The Sickle Cell Disease Multidisciplinary Clinic at the Lifespan Cancer Institute

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Sickle cell disease (SCD) is one of the world's most common monogenic disorders, affecting about 100,000 people in the United States. The illness is manifested by sudden, unpredictable and severe bouts of pain, termed vaso-occlusive episodes (VOEs). In addition to the classic presentation of severe VOEs, SCD leads to end-organ damage in multiple systems (**Table 1**). This damage is cumulative, and ultimately leads to a decreased average lifespan and quality of life.[1] As is the case for many genetic diseases, pediatricians have been at the forefront of research and treatment for SCD. Nevertheless, as patients with SCD mature into adulthood, they face the unique problems of adults, along with the accumulating burden of symptoms and end-organ damage from hemoglobinopathy, and care in adult medicine practices becomes appropriate. Current guidelines for the management of SCD call for the care of patients with SCD to be coordinated throughout the lifespan and across care settings as in the patient-centered medical home model.[2]

Table 1. Systemic Effects of SCD

Organ or System	Manifestations of end-organ damage
Nervous system	Stroke, neurocognitive impairment, psychiatric disease, neuropathic pain
Eyes	Retinopathy
Heart	Cardiomyopathy, congestive heart failure, cardiomegaly, valvulopathy
Lungs	Interstitial lung disease, pulmonary hypertension, intrapulmonary shunt
Liver	Hepatopathy, gallstones, nausea, constipation
Immunohematologic system	Hemolysis, thromboembolic disease, hyposplenism
Genitourinary system	Isosthenuria, acute kidney injury, chronic kidney disease, papillary necrosis, renal medullary carcinoma, priapism, erectile dysfunction
Skeleton	Avascular necrosis, osteoporosis, compression fractures
Skin	Leg ulcers
Social function	School and work absenteeism, interrupted education, underemployment, underinsurance

Data on the number of patients with SCD in Rhode Island are scarce. Nevertheless, one can arrive at a rough estimate based on the number of African Americans in Rhode Island and the known prevalence of SCD in the African American population. There are about 60,000 people of African descent in Rhode Island.[3] The prevalence of SCD in African Americans is about 1 in 365.[4] The expected number of patients with SCD is therefore about 150 to 200 patients. Hasbro Children's Hospital (HCH) has long had a clinical program in SCD, but no similar multidisciplinary clinic has existed for adults whose care was divided among different community and academic hematologists in Rhode Island.

In the last quarter of 2017, The Lifespan Cancer Institute (LCI) established the SCD Multidisciplinary Clinic (SCDMDC). The clinic was modeled after two successful programs within the Lifespan Academic Medical Center – the Pediatric SCD program at Hasbro's Tomorrow Fund Clinic and the various disease-centered multidisciplinary clinics within LCI. The first patients were cared for in the clinic on January 2, 2018. The mission of the SCDMDC is to facilitate the achievement by patients with SCD of their self-identified life and health-care goals, while mitigating as much as possible the impact of SCD on achieving these goals. The SCDMDC uses three strategies to facilitate care of adult patients with SCD: patient-centered care, multidisciplinary care, and high-touch care.

Patient-centered care is foundational in SCD. By the time they have reached adulthood, most patients with SCD have extensive experience with the health care system, and this experience has left lasting impressions for both good and ill.[5] As with any other specialty clinic, the first visit to the SCDMDC is concerned with gathering records and clarifying the patient's previous disease history. But, in addition to collecting the medical facts, such as number and frequency of hospitalizations, previous treatments and end-organ damage, time is spent elucidating the patient experience of SCD. Certain aspects of the clinical presentation and pathophysiology of SCD make discussion and validation of the patient's experience of disease particularly important.

Despite its prevalence among African-Americans, South Asian-Americans and Arab-Americans, SCD as a whole is

considered to be a rare disease.[6] Patients with SCD are frequently cared for by practitioners with little personal experience with the disease.[7] Furthermore, the episodic nature of VOEs contributes to frequent emergency treatment, and this often comes from nurses and doctors who do not know the patient personally. The primary symptom of VOEs, pain, is entirely subjective. Successful treatment of acute exacerbations of SCD-related pain requires a foundation of trust between the patient and health-care providers. The provider must trust that the patient's description of his or her symptoms is accurate. In turn, the patient must trust that the provider will accept the patient's description of his or her symptoms without objective correlation to laboratory tests or imaging studies. Such deep trust can be built over multiple patient encounters during an ongoing provider-patient relationship, but is often difficult to achieve when providing care to an unfamiliar patient or receiving care from an unfamiliar practitioner.[8] For this reason, patient-centered care relies on providing care within the context of a familiar practitioner-patient relationship. Patients in the SCDMDC are encouraged to receive urgent care within LCI, either through unscheduled visits to their primary practitioner or through parenteral treatment in the LCI infusion suite. In either setting, patients have a better chance of being cared for by someone whom they know and who knows them personally. If patients cannot be cared for within LCI, they are encouraged to present to the emergency department of a Lifespan hospital. In order to facilitate consistent care in this less familiar setting, each patient in the SCDMDC has a personalized plan for treatment of VOEs in his or her chart. This plan includes documentation of the patient's baseline analgesic regimen as well as analgesic suggestions for unscheduled care in the emergency department and if admitted to the hospital. Plans are readily visible in a care co-ordination note in the patient's electronic medical record.

Another aspect of patient-centered care in the SCDMDC is collaborative development and prioritization of goals. While the SCDMDC staff identifies specific treatment goals within the first few provider-patient encounters based on the extent and severity of end-organ damage, patients of the SCDMDC may have more immediate goals such as relief of symptoms. Furthermore, there are only a few therapies known to be helpful in SCD, and all these therapies have significant shortcomings in terms of effectiveness and adverse events. Therapy for SCD typically must be initiated at low doses and titrated up slowly before it can be expected to lead to clinical benefit, whereas side effects are often noticeable shortly after starting therapy. Given these difficulties with the therapeutic tools available to patients with SCD, patients may be reluctant to accept recommended therapies based on prior experiences. Typically, early prioritization of patient goals, such as symptom management, is necessary prior to beginning treatment based on practitioner-identified goals, such as initiation of disease-modifying therapy and prevention of end-organ damage.

Table 2. Disease-specific treatments of SCD

Treatment	Advantages	Disadvantages
Hydroxyurea	Extends life, reduces VOEs, inexpensive	GI discomfort, leg ulcers, leukemogenic, cytopenias
Transfusion	Prevents stroke in children	Hemosiderosis, alloimmunization, vascular access
Glutamine	Reduces VOEs	Nausea, expensive
Crizalinzumab	Reduces VOEs	Expensive, vascular access, infusion reactions
Voxelotor	Increases hemoglobin	No demonstrated effect on VOEs, expensive
Allogeneic hematopoietic cell transplantation	Curative	Expensive, upfront morbidity and mortality, not available for SCD in Rhode Island

VOE – vaso-occlusive episode

Finally, patient-centered care requires offering the full range of therapies for SCD. Until 2017, there was only one approved drug for SCD. Since then, three new drugs have been approved. With respect to non-drug therapy, supportive care includes both simple and exchange transfusion, while hematopoietic cell transplantation (HCT) remains the only curative treatment for SCD. Every patient who is interested in the procedure is offered referral to an HCT program or to the SCD gene therapy program at Boston Children's Hospital.[9] All other disease-specific therapies are available directly through the SCDMDC at Rhode Island Hospital. Individualized treatment plans use any of these therapies either as single agents or in combination. Because there are no experimental data comparing any therapy for SCD to another, the most appropriate sequencing and combination of treatments is unclear. Selection of treatments is based on the known advantages and disadvantages of each therapy (**Table 2**) but ultimately requires a shared decision-making process in which the patient is the ultimate arbiter of which therapies will be used.

The second strategy used for all patients in the SCDMDC is multidisciplinary care. SCD can affect almost any organ system, and most typically affects multiple systems.[1] Specialists from many different disciplines are required to provide comprehensive care. The dedicated clinic staff of the SCDMDC includes three physicians, two nurse practitioners, two social workers, two patient navigators, a pharmacist, an infusion nurse, a psychologist and a chaplain. A nurse coordinator leads the clinic. Weekly pre-clinic and post-clinic meetings are organized to co-ordinate care among the different disciplines. Monthly meetings of the SCDMDC steering committee are dedicated to systematic issues and to the discussion of complicated patients.

In addition to the above-mentioned core clinical staff, the SCDMDC has developed working relationships with practitioners in other key disciplines, including pain and palliative care, psychiatry, cardiology, pulmonology, nephrology, acupuncture, music and art therapy, emergency medicine, hospital medicine and orthopedics. Colleagues at the Lifespan Recovery Center have been available to treat the few patients with substance use disorder while the patients remain on indicated narcotic analgesics, a problem that is notoriously complicated to treat.[10]

Such complex multidisciplinary and longitudinal care requires considerable co-ordination. Patients of the SCDMDC are strongly encouraged to identify primary care providers and are typically referred to a primary care practice if no such provider has been identified.

The third strategy used by the SCDMDC is high-touch care. Care is based on the 2014 NHLBI expert panel report on evidence-based management of SCD.[4] Where the evidence is not clear, the SCDMDC tends to favor screening for known complications of SCD. After the first few visits, it is often the case that several opportunities for screening and treatment are identified. Patients are usually followed monthly until these interventions have been provided or deferred. Thereafter, patients are followed monthly during titration of treatments. Patients with complicated pain management needs, such as patients on high doses of opiates, patients whose opiates are being tapered and patients with co-morbid substance abuse, are typically seen weekly, whereas patients with very complicated analgesic regimens requiring parenteral treatment may be seen several times a week. In the last case, the LCI infusion nurses and advanced practice providers lead care. When patients are on stable therapy, they are seen 2–4 times per year. Patients admitted to hospital are cared for by the RIH house staff and inpatient physicians with consultation from SCDMDC physicians and frequent visits from other clinic staff.

The LCI SCDMDC is now 2 years old. Approximately 60 patients have been treated, with anecdotal benefit to several patients. One clinic patient has died in the last two years. Overall, hospital days have been reduced by about 30% and the number of ER visits for SCD has been reduced by about 50%. Research collaborations have been initiated with the Department of Emergency Medicine and with other SCD centers in New England, as part of the American Society of Hematology SCD Research Network. The staff of the SCDMDC continues to strive to build on these accomplishments. Patients with SCD can be referred to the MDC via the main LCI number, 844-222-2881.

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