Lessons Learned:
Calming the COVID-19 Storm

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Outcomes

At the conclusion of the presentation, participants will meet the following outcomes:

- Define the etiology, pathophysiology, and clinical presentation of COVID-19 and identify how to protect yourself and others from transmitting and acquiring COVID-19.
- Identify the current pharmacologic and non-pharmacologic treatment modalities including strategies to optimize oxygenation, ventilation, and perfusion and manage systemic effects and complications of COVID-19.
- Summarize how COVID-19 has transformed the care environment, the nursing workforce and education and how it will continue to impact the future of healthcare.

Disclaimers

The speakers declare that there are no financial relationships to disclose.

The speakers declare that there will be non-FDA approved drug and treatment trials discussed including: IL-6 antagonists, remdesivir, interferons, monoclonal antibodies, dexamethasone, and convalescent plasma.

Let’s talk about COVID-19…

COVID-19

- Most impactful pandemic since 1918 Spanish Flu
- SARS-CoV-2 first recognized in Wuhan, China in December 2019
- Declared a pandemic March 11, 2020
- March 2021 – more than 500,000 dead in the U.S. and more than 2.5 million deaths reported to WHO.

COVID-19 Transmission

Transmission

- Primarily transmitted through respiratory droplets
- Evidence of some airborne transmission
- Asymptomatic transmission
- Incubation period 2 to 14 days; median 4 to 5 days

Signs and symptoms

- Most people experience at least one of the following:
  - Congestion or rhinorrhea
  - Cough
  - Diarrhea
  - Fatigue
  - Fever or chills
  - Headache
  - Muscle or body aches
  - Nausea or vomiting
  - Shortness of breath and difficulty breathing

Severe to critical illness

- Some individuals rapidly deteriorate 1 week after illness onset; median time to acute respiratory distress syndrome ranges from 8 to 12 days.

- Signs of severe illness:
  - Dyspnea
  - Hypoxia
  - More than 50% lung involvement on chest imaging

  - Signs of critical illness:
    - Multisystem organ failure
    - Respiratory failure
    - Shock

How do we prevent transmission?

When SARS-CoV-2 infection isn't suspected

- For protection against exposure from asymptomatic or presymptomatic patients:
  - Facemask, N95 respirator, or respirator similar to NIOSH-approved filtering facepiece respirator
  - Eye protection
- For aerosol-generating procedures or surgical procedures that pose a higher risk for transmission:
  - N95 respirator, equivalent, or higher-level respirator
  - Eye protection

For suspected or confirmed SARS-CoV-2 infection

- Healthcare personnel who enter the patient's room should wear:
  - NIOSH-approved N95 or equivalent or higher-level respirator
  - Gown
  - Gloves
  - Eye protection

Vaccine approval

- December 11, 2020 Emergency Use Authorization (EUA) for Pfizer-BioNTech COVID-19 vaccine
- December 18, 2020 EUA for Moderna COVID-19 vaccine
- February 27, 2021 EUA for Johnson & Johnson's Janssen COVID-19 vaccine

Pfizer-BioNTech COVID-19 vaccine

- Messenger RNA vaccine; does not contain live virus
- Stored in an ultra-low temperature freezer until the expiration date printed on the label; or vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks
- May be thawed at room temperature for immediate use; or thawed under refrigeration for up to 5 days
- Requires 2 IM injections (0.3 mL each), 3 weeks apart
- Adverse reactions—anaphylaxis; other hypersensitivity reactions; injection site pain, swelling, and redness; fatigue; headache; muscle pain; chills; joint pain; fever, nausea, malaise, and lymphadenopathy

Moderna COVID-19 vaccine

- Messenger RNA vaccine; does not contain live virus
- Requires storage in a freezer between -25°C and -15°C (-13°F and 5°F); or may be stored in the refrigerator between 2°C and 8°C (36°F and 46°F) for up to 30 days before vials are punctured
- Maybe thawed in the refrigerator or thawed at room temperature for immediate use
- Requires 2 IM injections (0.5 mL each), one month apart
- Adverse reactions—anaphylaxis, pain, swelling, and erythema at the injection site; fatigue; headache; myalgia; arthralgia; chills; nausea; vomiting; axillary swelling and tenderness; and fever

Johnson & Johnson's Janssen COVID-19 vaccine

- Viral vector vaccine; uses a different virus as a vector
- Requires storage of unpunctured vials at 2°C to 8°C (36°F to 46°F); unpunctured vials may also be stored between 9°C to 25°C (47°F to 77°F) for up to 12 hours
- May be thawed in the refrigerator or thawed at room temperature for immediate use
- Requires one IM injection (0.5 mL)
- Adverse reactions—anaphylaxis; pain, swelling, and erythema of the injection site; fatigue; headache; myalgia; arthralgia; chills; nausea; vomiting; axillary swelling and tenderness; and fever

Vaccine administration

- April 25, 2021 CDC reports 228.6 million total vaccine doses administered; 42.2% of the population received one or more doses
- 94.7 million individuals fully vaccinated; 28.5% of total population

Let’s talk about testing and testing capacity

Testing

- Sensitivity versus specificity
- Polymerase chain reaction (PCR) testing detects viral genetic material; highly sensitive and highly specific
- Rapid antigen testing detects one or more proteins from a virus particle; less sensitive, but highly specific

Testing in the U.S.

- January 20, 2020 U.S. document the first U.S. case of COVID-19
- By May 4, 2020, U.S. performed 7.1 million tests
- April 23, 2021 CDC reports 408,792,038 tests performed; 33,944,127 total positive tests; 8.3% total % positive

Why test?

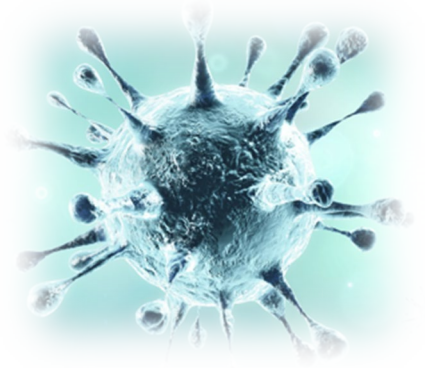
- Helps determine the true number of cases and their location
- Assists with understanding asymptomatic transmission
- Helps guide restrictions and reopening

Let’s talk about managing COVID-19…

Management of mild symptoms

- Mild – up to 80% of cases
  - S/S: “Fever, dry cough, shortness of breath”
    - Loss of taste and smell
    - Others: myalgias, headache, nasal congestion, rhinorrhea, viral conjunctivitis, sore throat, diarrhea
- Management – stay at home
  - Self isolation
  - Symptom management
  - Rest
  - Nighttime is worse for symptoms - sleep propped on pillows

Cytokine storm – driving the severity of illness



Immune cells recognize virus

Cytokines (interferon, TNF's) released

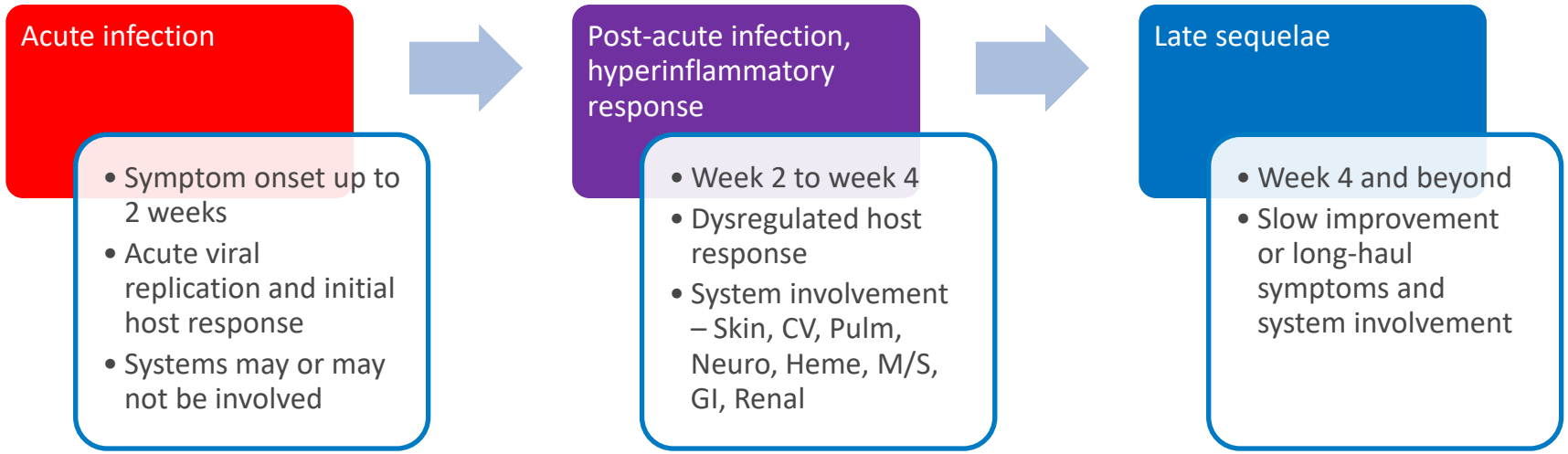
Chemokines (IL-6, IL 10, more TNF-alpha) released

Macrophages, CD-4, CD-9 recruited

Inflammatory overdrive- multi-organ dysfunction (vascular leakage, coagulopathy, DIC, cardiomyopathy)

Normal immune response

Timeline for infection and inflammation



Oxygen demand is higher than oxygen supply!

Goal: Optimize oxygenation

- Cardinal symptom: They can’t breathe no matter what position!
- Management recommendations (AACN, NIH, SCCM)
  - Supplemental oxygen if the SpO2 is less than 90%; consider if less than 92%
  - Oxygen therapy
    - Nasal cannula
    - High flow nasal cannula – preferred in acute hypoxemic respiratory failure
      - Use low flow in non-negative pressure room
    - 100% non-rebreather mask
    - HFNC with non-rebreather mask

Non-invasive ventilation

- CPAP (Continuous Positive Airway Pressure)
  - Method of choice – delivers constant flow of pressure during inspiration and expiration
  - Does not cause increase in tidal volume (Vt); less barotrauma
  - Initial settings: CPAP 10 cm H2O; 60% to 100% FiO2; titrate to keep SpO2 between 92% and 96%
  - CPAP methods
    - Full face mask
    - Nasal mask
    - Nasal pillows
    - Helmet – can result in claustrophobia

- BiPAP (Bi-Level Positive Airway Pressure)
  - Most commonly used in patients with underlying COPD
  - Can increase tidal volume (Vt) resulting in barotrauma
  - Gives different pressures for inspiration (IPAP) and expiration (EPAP)
  - Monitor closely for pneumothorax

COVID-19 Sepsis

- Definition: life-threatening organ dysfunction caused by dysregulated host response to suspected or proven infection

- Signs and Symptoms
  - Severe dyspnea and hypoxemia
  - Renal impairment with reduced urine output
  - Tachycardia
  - Altered mental status
  - Hyperbilirubinemia
  - Acidosis
  - High lactate level
  - Coagulopathy
  - Thrombocytopenia

COVID-19 Sepsis diagnostics

- Diagnostics
  - CXR
  - Consider CT Scan of Chest
- 12 lead ECG – medications effect QTc
- Labs
  - Cultures – blood, urine, sputum
  - CBC with differential
  - Chemistry, Mg, Phosphorus
  - Liver function tests
  - Lactate level
  - Inflammatory markers – CRP, D-Dimer, ferritin
  - Troponins
  - Coagulation studies
  - LDH
  - Hepatitis B, Hepatitis C, HIV, QuantiFERON BP Gold (for latent TB) – if considering tocilizumab

COVID-19 Septic Shock management

- Antibiotics for secondary bacterial pneumonia
- MAP > 60 to 65 mm Hg
  - Conservative versus liberal volume resuscitation - use buffered crystalloid – lactated ringers solution
  - Vasopressors
    - Norepinephrine 1st line
    - Vasopressin 2nd line
    - Epinephrine
    - Dobutamine – to increase cardiac output

Let’s talk about acute respiratory failure…

Acute Respiratory Failure

Type 1

- **Hypoxemia (PaO2 less than 60 mm Hg)**
- **Problem is oxygen**
- Cardiogenic cause
  - Pulmonary edema
- Noncardiogenic cause
  - COVID-19 Pneumonia
  - Pneumonia
  - Pulmonary hemorrhage
  - Pulmonary embolism

Type 2

- **Hypercarbia (PaCO2 greater than 50 mm Hg)**
- **Problem is carbon dioxide**
  - Hypoventilation secondary to
    - Drug overdose
    - Neuromuscular disease
  - Hypercarbia secondary to
    - Asthma
    - COPD
    - Pulmonary embolism

Can you tell who is at risk for intubation?

- Overweight and obese people make up 78% of patients hospitalized for COVID-19
- Pulmonary involvement – rapidly progressing infiltrates on CXR
- Acute hypoxic respiratory failure
  - Pa02/FiO2 ratio less than 300
  - SpO2 decreasing – less than 92%-93%
- Elevated inflammatory markers
  - CRP greater than 10 times normal
  - D-Dimer greater than 10 times normal
  - Ferritin greater than 1,000 ng/mL
  - LDH greater than 2 times the upper limit

Defining acute respiratory distress syndrome (ARDS)

- Definition – acute onset of hypoxia and pulmonary infiltrates and incited by conditions such as sepsis, pneumonia, trauma, burns, pancreatitis, blood transfusions
- Berlin Criteria (ARDS Task Force, 2012)
  - PaO_2 / FiO_2 ratio – degree of hypoxemia on 5 cm or greater of PEEP
    - Mild: 200 to 300
    - Moderate: 100 to 199
    - Severe: less than 100
  - Variables – radiographic severity, PEEP, corrected expired volume/minute, respiratory compliance

Lung compliance is the differentiator

- Static compliance – “lungs not moving, lungs at rest”; pressure is the only variable
- Dynamic compliance – “lungs moving, lungs at work”

- Examples
  - COPD – elastic recoil is damaged which leads to high compliance – needs less pressure to inflate lungs
  - Pulmonary fibrosis – collagen buildup in fibers which makes them stiff and leads to low compliance – needs more pressure to inflate lungs
  - Typical ARDS – hypoxemia with atelectasis in dependent lung areas – low compliance – needs more pressure to inflate lungs

COVID-19 ARDS: Ventilation and perfusion issues

Things to consider

- Severe hypoxemia
  - Beware of silent hypoxemia
- New research is pointing to local lung inflammation from COVID virus and inflammatory response as causing respiratory dysfunction
- Higher lung compliance than typical ARDS initially; as lungs worsen – need more pressure to inflate the lungs – require higher PEEP
- Inability to regulate lung perfusion and hypoxic vasoconstriction
- Remember: Ventilation is as important as perfusion!
- Have end of life discussion early! – Low chance of getting off ventilator

Intubation

- Intubation – high risk of aerosolization!
  - Performed by most experienced person present – use PAPR if available
  - Negative pressure room
  - Airborne precautions
  - Preoxygenate using 100% NRB or CPAP; do not use bag-valve-mask
- Insert arterial and central venous lines at this time to bundle care while patient is sedated, and clinicians are in full PPE
- Put lines on same side in anticipation of prone positioning

Managing the mechanically vented patient

- Low tidal volume (Vt) ventilation strategy
  - Vt 4 to 8 mL/kg predicated body weight; most common 6 mL/kg PDW
- Target plateau pressure less than 30 cm H2O
  - If elevated – decrease Vt or PEEP
- Moderate to severe ARDS, consider higher PEEP strategy (greater than 10 cm H2O)
  - PEEP must be high enough to maintain the driving pressure (Pplat-PEEP) as low as possible (less than 14 cm H2O)
- Consider pressure-limited modes or volume targeted pressure-controlled ventilation modes with vent dyssynchrony
- Patients with hypoxemia despite optimized ventilation – consider recruitment maneuvers

Sedation and analgesia

- Keep RASS lower – commonly 3 to 4; give sedation vacations daily
  - Agents
    - Opioid infusion preferred; can use opioid via feeding tube if shortage
    - Propofol infusion – monitor triglycerides every 3 days
    - Dexmedetomidine infusion
    - Benzodiazepine infusion
    - Paralytics – prefer bolus dosing; may need infusion with proning
      - Always sedate when giving a paralytic agent

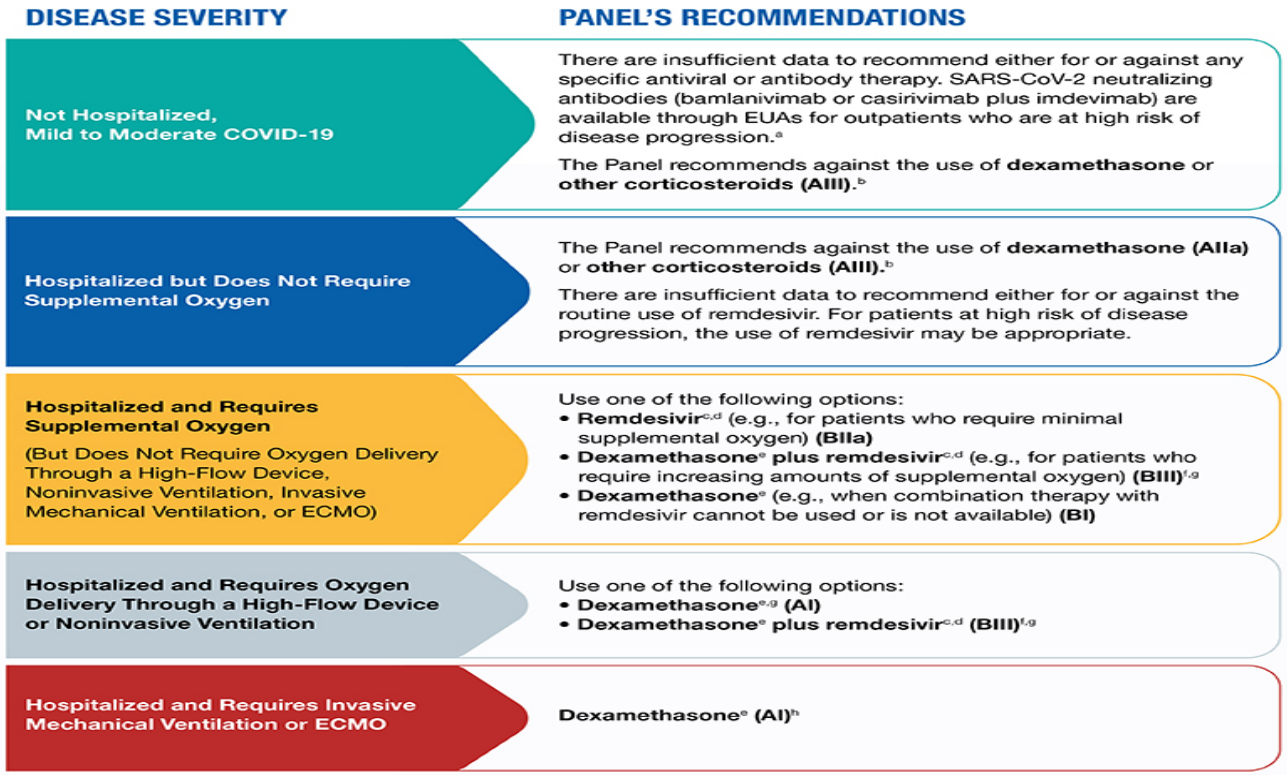
Ventilator weaning and extubation

- Ventilator weaning
  - Slower is better
  - Patients look stable, and then decline rapidly
- Consider tracheostomy
  - After 14 to 21 days; sooner maybe better
  - Consider trach team
- Extubation – high risk of aerosolization
  - Negative pressure room
  - Minimal number of people present
  - PAPR if available

What medications are available to manage COVID-19?

Figure 1. Pharmacologic Management of Patients with COVID-19 Based on Disease Severity

Doses and durations are listed in the footnote.



DISEASE SEVERITY	PANEL'S RECOMMENDATIONS
Not Hospitalized, Mild to Moderate COVID-19	There are insufficient data to recommend either for or against any specific antiviral or antibody therapy. SARS-CoV-2 neutralizing antibodies (bamlanivimab or casirivimab plus imdevimab) are available through EUAs for outpatients who are at high risk of disease progression.[a] The Panel recommends against the use of **dexamethasone** or **other corticosteroids (AIII)**.[b]
Hospitalized but Does Not Require Supplemental Oxygen	The Panel recommends against the use of **dexamethasone (AIIa)** or **other corticosteroids (AIII)**.[b] There are insufficient data to recommend either for or against the routine use of remdesivir. For patients at high risk of disease progression, the use of remdesivir may be appropriate.
Hospitalized and Requires Supplemental Oxygen (But Does Not Require Oxygen Delivery Through a High-Flow Device, Noninvasive Ventilation, Invasive Mechanical Ventilation, or ECMO)	Use one of the following options: • **Remdesivir**[c,d] (e.g., for patients who require minimal supplemental oxygen) **(BIIa)** • **Dexamethasone**[e] **plus remdesivir**[c,d] (e.g., for patients who require increasing amounts of supplemental oxygen) **(BIII)**[f,g] • **Dexamethasone**[e] (e.g., when combination therapy with remdesivir cannot be used or is not available) **(BI)**
Hospitalized and Requires Oxygen Delivery Through a High-Flow Device or Noninvasive Ventilation	Use one of the following options: • **Dexamethasone**[e,g] **(AI)** • **Dexamethasone**[e] **plus remdesivir**[c,d] **(BIII)**[f,g]
Hospitalized and Requires Invasive Mechanical Ventilation or ECMO	**Dexamethasone**[e] **(AI)**[h]

Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

[a] See the Anti-SARS-CoV-2 Monoclonal Antibodies section for more information on using bamlanivimab and casirivimab plus imdevimab in patients with mild to moderate COVID-19.
[b] Patients who are receiving corticosteroids for other indications should continue therapy for their underlying conditions as directed by their health care providers.
[c] The remdesivir dose is 200 mg IV for one dose, followed by remdesivir 100 mg IV once daily for 4 days or until hospital discharge (unless the patient is in a health care setting that can provide acute care that is similar to inpatient hospital care). Treatment duration may be extended to up to 10 days if there is no substantial clinical improvement by Day 5.
[d] For patients who are receiving remdesivir but progress to requiring oxygen through a high-flow device, noninvasive ventilation, invasive mechanical ventilation, or ECMO, remdesivir should be continued until the treatment course is completed.
[e] The dexamethasone dose is 6 mg IV or PO once daily for 10 days or until hospital discharge. If dexamethasone is not available, equivalent doses of other corticosteroids (e.g., prednisone, methylprednisolone, hydrocortisone) may be used. See the Corticosteroids section for more information.
[f] The combination of dexamethasone and remdesivir has not been studied in clinical trials.
[g] In the rare circumstances where corticosteroids cannot be used, **baricitinib plus remdesivir** can be used **(BIIa)**. The FDA has issued an EUA for baricitinib use in combination with remdesivir. The dose for baricitinib is 4 mg PO once daily for 14 days or until hospital discharge.
[h] The combination of **dexamethasone and remdesivir** may be considered for patients who have recently been intubated **(CIII)**. The Panel **recommends against** the use of remdesivir monotherapy in these patients.

Key: ECMO = extracorporeal membrane oxygenation; EUA = Emergency Use Authorization; FDA = Food and Drug Administration; IV = intravenous; the Panel = the COVID-19 Treatment Guidelines Panel; PO = orally; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2

Outpatient therapies

- 2 therapies available
- Bamlanivimab + etesevimab
- Casirivimab + imdevimab
- Mechanism of action: SARS CoV2 monoclonal antibody; targets spike proteins; prevents replication and decreases symptoms and limits disease progression
- Indication: Patients with mild to moderate COVID-19 who are at high risk of progressing to severe disease and hospitalization
- Dosage and administration
  - Bamlanivimab + etesevimab Administration: banlanivimab 700 mg + etesevimab 1400 mg IV infusion x 1
  - Casirivimab + imdevimab administration: 1200mg of casirivimab and 1200mg of imdevimab via IV infusion x 1
  - Infusion rate dependent on diluent amount – see package insert
  - Should not receive Messenger RNA vaccine for 3 months after receiving these medications

Dexamethasone

- Dexamethasone
  - Mechanism of action: decreases the inflammatory response
  - Indication: COVID-19 + patients on supplemental oxygen
  - Dose:
    - 6 mg IV or orally for 10 days
    - What if dexamethasone isn’t available:
      - Prednisone 40 mg daily
      - Methylprednisolone 32 mg daily
      - Hydrocortisone 160 mg daily

Remdesivir

- Remdesivir – only drug approved to treat COVID-19 by FDA; all others have emergency use authorization
  - Mechanism of Action: binds to viral RNA inhibiting viral replication
  - Indication: hospitalized patients requiring supplemental oxygen
  - Pretests:
    - Liver function tests
    - Coagulation studies (PT/INR, PTT)
    - Creatinine, BUN and GFR
  - Dose:
    - 200 mg IV for day 1; 100 mg IV daily for 4 more days; total of 5 days
    - Caution: can cause GI upset and increase in transaminases (alanine transaminase (ALT); if ALT increases to 10 times the upper limits; stop the drug
    - Don’t use if the patient has elevated LFTs (metabolized through CYP450 system)or GFR less than 30 ml/minute (component cleared through kidneys)

Tocilizumab

- Tocilizumab (IL-6 inhibitor; blocks IL-6 receptor)
  - Mechanism of action: IL-6 promotes endothelial dysfunction and development of vascular permeability; the drug blocks the IL-6 receptor decreasing endothelial dysfunction and vascular permeability
    - Decreases fever
    - Decreases use of oxygen support and mechanical ventilation
    - Decreases lung manifestations/involvement
  - Indication: +COVID, progressing pulmonary involvement, SpO2 less than 93%, Pa02/Fi02 ratio less than 300 and at least 3 of the following:
    - CRP greater that 10x normal (equal or over 75)
    - Ferritin greater than 1,000 ng/mL
    - D-Dimer greater than 10 times normal
    - LDH greater than 2 times the upper limit
  - Pretests:
    - Hepatitis B, Hepatitis C, HIV and QuantiFERON TB Gold
  - Dose: 8 mg/kg (maximum dose is 800 mg) IV over 60 minutes

Other treatments

- Convalescent plasma
  - Inadequate evidence to recommend use except in clinical trials

- Extracorporeal membrane oxygenation (ECMO) – for refractory hypoxemia despite lung-protective ventilation, prone positioning, PEEP and recruitment maneuvers, neuromuscular blocking agents, pulmonary vasodilators (NIH – evidence not adequate for recommendation)
  - Criteria exclusion: age > 65-70 years, morbid obesity, severely immunocompromised, advanced chronic systolic heart failure
  - Absolute Contraindications:
    - Multiorgan failure
    - Severe neurologic injury or hemorrhage
    - Cardiac arrest with prolonged down time

Let’s talk about proning…

Prone positioning

- Positioning on the stomach with the head to the side
- Prone positioning:
  - improves ventilation/perfusion matching
  - reduces hypoxemia
  - reduces shunting
  - improves recruitment of posterior lung segments
  - helps clear secretions

Proning the nonventilated patient

- To prone or not to prone?
  - Prior recommendations--may prevent intubation in patients with acute respiratory failure or delay intubation until patient further deteriorates and becomes more hypoxemic
  - January 2021 Society of Critical Care Medicine COVID treatment guidelines state that there's insufficient evidence to issue a recommendation on the use of prone positioning for in nonintubated adults with severe COVID-19.
  - February 2021 NIH COVID-19 treatment guidelines recommend considering awake prone positioning for patients with persistent hypoxemia despite increasing supplemental oxygen if endotracheal intubation isn't otherwise indicated.
  - NIH recommends against using awake prone positioning as a rescue therapy for refractory hypoxemia to avoid intubation in patients who otherwise meet the indications for intubation and mechanical ventilation.

Proning the ventilated patient

- Use a systematic team approach to prevent:
  - Accidental extubation
  - Airway occlusion
  - Catheter dislodgement
- Relocate ECG leads to patient's back.
- Maintain lines on one side of the patient, if possible
- Protect the eyes and skin
- Preoxygenate, and suction, as needed before turning
- Secure artificial airway
- Provide adequate sedation
- Compensate for decompensation with hyperoxygenation and vasopressor titration, as needed
- Maintain prone positioning for more than 12 hour per day (Wilson, 2020)

Let’s talk about multi-organ dysfunction and failure…

Recognizing myocardial dysfunction

Increased risk for acute coronary syndrome, secondary to increased myocardial demand, or plaque rupture or instability. May also develop cardiomyopathy and heart failure.

- Elevated troponin levels
- Elevated creatine kinase
- Elevated myoglobin
- Elevated BNP
- Evidence of more severe systemic inflammation
  - Higher WBC counts
  - Higher C-reactive protein levels
  - Higher procalcitonin levels

Managing myocardial dysfunction

Treatment for myocardial injury

- Emergent thrombolysis, unless contraindicated, for ST-segment elevation MI
- Avoid aggressive fluid resuscitation because of oxygenation challenges
- Norepinephrine for hypotension to achieve a MAP of 60 to 65 mm Hg
- Dobutamine for worsening hypotension with cardiac dysfunction
- Epinephrine and vasopressin for refractory hypotension
- NIH guidelines now suggest there are insufficient data to recommend either for or against ECMO in patients with COVID-19 and refractory hypoxemia.

Recognizing neurologic effects

- Most hospitalized patients have neurologic symptoms, which may include
  - Headache
  - Dizziness
  - Altered taste and smell
  - Muscle weakness
  - Delirium
  - Seizures
  - Stroke
- Neurologic symptoms likely a result of immune response to infection; not viral infection of the brain or nervous system

A look at coagulopathy

COVID-19-associated coagulopathy differs from DIC.

- Elevations in fibrinogen
- Elevations in D-dimer
- PTT elevation, less than PT elevation (may be caused by increased factor VIII levels)
- Mild thrombocytopenia

Some patients with severe COVID-19 infection do develop traditional DIC

- Decreased fibrinogen (drops dramatically over a few days)
- Marked elevations in D-dimer
- PTT and PT elevations
- Moderate to severe thrombocytopenia

Managing the clot burden and bleeding

Treatment for COVID-associated coagulopathy

- Avoid blood products unless active bleeding
- For active bleeding
  - Transfuse platelets for platelet count less than 50 x 10^9/L
  - Transfuse plasma for INR greater than 1.8
  - Transfuse cryoprecipitate for fibrinogen less than 1.5 g/L
- Prophylactic low-molecular-weight heparin (unless platelet count falls below 25 x 10^9/L, or fibrinogen falls below 0.5 g/L)

VTE prophylaxis and treatment recommendations

- Patients not requiring intensive care
  - Without evidence of venous thromboembolism (VTE) – standard dose for VTE prophylaxis
  - Evidence of VTE – therapeutic anticoagulation dose
- Patients requiring intensive care
  - Without evidence of VTE—standard dose if in noninflammatory phase; evidence variable for inflammatory phase
  - Evidence of VTE – therapeutic anticoagulation dose
- Extended out of hospital prophylaxis for VTE no longer recommended, unless patient at high risk

Anticoagulation Regimes

Clinical Consideration	Standard	Intermediate (evidence variable)	Therapeutic (for Dx VTE)
CrCL greater than 30 mL/minute	LMWH 40 mg every 24 hours	LMWH 0.5 mg/kg every 12 hours	LMWH 1 mg/kg every 12 hours
CrCL greater than 15 mL/minute or less than 30 mL/minute	LMWH 30 mg every 24 hours or UFH 5,000 units every 8 or 12 hours	UFH 7,500 units every 8 hours	LMWH 1 mg/kg daily or UFH bolus + infusion
CrCL less than 15 mL/minute or receiving CRRT	UFH 7,500 units every 8 hours	UFH 7,500 units every 8 hours	UFH bolus + infusion

Recognizing acute kidney injury

In addition to insults associated with shock, novel coronavirus damages the kidneys.

Imbalances more profound than commonly seen in acute kidney injury

- Hyperkalemia
- Hyperphosphatemia
- Profound metabolic acidosis

A look at treatment for acute kidney injury

- Patients develop coagulopathy– run UFH or argatroban precircuit
- Continuous renal replacement therapy (CRRT)
  - Dialysis provided around-the-clock for those who develop hemodynamic instability
  - Complicated by circuit clotting
  - Limited number of dialysis machines due to demand
- Sustained low-efficiency daily dialysis (SLEDD)
  - Standard dialysis machine, and lower dialysate and blood-flow rates over a longer period of time
- Prolonged intermittent renal replacement therapy (PIRRT)
  - Uses CRRT machines running at higher clearances for 8 to 12 hours so the machine can be used for the next patient

Recognizing and managing GI dysfunction

- Nausea and vomiting
- Diarrhea – can signify a higher viral load burden
  - Dehydration risk – difficult to manage with conservative volume replacement strategy
- Hepatic dysfunction
  - AST, ALT, total bilirubin and direct bilirubin – possible damage due to direct virus effects, excessive immune reaction, shock and hypoperfusion, drug induced injury

How has healthcare transformed as a result of COVID-19?

What did we learn from 2020?

- **The healthcare system was fractured and started going off the rails**
  - Supply and demand issues – space, equipment, etc.
  - Lack of the latest evidence and clinical guidelines
  - The primary care delivery model failed in the crisis
  - The financial impact was catastrophic
  - Nursing education needed to evolve

- **Innovation and creativity created a healthcare revolution**
  - Repurpose the old to make way for the new - space, older equipment
  - New medical devices, medications and procedures
  - Nursing education goes virtual including simulation replacing clinical hours
  - Focus on workforce agility and efficiency
    - Educate differently – rapid onboarding/cross-training, simulation in practice and academia
    - Developed new care delivery models – Interdisciplinary Team model, Telehealth
    - Leverage transition to practice – practice/academic partnerships, residency programs, developing clinical judgement in new nurses

- **The most valuable commodity in healthcare is the workforce; workforce resiliency is the cornerstone of the future**

Thoughts for the future…

1. The nursing workforce needs to be agile and efficient to meet the needs of the people it serves – “multispecialty nurse”
   - Rapid-onboarding, cross-training
   - It’s all about supply and demand - Nursing workforce supply must meet the patient demand
2. In practice settings, training and onboarding need to change
   - Microlearning
   - No time or budget to take workforce off the units – virtual learning and training
3. Alternative care models are here to stay
   - Care models need to evolve based on the situation
   - Telehealth - the future of patient access to care
4. Nursing education will need to continue to evolve and innovate quickly and partner with practice
   - On-line and hybrid models – will be the norm
   - Simulation – more important since clinical time has been reduced
   - Faculty shortage – needs to be addressed
   - Need to feed the nurse pipeline - will preceptors be available?
5. It takes a collaborative team…Collaboration between education settings, practice settings, and between disciplines has never been more important
6. Resilience of the nursing and healthcare workforce is key to future healthcare success
   - Value the workforce to keep the talent inhouse – provide the evidence, adequate staffing, and a safe environment
   - Give the workforce time-off, address the issues of burnout, moral injury and resilience

Let’s sum it up…

Just the facts…

- Case mortality rate – .25% to 10% compared to .1% seasonal influenza (depends on age, comorbidities, and country)
- 80% of patients will be asymptomatic or have mild illness
- 20% or less of patients will have moderate to severe disease and need hospitalization
- Moving less patients to the ICU because we have therapies that are decreasing the need for mechanical ventilation
- Highest risk patients – over 65 years, have comorbidities (heart, lung, and kidney disease, immunocompromised

Take-aways…

- Vaccine distribution remains slow, but the number of vaccinated individuals increases daily
- Hand hygiene, social distancing, and masking wearing makes a difference
- We continue to learn how to better treat patients with COVID-19

Thank you for being a frontline hero!

A health care worker in the Atlas pose holding up the earth by Brigitte Dawson and Melissa Turner of Melbourne's Murals.

Location: Black Rock

Questions?

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