CT Children's CLASP Guideline

Post-COVID Conditions and COVID-19 Long Haul Management

INTRODUCTION

As of September 2021, the COVID-19 pandemic has infected over 5 million children (of over 33 million infections worldwide), representing over 15% of all COVID-19 cases. This number continues to rise with the delta variant of SARS-CoV-2. Although pediatric hospitalizations and deaths remain relatively low, children may be left with long-lasting, post-acute sequelae from their infection, even if the child was initially asymptomatic. "Post-COVID Conditions" is a term to describe the wide range of physical and mental health consequences that are present for ≥4 weeks after an initial COVID-19 infection, even in children who were initially asymptomatic (*CDC, 2021)*. Post-COVID Conditions are thought to affect 5% to 80% of individuals who have had COVID-19 infection of any severity, but the data is limited on its impact on the pediatric population. Because of the uncertainty surrounding Post-COVID Conditions, including the wide range of presentations, difficulty in assessing potential alternative etiologies, and lack of standardized guidance, a thorough, systematic and multi-disciplinary approach to evaluation and management is warranted.

Important note: It is important to distinguish between the care outlined below for Post-COVID Conditions and that of **Multisystem Inflammatory Syndrome in Children (MIS-C)**, which can appear weeks after a child's initial infection as well. MIS-C can be a medical emergency and the management should not follow this referral guideline. The CDC defines MIS-C as an individual <21 years of age with fever, laboratory evidence of inflammation, and evidence of clinically severe illness requiring hospitalization, with multisystem (≥2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic, or neurological) AND no alternative plausible diagnosis; AND positive for current/recent SARS-CoV-2 infection (or exposure to suspected/confirmed COVID-19 case within the 4 weeks prior to the onset of symptoms).

INITIAL EVALUATION

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PCPs should be mindful of the presence of post-COVID conditions after any documented SARS-CoV-2 infection, even if the child is initially asymptomatic. New or persisting symptoms are present for ≥4 weeks from acute infection (i.e., ≥4 weeks from symptom onset and/or first positive test). Note that patients who present with possible MIS-C should be excluded from this guideline.

RELEVANT CLINICAL HISTORY/REVIEW OF SYSTEMS:

- **Past Medical History:**
  - Confirmation of SARS-CoV-2 infection and date of onset
  - Symptom severity (if any) during acute infection
  - History of thrombosis
  - Other physical or mental underlying disease states present that may contribute to presentation
- **Family History:**
  - Note if any immediate family with inherited thrombophilia (i.e., Factor V Leiden, Prothrombin Gene Mutation, Protein S or Protein C deficiency, Anti-thrombin III deficiency)
- **Symptoms Associated with Post-COVID Conditions (most common):**

  *****Symptoms present for ≥4 weeks from acute infection (i.e., ≥4 weeks from symptom onset and/or first positive test)*****
  - **Overall Wellness:**
    - Post-exertional malaise and/or poor endurance (worsening of symptoms following minor physical/mental exertion, worsening 12-48 hours after activity and lasting for days or even weeks
  - **Cognitive/Mental:**
    - Insomnia/difficulty sleeping or hypersomnia

- Fatigue (compared to before COVID-19 infection)
- Depression, anxiety, or mood/behavioral changes compared to before COVID-19 infection
- Brain fog, cognitive impairment
  - → Complete **Appendix A: Pediatric Cognitive Function – Short Form**

- **Head:**
  - Mild-moderate, intermittent headache
  - Seizures
- **ENT:**
  - Anosmia (loss of smell)
  - Change or loss of taste
  - Persistent nasal congestion
- **Lungs:**
  - Intermittent dyspnea
  - Persistent cough
  - Exercise intolerance
  - Chest tightness
- **Heart:**
  - Palpitations and/or tachycardia
  - Lightheadedness
  - Chest pain
- **GI:**
  - Abdominal pain
  - Diarrhea
  - Constipation
  - Nausea/vomiting or inability to tolerate intake
- **GU:**
  - Difficulty or painful urination
- **MS:**
  - Pain
  - Arthralgia
  - Myalgia
  - Paresthesia, neuropathy
  - Muscle weakness
  - Abnormal movements
- **Skin:**
  - Rash or abnormal discoloration
- **Endocrine:**
  - Menstrual cycle irregularities
  - Significant weight loss or weight gain
- **Infectious:**
  - Fever *without concern for MIS-C*
- **Heme:**
  - Signs of thrombosis or anemia
- **Other:**
  - Any new symptoms that have persisted for more than 4 weeks after a confirmed SARS-CoV-2 infection

	• **Timing of Onset:**
	  ○ Confirm timing of initial infection
	  ○ Note persisting or new symptoms that are present ≥4 weeks after initial acute infection (i.e., ≥4 weeks from symptom onset and/or first positive test) that are not easily explained by an alternative etiology
	
	FULL PHYSICAL EXAM:
	***A full physical examination should be completed by the PCP and should note the following components:**
	  ○ Vitals: HR, RR, O2 sat, BP, temperature
	  ○ Anthropometrics: Weight, height, BMI
	  ○ Skin: Full skin examination; include any swelling, pigmentation, varicosities, ulcers
	  ○ HEENT: standard examination; include any oral ulcerations
	  ○ Cardiac: include heart sounds, perfusion, liver edge, edema
	  ○ Lung: include SpO2, location/presence of abnormalities
	  ○ GI: include presence of hepatoslenomegaly, distention, abnormal bowel sounds
	  ○ GU: standard examination, if needed
	  ○ MS: include joint examination, ROM, pain, edema
	  ○ Neuro: include a gross neurological examination
	  ○ Heme: assess for any indication of thrombosis, DVT, PE, or stroke
	• **RED FLAGS:**
	  ○ Any abnormalities on examination should be further investigated and referred, as appropriate
	• **URGENT/EMERGENT RED FLAGS**:
	  ○ Any symptoms or signs of clinical instability, including, but not limited to:
	  • severe chest pain, severe shortness of breath, severe persistent headache, severe abdominal pain, persistent fever with concern for MIS-C, signs of thrombosis/DVT/PE/stroke
	  • active suicidality or mental health instability placing child at immediate risk of harm to self or others

INITIAL PCP MANAGEMENT	**Initial Management by PCP:**
	• Establish if the patient needs urgent/emergent referral (see URGENT/EMERGENT RED FLAGS above):
	  ○ Refer patient to emergency care, as appropriate
	• Establish if acute intervention is needed (see RED FLAGS above):
	  ○ Standard clinical management should be initiated by the PCP on a case-by-case basis of patient's presenting signs and symptoms
	• Establish if above signs and symptoms could be due to re-infection with SARS-CoV-2:
	  ○ Although rare, reinfection within 90 days of initial infection could occur
	  ○ Consider symptoms, risk factors/exposures, and discussing case with CT Children's Infectious Diseases providers

WHEN TO REFER TO LONG HAUL CLINIC	All patients with a concern for post-COVID conditions can be referred to CT Children's "Long Haul" Clinic in Infectious Diseases. All referrals are considered routine and will be scheduled in 2-3 weeks.
	• **Routine referral to Long Haul Clinic if all of the following criteria met:**
	  ○ Documented SARS-CoV-2 infection ≥4 weeks prior
	  ○ New or persisting symptoms listed above are present for ≥4 weeks from acute SARS-CoV-2 infection (i.e., ≥4 weeks from symptom onset and/or positive test result)
	  ○ Abnormal/positive **Pediatric Cognitive Screen: Appendix A**
	• **Defer referral if any of the following criteria are present:**
	  ○ Absence of acute SARS-CoV-2 infection

	○ New or persisting symptoms have been present for <4 weeks (i.e., <4 weeks from symptom onset and/or first positive test result) ○ New or persisting symptoms are easily attributable to alternative, underlying disease process • **Emergency management if URGENT/EMERGENT RED FLAGS are present. Routine referrals are not clinically appropriate in these instances.**
HOW TO REFER	**Routine Referral to Department of Infectious Diseases and Immunology via CT Children's One Call Access Center** **Phone:** 833.733.7669 **Fax:** 833.226.2329 ***Information to be included with the referral:*** ▪ Notes from recent visits that document specific Post-COVID Conditions that are present ▪ Growth charts (height, weight, BMI) ▪ Copy of documented laboratory report of SARS-CoV-2 infection (include date of test) ▪ Copy of **Pediatric Cognitive Function – Short Form (Appendix A)** ▪ Copies of other relevant laboratory studies and imaging studies
WHAT TO EXPECT – PCPs	**What to expect from CT Children's Visit:** ▪ Initial evaluation by Long Haul Clinic in Infectious Diseases within 2-3 weeks. This may be an in-person or telemedicine visit. ▪ Comprehensive history, review of systems and physical exam ▪ Confirmation of Long Haul diagnosis by Infectious Diseases provider ○ Baseline laboratory studies ○ Additional laboratory and imaging studies, as indicated ○ Referral to appropriate subspecialists to assess for other organic causes, as appropriate ○ If appropriate, patient will be referred to CT Children's Pain Team to assist with a multi-disciplinary approach for symptomatic management of certain symptoms such as fatigue, brain fog, etc. ▪ If Long Haul diagnosis is unlikely to be the etiology of current presentation, patient will be transitioned back to the PCP for further management.
WHAT TO EXPECT – Patients/Families/ Caregivers	**PCPs to review with patients/families/caregivers:** ▪ Initial evaluation by Long Haul Clinic in Infectious Diseases within 2-3 weeks, to confirm Post-COVID Condition diagnosis. There is no specific cure for Post-COVID Conditions and much is still unknown. Your child will be managed on a case-by-case basis, and resolution of symptoms may take some time. Symptoms may initially be managed by your primary care provider. ▪ Your initial visit with the Long Haul Clinic may be in-person or through a telemedicine visit. ▪ The provider may order further lab tests and studies, as appropriate. ▪ If appropriate, your symptoms may be managed by a multi-disciplinary group of specialists, with further specialty follow up to assess for any other causes of your symptoms. It may take 2-3 weeks to be seen by other specialists after your initial visit with Infectious Diseases. ▪ Your specialists will be communicating closely with your primary care provider.

Appendix A: Pediatric Cognitive Function – Short Form

Screening is positive if: score <25 or ≥2 items are "quite/very much".
If patient has baseline ADHD, a significant change from baseline (prior to COVID-19 infection) should prompt a referral.

Neuro-QOL Item Bank v2.0 –Pediatric Cognitive Function – Short Form

Pediatric Cognitive Function – Short Form

Please respond to each question or statement by marking one box per row.

		Not at all	A little bit	Somewhat	Quite a bit	Very much
NQCOGped03	I forget schoolwork that I need to do……	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
NQCOGped05	I sometimes forget what I was going to say……	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
NQCOGped08	I react slower than most people my age when I play games. ……	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
NQCOGped15	I forget things easily……	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
NQCOGped17	I have trouble remembering to do things (e.g., school projects)……	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
NQCOGped18	It is hard for me to concentrate in school……	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
NQCOGped19	I have trouble paying attention to the teacher……	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
NQCOGped20	I have to work really hard to pay attention or I will make a mistake……	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1

Key References:

- Children and COVID-19: State-Level Data Report (aap.org)
- Key Points | Evaluating and Caring for Patients with Post-COVID Conditions | CDC
- Tracking - Johns Hopkins Coronavirus Resource Center (jhu.edu)

Other References:

- Brackel, C.L.H., Lap, C.R., Buddingh, E.P., et al. Pediatric long-COVID: an overlooked phenomenon?. *Pediatr Pulmonol*. Published online June 8, 2021. doi:10.1002/ppul.25521.
- Buonsenso, D., Munblit, D., De Rose, C., et al. Preliminary evidence on long COVID in children. *Acta Paediatr*. 2021;110(7):2208-2211. doi:10.1111/apa.15870PubMed.
- Ludvigsson, J.F. Case report and systematic review suggest that children may experience similar long-term effects to adults after clinical COVID-19. *Acta Paediatr*. 2021;110(3):914-921. doi:10.1111/apa.15673PubMed.
- Say, D., Crawford, N., McNab, S., Wurzel, D., Steer, A., Tosif, S. Post-acute COVID-19 outcomes in children with mild and asymptomatic disease. *Lancet Child Adolesc Health*. 2021;5(6):e22-e23. doi:10.1016/S2352-4642(21)00124-3PubMed.