with RT-PCR results, indicating progression and new positive cases.
Screening for COVID 19

- Logistics of screening
- Co-infections may occur with COVID 19
- Procedure of obtaining NP swab
- False negatives – more to come as we learn
Clinical Features and Course

Katie Auriemma
Actual Patients admitted in UPHS System

- 72M with confusion and a fever
- 80M with disequilibrium – activated for code stroke
- 68W with fever and SOB
- 72M with 1 week of diarrhea and emesis

All Covid-19 Positive
Early Reports of Epidemiology and Clinical Characteristics

Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study

Nanshan Chen*, Min Zhou*, Xuan Dong*, Jiemei Qu*, Fengyuan Gong, Yang Han, Yang Qiu, Jingli Wang, Ying Liu, Yuan Wei, Jia’an Xia, Ting Yu, Xinmin Zhang, Li Zhang

- Lancet, February 15, 2020
- Largest early cohort of hospitalized patients
- Fever, cough, shortness of breath

<table>
<thead>
<tr>
<th>Signs and symptoms at admission</th>
<th>Patients (n=99)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>82 (83%)</td>
</tr>
<tr>
<td>Cough</td>
<td>81 (82%)</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>31 (31%)</td>
</tr>
<tr>
<td>Muscle ache</td>
<td>11 (11%)</td>
</tr>
<tr>
<td>Confusion</td>
<td>9 (9%)</td>
</tr>
<tr>
<td>Headache</td>
<td>8 (8%)</td>
</tr>
<tr>
<td>Sore throat</td>
<td>5 (5%)</td>
</tr>
<tr>
<td>Rhinorrhoea</td>
<td>4 (4%)</td>
</tr>
<tr>
<td>Chest pain</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>More than one sign or symptom</td>
<td>89 (90%)</td>
</tr>
<tr>
<td>Fever, cough, and shortness of breath</td>
<td>15 (15%)</td>
</tr>
</tbody>
</table>
NEJM, February 28, 2020
1099 patients – 93.6% hospitalized
Less than half of patients presented with fever
Vast majority did develop fever during hospitalization
Wide range of other reported symptoms
Cough, sputum, and fatigue most common

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Patients (N = 1099)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever on admission</td>
<td>473/1081 (43.8)</td>
</tr>
<tr>
<td>Patients — no./total no. (%)</td>
<td></td>
</tr>
<tr>
<td>Fever during hospitalization</td>
<td>975/1099 (88.7)</td>
</tr>
<tr>
<td>Patients — no./total no. (%)</td>
<td></td>
</tr>
</tbody>
</table>

| Symptoms — no. (%)             |                         |
| Conjunctival congestion        | 9 (0.8)                 |
| Nasal congestion               | 53 (4.8)                |
| Headache                       | 150 (13.6)              |
| Cough                          | 745 (67.8)              |
| Sore throat                    | 153 (13.9)              |
| Sputum production              | 370 (33.7)              |
| Fatigue                        | 419 (38.1)              |
| Hemoptysis                     | 10 (0.9)                |
| Shortness of breath            | 205 (18.7)              |
| Nausea or vomiting             | 55 (5.0)                |
| Diarrhea                       | 42 (3.8)                |
| Myalgia or arthralgia          | 164 (14.9)              |
| Chills                         | 126 (11.5)              |
## Table 3. Complications, Treatments, and Clinical Outcomes.

<table>
<thead>
<tr>
<th>Variable</th>
<th>All Patients (N=1099)</th>
<th>Disease Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Nonsevere (N=926)</td>
</tr>
<tr>
<td>Complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septic shock — no. (%)</td>
<td>12 (1.1)</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>Acute respiratory distress syndrome — no. (%)</td>
<td>37 (3.4)</td>
<td>10 (1.1)</td>
</tr>
<tr>
<td>Acute kidney injury — no. (%)</td>
<td>6 (0.5)</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>Disseminated intravascular coagulation — no. (%)</td>
<td>1 (0.1)</td>
<td>0</td>
</tr>
<tr>
<td>Rhabdomyolysis — no. (%)</td>
<td>2 (0.2)</td>
<td>2 (0.2)</td>
</tr>
<tr>
<td>Physician-diagnosed pneumonia — no./total no. (%)</td>
<td>972/1067 (91.1)</td>
<td>800/894 (89.5)</td>
</tr>
<tr>
<td>Median time until development of pneumonia (IQR) — days*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>After initial Covid-19 diagnosis</td>
<td>0.0 (0.0–1.0)</td>
<td>0.0 (0.0–1.0)</td>
</tr>
<tr>
<td>After onset of Covid-19 symptoms</td>
<td>3.0 (1.0–6.0)</td>
<td>3.0 (1.0–6.0)</td>
</tr>
</tbody>
</table>

15.7% of 1099 patients had “severe disease”
Clinical Characteristics of Coronavirus Disease 2019 in China


- 6.1% experienced the primary composite endpoint:
  - ICU admission - 5%
  - invasive MV - 2.3%
  - death - 1.4%

- Characteristics associated with worst outcomes
  - Older age
  - Comorbid illness

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Presence of Primary Composite End Point‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (N=67)</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
</tr>
<tr>
<td>Median (IQR) — yr</td>
<td>63.0 (53.0–71.0)</td>
</tr>
<tr>
<td>Distribution — no./total no. (%)</td>
<td></td>
</tr>
<tr>
<td>0–14 yr</td>
<td>0</td>
</tr>
<tr>
<td>15–49 yr</td>
<td>12/65 (18.5)</td>
</tr>
<tr>
<td>50–64 yr</td>
<td>21/65 (32.3)</td>
</tr>
<tr>
<td>≥65 yr</td>
<td>32/65 (49.2)</td>
</tr>
<tr>
<td><strong>Coexisting disorder — no. (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>39 (58.2)</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>7 (10.4)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>18 (26.9)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>24 (35.8)</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>6 (9.0)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>4 (6.0)</td>
</tr>
<tr>
<td>Hepatitis B infection</td>
<td>1 (1.5)</td>
</tr>
<tr>
<td>Cancer</td>
<td>1 (1.5)</td>
</tr>
<tr>
<td>Chronic renal disease</td>
<td>2 (3.0)</td>
</tr>
<tr>
<td>Immunodeficiency</td>
<td>0</td>
</tr>
</tbody>
</table>
4,226 total US cases at that time

Highest fatality in age ≥ 85 (10-27%)

Overall in US, persons age ≥ 65:
- 31% of cases
- 45% of hospitalizations
- 53% of ICU admissions
- 80% of deaths

Of ICU admissions
- 36% age 45-64
- 12% age 20-44
NYC and Philadelphia

▶ In Philadelphia, half of cases <40 years

▶ In NYC, majority of cases <65 years

NYC COVID-19 Cases

<table>
<thead>
<tr>
<th></th>
<th>Total Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>32308</td>
</tr>
<tr>
<td>Median Age (Range)</td>
<td>48 (0-105)</td>
</tr>
<tr>
<td>Age Group</td>
<td></td>
</tr>
<tr>
<td>- 0 to 17</td>
<td>611 (2%)</td>
</tr>
<tr>
<td>- 18 to 44</td>
<td>13794 (43%)</td>
</tr>
<tr>
<td>- 45 to 64</td>
<td>11146 (35%)</td>
</tr>
<tr>
<td>- 65 to 74</td>
<td>3790 (12%)</td>
</tr>
<tr>
<td>- 75 and over</td>
<td>2897 (9%)</td>
</tr>
<tr>
<td>- Unknown</td>
<td>70</td>
</tr>
<tr>
<td>Age 50 and over</td>
<td></td>
</tr>
<tr>
<td>- Yes</td>
<td>15074 (47%)</td>
</tr>
<tr>
<td>- No</td>
<td>17164 (53%)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>- Female</td>
<td>14293 (44%)</td>
</tr>
<tr>
<td>- Male</td>
<td>17971 (56%)</td>
</tr>
<tr>
<td>- Unknown</td>
<td>44</td>
</tr>
<tr>
<td>Borough</td>
<td></td>
</tr>
<tr>
<td>- Bronx</td>
<td>6145 (19%)</td>
</tr>
<tr>
<td>- Brooklyn</td>
<td>8451 (26%)</td>
</tr>
<tr>
<td>- Manhattan</td>
<td>5438 (17%)</td>
</tr>
<tr>
<td>- Queens</td>
<td>10373 (32%)</td>
</tr>
<tr>
<td>- Staten Island</td>
<td>1866 (6%)</td>
</tr>
<tr>
<td>- Unknown</td>
<td>35</td>
</tr>
<tr>
<td>Deaths</td>
<td>678</td>
</tr>
</tbody>
</table>
Imaging Findings

- A: 56M, d3 after Sx onset
- B: 74W, d10 after Sx onset
- C: 61W, d20 after Sx onset
- D: 63W, d17 after Sx onset

Shi H et al Lancet 2020
Imaging Findings

- Distribution CT patterns at various timepoints from symptom onset

Shi H et al. Lancet 2020
Laboratory Findings

- Leukopenia and lymphopenia (80%+)
- IL-6, Ferritin elevated
- D-Dimer, CRP, LDH elevated
- Procalcitonin generally low → may be high with bacterial superinfection
Disease Progression

Median time from onset to recovery:
- Mild: 2 weeks
- Severe: 3-6 weeks

Onset to development of severe disease:
- 1 week

Among those who have died, time of symptom onset to death:
- 2-8 weeks
Decompensation – Mainly Anecdotal

- **Respiratory Failure**
  - Rapidly progressive from hospital admission (often 7-10d out from symptom onset)

- **Shock**
  - Onset described when respiratory failure seems to be resolving
  - Described as cold/clamped, POCUS demonstrating impaired cardiac function

- **Cardiac Arrest**
  - VT/VF
  - PEA
Washington ICU Outcomes

- Case series of 21 critically ill patients from Washington State
- Published 3/19/20

- Over half had severe ARDS
- 2/3 developed shock requiring vasopressors
- 19% AKI
- 1/3 developed a cardiomyopathy

Table 2. Clinical Measures During the Course of Illness and Outcomes of 21 Critically Ill Patients With Coronavirus Disease 2019

<table>
<thead>
<tr>
<th>Clinical measures</th>
<th>No. (%) of patients³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute respiratory distress syndrome (ARDS)ᵇ</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1 (4.8)</td>
</tr>
<tr>
<td>Mild</td>
<td>2 (9.5)</td>
</tr>
<tr>
<td>Moderate</td>
<td>6 (28.6)</td>
</tr>
<tr>
<td>Severe</td>
<td>12 (57.1)</td>
</tr>
<tr>
<td>Required mechanical ventilation</td>
<td>15 (71.0)</td>
</tr>
<tr>
<td>Use of vasopressors</td>
<td>14 (67.0)</td>
</tr>
<tr>
<td>Acute kidney failureᵈ</td>
<td>4 (19.1)</td>
</tr>
<tr>
<td>Cardiomyopathyᵉ</td>
<td>7 (33.3)</td>
</tr>
<tr>
<td>Acute hepatic injuryᶠ</td>
<td>3 (14.3)</td>
</tr>
<tr>
<td>Seizures</td>
<td>1 (4.8)</td>
</tr>
<tr>
<td>Length of follow-up, mean (range), d</td>
<td>5.2 (1-10)</td>
</tr>
</tbody>
</table>

Outcomes

| Died                                                   | 11 (52.4)             |
| Survived to transfer out of ICU                        | 2 (9.5)               |
| Remains critically ill and requires mechanical ventilation | 8 (38.1)           |
| Length of follow-up for those who survived or remain critically ill, mean (range), d | 7.5 (5-10) |

Arentz M et al JAMA 2020
Critical Care Management

Roger Kim
Outline

- Respiratory failure
- Mechanical ventilation
- Hemodynamic management
- Novel strategies / future directions
Respiratory failure algorithms

UPHS guidelines
March 27, 2020
Respiratory support general principles

- Favor early intubation
- Avoid NIPPV (i.e. CPAP, BiPAP)
- Limit HFNC use to 10-20 L/min flow rate and 60% FiO2
Acute hypoxic respiratory failure

1. **SaO2 <92% +/- ↑ WOB Despite 6 L/min NC**

   - Transfer to airborne isolation room and use airborne, droplet, & contact isolation PPE

2. **Early intubation**
   - *call anesthesia STAT*
   - Yes
   - Rapidly worsening?
   - No

   - Consider HFNC up to 10-20 L/min + 60% FiO2
     - *surgical mask over patient’s nose + mouth*

   - No

   - Clinical stability within 1 hour?
     - No
     - Yes
Acute on chronic hypoxic respiratory failure

1. \( \text{SaO}_2 <88\% \pm \uparrow \text{WOB} \)
   Despite baseline \( >6 \text{ L/min NC} \)

2. Transfer to airborne isolation room and use airborne, droplet, & contact isolation PPE

3. Intubation
   - *call anesthesia STAT*

4. HFNC up to 10-20 L/min + 60% FiO2
   - or NRB up to 10-12 L/min
   - *surgical mask over patient's nose + mouth*

5. Clinical stability?
   - No
   - Yes

---

Penn Medicine
Acute / acute on chronic hypercapnic respiratory failure

- Acutely rising PCO2 with respiratory acidosis
- Transfer to airborne isolation room and use airborne, droplet, & contact isolation PPE
- Early intubation
  *call anesthesia STAT
Stable chronic hypercapnic respiratory failure

Baseline NIPPV use

Transfer to airborne isolation room and use airborne, droplet, & contact isolation PPE

NIPPV prohibited

Indication for NIPPV strictly OSA?

Yes

No

Contact NIPPV team
HUP: 215-964-7480
PMC: 267-591-3767
PAH: 610-529-5171
CCH: 610-731-9736
MCP: 732-672-6450
LGH: 412-491-7603
ARDS mechanical ventilation strategies

UPHS guidelines
March 27, 2020

SCCM COVID-19 guidelines
March 2020
ARDS mechanical ventilation general principles

- Low-stretch (lung protective) ventilation

- High PEEP strategy

- Conservative fluid strategy

- Refractory hypoxemia
  - Neuromuscular blocking agents (NMBA)
  - Prone ventilation
ARDS mechanical ventilation general principles

- Low-stretch (lung protective) ventilation
- High PEEP strategy
- Conservative fluid strategy
- Refractory hypoxemia
  - Neuromuscular blocking agents (NMBA)
  - Prone ventilation
Low-stretch (lung protective) ventilation

- **Volume assist control (VAC) with low tidal volumes**
  - Vt 4-8 mL/kg of predicted ideal body weight (start at 6 mL/kg)

- **Target plateau pressure (P_{plat})<30 cm H_2O**

- **Goal pH: 7.30-7.45**

- **Goal SpO2: 92-96%**

- **Ventilator dyssynchrony is common**
  - Adequate sedation is required
  - Consider RASS goal of -2 to -3
High PEEP strategy

- PEEP-responsive ARDS with driving pressures <15 cm H₂O consistently reported

- Start with PEEP of >14-18 cm H₂O

- Risk of PTX and hemodynamic compromise
Peak inspiratory pressure ($P_{\text{peak}}$)

Driving Pressure ($\Delta P$) = $P_{\text{plateau}}$ - PEEP

Average pressures represented by AUC / time → Mean airway pressure

$C_{\text{dyn}} = TV / [P_{\text{peak}} - \text{PEEP}]$

$C_{\text{stat}} = TV / [P_{\text{plateau}} - \text{PEEP}]$
High PEEP strategy

- PEEP-responsive ARDS with driving pressures <15 cm H₂O consistently reported
- Start with PEEP of ≥14-18 cm H₂O
- Risk of PTX and hemodynamic compromise

<table>
<thead>
<tr>
<th>FiO₂</th>
<th>0.3</th>
<th>0.3</th>
<th>0.3</th>
<th>0.3</th>
<th>0.3</th>
<th>0.4</th>
<th>0.4</th>
<th>0.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEEP</td>
<td>5</td>
<td>8</td>
<td>10</td>
<td>12</td>
<td>14</td>
<td>14</td>
<td>16</td>
<td>16</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>FiO₂</th>
<th>0.5</th>
<th>0.5-0.8</th>
<th>0.8</th>
<th>0.9</th>
<th>1.0</th>
<th>1.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEEP</td>
<td>18</td>
<td>20</td>
<td>22</td>
<td>22</td>
<td>22</td>
<td>24</td>
</tr>
</tbody>
</table>
Conservative fluid strategy

- No consensus on definition
- Diurese to avoid obvious volume overload
- Diurese if SpO2 <92% despite optimization of ventilator mechanics
- Consider diuresis if on low-dose pressors with normal renal function
Neuromuscular blocking agents (NMBA)

- Intermittent boluses to facilitate lung protective ventilation

- Continuous infusion <48 hrs for prone ventilation, persistent $P_{plat} > 30$ cm H$_2$O, or persistent ventilator dyssynchrony

Prone ventilation

- Use if $P:F < 150$, FiO$_2 > 60\%$, and PEEP $> 5$ cm H$_2$O after $> 12$ hours of ventilator support

- Prone 16-18 hours per day

- Stop:
  - When $P:F > 150$ with PEEP $\leq 10$ cm H$_2$O and FiO$_2 \leq 60\%$ in supine position for $\geq 4$ hours
  - If prone position decreases $P:F$ by $> 20\%$ compared to supine position
# Refractory hypoxemia – strategies to consider

<table>
<thead>
<tr>
<th>Traditional recruitment maneuvers</th>
<th>Bronchoscopy ONLY in following situations:</th>
<th>VV-ECMO Consider if all other interventions exhausted AND any 1 of following:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 30-40 cm H₂O for 30-40 s</td>
<td>• Complete lung atelectasis from mucous plugging with worsening hypoxemia</td>
<td>• Injurious ventilator settings necessary to achieve adequate oxygenation</td>
</tr>
<tr>
<td>• If oxygenation improves, use higher PEEP</td>
<td>• Massive hemoptysis with need to clear blood/clot and place bronchial blocker</td>
<td>• Uncontrolled respiratory acidosis</td>
</tr>
<tr>
<td></td>
<td>• Unable to obtain tracheal aspirate for VAP workup</td>
<td>• Right heart failure with persistent organ dysfunction despite lung protective ventilation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• May need to switch to VA-ECMO if does not improve with VV-ECMO</td>
</tr>
</tbody>
</table>
Refractory hypoxemia – NOT recommended strategies

**Inhaled epoprostenol (i.e. Flolan, Veletri)**

- No mortality benefit
- May clog vent filter and increase risk of aerosolization
- Can consider a trial of inhaled nitric oxide after discussion with pharmacy

**Staircase (incremental PEEP) recruitment maneuvers**

- Defined as incremental increases in PEEP from 25 to 35 to 45 cm H$_2$O for 1-2 min. each
- May be associated with increased mortality
Hemodynamic management

UPHS guidelines
March 27, 2020

SCCM COVID-19 guidelines
March 2020
Septic shock management

- Empiric antibiotics in mechanically ventilated patients
- Conservative isotonic crystalloid fluids (LR > NS) for acute resuscitation
  - Preferred over hydroxyethyl starches, dextrans, gelatins, or albumin
- Norepinephrine = preferred 1st line vasoactive agent
  - If not available, consider vasopressin or epinephrine
  - Preferred over dopamine
- Vasopressin = preferred 2nd line vasoactive agent
  - If not available, consider epinephrine
- MAP goal: 60-65 mmHg
- Consider “stress-dose” steroids (hydrocortisone 200 mg/d) for refractory shock
COVID-19 hemodynamic considerations

- Start norepinephrine at 0.05-0.1 mcg/kg/min immediately after intubation and titrate accordingly

- Presumed viral myocarditis → cardiac dysfunction / fluid overload
  - Favor negative fluid balance without causing organ hypoperfusion
  - Consider diuresis if POCUS reveals non-collapsible IVC
  - Dynamic hemodynamic reassessment with POCUS TTE
  - Consider VA-ECMO for severe myocarditis causing cardiogenic shock

- Ensure adequate preload in setting of high PEEP ventilatory strategy
  - Consider careful IVF boluses if PEEP >15cm H₂O
Novel strategies / future directions
Awake prone ventilation

- Floor patients with hypoxic respiratory failure on supplemental O2 (including HFNC)

- **NOT** recommended in patients with:
  - Chronic lung disease
  - Chest tubes
  - Spinal instability
  - Cardiogenic pulmonary edema
  - GCS <15
  - PaCO2 >45 mmHg

- Prone for ≥2-4 hours bid as tolerated
BMI-based PEEP ventilatory strategy

<table>
<thead>
<tr>
<th>BMI</th>
<th>Starting PEEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35</td>
<td>10</td>
</tr>
<tr>
<td>35-50</td>
<td>12</td>
</tr>
<tr>
<td>&gt;50</td>
<td>15</td>
</tr>
</tbody>
</table>
Future directions

- Define PEEP weaning and prolonged SBT protocol

- Standardize approach to cardiac monitoring
  - Daily EKG not recommended
  - Early POCUS vs. TTE?

- Standardize sedation protocol
  - Concerns about propofol (↑TG’s & LFT’s)
  - Cisatracurium shortage

- Standardize laboratory testing frequency
  - D-dimer, procalcitonin, LFT’s, LDH, ferritin, WBC w/ diff, CRP, IL-6, coags
Supplemental slides / figures
**Penn Medicine Tip Sheet: Escalation of Care for Respiratory Failure**

**ACUTE RESPIRATORY FAILURE**
Are O₂ requirements or work of breathing rapidly escalating?

**COVID-19 STATUS**

<table>
<thead>
<tr>
<th>Non-COVID / Non-PUI</th>
<th>COVID-19 PUI</th>
<th>COVID-19 Confirmed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upgrade to droplet + contact isolation Close door, minimize entry</td>
<td>Upgrade to airborne + contact isolation Move to negative pressure room if possible</td>
<td>Call lab to expedite results</td>
</tr>
<tr>
<td>Call ID for testing (hypercapnia only)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**HYPOXEMIA** (↑WOB or SaO₂ <92% on ≥6L RPM)

<table>
<thead>
<tr>
<th>Normal management</th>
<th>Trial HFNC Flow: 10-20 LPM; FiO₂: up to 60%</th>
<th>Only if chronic baseline O₂ ≥6 LPM</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Trial NRB Flow: 10-12 LPM</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**HYPERCAPNIA**

- Start NPPV Non-vented mask
  - Active ventilation circuit w/ exhalation filter
  - Healthcare workers to wear N95 until COVID testing is negative
- Consider Early Intubation if high risk for COVID-19 or impending respiratory failure
- Early Intubation
  - Risk of rapid progression of respiratory failure requiring mechanical ventilation

**EARLY INTUBATION**

- All intubations, including ICU intubations should be called overhead STAT
  - Ward (neg pressure): intubate in room prior to ICU transfer
  - Ward (regular): transfer to ICU with mask on patient, then intubate
    - For most patients, use Low Stretch Protocol for ARDS
      - SaO₂ < 92% or pH < 7.3 despite maximal interventions

**Stable Chronic Hypercapnia**

- Upgrade isolation by COVID-19 status as per acute respiratory failure algorithm.
  - OSA: No NPPV allowed
  - COPD, OHS, NMD: contact hospital NIV team
  - HUP: 215-964-7480 CCH: 610-731-9736
  - PMC: 267-591-3767 MCP: 732-672-6450
  - Pah: 610-529-5171 CHH: 412-491-7603
  - 215-498-6357 acute

Adapted from the UPHS Critical Care Clinical Operations COVID-19 guidelines. UPHS CCOG guidelines are rapidly evolving - check Penn SharePoint for most updated information. Email Jeff Min & Jennifer Giavrieta for corrections.
COVID-19 with hypoxia

Indication for endotracheal intubation?

Yes

Tolerating supplemental oxygen?

No

Tolerating HFNC

Consider: HFNC

Not tolerating HFNC or HFNC is not available

No

Indication for endotracheal intubation?

Yes

Consider: a trial of NIPPV

Do it: Monitor closely at short intervals

Do not: Delay intubation if worsening

Do it: Monitor closely for worsening

Do it: Target SPO₂ 92 to 96%

Do it: Appropriate infection control precautions

Do not: Delay intubation if worsening

Do it: Endotracheal intubation

Do it: Expert in airway to intubate

Do it: Use N-95/FFP-2 or equivalent and other PPC/Infection control precautions

Do it: Minimize staff in the room

Consider: if available Video-laryngoscope
<table>
<thead>
<tr>
<th>Timing</th>
<th>Within 1 week of a known clinical insult or new or worsening respiratory symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest imaging(^a)</td>
<td>Bilateral opacities—not fully explained by effusions, lobar/lung collapse, or nodules</td>
</tr>
<tr>
<td>Origin of edema</td>
<td>Respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (eg, echocardiography) to exclude hydrostatic edema if no risk factor present</td>
</tr>
<tr>
<td>Oxygenation(^b)</td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>200 mm Hg &lt; Pao(_2)/FiO(_2) ≤ 300 mm Hg with PEEP or CPAP ≥ 5 cm H(_2)O(^c)</td>
</tr>
<tr>
<td>Moderate</td>
<td>100 mm Hg &lt; Pao(_2)/FiO(_2) ≤ 200 mm Hg with PEEP ≥ 5 cm H(_2)O</td>
</tr>
<tr>
<td>Severe</td>
<td>Pao(_2)/FiO(_2) ≤ 100 mm Hg with PEEP ≥ 5 cm H(_2)O</td>
</tr>
</tbody>
</table>

Abbreviations: CPAP, continuous positive airway pressure; FiO\(_2\), fraction of inspired oxygen; Pao\(_2\), partial pressure of arterial oxygen; PEEP, positive end-expiratory pressure.

\(^a\) Chest radiograph or computed tomography scan.

\(^b\) If altitude is higher than 1000 m, the correction factor should be calculated as follows: [Pao\(_2\)/FiO\(_2\) × (barometric pressure/760)].

\(^c\) This may be delivered noninvasively in the mild acute respiratory distress syndrome group.
<table>
<thead>
<tr>
<th>Height</th>
<th>PBW</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>4'10&quot;</td>
<td>58</td>
<td>45.4</td>
<td>180</td>
<td>230</td>
<td>270</td>
<td>320</td>
</tr>
<tr>
<td>4'11&quot;</td>
<td>59</td>
<td>47.7</td>
<td>190</td>
<td>240</td>
<td>290</td>
<td>330</td>
</tr>
<tr>
<td>5'0&quot;</td>
<td>60</td>
<td>50</td>
<td>200</td>
<td>250</td>
<td>300</td>
<td>350</td>
</tr>
<tr>
<td>5'1&quot;</td>
<td>61</td>
<td>52.3</td>
<td>210</td>
<td>260</td>
<td>310</td>
<td>370</td>
</tr>
<tr>
<td>5'2&quot;</td>
<td>62</td>
<td>54.6</td>
<td>220</td>
<td>270</td>
<td>330</td>
<td>380</td>
</tr>
<tr>
<td>5'3&quot;</td>
<td>63</td>
<td>56.9</td>
<td>230</td>
<td>280</td>
<td>340</td>
<td>400</td>
</tr>
<tr>
<td>5'4&quot;</td>
<td>64</td>
<td>59.2</td>
<td>240</td>
<td>300</td>
<td>360</td>
<td>410</td>
</tr>
<tr>
<td>5'5&quot;</td>
<td>65</td>
<td>61.5</td>
<td>250</td>
<td>310</td>
<td>370</td>
<td>430</td>
</tr>
<tr>
<td>5'6&quot;</td>
<td>66</td>
<td>63.8</td>
<td>260</td>
<td>320</td>
<td>380</td>
<td>450</td>
</tr>
<tr>
<td>5'7&quot;</td>
<td>67</td>
<td>66.1</td>
<td>270</td>
<td>330</td>
<td>400</td>
<td>460</td>
</tr>
<tr>
<td>5'8&quot;</td>
<td>68</td>
<td>68.4</td>
<td>280</td>
<td>340</td>
<td>410</td>
<td>480</td>
</tr>
<tr>
<td>5'9&quot;</td>
<td>69</td>
<td>70.7</td>
<td>290</td>
<td>350</td>
<td>420</td>
<td>490</td>
</tr>
<tr>
<td>5'10&quot;</td>
<td>70</td>
<td>73</td>
<td>300</td>
<td>370</td>
<td>440</td>
<td>510</td>
</tr>
<tr>
<td>5'11&quot;</td>
<td>71</td>
<td>75.3</td>
<td>310</td>
<td>380</td>
<td>450</td>
<td>530</td>
</tr>
<tr>
<td>6'0&quot;</td>
<td>72</td>
<td>77.6</td>
<td>320</td>
<td>390</td>
<td>470</td>
<td>540</td>
</tr>
<tr>
<td>6'1&quot;</td>
<td>73</td>
<td>79.9</td>
<td>330</td>
<td>400</td>
<td>480</td>
<td>560</td>
</tr>
<tr>
<td>6'2&quot;</td>
<td>74</td>
<td>82.2</td>
<td>340</td>
<td>410</td>
<td>490</td>
<td>580</td>
</tr>
<tr>
<td>6'3&quot;</td>
<td>75</td>
<td>84.5</td>
<td>350</td>
<td>420</td>
<td>510</td>
<td>590</td>
</tr>
<tr>
<td>6'4&quot;</td>
<td>76</td>
<td>86.8</td>
<td>360</td>
<td>430</td>
<td>520</td>
<td>610</td>
</tr>
<tr>
<td>6'5&quot;</td>
<td>77</td>
<td>89.1</td>
<td>370</td>
<td>450</td>
<td>530</td>
<td>620</td>
</tr>
<tr>
<td>6'6&quot;</td>
<td>78</td>
<td>91.4</td>
<td>380</td>
<td>460</td>
<td>550</td>
<td>640</td>
</tr>
</tbody>
</table>
INCLUSION CRITERIA: Acute onset of
1. \( P_{a}O_{2}/FiO_{2} \leq 300 \) (corrected for altitude)
2. Bilateral (patchy, diffuse, or homogeneous) infiltrates consistent with pulmonary edema
3. No clinical evidence of left atrial hypertension

PART I: VENTILATOR SETUP AND ADJUSTMENT
1. Calculate predicted body weight (PBW)
   - Males = 50 + 2.3 \[\text{height (inches)}\] - 60
   - Females = 45.5 + 2.3 \[\text{height (inches)}\] - 60
2. Select any ventilator mode
3. Set ventilator settings to achieve initial \( V_{T} = 8 \text{ ml/kg PBW} \)
4. Reduce \( V_{T} \) by 1 ml/kg at intervals ≤ 2 hours until \( V_{T} = 6 \text{ ml/kg PBW} \).
5. Set initial rate to approximate baseline minute ventilation (not > 35 bpm).
6. Adjust \( V_{T} \) and RR to achieve pH and plateau pressure goals below.

OXYGENATION GOAL: \( P_{a}O_{2} \geq 55-80 \) mmHg or \( SpO_{2} \geq 88-95\%
Use a minimum PEEP of 5 cm H\(_2\)O. Consider use of incremental \( FiO_{2}/PEEP \) combinations such as shown below (not required) to achieve goal.

**Lower PEEP/higher \( FiO_{2} \)**

<table>
<thead>
<tr>
<th>( FiO_{2} )</th>
<th>0.3</th>
<th>0.4</th>
<th>0.4</th>
<th>0.5</th>
<th>0.5</th>
<th>0.6</th>
<th>0.7</th>
<th>0.7</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEEP</td>
<td>5</td>
<td>5</td>
<td>8</td>
<td>8</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>12</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>( FiO_{2} )</th>
<th>0.7</th>
<th>0.8</th>
<th>0.9</th>
<th>0.9</th>
<th>0.9</th>
<th>1.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEEP</td>
<td>14</td>
<td>14</td>
<td>14</td>
<td>16</td>
<td>18</td>
<td>18-24</td>
</tr>
</tbody>
</table>

**Higher PEEP/lower \( FiO_{2} \)**

<table>
<thead>
<tr>
<th>( FiO_{2} )</th>
<th>0.3</th>
<th>0.3</th>
<th>0.3</th>
<th>0.3</th>
<th>0.3</th>
<th>0.4</th>
<th>0.4</th>
<th>0.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEEP</td>
<td>5</td>
<td>8</td>
<td>10</td>
<td>10</td>
<td>14</td>
<td>14</td>
<td>16</td>
<td>16</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>( FiO_{2} )</th>
<th>0.5</th>
<th>0.5</th>
<th>0.8</th>
<th>0.8</th>
<th>0.9</th>
<th>1.0</th>
<th>1.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEEP</td>
<td>18</td>
<td>20</td>
<td>22</td>
<td>22</td>
<td>22</td>
<td>22</td>
<td>24</td>
</tr>
</tbody>
</table>

PLATEAU PRESSURE GOAL: ≤ 30 cm H\(_2\)O
Check \( P_{p}lat \) (0.5 second inspiratory pause), at least q 4h and after each change in PEEP or \( V_{T} \).

- If \( P_{p}lat \geq 30 \) cm H\(_2\)O: decrease \( V_{T} \) by 1 ml/kg steps (minimum = 4 ml/kg).
- If \( P_{p}lat < 25 \) cm H\(_2\)O and \( V_{T} < 6 \) ml/kg, increase \( V_{T} \) by 1 ml/kg until Pplat > 25 cm H\(_2\)O or \( V_{T} = 6 \) ml/kg.
- If \( P_{p}lat < 30 \) and breath stacking or dys-synchrony occurs: may increase \( V_{T} \) in 1ml/kg increments to 7 or 8 ml/kg if Pplat remains ≤ 30 cm H\(_2\)O.
pH GOAL: 7.30–7.45

Acidosis Management: (pH < 7.30)
  If pH 7.15–7.30: Increase RR until pH > 7.30 or PaCO₂ < 25
  (Maximum set RR = 35).

If pH < 7.15: Increase RR to 35.
  If pH remains < 7.15, V̇₁ may be increased in 1 ml/kg steps until pH > 7.15 (Pplat target of 30 may be exceeded).
  May give NaHCO₃

Alkalosis Management: (pH > 7.45) Decrease vent rate if possible.

I: E RATIO GOAL: Recommend that duration of inspiration be ≤ duration of expiration.

PART II: WEANING

A. Conduct a SPONTANEOUS BREATHING TRIAL daily when:
   1. FiO₂ ≤ 0.40 and PEEP ≤ 8 OR FiO₂ ≤ 0.50 and PEEP ≤ 5.
   2. PEEP and FiO₂ ≤ values of previous day.
   3. Patient has acceptable spontaneous breathing efforts. (May decrease vent rate by 50% for 5 minutes to detect effort.)
   4. Systolic BP ≥ 90 mmHg without vasopressor support.
   5. No neuromuscular blocking agents or blockade.

B. SPONTANEOUS BREATHING TRIAL (SBT):
   If all above criteria are met and subject has been in the study for at least 12 hours, initiate a trial of UP TO 120 minutes of spontaneous breathing with FiO₂ ≤ 0.5 and PEEP ≤ 5:
   1. Place on T-piece, trach collar, or CPAP ≤ 5 cm H₂O with PS ≤ 5
   2. Assess for tolerance as below for up to two hours.
      a. SpO₂ ≥ 90: and/or PaO₂ ≥ 60 mmHg
      b. Spontaneous V̇₁ ≥ 4 ml/kg PBW
      c. RR ≤ 35/min
      d. pH ≥ 7.3
      e. No respiratory distress (distress = 2 or more)
         ➢ HR > 120% of baseline
         ➢ Marked accessory muscle use
         ➢ Abdominal paradox
         ➢ Diaphoresis
         ➢ Marked dyspnea
   3. If tolerated for at least 30 minutes, consider extubation.
   4. If not tolerated resume pre-weaning settings.

Definition of UNASSISTED BREATHING
(Different from the spontaneous breathing criteria as PS is not allowed)

1. Extubated with face mask, nasal prong oxygen, or room air, OR
2. T-tube breathing, OR
3. Tracheostomy mask breathing, OR
4. CPAP less than or equal to 5 cm H₂O without pressure support or IMV assistance.
COVID-19 with mild ARDS

- **Do:**
  - Vt 4-8 ml/kg and $P_{plat} < 30$ cm H$_2$O

- **Do:**
  - Investigate for bacterial infection

- **Do:**
  - Target SPO2 92% - 96%

- **Consider:**
  - Conservative fluid strategy

- **Consider:**
  - Empiric antibiotics

- **Uncertain:**
  - Systematic corticosteroids

COVID-19 with Mod to Severe ARDS

- **Consider:**
  - Higher PEEP

- **Consider:**
  - NMBA boluses to facilitate ventilation targets

- **Consider:**
  - If PEEP responsive
  - Traditional Recruitment maneuvers

- **Consider:**
  - Prone ventilation 12-16 h

- **Consider:**
  - If proning, high $P_{plat}$, asynchrony
  - NMBA infusion for 24 h

- **Consider:**
  - If proning, high $P_{plat}$, asynchrony
  - NMBA infusion for 24 h

- **Consider:**
  - Prone ventilation 12-16 h

- **Consider:**
  - STOP if no quick response
  - A trial of inhaled Nitric Oxide

- **Consider:**
  - V-V ECMO or referral to ECMO center

Rescue/Adjunctive therapy

- **Uncertain:**
  - Antivirals, chloroquine, anti-IL6

- **Consider:**
  - If proning, high $P_{plat}$, asynchrony
  - NMBA infusion for 24 h

- **Consider:**
  - Prone ventilation 12-16 h

- **Consider:**
  - STOP if no quick response
  - A trial of inhaled Nitric Oxide

- **Consider:**
  - If proning, high $P_{plat}$, asynchrony
  - NMBA infusion for 24 h

- **Consider:**
  - V-V ECMO or referral to ECMO center

- **Don’t do:**
  - Staircase Recruitment maneuvers

- **Consider:**
  - Short course of systemic corticosteroids

- **Uncertain:**
  - Antivirals, chloroquine, anti-IL6