Situation in United States

As of November 2020 in the U.S.

- Over 11 million total cases
- Nearly 250,000 deaths

SARS-CoV-2

Incubation period can be up to 14 days from time of exposure
- Median 4-5 days

Spectrum of illness asymptomatic to severe illness and death
### COVID-19

Primarily a pulmonary disease, however emerging data also suggests cardiac, dermatologic, hematological, hepatic, neurological, renal and other complications

Thromboembolic events are common, highest risk in critically ill patients

The long-term sequelae of COVID-19 survivors are currently unknown

<table>
<thead>
<tr>
<th>Infection Prevention and Control</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Limit potential facility exposure</strong></td>
</tr>
<tr>
<td>• Consider postponing elective procedures</td>
</tr>
<tr>
<td>• Use telehealth options when possible</td>
</tr>
<tr>
<td>• Limit points of entry</td>
</tr>
<tr>
<td>• Screen all patients and visitors for signs and symptoms of COVID-19</td>
</tr>
<tr>
<td>• This will miss asymptomatic / pre-symptomatic individuals</td>
</tr>
</tbody>
</table>

### COVID-19

80% infected have mild illness

15% severe: SpO2 < 94% on room air

5% critical: mechanical ventilation or ECMO

10% of all infections are hospitalized

• 10% requiring ICU level of care
Infection Prevention and Control
Patients and visitors should wear a mask upon arrival and throughout their stay
Restrict visitors who have suspected or confirmed SAR-CoV-2 infection, or have had close contact with SARS-CoV-2 person

Infection Prevention and Control
Symptomatic patients should be isolated in an exam room with the door closed
Airborne infection isolation rooms should be reserved for those undergoing aerosolizing procedures
Consider universal pre-admission or pre-procedural testing of patients
Re-evaluate admitted patients for signs and symptoms of COVID-19

Infection Prevention and Control
Healthcare workers (HCWs) should wear a facemask at all times within the facility
• This includes in breakrooms or other common areas
Encourage physical distancing (6 feet) as much as possible

Testing
Viral (nucleic acid or antigen) tests are recommended for diagnosis of acute infection
Antibody testing not approved or recommended as sole basis for diagnosis of acute infection
Nasopharyngeal, mid-turbinate or nasal swabs are preferred to oropharyngeal or saliva alone
Lower respiratory tract specimens can be tested if suspicion remains high
# Personal Protective Equipment (PPE)

Facemask and eye protection for all patient encounters
- Glasses are not sufficient

SARS-CoV-2 positive patients require addition of gown and gloves

N95 (or equivalent) or higher level respirator for AGP and surgical procedures with high risk of COVID transmission (nose, oropharynx, respiratory tract)

---

# Aerosol generating procedures

- Procedures:
  - Intubation / Extubation
  - Endoscopy (EGD, Bronchoscopy, TEE)
  - CPR
  - Tracheostomy placement

- Bedside Care:
  - Nasopharyngeal swab (testing for COVID)
  - NG / OG tube placement
  - Suctioning, sputum induction or tracheal aspiration

---

# PPE

- Follow the recommended sequence for safely donning and doffing PPE to avoid self contamination

- Hand hygiene should be performed before and after all patient contact, before putting on and after removing PPE
  - Alcohol based hand sanitizer or soap and water
Optimizing PPE supply

- Cancel elective and non-urgent procedures / appointments
- Reserve PPE for healthcare workers
- Use re-usable PPE that can be reprocessed if able
- Consider extending use of respirators, facemasks and eye protection beyond a single patient contact

Occupational Exposure

HCW with prolonged close contact with SARS-CoV2- positive patient, visitor or staff (cumulative period of 15 minutes or longer)

- No facemask or respirator: quarantine for 14 days
- Face mask / respirator: continue to work, monitor symptoms and quarantine if symptoms develop
Community Exposure

HCW with prolonged close contact with SARS-CoV2-positive person in community should quarantine until 14 days from last exposure

Return to work

Confirmed or suspected SARS-CoV-2 infection:
• Mild-moderate: 10 days since symptom onset, 24 hours afebrile, symptoms improved
• Moderate-severe: 10-20 days

Test based strategy no longer recommended

Discontinuation of Isolation

Mild to Moderate:
• 10 days from symptom onset
• 24 hours afebrile
• Symptoms overall improved

Moderate to Severe
• At least 10 days from symptom onset, can extend up to 20
• 24 hours afebrile
• Symptoms overall improved

Treatment
**Dexamethasone**

RECOVERY trial
- Lower 28 day mortality seen in those on supplemental O2 or mechanical ventilation
- No benefit among those not requiring respiratory support

Dexamethasone 6 mg IV or PO daily for 10 days
- Equivalent glucocorticoid may be used if dexamethasone unavailable

**Remdesivir**

Inhibitor of the viral RNA-dependent RNA polymerase

FDA approved October 22, 2020

In setting of limited resource, remdesivir is most beneficial in those with severe illness, not critical

Given as 5 day course in severe illness, extended to 10 days in critical illness

**Bamlanivimab**

Monoclonal antibody against SARS-CoV-2 spike protein

Designed to block virus' attachment and entry into human cells

FDA issued EUA November 9, 2020

Authorized for outpatients with high risk for severe COVID-19

Not authorized for hospitalized patients or those requiring oxygen therapy due to COVID-19

**Convalescent Plasma**

FDA issued EUA on August 23, 2020

IDSA guidelines recommend convalescent plasma be used in setting of a clinical trial
Casirivimab and Imdevimab (Regeneron)
Recombinant human IgG1 monoclonal antibody that targets receptor binding domain of the spike protein of SARS-CoV-2
FDA issued EUA November 21, 2020
Indicated for mild to moderate COVID-19
NOT indicated for hospitalized patients or those requiring oxygen therapy

Therapies not recommended
Hydroxychloroquine or Chloroquine with or without Azithromycin
Lopinavir / ritonavir, except in setting of a clinical trial
Tocilizumab, except in setting of a clinical trial
Famotidine

Vaccine

Operation Warp Speed
Partnership between multiple federal and private agencies to expedite vaccine development
Goal is to deliver 300 million doses of vaccine, initial doses by January 2021
Three vaccine candidates have been funded for phase 3 trials
### Vaccine

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Mechanism</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderna mRNA-1273</td>
<td>mRNA-based vaccine</td>
<td>Phase 3</td>
</tr>
<tr>
<td>Pfizer / BioNTech BNT162</td>
<td>mRNA-based vaccine</td>
<td>Phase 3</td>
</tr>
<tr>
<td>University of Oxford / AstraZeneca AZD1222</td>
<td>Replication-deficient viral vector (chimpanzee adenovirus)</td>
<td>Phase 3</td>
</tr>
</tbody>
</table>

### Inpatient Management of COVID-19

**Rachel Quaney, MD**  
Clinical Instructor of Internal Medicine  
Division of Pulmonary, Critical Care, and Sleep Medicine  
The Ohio State University Wexner Medical Center

#### Outline
- Respiratory failure
- ARDS
- Coagulopathy
- Special groups
- Outcomes

#### Outline
- Respiratory failure
- ARDS
- Coagulopathy
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- Outcomes
**Hospital course**

- Median time from illness to dyspnea → 5-8 days
- Median time from illness to ARDS → 8-12 days
- Median time from illness to ICU admission → 9.5-12 days

**Respiratory failure**

- Conventional oxygen therapy

  ![Diagram](https://www.covid19treatmentguidelines.nih.gov/critical-care/)

  - High-flow nasal cannula (HFNC)

  - Closely monitored trial of noninvasive positive pressure ventilation (NIPPV) if intubation not indicated and HFNC not available

**ARDS definition**

<table>
<thead>
<tr>
<th>Imaging</th>
<th>Bilateral opacities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etiology</td>
<td>Not fully explained by heart failure or volume overload</td>
</tr>
<tr>
<td>Timing</td>
<td>≤ 1 week since onset or insult</td>
</tr>
<tr>
<td>( \frac{\text{PaO}_2}{\text{FiO}_2} ) (P:F) ratio</td>
<td>calculated with ( \text{PaO}_2 ) as whole number (mmHg) and ( \text{FiO}_2 ) as decimal</td>
</tr>
<tr>
<td></td>
<td>(&lt; 300) (measured with PEEP ≥ 5 cmH2O)</td>
</tr>
</tbody>
</table>
ARDS

A1. low tidal volume ventilation over higher tidal volumes
(VT 4-8 mL/kg)

B2. prone ventilation for 12-16 hours per day for refractory hypoxemia despite optimized mechanical ventilation

C3. if still hypoxemic, recommend trial of inhaled pulmonary vasodilator; but if no rapid improvement in oxygenation, should be tapered off

Principles of ventilator settings

- We determine \( \rightarrow \) independent variables
- Ventilator Mode: volume or pressure cycled
- We measure \( \rightarrow \) dependent variables
- Peak pressure or tidal volume

Principles of ventilator settings

- We determine \( \rightarrow \) independent variables
  - Ventilator Mode: volume or pressure cycled
  - Oxygen Concentration (FiO\(_2\)): 0.21 - 1.0
  - Minimum Respiratory Rate: set rate
  - PEEP
- We measure \( \rightarrow \) dependent variables
  - Peak pressure or tidal volume
  - Plateau pressure
  - Auto PEEP (sometimes)

Ventilator mode most appropriate for acute hypoxemic respiratory failure

- Vent supports all breaths to a targeted tidal volume
- A minimum rate (RR) is set and delivered to the patient
- All spontaneous breaths will be supported to the same targeted volume
Independent Regulation of Ventilation and Oxygenation

**Assist/Control – Volume Control**


text: RR, VT, PEEP, FiO2

- Ventilation
- Oxygenation

\[ RR \times VT = \text{minute ventilation} = \text{volume of air moved per minute} \]

Initial settings — Hypoxemic respiratory failure with or at risk for ARDS

**Assist/Control – Volume Control**


text: RR, VT, PEEP, FiO2

- RR 18-24 bpm
- VT 6 mL/kg PBW
- PEEP 12-18 cmH₂O
- FiO₂ 1.0

**Key point:** The 6 mL/kg tidal volume is based on “predicted body weight”
- Males: PBW = 50 kg + 2.3 kg for each inch over 5 feet
- Females: PBW = 45.5 kg + 2.3 kg for each inch over 5 feet

**Key point:** Permissive hypercapnia is okay – low VT may require pH as low as 7.2

**Goals for “lung protection”**
- Low tidal volume: 4-8 mL/kg
- Plateau pressure < 30 cmH₂O
- Driving pressure < 15 cmH₂O

**Data:** Lung protective ventilation strategy is the only intervention that has been definitively shown to reduce mortality in patients with ARDS

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  - Minimum Respiratory Rate: set rate
  - PEEP

- We measure → dependent variables
  - Peak pressure or tidal volume
  - Plateau pressure
  - Auto PEEP (sometimes)

- We look for and respond to:
  - Oxygenation (PaO₂ or SpO₂)
  - Ventilation (pCO₂ and pH)
  - The Obvious: ventilator dysynchrony or “blowouts” like pneumothorax
  - The Occult: auto PEEP
Monitors
- Blood gas (arterial)
  - pH
  - PaCO2
  - PaO2
- Pulse oximetry
  - SpO2

Goals
- Oxygenation (FiO2 and PEEP)
  - PaO2 ~65 mmHg
  - SpO2 ~90%
- Ventilation (RR and Vt)
  - pH 7.2-7.45
- PaCO2
  - permissive hypercapnia except with increased intracranial pressure

Using plateau pressure
- Goal plateau < 30 cmH2O
- Goal driving < 15 cmH2O

Adjusting PEEP and FiO2
- OXYGENATION GOAL: PaO2 55-80 mmHg or SpO2 88-95%

<table>
<thead>
<tr>
<th>FiO2</th>
<th>PEEP</th>
<th>PIP/Drive</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>5</td>
<td>15/10</td>
</tr>
<tr>
<td>0.6</td>
<td>5</td>
<td>15/10</td>
</tr>
<tr>
<td>0.7</td>
<td>5</td>
<td>15/10</td>
</tr>
<tr>
<td>0.8</td>
<td>5</td>
<td>15/10</td>
</tr>
</tbody>
</table>

Lower PEEP/higher FiO2

<table>
<thead>
<tr>
<th>FiO2</th>
<th>PEEP</th>
<th>PIP/Drive</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>10</td>
<td>20/15</td>
</tr>
<tr>
<td>0.6</td>
<td>10</td>
<td>20/15</td>
</tr>
<tr>
<td>0.7</td>
<td>10</td>
<td>20/15</td>
</tr>
<tr>
<td>0.8</td>
<td>10</td>
<td>20/15</td>
</tr>
</tbody>
</table>

Higher PEEP/loweFiO2

<table>
<thead>
<tr>
<th>FiO2</th>
<th>PEEP</th>
<th>PIP/Drive</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>18</td>
<td>22/17</td>
</tr>
<tr>
<td>0.6</td>
<td>18</td>
<td>22/17</td>
</tr>
<tr>
<td>0.7</td>
<td>18</td>
<td>22/17</td>
</tr>
<tr>
<td>0.8</td>
<td>18</td>
<td>22/17</td>
</tr>
</tbody>
</table>
Prone positioning

- Early prone positioning in severe ARDS improves oxygenation and may have a mortality benefit
  - Consider early if P:F < 150 despite low tidal volume ventilation

- How it works:
  - ↓ compression of left lung by the heart
  - ↓ dependent atelectasis from interstitial edema
  - Allows more lung regions to be functional
  - Improves V/Q mismatch by impacting both blood flow and ventilation in more alveoli

Neuromuscular blockade

- 2010 ACURASYS trial → mortality benefit
- 2019 ROSE trial → no mortality benefit compared to lighter sedation

- Bottom line:
  - Not needed for all ARDS patients
  - Still useful for significant vent dysynchrony OR refractory hypoxemia/hypercapnia
  - If used:
    - Ensure adequate continuous sedation and analgesia
    - Ensure VTE prophylaxis

Troubleshooting

Using plateau pressure

- May be helpful in identifying/differentiating complications
  - Peak pressure (PIP) reflects airway resistance
  - Plateau pressure (Pplat) reflects lung/pleural compliance, elastic recoil
  - Peak minus plateau is normally < 5 cmH₂O
Causes of high peak pressure

- Mucus plugging
- Bronchospasm
- Biting endotracheal tube

Auto PEEP

- Also known as “dynamic hyperinflation” or “breath stacking”
- Incomplete exhalation before a new breath is delivered
- Why it is bad:
  - Inadequate ventilation
  - Increased intrathoracic pressure, can lead to cardiovascular compromise

Mucus plugging

- Increase in peak pressure, usually WITHOUT plateau pressure
- Decreased breath sounds on affected side, or bilaterally if plug is in ET tube or trachea
- May have asymmetric chest rise
- Should still have lung sliding on ultrasound, though may be lessened
- Confirmation with chest X-ray if not acutely hypoxemic
**Pneumothorax**

- Increase in peak pressure AND plateau pressure
- Decreased breath sounds, or hyperresonance, on affected side
- May have asymmetric chest rise, subcutaneous emphysema (later)
- Due to closed ventilator circuit, increasing intrathoracic pressure can have hemodynamic consequences = TENSION
- Lack of lung sliding on ultrasound
- Confirmation with chest X-ray if not acutely hypotensive

---

**Coagulopathy**

Incidence of VTE in COVID-19 ranges from 1.1% to 69%

---

**Outline**

- Respiratory failure
- ARDS
- Coagulopathy
- Special groups
- Outcomes

---

**Coagulopathy**

<table>
<thead>
<tr>
<th></th>
<th>American Society of Hematology</th>
<th>National Institutes of Health</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapeutic anticoagulation</td>
<td>continue some form</td>
<td>continue some form</td>
</tr>
<tr>
<td>Thromboprophylaxis</td>
<td>LMWH &gt; UFH &gt; mechanical</td>
<td>per standard of care</td>
</tr>
<tr>
<td>Empiric anticoagulation</td>
<td>clinical trials</td>
<td>clinical trials</td>
</tr>
<tr>
<td>Clotting devices</td>
<td>may be reasonable to increase intensity or switch anticoagulant</td>
<td>antithrombotic therapy per standard institutional protocols</td>
</tr>
<tr>
<td>Post-discharge thromboprophylaxis</td>
<td>not routinely, but consider VTE risk, bleeding risk, and feasibility</td>
<td>not routinely, but consider only if high VTE risk &amp; low bleeding risk</td>
</tr>
</tbody>
</table>

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*NIH treatment guidelines found at nih.gov
ASH treatment guidelines found at hematology.org*
Special groups increased need for precautions

<table>
<thead>
<tr>
<th>Individual situation</th>
<th>Living situation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Racial and ethnic minority</td>
<td>Rural communities</td>
</tr>
<tr>
<td>Disabled</td>
<td>Experiencing homelessness</td>
</tr>
<tr>
<td>Developmental disorders</td>
<td>Refugee populations</td>
</tr>
<tr>
<td>Behavior disorders</td>
<td>Nursing homes</td>
</tr>
<tr>
<td>Drug and substance use</td>
<td>Longer-term care facilities</td>
</tr>
<tr>
<td>disorders</td>
<td>Group homes</td>
</tr>
</tbody>
</table>

Pregnancy

↑ risk of hospitalization, ICU admission, and mechanical ventilation

• Management nuances:
  • Presume difficult airway
  • Left lateral decubitus position improves pre-load
  • Maintain SpO2 > 95%

Pregnancy and steroids

- betamethasone
- dexamethasone
- prednisolone

ARDS and steroids

- methylprednisolone
- dexamethasone

Steroids for pregnancy and COVID-19

- methylprednisolone
- dexamethasone

Steroids for pregnancy and COVID-19

- methylprednisolone
- dexamethasone
Steroids for pregnancy and COVID-19

- Methylprednisolone
- Dexamethasone

Pregnant with COVID-19 requiring supplemental oxygen

Glucocorticoids indicated for fetal lung maturity?
(24.0/7 to 33.6/7 weeks)

- No
- Yes

Methylprednisolone 32 mg/day x 10 days
Dexamethasone 6 mg IM q12hrs x 4 doses

Steroids for breastfeeding and COVID-19

- Methylprednisolone
- Dexamethasone

Pregnant with COVID-19 requiring supplemental oxygen

Glucocorticoids indicated for fetal lung maturity?
(24.0/7 to 33.6/7 weeks)

- No
- Yes

Methylprednisolone 32 mg/day x 10 days
Dexamethasone 6 mg IM q12hrs x 4 doses

Outline

- Respiratory failure
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Outcomes

• 1648 patients hospitalized with COVID-19 in Michigan March - July
  
  \[
  \begin{array}{|c|c|}
  \hline
  \text{24.2% mortality} & \text{75.8% survival} \\
  \hline
  \end{array}
  \]

• 60 days after discharge
  
  \[
  \begin{array}{|c|c|}
  \hline
  \text{29.2% mortality} & \text{70.8% survival} \\
  \hline
  \end{array}
  \]


Outcomes

• 405 patients receiving ICU treatment
  
  \[
  \begin{array}{|c|c|}
  \hline
  \text{63.5% mortality} & \text{36.5% survival} \\
  \hline
  \end{array}
  \]

• 15.1% of hospital survivors were rehospitalized within 60 days


Issues after discharge

• 488 (41.8%) were able to be contacted 60 days postdischarge
  • 159 with cardiopulmonary symptoms
  • 65 with anosmia or ageusia
  • 58 with ADL difficulties

• Of 195 employed prior to hospitalization:
  • 117 returned to work but 30 of those with reduced or modified duties
  • 78 could not return to work

• 238 emotionally affected by their health
• 179 financially impacted


Summary

Respiratory failure
ARDS
Coagulopathy
Special groups
Outcomes
References


Acknowledgements

• Drs. Lynn Fussner and Jeff Horowitz