# 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 as data and evidence emerge.***

**May 27, 2020** - Sickle cell disease (SCD) affects 100,000 individuals in the United States 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 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.
- Halt all new subject enrollments for research requiring patient visits unless it is deemed in the patient's best interest or involves COVID-19 clinical investigation or compassionate use protocols for very ill patients.

## Management of Acute Sickle Cell Pain

- 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. **Note that some patients with SCD present initially with acute sickle cell pain therefore close telephone contact should be employed with low threshold for in-person evaluation and COVID-19 testing.**
- 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 COVID-19. 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 simple transfusion if patient is symptomatic or there is significant anemia (hemoglobin < 9 g/dl or greater than a 2 g/dl fall in hemoglobin; modified from NIH Recommendations). 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.

- **Management of hypercoagulability:**

    - COVID is associated with elevated D-dimer, prolongation of the prothrombin time, thrombocytopenia, reduction fibrinogen and these have prognostic significance in infected individuals without sickle cell disease. Such findings are also common in sickle cell patients with severe acute chest and multiorgan failure. These should be measured and monitored in all patients admitted with COVID infection and a risk stratification algorithm has been developed by the International Society of Thrombosis and Hemostasis. https://onlinelibrary.wiley.com/doi/abs/10.1111/jth.14810. Also see ASH recommendations. https://hematology.org/covid-19/covid-19-and-coagulopathy.

    - There also appears to be an increased risk of thrombosis with or without SCD. ISTH also recommends that prophylactic heparin be considered in all hospitalized patients that are not bleeding and who have platelet counts greater than 25,000. Anticoagulation and risk stratification recommendations for children and adults hospitalized with COVID are available from the American Society of Hematology https://hematology.org/covid-19/covid-19-and-vte-anticoagulation

- **Kawasaki-like syndrome.**

    - Recent reports highlight an increase in children of a Kawasaki–like disease, a systemic vasculitis, sometimes presenting in a very severe form. While the connection with COVID-19 has yet to be demonstrated, these data should be taken into careful consideration in the upcoming months. (See https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31103-

X/fulltext)

- **Managing the COVID-19+ SCD patient following discharge from the hospital.**

    - Patients with SCD who are discharged from the hospital and known to be COVID-19 positive remain at risk for serious complications including the acute chest syndrome and secondary bacterial infection.
    - Patients should only be discharged if close outpatient follow up can be instituted, preferably with daily phone calls to the patient by an outpatient provider (physician or nurse) to assess for symptoms suggesting progression of COVID-19 disease severity or the development of sickle cell-related complications.

## 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, 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 you match 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 or partial exchange 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.

# Frequently Asked Questions

## What should I do if a patient or a parent asks for a letter for work?

- Prepare a form letter that supports their request to work at home and can be easily customized for each patient. Highlight that SCD is considered to be a high-risk condition for severe COVID-19 infection. www.sicklecelldisease.org/template-letters-for-caregivers-2/

## How can I get information for my patients about COVID-19?

- Please have them go to www.sicklecelldisease.org where they can get updated information that is specific for patients and their caregivers.

# SCDAA Medical and Research Advisory Committee Members

Miguel R Abboud, MD
Professor of Pediatrics and
Pediatric Hematology-Oncology
Chairman
Department of Pediatrics and Adolescent Medicine
American University of Beirut
Beirut, Lebanon

Biree Andemariam, MD
Chair, Medical and Research Advisory Committee, Sickle Cell Disease Association of America
Chief Medical Officer, Sickle Cell Disease Association of America
Director, New England Sickle Cell Institute
Associate Professor of Medicine
University of Connecticut Health
Farmington, Connecticut

Shawn Bediako, PhD
Associate Professor
Department of Psychology
University of Maryland Baltimore County
Baltimore, Maryland

Andrew Campbell, MD
Center for Cancer and Blood Disorders
Children's National Health System
Associate Professor of Pediatrics
George Washington University School of Medicine and Health Sciences
Washington, District of Columbia

Raffaella Colombatti, MD, PhD
Physician Azienda Ospedaliera-Università di Padova
Department of Womens' and Child Health Clinic of Pediatric Hematology Oncology Via Giustiniani 3
35129 Padova, Italy

Lori Crosby, PsyD
Co-Director, Innovations in Community Research, Division of Behavioral Medicine & Clinical Psychology
Co-Director, CCTST, Community Engagement Core
Psychologist, Research, Behavioral Medicine
& Clinical Psychologist
Cincinnati Children's
Professor, UC Department of Pediatrics
Cincinnati, OH

Deepika Darbari, MD
Center for Cancer and Blood Disorders Children's National Health System Associate Professor of Pediatrics
George Washington University
School of Medicine and Health Sciences
Washington, DC

Payal Desai, MD
Associate Professor
Director of Sickle Cell Research
The Ohio State University
JamesCare at Ohio State East Hospital
Columbus, Ohio