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

(Adapted for Sub-Saharan Africa)

This document will be updated weekly as data and evidence emerge.

April 1, 2020- Sickle cell disease (SCD) affects ~100,000 individuals in the United States, 3,000,000 in Africa, and millions globally. Individuals living with SCD suffer from both acute and chronic complications that require close contact with the medical system. These include acute sickle cell pain, fever, and the acute chest syndrome (ACS) which is the term used for a constellation of findings that includes chest pain, cough, fever, hypoxia and new lung infiltrates. There is a significant concern that the overlap of fever and lung disease from COVID-19 with ACS may result in increased complications and amplification of healthcare utilization among individuals with SCD. Moreover, individuals with SCD, in general, experience 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 during the COVID-19 pandemic.

Here, we provide suggested guidelines for the acute and chronic disease management of patients with SCD given the multidimensional and evolving changes and challenges in our healthcare operational landscape.

Routine Clinical Care

- If possible, convert all routine in-person appointments to virtual or telephonic appointments. **Do not simply cancel appointments as patients need guidance and planning now more than ever.**
- Educate patients and parents over the telephone about COVID-19 signs and symptoms and the importance of **physical distancing** to limit chances of exposure and infection. **Encourage enhanced emotional connection through virtual or cellular-based modalities.**
- Counsel patients and parents to continue to seek medical help for fever and other signs of infection. Counsel them to **call first** - their hospital, doctor, or nurse - for advice on where to go safely for evaluation.
- Make sure patients have a thermometer and know how to use it and clean it after each use.

- Make certain your patients have an ample supply of all prescribed medication at home (including analgesics) to manage both acute and chronic pain. If needed, reach out to your state medical board to institute a waiver on duration of opioid prescriptions.

- Prioritize the use of pharmacies who deliver medications to patients.

- **Counsel patients to adhere closely to use of hydroxyurea and other chronic medications such as L-glutamine, Voxelotor and Crizanlizumab as prescribed.**

- Consider starting and/or optimizing existing therapies known to reduce sickle cell pain frequency (hydroxyurea, L-glutamine, crizanlizumab) as this is what most commonly brings older children and adults in direct contact with emergency departments and hospitals. The goal is to reduce this contact, if possible, to limit exposure to COVID-19.

- Consider active e-consultation (telephone, texting, web-based or video conferencing) where possible for participants who are enrolled in research or health registries.

Management of Acute Sickle Cell Pain or Other Complications

- Encourage patients without fever or signs of infection to manage pain at home with oral medications to reduce hospitalizations and visits to the emergency department.

- Consider prescribing naloxone for home use and educating patients and parents on when and how to use it.

- Call in or e-prescribe analgesic medications to the patient's pharmacy and preferentially use pharmacies that deliver medications to patients' homes.

- Call patient frequently to assess response to home-based treatment and offer in-person evaluation if this fails.

- Urge patients to continue strict adherence to agents that reduce acute sickle cell pain frequency (e.g. hydroxyurea, L-glutamine, crizanlizumab) to reduce the likelihood of another pain episode.

Triage for possible COVID-19

We recognize that almost all institutions have established COVID-19 task forces with specific protocols. We underscore that it is essential that every institution includes SCD patients as a high risk category, thus we advise taking the following into consideration:

- Make every effort to interview the patient by telephone, text monitoring system, or video conference. Temperature monitoring could be reported by phone or shown to a provider via video conferencing.

- For patients with COVID-19 symptoms (fever, cough, or shortness of breath):

- Schedule patient for an outpatient visit immediately. Avoid the emergency department (ED), if possible. If the ED must be used, call ahead to facilitate care and isolation.

- If it is possible at your center, test patient for SARS-CoV-2. If it is not possible, follow guidelines and collect appropriate sample and send to a testing facility.

- Follow standard of care for managing SCD and fever including culturing of blood and other specimen (as indicated), testing for typical viral infections, administration of empiric broad-spectrum antibiotics to cover encapsulated organisms (e.g., ceftriaxone), and assessing for signs of acute chest syndrome.

- If the patient is COVID-19 negative and close telephone contact is possible to assess routinely for progression of symptoms, consider management at home with oral antimicrobials.

- If possible, give the patient an incentive spirometer to use at home.

Treatment of COVID-19 in Patients with Sickle Cell Disease

This is a rapidly evolving area of medicine without fully established standard of care for any population of patients, thus we advise taking the following into consideration when treating SCD patients with COVID-19:

- **Monitor closely for signs of ACS and treat aggressively**.

    - Be vigilant for signs of rapidly progressive ACS, especially in adults: thrombocytopenia, acute kidney injury, hepatic dysfunction, altered mental status, and multi-organ failure (Chaturvedi et al. Am J Hematol. 2016). Use standard treatment protocols for ACS.

    - Standard of care for ACS includes empiric antibiotics and use of oseltamivir until influenza is ruled out, supplemental oxygen, incentive spirometry, and good pain control to reduce atelectasis.

    - Transfusion for ACS – Transfusion should be performed in patients with worsening anemia, evidence of hypoxia and chest x-ray changes. Initiate exchange transfusion for progression of hypoxia or clinical deterioration.

- Be vigilant for signs of Fat Emboli Syndrome: worsening anemia and mental status, hemolysis, thrombocytopenia, hypoalbuminemia, respiratory distress, and petechial rash. Can progress rapidly and mortality can be >60% in 48hrs.

- SCD patients often have undiagnosed pulmonary hypertension (PH) which could affect management of COVID-19. This should be considered in those who are acutely ill as patients can develop increased pulmonary pressures and, at times, right sided heart failure during ACS (particularly in those with known PH) and if these are present, consultation with Cardiology or Pulmonary is warranted.

- Significant numbers of patients with SCD have co-morbid asthma which may be exacerbated by acute viral illnesses. Review your hospital policies regarding the use of nebulizers during the COVID-19 pandemic as many institutions have advised against the use of aerosol-based interventions. Under such circumstances, consider using metered-dose inhaler instead.

- Many SCD patients are chronically prescribed NSAIDs, angiotensin converting enzyme inhibitors, and angiotensin II receptor blockers. Data are emerging regarding possible negative effects of these classes of drugs on people being treated for COVID-19. We suggest regular review of emerging data to guide decision-making about these drugs on a case-by-case basis.

Scheduled Chronic Blood Transfusions for Sickle Cell Disease

In the setting of blood shortage, clinicians will need to prioritize transfusions according to clinical need. Highest priority indications for continued transfusion include stroke prevention, progressive or critical neurovascular disease and those with recurrent acute chest syndrome unresponsive to hydroxyurea, and significant cardiac or respiratory co-morbidity. To date, data suggest that transfusions remain safe.

- Monitor the availability of blood in your community closely as you may have to adjust your transfusion practices (e.g. apheresis vs manual/simple transfusion) to maintain current individual patient treatment goals.

- Consider transitioning to hydroxyurea for patients eligible according to TWITCH criteria. (Ware et al Lancet 2016).

- If your institution matches red cells for CEK antigens, please continue.

- Indications where maintenance of current transfusion strategy is imperative:

    - Children with history of stroke/abnormal TCD: maintain HbS < 30% or continue current strategy*.

    - Adults with history of stroke or abnormal TCD as children: maintain HbS < 30% or continue current strategy*.

- Consider modification of transfusion strategy in order to conserve blood in the following:

    - Patients receiving chronic transfusion for recurrent acute chest syndrome: continue current strategy*, individualize for maintenance of HbS < 30% vs < 50%, consider adding disease-modifying drug (hydroxyurea).

    - Patients on RBC exchange for end organ damage, priapism, or other non-neurologic indication: switch to simple transfusion and higher HbS% goal for 3-6 months or until blood supply recovers, if baseline hematocrit allows (individualize, generally maintain hematocrit <33%).

**for patients who may be stable with a HbS goal that is ≥ 30%, maintain current goal*

Need for Widespread Blood Donation

- **Encourage people to Donate, Donate, Donate.**
    - Medical leaders should encourage local communities and political leadership to support local blood drives as blood shortages are anticipated.
    - During “shelter in place”, blood donation probably is considered an essential activity.

Clinical Trials, COVID-19, and Sickle Cell Disease

- We are not aware of any clinical trials in COVID-19 specifically for SCD. However, a non-research global registry collecting only de-identified data has been established as a voluntary effort to identify the impact of COVID-19 on people with SCD: https://covidsicklecell.org/
- People with SCD should not be excluded *a priori* from COVID-19 clinical trials.
- Modify other ongoing clinical trials for the safety of patients and staff.
- Halt all other new research enrollment requiring a patient visit, including gene therapy/bone marrow transplantation, unless it is deemed in the patient’s best interest or involves COVID-19 clinical investigation or compassionate use protocols for very ill patients.

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