Sickle Cell Disease and COVID-19:
An Outline to Decrease Burden and Minimize Morbidity

Medical and Research Advisory Committee
Sickle Cell Disease Association of America

This document will be updated once weekly on Friday afternoons as data and evidence emerge.

As of March 17, 2020, there are 188,421 infected and 7,499 deaths from COVID-19 worldwide. While most of these patients are in the Hubei province of China, the numbers in the United States are climbing exponentially with 4,748 cases and 93 deaths. The major morbidity and mortality from COVID-19 is described by Guan et al. NEJM 2020. In a cohort of 1099 patients, the median age of the patients was 47 years; 41.9% of the patients were female. Of this cohort, 5.0% were admitted to the ICU, 2.3% underwent invasive mechanical ventilation, and 1.4% died. The most common symptoms were fever (43.8% on admission and 88.7% during hospitalization) and cough (67.8%). On admission, ground-glass opacity was the most common radiologic finding on chest computed tomography (CT) (56.4%). No radiographic or CT abnormality was found in 157 of 877 patients (17.9%) with non-severe disease and in 5 of 173 patients (2.9%) with severe disease. It is clear from the work of our colleagues in China and Italy, that the disease is particularly devastating to individuals with pre-existing conditions.

Sickle cell disease (SCD) affects 100,000 individuals in the United States and many more world-wide. A major cause of morbidity and mortality in these individuals is acute chest syndrome (ACS) which is the term used for a constellation of findings that includes chest pain, cough, fever,

hypoxia (low oxygen level) and lung infiltrates. Acute chest syndrome may be the result of sickling in the small blood vessels, pulmonary infarction/emboli or viral or bacterial pneumonia. The management of ACS is challenging and requires vigilance from the medical team. There is a significant concern that the overlap of lung disease from COVID-19, in the setting of sickle cell lungs already primed for and scarred from acute chest syndrome may result in significant complications and amplification of healthcare utilization. Moreover, individuals with sickle cell disease have high utilization of acute care services including emergency departments and hospitals and often present with fever, signs and symptoms of pneumonia or evolving ACS, as well as acute sickle cell pain requiring parenteral therapy. Thus, there may be specific diagnostic, treatment and logistical challenges in meeting the healthcare needs of this population in the midst of the COVID-19 pandemic.

Here, we provide guidelines for providers who may encounter patients suspected of being infected with COVID-19 and having sickle cell disease.

Specifically, for sickle cell disease patients:

- **Clinic Flow and Strategies to Meet Transfusion Demands**
    - Over the next several weeks, we will be inundated with persons under investigation (PUI) for COVID-19. Make every effort to interview the “person of interest” by telephone, text monitoring system, or video conference. Temperature monitoring could be reported by phone or shown to a provider via video conferencing.
    - If possible, reschedule all routine appointments for the next 4-6 weeks. Push your institution to have virtual appointments and electronic refills.
    - Reach out to your state board to have a waiver on duration of opioid prescriptions. (for example, the New York State Board has given three-month waivers to sickle cell patients).

- Halt all new research enrollment, including gene therapy/bone marrow transplantation
- Use enhanced discretion when ordering transfusions in sickle and non-sickle cell patients in the hospital and require all transfusions to be approved by hematology.
- Medical leaders should encourage local communities and political leadership to support local blood drives as blood shortages are anticipated.
- In the setting of blood shortage, clinicians will need to prioritize transfusion according to clinical need. Highest priorities include patients with recent stroke, progressive or critical neurovascular disease and those with repeated acute chest syndrome despite Hydroxyurea and significant cardiac or respiratory co-morbidity. Consider transitioning to Hydroxyurea for patients eligible according to TWITCH criteria. (Ware et al Lancet 2016)
- For patients with fever and cough
  - If possible at your center – test ALL patients for COVID-19.
  - Follow standard operating procedures for sickle cell disease and fever.
  - Consider minimizing hospitalizations if COVID-19 negative and manageable with outpatient antibiotics.

COVID-19+ Treatment in Patients with Sickle Cell Disease

- Consider early aggressive simple or exchange transfusion for patients with SCD and COVID-19 with fever and cough. This should certainly be done in patients with worsening anemia, evidence of hypoxia and chest x-ray changes, but may be done in the absence of these indications. This recommendation is based on H1N1 and sickle cell disease experience (Inusa et al Blood 2011, Jacobs et al PBC 2011).

- General respiratory measures for infected patients are to avoid aerosol-based interventions.
    - Nebulizers should not be used in a non-negative pressure room, instead use metered-dose inhaler for Albuterol
    - No non-invasive ventilation or high flow oxygen, or bronchoscopy on the general floors; should only be done in negative pressure rooms
    - Non-invasive oxygen therapy should progress to intubation to limit aerosolization and infection risk.
- Prophylactic antibiotic management and use oseltamivir until influenza ruled out
- Steroids are contraindicated until we have more data on immune system responses.
- Patients should be assessed for pulmonary hypertension and right ventricle dysfunction. Providers may consider inhaled nitric oxide in the setting of these entities.
- For severe and progressive cases, consider prone ventilation, inhaled nitric oxide (preferred) or Epoprostenol therapy, paralysis, and extra-corporeal membrane oxygenation.
- At the discretion of providers, Ritonavir/Lopinovir, Tocilizumab or Hydroxychloroquine may be used.
- The data around non-steroidal anti-inflammatory drugs, angiotensin converting enzyme inhibitors and angiotensin II receptor blockers are not clear and decisions about these drugs should be made on a case-by-case basis.

The coming months will be unprecedented in the history of healthcare. These recommendations serve as a template that may be beneficial when navigating this unchartered territory.

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