Fever, as a potential sign of serious infection, is present in more than one-third of emergency department (ED) encounters in children and young adults with sickle cell disease (SCD). This study by Rineer et al used the Pediatric Health Information Systems database to describe the risk of bacteremia in 35,548 ED visits with fever in children and young adults with SCD at 36 children's hospitals from 2016 to 2021. Rineer et al identified bacteremia in 405 encounters (1.1%) and increased risk of bacteremia associated with a history of bacteremia (odds ratio [OR], 1.36; 95% CI, 1.01-1.83), central line–associated blood stream infection (OR, 6.39; 95% CI, 3.02-13.52), and apheresis (OR, 1.77; 95% CI, 1.22-2.55). Acute chest syndrome occurred in 8,116 encounters (22.8%), and urinary tract infections (492 encounters [1.4%]) were identified more frequently than bacteremia, while meningitis (7 encounters [<0.1%]), osteomyelitis (172 encounters [0.5%]), and septic arthritis (39 encounters [0.1%]) were rare.

Infection (mostly pneumococcal bacteremia and malaria) remains the leading cause of death in children with SCD worldwide. The implementation of universal newborn screening for SCD in the United States and early prophylaxis with penicillin were associated with greatly reducing the rate of invasive pneumococcal infections in children aged 3 to 36 months with sickle cell anemia from 9.8 infections to 1.5 infections per 100 person-years. These rates decreased further with the widespread use and expanded serotype coverage of the conjugate pneumococcal vaccines, such that invasive pneumococcal infections, although still much more frequent than the general population, have become a rare cause of serious illness and death in children with SCD in the United States.

What are the other causes of fever in children and young adults with SCD? Acute chest syndrome is by far the most common, occurring in 10% to 23% of the ED visits for fever and can be caused by viral or bacterial infections, fat emboli from bone marrow infarction, or vaso-occlusion in the vasculature of the lung. Viral infections, including respiratory viruses (eg, influenza, respiratory syncytial virus, and COVID-19), Epstein Barr virus, and parvovirus B19, often present with fever as an initial symptom, and many of these infections have greater severity or increased complications in people with SCD. Urinary tract infections are identified in 1% to 4% of children, with the highest rates in children younger than 3 years. Additional noninfectious causes of fever include pulmonary embolism and acute sickle vaso-occlusive events affecting bone or bone marrow infarction.

While Streptococcus pneumoniae continues to be the most commonly isolated organism in recent studies, clinicians should be aware of the increasing, albeit still rare, prevalence of other microbes. Bacteremia with gram-positive species, such as Streptococcus viridans and Staphylococcus aureus, and gram-negative species, including Escherichia coli, Bordetella holmesii, Haemophilus influenzae, Salmonella species, Acinetobacter baumannii complex, Klebsiella oxytoca, Pseudomonas aeruginosa, and Stenotrophomonas maltophilia, have been reported. Atypical mycobacterium and Candida bloodstream infections have also been identified in children with SCD. B. holmesii, a fastidious gram-negative coccobacillus with predilection for asplenic hosts, is particularly notable for its delayed detection time in the laboratory, in contrast to other pathogens known to affect people with SCD. Babesiosis can also cause severe infections in asplenic hosts and has been transmitted to people with SCD by transfusion.

The landscape of fever management in children with SCD has evolved due to advances in preventative care and declining rates of bacteremia. For more than 10 years, most institutions have
used some form of risk stratification to differentiate patients who can be safely discharged home after parenteral antibiotics from those who require admission. Often this includes an extensive clinical and laboratory evaluation (blood culture, complete blood and reticulocytes counts, chest radiograph for those with respiratory symptoms, and urinalysis and urine culture in children aged <3 years and with those with symptoms of urinary tract infection). Mortality rates have remained extremely low using these principles. Less is known about the costs of this strategy. For instance, the incidence and consequences of ceftriaxone-induced hemolytic anemia have not been widely measured. The rate of false-positive blood cultures in this population is not known. The impact of emotional trauma to young children who undergo repeated blood cultures or work time lost for parents who must bring their child for evaluation has not been measured. Perhaps it is time to critically reexamine our approach to fever in children with SCD with a more comprehensive analysis of contemporary risks and benefits.

ARTICLE INFORMATION
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