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Mini Review

COVID-19 Cliff Notes: A COVID-19 Multidisciplinary Care Compendium

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A B S T R A C T

As we pass the nearly 9 month mark of the coronavirus virus disease 2019 (COVID-19) pandemic in the United States, we sought to compile a brief multi-disciplinary compendium of COVID-19 information learned to date. COVID-19 is an active viral pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that confers high morbidity and mortality. COVID-19 has been associated with: pulmonary compromise and acute respiratory distress syndrome, thrombotic events, inflammation and cytokine, and post-infectious syndromes. Mitigation of these complications and expeditious therapy are a global urgency; this is brief summary of current data and management approaches synthesized from publications, experience, cross-disciplinary expertise (Figure 1).

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PULMONARY AND SUPPORTIVE CARE

Progressive COVID-19 requires critical care. Priorities include appropriate personal protective equipment, negative-pressure rooms, and minimization of particle aerosolization: regular- or high-flow nasal cannula (limited to ≤ 30 L/minute), oxygen mask, and in very select cases a trial of noninvasive ventilation [1]. Progressive failure necessitates safe endotracheal intubation by experienced providers and lung-protective mechanical ventilation (high positive end-expiratory pressure and low tidal volumes), with adjunct therapies including proning, inhaled pulmonary vasodilators, extracorporeal

membrane oxygenation, vasopressors, nutrition, and renal replacement therapy. Safe and expedient extubation must be prioritized in patients with successful spontaneous breathing trials [1]. Adult respiratory distress syndrome (ARDS) is a life-threatening complication, with data suggesting that low-dose, short-term dexamethasone therapy may have a critical role [2]. Cardiac complications, including myocarditis, heart failure, and arrhythmias, are being increasingly recognized in COVID-19; thus, cardiac evaluation is recommended in children and adults with severe disease. Additional risks of ulcers, thrombi, and fluid overload should be minimized. Evaluation for coinfections is warranted, as data have shown that bacterial and fungal pathogens contribute to mortality, and some have suggested therapy with empiric antimicrobials [1].

Fig. 1.

COVID-19 TREATMENT

Two therapies continue to show promise for primary treatment of COVID-19. Convalescent plasma—plasma containing antibodies to SARS-CoV-2, obtained from individuals who

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COVID-19 Care Considerations

Pulmonary/ Supportive Care

Tidal volumes: 6cc/kg predicted body weight
Plateau Pressure (Pplat): ≤30mmHg
Goal SaO₂: 88-95%
FiO₂ & PEEP (per ARDSNet):

FiO ₂	PEEP
0.3	5
0.4	5
0.4	8
0.5	8
0.5	10
0.6	10
0.7	10
0.7	12
0.7	14
0.8	14
0.9	14
0.9	16
0.9	18
1.0	18-24

Adjunct considerations:

- Proning; oxymask
- Regular/hi flow NC ≤ 30 L/min
- Inhaled pulmonary vasodilator
- ECMO
- Vasopressors
- Renal replacement therapy
- Evaluation of co-infection: Blood, Sputum cultures
- Nutrition; pharmacy dosing for multi-organ failure
- Echocardiogram

ARDS: Dexamethasone 6 mg q24 x ≤10 days

Inflammatory/ Cytokine storm

Uncompensated shock: pulmonary edema, hypoxemia, hypotension, tachycardia, confusion
Monitor: Ferritin, CRP, D-dimer
TREATMENT: Tocilizumab (Toci), (monoclonal antibody against IL-6)

- **Pediatric:** < 30 kg: 12 mg/kg/dose IV q12 hours x 2 if no adverse events (AE); ≥30 kg: 8 mg/kg/dose IV q12 hours x 2 if no (AE)
- **Adult:** 8 mg/kg/dose max 800 mg/dose IV q 12 hours x 2 if no (AE)

Monitor: CRP as surrogate for IL-6 vs. IL-6 levels
Note: Neutrophil & T cell function should be preserved
TREATMENT: Cytosorb (EUA designation), consider if refractory to Toci; www.cytosorbents.com
Systemic glucocorticoids limited role

Thrombotic/ Hematological

Monitor: CBC, D-dimer, PT and aPTT, Fibrinogen daily
 • low threshold for chest CTA or leg ultrasound.

Prophylaxis Enoxaparin dose for ill hospitalized:

- **Pediatric:** 0.5 mg/kg BID (max 40mg); *consider checking anti-Fxa in children >60kg.
- **Adult:** 40 mg BID, *adjust dose & check anti-Fxa if BMI>40, CrCl <30

Consider Post Discharge (adults): Betrixaban, Rivaroxaban, Enoxaparin for up to 4-5 weeks

COVID-19 infection

Convalescent Plasma (ABO compatible):

- **Pediatric:** 10mL/kg/dose to max 2 units (250 mL/unit) IV 2-4 hours q12 hours x1;
- **Adult:** 2 units per dose q12 hours x 1

Remdesivir:

- **Pediatric (<40 kg):** 5mg/kg/dose IV x1 on day 1, 2.5mg/kg/dose IV daily days 2-10. If improved, complete 5 days; if not improved, complete 10 days.
- **Adult (> 40kg):**
 - **ICU:** 200mg IV x1 on day 1, 100mg QD days 2-10
 - **Non-ICU:** 200mg IV x1 day 1, 100 mg QD days 2-5

Monoclonal antibody: > 12 years (> 40kg) & mild disease (recent infection <10 days of symptoms):

- **Casirivimab/ Imdevimab:** 1200 mg IV each rx x 1
- **Bamlanivimab:** 700 mg IV x1

Post-infectious syndromes/ PIMS-TS

DIAGNOSTIC CRITERIA:

- **Fever + recent COVID-19 (within 4 wks) AND:**
One of: hypotension, shock, severe cardiac illness, severe end organ involvement,
Two or more: maculopapular rash, bilateral non-purulent conjunctivitis, mucocutaneous inflammatory signs, acute gastrointestinal symptoms; and not explained by another diagnosis
- **Echocardiogram:** Function and coronary arteries baseline and then 1-2 weeks

KAWASAKI-LIKE TREATMENT:

- **IVIG:** 2 gram/kg/dose (max 100g/dose);
- **Aspirin:** Moderate dose (30-50 mg/kg/day) to high dos (80-100 mg/kg/day) until afebrile (max 4 gm/day)

SEVERE CARDIAC DISEASE TREATMENT:

- **Methylprednisolone** 2mg/kg/day (max 60 mg/day); if refractory, **Anakinra** 2-10mg/kg/day

Additional websites:

- <https://www.covid19treatmentguidelines.nih.gov>
- <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/patient-management>
- <https://www.cdc.gov/coronavirus/2019-ncov/index.html>
- www.hematology.org/COVIDguidelines

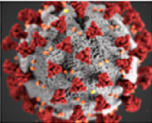


Figure 1. COVID-19 care considerations.

have recovered from COVID-19—has a good safety record, data to suggest efficacy in severe disease, and recently received emergency use authorization (EUA) from the Food and Drug Administration for use in COVID-19 [3]. Studies in children and adults are ongoing, with the best results anticipated in patients who receive products with high neutralization titers. To date, the most encouraging antiviral agent is remdesivir, with some data linking it to decreased time to recovery in adults [4]. Antiviral treatment is likely most effective earlier in the illness (days 0 to 7) when there is active viral replication. It

has been given emergency use authorization for the treatment of SARS-CoV-2 in hospitalized adult and pediatric patients with severe disease. Emerging data suggests that monoclonal antibody therapy to SARS-CoV2 may mitigate severe disease in outpatients early in the disease process, with either casirivimab and imdevimab or bamlanivimab (under an EUA) [5,6].

COAGULOPATHY AND BLEEDING DIATHESIS

SARS-CoV-2 infection predisposes patients to venous and arterial thrombosis, due to excessive inflammation, platelet

activation, endothelial dysfunction and stasis [7]. Venous thromboembolism incidence risk is associated with disease severity, $\leq 70\%$ in intensive care patients [7]. Bleeding diatheses also occur in up to 5% of patients with COVID-19 and can be accompanied by hypofibrinogenemia [7]. To risk stratify, follow coagulation and hematology labs daily. Intermediate dose prophylaxis should be considered in ill patients, using anti-FXa to evaluate resistance and adjust dosage, including those on therapeutic dosing [7]. Careful consideration of changing renal function, thrombocytopenia, and impact of BMI on dosing of anticoagulation. Consider a very low threshold for chest computer tomography angiography, venous ultrasound. In ill adults, post-discharge thromboembolism prophylaxis could be considered for up to 4-5 weeks.

INFLAMMATION/CYTOKINE STORM

Severe COVID-19 may present with life-threatening, uncompensated shock similar to cytokine release or macrophage activation syndromes with elevated ferritin, C-reactive protein, and d-dimers. Hallmarks include lymphopenia, elevated IL-6, and TNF- α . Tocilizumab, an IL-6 antagonist, has shown survival benefit in the treatment of COVID-19 without affecting viral clearance [8]. This may be especially important for immunocompromised patients, such as after cellular transplantation [9]. In contrast, the risks of secondary infections have cautioned against systemic steroids in patients who do not have ARDS. For patients refractory to tocilizumab, a method for in-line cytokine removal, CytoSorb, has received an EUA for adults, although data remain limited.

POSTINFECTIOUS SYNDROMES

Postinfectious syndromes such as Guillain-Barré and a severe multisystem disease inflammatory syndrome in children (MIS-C; also called pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2) are emerging. MIS-C is characterized by fever with one of the following: hypotension or shock, severe cardiac illness, and severe end-organ involvement; or 2 or more of the following: maculopapular rash, bilateral nonpurulent conjunctivitis, mucocutaneous inflammatory signs, acute gastrointestinal symptoms; and not explained by another diagnosis [10]. Echocardiography should be performed at presentation and repeated in 1 to 2 weeks. Treatment includes supportive care along with consideration of immunomodulation with, for example, steroids and i.v. immunoglobulin, with uncommon use of IL-1 and IL-6 inhibitors, and anticoagulation [10].

This perspective is not a guideline but provides a brief summary of current considerations for the care of patients with COVID-19, including details of pulmonary and intensive care

management, and specific treatments for severe disease, coagulopathy, dysregulated inflammation, and postinfectious syndromes. The care of COVID-19 patients is a rapidly evolving field that will require continued collaborations across disciplines and age groups to best care for these patients and improve outcomes, as highlighted by the patient synopsis.

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