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Updates to COVID Treatment Pathway

8-20-21
-Added REGEN-COV Treatment/Prophylaxis algorithm (see pg. 1 of document)
-Added Baricitinib to treatment page (see pg. 4 of document)
-Updated REGEN-COV dosing for COVID+/direct exposure/high risk for ongoing exposure (see pgs. 1 & 4 of document

9-15-21
-Removed obesity from anticoagulation treatment portion of the pathway. Obesity will remain a risk factor for prophylaxis.

12-27-21
-Removed REGEN-COV monoclonal Ab treatment due to non-effectiveness secondary to the omicron variant

1-3-22
-Added Sotrovimab dosing for high risk conditions only at this point due to limited supply

1-27-22
-Added pre-exposure prophylaxis – Evusheld.
-Added Paxlovid to treatment options for inpatient and outpatient

4-12-22
-Changed Sotrovimab to Bebtelovimab and updated dosing
-Changed dosing on Evusheld to 300 mg for each component

COVID-19 Treatment Pathway

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Pre-Exposure Prophylaxis
- Only for use in patients with moderate-severe compromise who may not mount adequate immune response to vaccine.
- Patients are not COVID + and have had no recent exposure to COVID
- **Evusheld – requires ID consult**

Referring Hospitals -
If you need to transfer a child:
Contact Angel One
for transfer to Arkansas Children's Hospital
1-800-ACH-HELP

! **Special Respiratory Enhanced Contact Isolation**

COVID-19 (+) or suspected acute COVID infection

Consider MIS-C throughout evaluation

Mild/Moderate
- No new O2 requirement
- No respiratory distress

- Supportive care
- ID consult for consideration of Bebtelovimab based on high risk criteria**
- Paxlovid (for inpatient use, consult ID)

Severe
- New O2 requirement
- Increased O2 from baseline
- Not rapidly progressing

- Steroids*
- Consider remdesivir
- ID consult
- Consider addition of tocilizumab or baricitinib for rapidly increasing oxygen needs
- Consider anticoagulation – see guideline (pg. 3&4)
- Consider CRP/Procalcitonin

Critical
- Rapidly progressing O2 requirement
- Requires intubation or non-invasive ventilation in PICU
- Shock or organ failure

- Steroids*
- Tocilizumab
- ID consult
- Consider anticoagulation – see guideline (pg. 3&4)
- Consider CRP/Procalcitonin

Clinical judgement for transfer of patients to AC Little Rock:
- Current ID recommendation - transfer of all adolescent patients with new O2 requirement or increasing O2 requirement, rapidly progressing O2 requirement, or respiratory distress
- Shock, ARDS, or organ failure

! High suspicion for bacterial infection:
Sepsis Pathway – ED/Inpatient
Sepsis Pathway – PICU

***Refer to the following page for details regarding eligibility, treatment, and dosing**

COVID-19 Treatment Agents

Medication (recommended or authorized)	Recommended Dose and Comments
Corticosteroids	Dexamethasone **0.15** mg/kg (max **6** mg) IV or PO once daily (preferred) OR Equivalent dose of substitute – methylprednisolone **0.8** mg/kg (max **32** mg) IV once daily **Duration** 10 days or until discharge
Remdesivir (Veklury®) *ID Consult Required*	3.5-40 kg: **5** mg/kg IV on day 1 then **2.5** mg/kg IV once daily on day 2 – 5 (or 10) ≥ 40 kg: **200** mg IV on day 1 then **100** mg IV once daily on day 2 – 5 (or 10) **Duration:** 5 or 10 days **Indication:** Hospitalized patients confirmed COVID (+) requiring supplemental oxygen **Exclusion:** Renal impairment – Age > 28 days with eGFR < 30 mL/min Age 7-28 days with Cr > 1 mg/dL Hepatic impairment – ALT > 5x upper limit of normal
Tocilizumab - IL-6 receptor antagonist *ID Consult Required*	Required testing before dose: • T-Spot • Consider Hep B titers based on risk factors Dosing <30 kg: 12 mg/kg x1 ≥30 kg: 8 mg/kgx1 (max 800 mg)
Baricitinib -Janus Kinase Inhibitor	For children 2 - <9 years of age 2 mg once daily for 14 days For children 9 years of age and older 4 mg once daily for 14 days
Bebtelovimab **-**Monoclonal antibody *ID Consult Required*	For children 12 years of age weighing over 40 kg 175 mg IV x1 (in 2 mL syringe) IV push over 30 seconds
Paxlovid -Antiviral -Given with Ritonavir	For children 12 years of age weighing over 40 kg 300 mg Nirmatrelvir with 100 mg Ritonavir PO BID x 5 days Numerous drug interactions with Ritonavir. Review patient medication list prior to prescribing.
Evusheld -Tixagevimab -Cilgavimab	300 mg Tixagevimab and 300 mg Cilgavimab IM x1 **Requires observation for 1 hour post-injection**. These come in 2 separate vials, draw up each vial in 2 separate syringes. Administer each IM injection in 2 separate sites, preferably each gluteal muscle. Estimated efficacy is 6 months.

<u>Not</u> recommended for treatment of COVID-19

- **Hydroxychloroquine**
- **Azithromycin**
- **Lopinavir-ritonavir**
- **Ivermectin**

Anticoagulation Guidelines for Acute COVID-19

Guidelines are derived from adult guidelines and various adaptations from pediatric hospitals.

Pharmacologic thromboprophylaxis should be considered in all pediatric and adolescent patients admitted to Arkansas Children's Hospital unless contraindicated (active bleeding, thrombocytopenia, recent or upcoming surgical intervention, etc.)

Anticoagulation

Inclusion Criteria:

All hospitalized patients who have been diagnosed with COVID-19 who meet one or ore of the following criteria of high-risk*:

- Any patient admitted to intensive care unit
- Patients admitted with suspected MIS-C
- Patients with active cancer, autoimmune disorders, decreased mobility, sickle cell disease, central line, diabetes, personal or family history of thrombosis, inherited thrombophilia, estrogen therapy
- Elevated D-dimer that is ≥5 times the upper limit normal or with evidence of inflammation (elevated CRP, etc.)

Special Considerations

- MIS-C/Kawasaki patients – if Cardiology recommends aspirin therapy (due to concern for abnormal coronary arteries or persistently diminished systolic function), carefully review clinical indication for additional prophylactic Lovenox. May not be required unless high risk for VTE based on above criteria. Concomitant use of low dose aspirin (<5 mg/kg/day) with prophylactic anticoagulation likely does not confer a high risk of bleeding in the absence of other bleeding risk factors.
- Daily assessment for signs/symptoms of DVT or PE with impaging (US or CTA chest) if VTE suspected.

Labs to be drawn at admission or upon consult:

- CBC, PT/PTT, D-dimer, fibrinogen, CRP, BUN, creatinine

Repeat every 2-3 days as clinically indicated and prior to discharge:

- CBC, D-dimer, fibrinogen, creatinine and inflammatory markers

D-dimer ≥ 5 times upper limit normal/ high risk* factor

Signs/symptoms or very high risk of thrombosis

Treatment Considerations:

If D-dimer ≥ 5 times upper limit normal or other high risk* factor present and no contraindications to anticoagulation:

- Start enoxaparin (e.g. Lovenox) 0.5 mg/kg/dose SQ q12h (prophylaxis dose)
- At least weekly anti-Xa testing while critically ill with goal anti-Xa 0.2-0.5 (follow ACH Anticoagulation guidelines)

!

Direct Oral Anticoagulants not preferred inpatient (can interact with medications used to treat COVID-19)

Treatment Considerations:

If signs/symptoms of microvascular thrombosis, or very high risk of thrombosis based on clinical impression (obesity, active cancer, sickle cell disease, or history of thrombosis):

- Consider increase in enoxaparin (e.g. Lovenox) to 1 mg/kg/dose SQ q12h (treatment dose)
- Target low molecular weight anti-Xa 0.5-1
- If contraindicated to anticoagulation (bleeding, thrombocytopenia, surgery):
  - -Strongly consider mecahnical thromboprophylaxis (SCD)
- If CrCl <30 or very high risk of bleeding, utilize unfractionated heparin instead of enoxaparin (follow ACH Anticoagulation guidelines)

Hematology Follow-Up:

- Assess patient for ongoing risk of thrombosis
- If ready for discharge, it is likely the patient no longer has risk factors for VTE
- If high risk (active cancer, SCD, thrombophillia, or history of thrombosis), discuss with Hematology the need for anticoagulation upon discharge
- No need to trend D-dimer or inflammatory markers after discharge
- If discharged home on Lovenox, follow up with Hematology within 2 weeks.

See pg. 6 for Anticoagulation Guidelines

Anticoagulation Guidelines for Acute COVID-19

Guidelines are derived from adult guidelines and various adaptations from pediatric hospitals.

Pharmacologic thromboprophylaxis should be considered in all pediatric and adolescent patients admitted to Arkansas Children's Hospital unless contraindicated (active bleeding, thrombocytopenia, recent or upcoming surgical intervention, etc)

Target population to be considered for VTE prophylaxis:

- All hospitalized patients who have been diagnosed with COVID-19 who meet one or more of the following criteria of high-risk*:
  - Any patient admitted to intensive care unit
  - Patients admitted with suspected MIS-C
  - Patients with active cancer, autoimmune disorders, decreased mobility, sickle cell disease, obesity, central line, diabetes, personal or family history of thrombosis, inherited thrombophilia, estrogen therapy.
  - Elevated D-dimer that is ≥ 5 times the upper limit normal or with evidence of inflammation (elevated CRP, etc.).

Laboratory monitoring:

- Labs to be drawn at admission or upon consult:
  - CBC, PT/PTT, D-dimer, fibrinogen, CRP, BUN, Creatinine
  - Repeat CBC, D-dimer, fibrinogen, creatinine and inflammatory markers every 2-3 days as clinically indicated and prior to discharge.

Treatment considerations:

- If **D-dimer ≥ 5 times upper limit normal or other high-risk* feature** present and no contraindication to anticoagulation:
  - **Start enoxaparin (e.g. Lovenox) 0.5mg/kg/dose SQ q12h (prophylaxis dose)**
  - At least weekly anti-Xa testing while critically ill with goal anti-Xa 0.2-0.5 (follow ACH Anticoagulation guidelines)
- If **signs/symptoms of microvascular thrombosis, or very high risk** of thrombosis based on clinical impression (e.g. active cancer, sickle cell disease, diabetes, or history of thrombosis)
  - Consider **increase in enoxaparin (e.g. Lovenox) to 1mg/kg/dose SQ q12h (treatment dose)**
  - Target low molecular weight anti-Xa 0.5-1
- If contraindication to anticoagulation (bleeding, thrombocytopenia, surgery)
  - Mechanical thromboprophylaxis should be strongly considered (SCD)
- If CrCl <30 or very high risk of bleeding, utilize unfractionated heparin instead of enoxaparin (follow ACH Anticoagulation Guidelines)

Special considerations:

- MIS-C/Kawasaki patients – If cardiology recommends aspirin therapy (due to concern for abnormal coronary arteries or persistently diminished systolic function), carefully review clinical indication for additional prophylactic Lovenox. May not be required unless high risk for VTE based on above criteria. Concomitant use of low dose aspirin (<5 mg/ kg/day) with prophylactic anticoagulation likely does not confer a high risk of bleeding in the absence of other bleeding risk factors.
- Direct Oral Anticoagulants (DOAC) are not preferred inpatient as they can interact with medications (antivirals) used to treat COVID-19.
- Daily assessment for signs/symptoms of DVT or PE with imaging (US or CTA chest) if VTE suspected.

Hematology follow-up:

- Assess patient for ongoing risk of thrombosis. If ready for discharge, it is likely patient no longer has risk factors for VTE.
- If high risk (active cancer, sickle cell disease, thrombophillia or history of thrombosis), discuss with Hematology the need for anticoagulation upon discharge.
- No need to trend D-dimer or inflammatory markers after discharge.
- If discharged home on Lovenox, follow up with Hematology within 2 weeks.

References

Massgeneral.org/news/coronavirus/treatment-guidelines.

American Society of Hematology. https://www.hematology.org/covid19/covid-19-and-coagulopathy. http://www.hematology.orgcovidcovid-and-coagulopathy.

Loi, M., Branchford, B., Kim, J., Self, C. & Nuss, R. COVID-19 anticoagulation recommendations in children. *Pediatric Blood & Cancer* **67**, e28485 (2020).

ASPHO Summer Virtual Learning Series. "Clinical aspects of evaluating and treating COVID-19 patients in pediatric hematology/oncology". Aspho.org/meetings/summer-virtual-learning-series.

"COVID-19 and venous thromboembolism prophylaxis: recommendations in children and adolescents." Texas Children's Hospital Supportive Care Practice Standard (S-20200011).

Goldenberg NA, Sochet A, Albisetti M, et al; the Pediatric/Neonatal Hemostasis and Thrombosis Subcommittee of the ISTH SSC. Consensus-based clinical recommendations and research priorities for anticoagulant thromboprophylaxis in children hospitalized for COVID-19–related illness. *J Thromb Haemost*. 2020;18:3099–3105.

https://doi.org/10.1111/jth.15073

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