Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

CHAPTER 8

Infectious Disease Emergencies

Sepsis and Septic Shock

Presentation

Sepsis is a potentially fatal emergency leading to more than 200,000 deaths in the United States each year.[1] Following the convening of the Third International Consensus Definitions Task Force by the Society of Critical Care Medicine and the European Society of Intensive Care Medicine, the Surviving Sepsis Campaign published updated sepsis guidelines in 2016.[2]

According to 2016 guidelines, sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. Definitions such as Systemic Inflammatory Response Syndrome and Severe Sepsis were removed from the guidelines. The guidelines recommend to use the Sequential (Sepsis-Related) Organ Failure Assessment (SOFA) score to rapidly identify patients with sepsis. Septic shock is defined as sepsis with persistent hypotension requiring vasopressors to maintain mean arterial pressure (MAP) $\geq$ 65 mmHg and a serum lactate $>$ 2 mmol/L (18 mg/dL) despite adequate volume resuscitation.[3]

Significant reduction in mortality was associated with early identification of sepsis, initiation of a 1-h care bundle, and rapid administration of broad-spectrum antibiotics. Risk factors for sepsis include ages 65–84,[1] chronic comorbidities, immunocompromised status, and traumatic injury.[2]

Symptoms include systemic symptoms such as fever, shaking chills, sweating, malaise, altered mental status, and localizing symptoms related to the source of infection. On examination, patient will have cold and clammy skin, tachycardia, tachypnea, and hypotension.

Causes for Rapid Response Activation

Tachycardia, hypotension, altered mental status.

Actions

INITIAL MEASURES

1. Maintain continuous pulse oximetry.
2. Administer supplemental oxygen to maintain $SpO_2 > 92\%$.
3. Maintain continuous cardiac monitoring.
4. Perform quickSOFA (qSOFA) score for patients outside the ICU:
   - Elevated respiratory rate $\geq$ 22 breaths per minute
   - Altered mental status (Glasgow Coma Scale score $<$ 15)
   - Systolic blood pressure of 100 mmHg or less
5. Calculate SOFA score for ICU patients based on the following factors:
   - PaO_2/FiO_2 (mmHg)
   - SaO_2/FiO_2

- Platelets $\times 10^3/mm^3$
- Bilirubin (mg/dL)
- Hypotension
- Glasgow Coma Scale
- Creatinine (mg/dL) or urine output (mL/day)

6. Patients with an increase of 2 or more in the SOFA score have an estimated in-hospital mortality of 10% due to sepsis and a 2- to 25-fold increased risk of death compared with patients with a SOFA score of < 2.[4]

DIAGNOSTIC WORK-UP

1. Labs: CBC (leukocytosis, left shift, bandemia, thrombocytopenia), CMP (hyperglycemia, organ dysfunction such as elevated creatinine or liver enzymes), procalcitonin (elevated in bacterial and fungal infection), lactate, coagulation studies (INR > 1.5), and UA (urinary tract infection).
2. Lactate levels greater than 2 mmol/L should be remeasured within 2–4 h to ensure the level is decreasing.
3. Order aerobic/anaerobic blood cultures prior to initiation of antibiotics, however, this should not delay administration of antibiotics within the first one hour of presentation.
4. Obtain other site-specific cultures, such as urine, sputum, and wound cultures.
5. Order EKG to assess for myocarditis or pericarditis.
6. Order site-specific imaging focused on source of infection.
7. Order site-specific invasive procedures to evaluate and/or treat source of infection—for example, transesophageal echo in patients with suspicion of valvular endocarditis; thoracentesis in patients with pleural effusion; paracentesis in patients with ascites, drainage of abscess, debridement and bone biopsy in osteomyelitis; and lumbar puncture.

TREATMENT

1. For fluid resuscitation, start normal saline 30 mL/kg IV within first 3 h for hypotension (mean arterial pressure ≤ 65 mmHg) or lactate ≥ 4 mmol/L.[5]
2. Further fluid administration is guided by:
   - Heart rate, blood pressure, arterial oxygen saturation, respiratory rate, temperature, and urine output
   - Passive leg raises
   - Bedside echocardiography
   - Other invasive and noninvasive techniques[5]
3. If hypotension (mean arterial pressure ≤ 65 mmHg) persists despite adequate volume resuscitation within first 3 h of presentation, add vasopressor and place arterial line.[5]
4. First-line vasopressors include:
   - Norepinephrine 5–15 μg/min IV infusion; usual maintenance dose range 2–80 μg/min[6]
   - Vasopressin 0.03 units/min to be added to decrease the dose of norepinephrine or to achieve the goal MAP ≥ 65 mmHg[5]
5. Second-line vasopressors include:
   - Epinephrine 1–15 μg/min IV infusion; usual maintenance dose range 1–40 μg/min[6]
6. Dobutamine is recommended for patients with persistent hypoperfusion despite adequate intravascular volume and vasopressor administration[5]:
   - Dobutamine 0.5–1 μg/kg/min IV infusion; usual maintenance dose range 2–20 μg/kg/min[6]
7. Initiate broad-spectrum empiric antimicrobials within 1 h of presentation[5]:
   - Administer piperacillin/tazobactam 4.5 g IV q 6 h[7] and vancomycin 15 mg/kg IV q 12 h with goal troughs of 15–20 mg/L.[8]
   - When candidemia is suspected, consider anidulafungin 200 mg IV day 1, followed by 100 mg IV daily starting day 2 thereafter.[9]

8. Deescalate antibiotics once pathogen and sensitivities are known.
9. Identify and control source of infection.
10. Remove old intravascular catheters.[5]
11. Administer hydrocortisone 200 mg IV daily in divided doses if fluid resuscitation and vasopressors fail to achieve hemodynamic stability, continue until vasopressors are no longer required.[1]
12. For blood products use:
    - Red blood cells if Hg < 7 g/dL, except in active ischemic myocardial disease, acute hemorrhage, or persistent severe hypoxia.
    - FFP in patients with bleeding and coagulation abnormalities or planned procedures.
    - Platelet transfusion for levels ≤ 10,000/mm^3 in the absence of bleeding or below ≤ 20,000/mm^3 if there is a high risk of bleeding, and for patients with active bleeding or planned surgery/invasive procedures if platelets ≤ 50,000/mm^3.
13. Start intubation and mechanical ventilation in sepsis-induced acute respiratory distress syndrome (ARDS):
    - Assist control or volume assist
    - Inspiratory to expiratory ratio (I/E) of 1:1 to 1:3
    - RR: 20–35 breaths per minute
    - Lower tidal volumes 6 mL/kg of predicted body weight:
      - Male: PBW (kg) = 50 + 2.3(height(in)-60)
      - Female: PBW (kg) = 45.5 + 2.3(height(in)-60)
    - Higher PEEP: start at 12 cm of H_2O, increase up to 28–30 cm of H_2O in severe ARDS
    - Plateau airway pressure ≤ 30 cmH_2O to avoid barotrauma[10]
14. Assure prone positioning in patients with PaO_2/FIO_2 ratio ≤ 150 mmHg.[5]
15. Use conservative fluid infusion in patients with ARDS.[5]
16. Use neuromuscular blocking agents for ≤ 48 h in patients with sepsis-induced ARDS and PaO_2/FIO_2 ratio ≤ 150 mmHg.[5]
17. Glucose control:
    - Glucose levels should be checked every 1–2 h until a stable insulin regimen is reached and every 4 h thereafter.
    - Target blood glucose level is 110–180 mg/dL.[5]
18. Administer sodium bicarbonate in patients with pH < 7.15.[5]

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Acute Hypoxemic Respiratory Failure Due to Severe Pneumonia

Presentation

Community-acquired pneumonia (CAP) is one of the most common infectious diseases. The American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA) 2019 guidelines recommend to abandon the healthcare-associated pneumonia category and place emphasis on local epidemiology and validated risk factors to determine the need for MRSA or *P. aeruginosa* coverage.[1]

This section will cover severe CAP. According to ATS/IDSA 2019 guidelines, the definition of severe pneumonia includes either one major criterion or three or more minor criteria.

Minor criteria:

- Respiratory rate > 30 breaths/min
- PaO_2/FIO_2 ratio < 250
- Multilobar infiltrates
- Confusion/disorientation
- Uremia (blood urea nitrogen level > 20 mg/dL)
- Leukopenia (white blood cell count < 4000 cells/μL)
- Thrombocytopenia (platelet count < 100,000/μL)
- Hypothermia (core temperature < 36°C)
- Hypotension requiring aggressive fluid resuscitation

Major criteria:

- Septic shock with need for vasopressors
- Respiratory failure requiring mechanical ventilation[1]

Causes for Rapid Response Activation

Progressively worsening tachypnea, use of accessory respiratory muscles, cyanosis, tachycardia/bradycardia, hypotension, altered mental status.

Actions

INITIAL MEASURES

1. Maintain continuous pulse oximetry.
2. Administer supplemental oxygen to maintain SpO_2 > 90% or PaO_2 > 60–65 mmHg; transition to high flow oxygen when patient requires high flow rates.
3. Maintain continuous cardiac monitoring.
4. Position the patient to minimize aspiration risk.

DIAGNOSTIC WORK-UP

1. Labs: CBC with differential (leukocytosis, left shift, bandemia, thrombocytopenia), BMP, procalcitonin (elevated in bacterial/fungal infection), C-reactive protein (elevated), lactate, and ABG.

2. Obtain blood cultures, culture of respiratory secretions, and nasal MRSA PCR for the following patients:
   - With severe pneumonia, especially if intubated
   - Empirically treated for MRSA or *P. aeruginosa*
   - Previously infected with MRSA or *P. aeruginosa*
   - Who were hospitalized and received parenteral antibiotics within the last 90 days[1]
3. Order urine pneumococcal antigen in patients with severe pneumonia.[1]
4. Order urine *Legionella* antigen for:
   - Association with *Legionella* outbreak
   - Recent travel to an area with *Legionella* outbreak
   - Severe pneumonia[1]
5. Collect lower respiratory tract secretions for *Legionella* culture on selective media or *Legionella* nucleic acid amplification testing in patients with severe pneumonia.[1]
6. Order imaging:
   - Chest X-ray is the standard imaging test for establishing the diagnosis of pneumonia; viral pneumonia imaging will show bilateral, interstitial, symmetric, perihilar infiltrates; typical bacterial pneumonia will show focal segmental or lobar consolidation; atypical bacterial pneumonia will show focal segmental or bilateral interstitial infiltrates; *P. jiroveci* pneumonia will show bilateral patchy interstitial infiltrates.[2]
   - Chest ultrasonography may facilitate assessment for pneumonia at bedside.
   - Chest CT scan may be considered if chest X-ray is negative in immunocompromised patient.[2]

TREATMENT

1. Use heated/humidified oxygen via high flow nasal prongs.
2. Start suctioning to clear secretions.
3. Order chest physiotherapy.
4. Administer bronchodilators: albumin nebulizer 2.5–5 mg q 20 min for three doses; follow with 2.5–10 mg q 1–4 h PRN or 10–15 min by continuous nebulization.[3]
5. Administer *N*-acetylcysteine nebulizer:
   - 10% solution in 6–10 mL; administer 2–20 mL every 2–6 h
   - 20% solution in 3–5 mL; administer 1–10 mL every 2–6 h[4]
6. In severe pneumonia without risk factors for MRSA or *P. aeruginosa*, standard empiric therapy includes β-lactam/macrolide combination or β-lactam/respiratory fluoroquinolone.[1]
7. In severe pneumonia with risk factors for MRSA or *P. aeruginosa* (prior respiratory isolation of MRSA or *P. aeruginosa*, recent hospitalization and parenteral antibiotics, or locally validated risk factors are present), add coverage for MRSA and *P. aeruginosa*.[1]
8. Empiric antibiotic options for MRSA include:
   - Vancomycin 15 mg/kg IV every 12 h; adjust based on levels
   - Linezolid 600 mg PO/IV every 12 h[1]
9. Empiric antibiotic options for *P. aeruginosa* include:
   - Piperacillin-tazobactam 4.5 g IV every 6 h
   - Cefepime 2 g IV every 8 h
   - Ceftazidime 2 g IV every 8 h
   - Aztreonam 2 g IV every 8 h
   - Meropenem 500 mg IV every 8 h
   - Imipenem 500 mg IV every 6 h[1]
10. Deescalate antibiotics when pathogen and sensitivities are established.[1]

11. Consider corticosteroids in patients with refractory septic shock.[1]
12. Consult pulmonologist for consideration of bronchoscopy and therapeutic lavage.
13. Start intubation and mechanical ventilation for patients with hypoxia or hypercapnia refractory to noninvasive forms of oxygen delivery or inability to protect airway. Initial ventilator settings:
    - Mode of ventilation: assist control support.
    - Initial FiO_2: 100%; once patient stabilizes, titrate down to maintain SpO_2 at 92%–94%.
    - Tidal volume (VT) 6–8 mL/kg of predicted (ideal) body weight:
        - Male: PBW (kg) = 50 + 2.3(height(in)-60)
        - Female: PBW (kg) = 45.5 + 2.3(height(in)-60)
    - Maintain inspiratory plateau pressure ≤ 30 cmH_2O to avoid barotrauma.
    - RR: 12–16 breaths per minute.
    - Inspiratory to expiratory ratio (I/E) of 1:2.
    - PEEP: 5 cm of H_2O.[5]

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Hypovolemic Shock Due to Acute Infectious Diarrheal Illness

Presentation

Acute infectious diarrheal illness is common in adults. The most common etiology is viral gastroenteritis. Other etiology can be bacterial or parasitic. The most common bacterial causes of acute diarrhea in the United States are *Salmonella*, *Campylobacter*, *Shigella*, and Shiga toxin–producing *Escherichia coli* (STEC).[1] Elderly patients, patients residing in nursing homes, and recently hospitalized patients are at high risk for acute infectious diarrheal illness. Recent use of antibiotics and recent sick contacts are other risk factors.

Acute diarrheal illness is classified as noninflammatory and inflammatory syndromes. Noninflammatory syndrome is milder and is characterized by intestinal secretion without disruption in intestinal mucosa. Inflammatory syndrome is characterized by disruption of intestinal mucosa resulting in tissue invasion and tissue damage and generally leads to more severe disease.[2] Examples of pathogens causing noninflammatory syndrome include enterotoxigenic *E. coli, Bacillus cereus, Rotavirus, Norovirus,* and *Staphylococcus aureus*. Examples of pathogens causing inflammatory syndrome include STEC, *Salmonella, Shigella,* and *Clostridium difficile*. Symptoms of inflammatory diarrheal illness include fever, tenesmus, and grossly bloody stools.[2]

Patients with severe GI loss of fluids can develop hypovolemia with decreased tissue perfusion. Elderly patients are at higher risk. Symptoms of severe dehydration include thirst, dizziness, decreased urinary output, and altered mental status. On examination, these patients will have a generally ill appearance, dry mucous membranes, tachycardia, and hypotension.

Causes for Rapid Response Activation

Progressively worsening tachycardia, hypotension, altered mental status.

Actions

INITIAL MEASURES

1. Maintain continuous pulse oximetry.
2. Administer supplemental oxygen to maintain SpO_2 > 90% or PaO_2 > 60–65 mmHg; transition to high flow oxygen when patient requires high flow rates.
3. Maintain continuous cardiac monitoring.
4. Raise patient's legs to improve circulation.
5. Establish adequate IV access: two large-bore lines or central line.

DIAGNOSTIC WORK-UP

1. Labs: CBC with differential (leukocytosis/leukopenia, eosinophilia in parasitic infections, bandemia (especially due to *Shigella*), anemia, thrombocytopenia), CMP (electrolytes, renal function), procalcitonin (elevated in bacterial and fungal infection), and lactic acid.
2. Order fecal occult blood test.

3. Fecal lactoferrin (marker for leukocytes released by damaged intestinal mucosal cells) has higher specificity and sensitivity compared to fecal leukocytes.[2]
4. Polymerase chain reaction (PCR)–based multiple GI pathogen panels have improved turnaround time compared to stool cultures; however, "reflex stool cultures" are needed for taxonomic classification and susceptibility[3]; stool studies are recommended in the following situations:
   - Severe dehydration
   - Sepsis
   - Fever
   - Grossly bloody stool
   - Symptoms last > 3–7 days
   - Immunocompromised patients
   - Inflammatory diarrhea
   - Inflammatory bowel disease
   - Nosocomial diarrhea (onset after more than 3 days in the hospital, antibiotic use within 3 months)
   - Patients older than 65years with significant comorbidities[4]
5. Order ova and parasites test in the following situations:
   - Diarrhea lasting > 7 days
   - Immunocompromised patients
   - Diarrhea associated with infants in daycare
   - Diarrhea associated with travel to mountainous regions
   - Diarrhea in patients with AIDS or men who have sex with men
   - Community waterborne outbreaks
   - Bloody diarrhea with few fecal leukocytes[5]
6. Patients with acquired immune deficiency syndrome (AIDS) with persistent diarrhea should undergo additional testing for organisms such as *Cryptosporidium*, *Cyclospora*, *Cystoisospora*, *Microsporidia*, *Mycobacterium avium* complex, and *Cytomegalovirus*.[6]
7. Test for *C. difficile* in symptomatic patients with new-onset ≥ 3 unformed stools in 24 h with:
   - History of diarrhea following antimicrobial use (within last 3 months)
   - Healthcare-associated diarrhea
   - Persistent diarrhea without an etiology and without recognized risk factors[6]
8. A single diarrheal stool specimen is recommended for detection of toxin or a toxigenic *C. difficile* strain (e.g., nucleic acid amplification testing); multiple specimens do not increase yield[6]; use rectal swab in patients with ileus.
9. Order blood cultures in febrile patients.
10. Imaging (ultrasonography, computed tomography, or magnetic resonance imaging) may detect small bowel/colonic wall circumferential thickening, intra-abdominal free air, and toxic megacolon.[6]

TREATMENT

1. Isotonic IV fluids such as normal saline or lactated Ringer's solution are recommended in severe dehydration, shock, ileus, or altered mental status; 1–2 L IV bolus is given initially, with close monitoring of vital signs, urinary output, and mental status.
2. Antimicrobial therapy for people with infections attributed to STEC O157 and other STEC that produce Shiga toxin 2 (or if the toxin genotype is unknown) should be avoided.[6]
3. Empiric antimicrobial therapy while waiting for the results of diagnostic work-up is recommended for the following patients with severe illness:
   - Immunocompromised patients

- Ill immunocompetent patients with fever and bloody diarrhea[6]

4. Empiric antimicrobial therapy options should be provided depending on the local susceptibility patterns:
   - Ciprofloxacin 400 mg IV q 12 h
   - Azithromycin 500 mg IV daily[2]
5. Antimicrobial therapy should be narrowed when antimicrobial susceptibility testing results become available; more prolonged therapy might be required for immunocompromised patients:
   - *Campylobacter*:
     - Azithromycin 500 mg IV for 5 days
   - Non-Shiga *toxin*-producing *E. coli*:
     - Ciprofloxacin 400 mg IV q 12 h for 7 days
     - Azithromycin 500 mg IV daily for 5 days[2]
   - *Salmonella*:
     - Ciprofloxacin 400 mg IV q 12 h for 7 days
     - Azithromycin 500 mg IV daily for 5 days
     - Ceftriaxone 2 g IV daily for 7 days[2]
   - *Shigella*:
     - Ciprofloxacin 400 mg IV q 12 h for 7 days
     - Azithromycin 500 mg IV daily for 5 days[2]
   - *C. difficile*:
     - Discontinue all inciting antibiotics
     - Vancomycin 125 mg orally four times per day for 10–14 days[7]
   - First *recurrence* of CDI:
     - Oral vancomycin as a tapered and pulsed regimen: 125 mg po four times a day for 10–14 days, two times a day for a week, once per day for a week, and then every 2 or 3 days for 2–8 weeks
     - Fidaxomicin 200 mg twice daily for 10 days[7]
   - Multiple *recurrences* of CDI:
     - Fecal microbiota transplantation[7]
   - CDI ileus:
     - Vancomycin 500 mg orally four times per day and 500 mg in approximately 100 mL normal saline per rectum every 6 h as a retention enema and metronidazole 500 mg IV every 8 h
     - Consultation with general surgeon for severely ill patients for consideration of subtotal colectomy with preservation of the rectum[7]

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Acute Respiratory Failure Due to Influenza Virus Infection

Presentation

Influenza is a common highly contagious airborne viral illness. It has seasonal activity and causes significant morbidity and mortality, especially in elderly patients and patients with chronic comorbidities. Three types of influenza viruses cause infection in humans: influenza A, B, and C. Influenza A infects multiple species, including humans, equines, swine, and birds. As Influenza A is more susceptible to antigenic variation, it contributes more to major pandemics.[1]

Common symptoms include chills related to fever, sweating, myalgias, malaise, sore throat, nasal discharge, cough, and headache. Some patients may have nausea, vomiting, and diarrhea. Symptoms usually continue for 2–8 days.[1] In severe pneumonia, patient will steadily deteriorate with development of dyspnea, tachypnea, and hypoxia. According to the 2010 guidelines of the World Health Organization (WHO),[2] severe influenza is defined as having at least one of the following clinical presentations:

- Dyspnea, tachypnea, or hypoxia
- Radiological signs of lower respiratory tract disease
- Central nervous system involvement (e.g., encephalopathy, encephalitis)
- Severe dehydration
- Acute renal failure
- Septic shock
- Exacerbation of underlying chronic disease, including asthma, chronic obstructive pulmonary disease (COPD), chronic hepatic or renal insufficiency, diabetes mellitus, or cardiovascular conditions
- Any other influenza-related condition or clinical presentation requiring hospital admission

Causes for Rapid Response Activation

Progressively worsening tachypnea, dyspnea, hypoxia, altered mental status.

Actions

INITIAL MEASURES

1. Maintain continuous pulse oximetry.
2. Administer supplemental oxygen to maintain SpO_2 > 90% or PaO_2 > 60–65 mmHg; transition to high flow oxygen when patient requires high flow rates.

3. Maintain continuous cardiac monitoring.

DIAGNOSTIC WORK-UP

1. Order influenza A and B tests: reverse transcription-polymerase chain reaction (RT-PCR) or viral culture of nasopharyngeal or throat secretions; rapid diagnostic tests for influenza usually have a 30-min turnaround time.[3]
2. Obtain sputum and blood cultures in superimposed bacterial pneumonia.
3. Order nasal MRSA PCR.
4. Check for urine streptococcal and *Legionella* antigens (see the earlier section on severe pneumonia for indications).
5. Labs: CBC (leukopenia, thrombocytopenia, leukocytosis in superimposed bacterial infection), CMP (electrolyte abnormalities, renal failure), and procalcitonin (elevated in superimposed bacterial or fungal infection).
6. Order chest X-ray: clear lungs or minimal bilateral symmetrical interstitial infiltrates in early disease; bilateral patchy infiltrates later in the course of illness; in superimposed bacterial pneumonia, chest X-ray will demonstrate nonsegmental homogeneous consolidation involving one, or less commonly, multiple lobes.[3]
7. CT scan of chest will show multifocal ground glass opacities; lobar consolidation will suggest superimposed bacterial pneumonia.

Treatment

1. As patients with severe influenza are at high risk of developing acute respiratory distress syndrome (ARDS), use IV fluids cautiously.
2. Start antiviral treatment as soon as possible (most effective if started within 48 h of symptom onset) for hospitalized patients regardless of illness duration:
   - Oseltamivir 75 mg orally twice daily for 5 days; adjust dose to renal function
   - Peramivir 600 mg IV single dose (for patients who are unable to take oseltamivir orally); adjust dose to renal function
   - Zanamivir 10 mg inhalation twice daily for 5 days (contraindicated in intubated patients, not recommended in patients with asthma or COPD)[4]
3. If clinical course remains severe, duration of the antiviral treatment can be extended until clinical improvement.[2]
4. Investigate and empirically treat bacterial co-infection, for example, bacterial pneumonia in the following patients:
   - Patients presenting initially with severe influenza (extensive pneumonia, respiratory failure, hypotension, fever)
   - Patients who deteriorate after initial improvement, particularly those treated with antivirals
   - Patients who fail to improve after 3–5 days of antiviral treatment[4]
5. Commonly isolated bacteria in patients with influenza complicated by bacterial pneumonia are *Staphylococcus aureus* (including MRSA), *Streptococcus pneumonia*, *Streptococcus pyogenes*, and *Moraxella catarrhalis*,[2] empiric antibiotic options for which (except MRSA) include:
   - Ampicillin/sulbactam 3 g IV q 6 h for 7 days
   - Ceftriaxone 2 g IV daily for 7 days
   - Levofloxacin 750 mg IV daily for 5 days
6. Patients with suspected MRSA pneumonia should preferably be treated with linezolid due to superiority in treatment for MRSA pneumonia and decreased risk for nephrotoxicity[5]:
   - Linezolid 600 mg PO/IV q 12 h for 10 days

- In case of contraindications for linezolid: vancomycin 15 mg/kg IV every 12 h; dose adjusted based on trough levels

7. Avoid corticosteroids unless there are other indications for them, such as asthma, COPD, or adrenal insufficiency.[2,4]
8. High-flow nasal cannula is preferred noninvasive respiratory support in patients with Influenza.[5]
9. Consider BiPAP in patients with asthma or COPD exacerbation[5]; however, if patient has evidence of ARDS, invasive PPV is the only strategy that improves mortality.
10. Start intubation and mechanical ventilation for patients with progressive hypoxia/hypercapnia despite optimal use of noninvasive respiratory support; ventilatory management principles for ARDS can be adopted in severe influenza.[6]
11. Initial ventilator settings:
    - Mode of ventilation: volume assist control.
    - Initial FiO_2: 100%; once the patient stabilizes, titrate it down to maintain SpO_2 at 88%–95% or PaO_2 55–80 mmHg.
    - PEEP: 18–24 cm of H_2O; titrate down as you titrate down FiO_2.
    - Tidal volume (VT) 6 mL/kg of predicted (ideal) body weight:
      - Male: PBW (kg) = 50 + 2.3(height(in)-60)
      - Female: PBW (kg) = 45.5 + 2.3(height(in)-60)
    - RR: 14–22 breaths per minute.
    - Inspiratory to expiratory ratio (I/E) of 1:2.
    - Maintain plateau pressure (Pplat) $\leq$ 30 cmH_2O to avoid barotrauma.
    - Monitor clinical response, Pplat, and ABGs closely.[7]

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Acute Respiratory Failure Due to COVID-19 (Coronavirus Disease of 2019) Pneumonia

Presentation

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a highly contagious respiratory disease that can spread in aerosols. Mean incubation period is 5 days; however, it can range from 2 days to 2 weeks.[1] The disease ranges from asymptomatic to severe illness with acute respiratory failure, multiorgan failure, and death. Initial symptoms may include fever, chills, sore throat, nasal congestion, cough, shortness of breath, loss of taste and smell, headache, nausea, vomiting, and diarrhea. Severe cases are mostly reported in patients older than 55 years with significant comorbidities, including obesity.[1]

In this chapter we will only address management of severe (RR > 30 breaths/min, severe respiratory distress or SpO_2 < 90%) and critical (presence of ARDS, respiratory failure requiring ventilation, sepsis or septic shock) COVID-19.

Causes for Rapid Response Activation

Rapidly worsening dyspnea, tachypnea, hypoxia.

Actions

INITIAL MEASURES

1. Maintain continuous pulse oximetry.
2. Administer supplemental oxygen to maintain SpO_2 > 92%–96% or PaO_2 > 60–65 mmHg; transition to high flow oxygen when patient requires high flow rates.
3. Maintain continuous cardiac monitoring.

DIAGNOSTIC WORK-UP

1. Order SARS-CoV-2 test (viral nucleic acid or antigen detection test).[1]
2. Other labs include CBC (leukopenia, lymphopenia); CMP (elevated LFTs); coagulation studies (PT, aPTT); inflammatory markers such as CRP, LDH, ferritin, D-dimer, fibrinogen, and IL-6 (if elevated, associated with increased risk of ARDS and death)[2,3]; ABG; and BNP (BNP < 100 pg/mL in a patient with hypoxia and bilateral pulmonary infiltrates supports ARDS rather than cardiogenic pulmonary edema).[4]
3. Order chest X-ray: bilateral consolidation and diffuse ground-glass opacities with highest severity around days 10–12 following the onset of symptoms.[1]
4. Consider chest CT scan: ground-glass and fine reticular opacities with mostly peripheral distribution and vascular thickening.[1]
5. Order compression Doppler ultrasound (US) of extremities when DVT is suspected.
6. Order chest CTA in patients with elevated D-dimer to rule out pulmonary embolism.

TREATMENT

1. Prone positioning for awake spontaneously breathing patient is associated with improved oxygenation and a lower rate of intubation,[5] however, overall evidence is insufficient, awaiting the results of ongoing RCT's.
2. High flow nasal cannula will deliver heated humidified oxygen through large-bore nasal prongs; oxygen flow rate can be titrated up to 50–60 L/min to maintain SpO_2 of 88%–95%; this mode is associated with improved patient comfort as it allows patient to talk, eat, and move around.[4]
3. As patients with severe COVID-19 pneumonia are at high risk for ARDS, a fluid-conservative strategy is preferred (improved oxygenation index, lower lung injury score, and increase in ventilator-free days); closely monitor urine output; consider diuretic to maintain low normal fluid balance.[6]
4. Administer dexamethasone 6 mg PO/IV daily for 10 days or until discharge (or equivalent glucocorticoid if dexamethasone is not available) for all patients with RR > 30 breaths/min, severe respiratory distress or SpO_2 < 90% on room air.[7]
5. Equivalent glucocorticoids if dexamethasone is not available include:
   - Methylprednisolone 32 mg PO/IV daily
   - Prednisone 40 mg PO daily[7]
6. Remdesivir (antiviral agent) is recommended for patients with severe COVID-19 (RR > 30 breaths/min, severe respiratory distress or SpO_2 < 90% on room air) and should ideally be started within 72 h of positive COVID-19 test, it is no longer recommended in adults undergoing mechanical ventilation.[7]
7. Convalescent plasma is recommended by IDSA only in the context of a clinical trial.[7]
8. BiPAP/CPAP is administered by full facemask for patients with progressive hypoxia despite optimal use of high flow oxygen.
9. Start intubation and mechanical ventilation for patients with progressive hypoxia/hypercapnia despite optimal use of noninvasive respiratory support.
10. Initial ventilator settings:
    - Mode of ventilation: volume assist control.
    - Initial FiO_2: 100%; once patient stabilizes, titrate it down to maintain SpO_2 at 88%–95% or PaO_2 55–80 mmHg.
    - PEEP: 18–24 cm of H_2O; titrate down as you titrate down FiO_2.
    - Tidal volume (VT) 6 mL/kg of predicted (ideal) body weight:
      - Male: PBW (kg) = 50 + 2.3(height(in)-60)
      - Female: PBW (kg) = 45.5 + 2.3(height(in)-60)
    - RR: 14–22 breaths per minute.
    - Inspiratory to expiratory ratio (I/E) of 1:2.
    - Maintain plateau pressure (Pplat) ≤ 30 cmH_2O to avoid barotrauma.
    - Monitor clinical response, Pplat, and ABGs closely.[8]
    - Prone ventilation for 12–16 h/day is suggested.
11. Administer prophylactic dose anticoagulation with enoxaparin, fondaparinux, or heparin (if CrCl < 30 mL/min) for patients with severe and critical COVID-19, in the absence of contraindications.[7]
12. Administer therapeutic dose of anticoagulation for patients with documented or presumptive pulmonary embolism or deep vein thrombosis.

References

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