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The Traveler with Sickle Cell Disease

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Abstract

Background—Sickle cell disease (SCD) is the most common genetic disease among persons with African ancestry. This article provides a background on SCD and reviews many important aspects of travel preparation in this population.

Methods—The medical literature was searched for studies about travel-associated preparedness and complications in individuals with SCD. Topics researched included malaria, bacterial infections, vaccinations, dehydration, altitude, air travel, and travel preparedness.

Results—There is very little published literature that specifically addresses the risks faced by travelers with SCD. Rates of medical complications during travel appear to be high. There is a body of literature that describes complications of SCD in indigenous populations, particularly within Africa. The generalizability of these data to a traveler are uncertain. Combining these sources of data and the broader medical literature we address major travel-related questions that may face a provider preparing an individual with SCD for safe travel.

Conclusions—Travelers with SCD face considerable medical risks when traveling to developing tropical countries; these include malaria, bacterial infections, hypovolemia, and sickle cell-associated vaso-occlusive crises. Frank counseling about risks, vigilant preventative measures, and contingency planning for illness while abroad are necessary parts of the pre-travel visit for individuals with SCD.

Sickle cell disease (SCD) is a group of inherited, autosomal recessive red blood cell disorders caused by hemoglobin S (HbS). This common, severe disease is the most important of the inherited red blood cell disorders. HbS results from a single amino acid substitution in the beta chain of hemoglobin. Heterozygous individuals with sickle cell trait (HbAS) are asymptomatic. In contrast, individuals with homozygous disease (HbSS) and other forms of SCD have varying degrees of hemolysis and vaso-occlusive disease, often colloquially referred to as “sickle crises.” Chronic organ damage to the spleen, kidneys,

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brain, lungs, and bones contributes significantly to morbidity experienced by children and adults with SCD. Individuals with SCD are also at risk for life-threatening complications, including sepsis, severe anemia, splenic sequestration, acute chest syndrome (ACS), and stroke. Despite improvements in care, individuals with SCD still suffer from substantial morbidity and mortality. Many patients with SCD have poor health-related quality of life, and are at high risk for mortality at a young age.[1] SCD is the most common genetic disease among persons with African ancestry. It will thus be reasonably common among people travelling to Africa to visit family. In addition, the trans-Atlantic slave trade brought many African people to Caribbean Islands and South America, particularly modern day Brazil. The East African slave trade brought many African people to the Arabian Peninsula and South Asia. It should thus be recognized that not all individuals with SCD have apparently African ancestry; such patients may travel to visit family in many parts of the tropical and/or developing world.

Sickle Cell Disease and Travel

There have been very few systematic studies or even case series of international travel in the SCD population, and yet fewer among the thalassemias and other erythrocyte disorders. Still, the general theme emerges that as compared with otherwise healthy travelers, the SCD population is at substantial risk of a medical complication while abroad. Table 1 While this body of literature is quite heterogeneous, one series of 148 travelers with SCD found that nearly 2/3 developed an acute medical condition while abroad, and more than 10% overall required hospitalization overseas.[2] This sobering finding should inspire frank discussions with SCD patients and their parents about the potential risks of international travel, especially to developing countries and for long durations. These discussions may include discouraging high risk travel altogether in some cases.

Global Burden and Epidemiology

Children born with SCD in the United States or in other high-income countries typically survive into adulthood, albeit with a variable degree of chronic illness. The median survival in the United States for males and females with SCD is now 42 and 48 years respectively.[3] This comparatively good survival can be attributed to universal newborn screening and early detection, prophylactic penicillin, and high quality, comprehensive, medical care.[4] By contrast, in Africa it is estimated that 50–80% of infants born with SCD die before the age of 5 years.[5] In sub-Saharan Africa, the leading cause of mortality in SCD is infection, most commonly due to *Streptococcus pneumoniae* and *Salmonella*.[4]

Care of Patients with Sickle Cell Disease

One of the primary components of caring for an individual with SCD is health care maintenance, which usually requires a team of physicians, nurses, health educators and medical social workers. By teaching patients and caregivers to recognize the early signs of specific illnesses and to understand the need for prompt evaluation of fever many of the complications of sickle cell anemia may be reduced.

Management of SCD involves management of complications, prevention of infection (see below) and prevention of vaso-occlusive complications. The only known preventive therapy for complications of SCD is hydroxyurea, a chemotherapeutic agent that induces fetal hemoglobin (HbF) expression in patients with SCD. Hydroxyurea prevents pain crises, acute chest syndrome (ACS), need for transfusion, and hospitalizations in children and adults. Hydroxyurea is safe and efficacious in children as young as 9 months of age.[6–9] Blood transfusions decrease anemia and can temporarily reduce amount of sickling. Blood transfusion is generally reserved for life threatening complications as well as secondary stroke prevention. Bone marrow transplantation is a rarely available but potentially curative option.

Vaso-occlusive pain crisis

One of the more common complications for travelers with SCD is vaso-occlusive pain crisis (VOC). A number of factors associated with travel, including dehydration, infection, altitude, and weather changes, are known to precipitate acute pain crisis. Literature review has demonstrated that of travelers with SCD hospitalized while abroad, 2–68% were hospitalized because of VOC [2,16,60]. A French study noted that VOC was the most common medical event affecting adult travelers with SCD. They also noted that those patients who developed VOC during travel were not necessarily those who suffered symptomatic disease prior to travel [2]. This emphasizes that even patients without frequent episodes of VOC should be made aware of the risk of this complication. Travelers should maintain adequate hydration and consider travelling with appropriate dosing of opioid analgesics.

Bacterial Infections

Individuals with SCD, particularly children, are at high risk for serious bloodstream infections. While VOC may be the most common complication in adult travelers with SCD, infection carries the highest risk among children.[16] This is primarily due to functional asplenia, which develops early in childhood. Because of the increased risk of bacterial sepsis in patients with SCD any fever (for children >38.3 once or persistently >38.0 and >38.5 for adults) must be urgently evaluated. Basic laboratory evaluation includes complete blood count (CBC), urinalysis, chest x-ray, and cultures of the blood and urine. Ill appearing children and those with a temperature greater than 40 degrees should be admitted to the hospital. Non-toxic appearing children with a temperature less than 40, without infiltrate on chest x-ray, without a history of sepsis, and with a reassuring compete blood count may be managed as an outpatient if close follow up can be ensured. These children can be observed at home after parenteral administration of a long-acting antibiotic that covers *Streptococcus pneumoniae* (pneumococcus) and *Haemophilus influenzae*.[10] Pneumococcus is the most common and important cause of bacteremia in SCD. This risk is substantial: before current preventative strategies were developed the incidence of invasive pneumococcal disease was high as six episodes of bacteremia per 100 patient years, with a peak in the first 3 years of life.[11]

Because the risk of pneumococcal bacteremia is so great the current standard of care is to initiate prophylactic penicillin therapy to children with SCD immediately upon diagnosis.[10, 12] The benefit of prophylactic penicillin diminishes after 5 years of age, and most hematologists with an expertise in SCD recommend cessation of prophylactic penicillin at this point.[13, 14] In select cases, such as a history of surgical splenectomy or a history of pneumococcal sepsis, antibiotics may be continued indefinitely. The role of prophylactic penicillin is controversial in patients with certain heterozygous SCD variants, such as type SC and $S\beta^+$ thalassemia.[15]

It is well-established that patients with SCD are vulnerable to complicated *Salmonella* infections, particularly bacteremia and osteomyelitis. The current medical literature contains relatively few documented cases of *Salmonella* infections among travelers with SCD, so the absolute risk to a traveler is uncertain. In one series of 39 children with SCD who had traveled to Africa, two children developed *Salmonella* bacteremia.[16] In one of the two cases the child had multifocal osteomyelitis. In a separate study of 42 children with SCD, of four hospitalizations occurring after return home one toddler suffered *Salmonella typhimurium* bacteremia complicated by osteomyelitis.[17] On the other hand, among 148 adult travelers with SCD none developed a *Salmonella* infection.[2]

International travel brings the additional challenge of exposure to travel-associated pathogens. The risk for developing an infection is increased by younger age, a longer duration of travel, or unsanitary living conditions.[17] The epidemiology of bacteremia among indigenous Africans with SCD varies by region and appears to differ from what patients experience in North America.[18] *Staphyloccocus aureus* and *H. influenzae* have been found to be important pathogens in studies from both West and East Africa.[19, 20] However, other studies have demonstrated the primary organisms causing bacteremia to be non-typhi *Salmonella* (NTS) and *Klebsiella*.[21, 22] A study focusing on East Africa found that 90% of isolates in bacteremia were due to five primary organisms, including *S. pneumoniae*, HiB, NTS, *Acinetobacter* species, and *Escherichia coli*.[23] It is not known whether these studies are generalizable to a traveler to Africa.

Malaria

The HbS gene and malaria share a fascinating co-evolutionary history. The HbS polymorphism has arisen multiple times independently within Africa, the Arabian Peninsula, and the Indian subcontinent during our recent evolutionary history, as have other hemoglobin polymorphisms such as hemoglobin C. The geographic concordance between HbS gene frequency and malaria transmission is more than coincidental. There is an abundance of evidence that individuals with sickle cell trait (i.e. heterozygous for the HbS allele) suffer less frequent and less severe bouts of malaria.[24, 25] Together these data suggest that malaria has produced a profound selective pressure on the hemoglobin beta chain gene.

What is less clear is how the sickle cell homozygous state, i.e. SCD itself, influences the risk of parasitemia and of severe malaria. Malaria appears to be common among African patients with SCD [26, 27], but some studies suggest that parasitemia [28–30] and severe malarial

anemia [31] are less common than they are in the general population. These studies are limited in a number of respects, including the fact that malaria transmission intensity varies greatly with season and locale. The denominator of patients studied, i.e. age group, rural versus urban, and hospitalized versus non-hospitalized patients makes it difficult to generalize from any one study. Finally, there are many confounders such as the improvement in standard of living and primary medical care in many regions of Africa; and on the other hand the crisis of antimalarial drug resistance.

While the HbS allele may be protective against malaria, this body of research should in no way diminish the importance of malaria prevention strategies for travelers to an endemic region. Even for healthy patients with sickle cell trait, it must be remembered that studies showing decreased severity of malaria have been conducted in indigenous populations. Because of repeated exposure, these subjects likely had a degree of acquired immunity that cannot be assumed in any traveler. Regardless of their risk compared with the general population, malaria remains a major cause of morbidity and mortality among SCD patients within Africa [3], and the risk in a nonimmune traveler with SCD who does not recognize the symptoms of malaria will almost certainly be higher. Indeed imported malaria has been documented among international travelers with sickle cell disease and trait; this includes a family in which two children with sickle cell disease and three with sickle trait developed *Plasmodium falciparum* malaria.[32] Three of the family members developed life-threatening infection.

All major prophylactic agents for malaria (mefloquine, atovaquone-proguanil, doxycycline, and chloroquine where it remains appropriate) are acceptable, and should be urged for all patients with SCD including young infants. In addition to chemoprophylaxis, the travel provider should urge patients with sickle cell disease to use appropriate insect repellents (e.g. *N*,*N*-diethyl-*m*-toluamide (DEET) or picaridin), insecticidal sprays for clothing (e.g. permethrin), and insecticide-impregnated bednets if sleeping in dwellings that are not climate-controlled with adequately screened windows and doors. Providing therapeutic antimalarials for presumptive self-treatment is only advisable in the rare case when an individual would not have prompt access to medical care while abroad. Not all malaria-like illnesses are malaria, and self-treatment for malaria should not mitigate the urgency of a medical evaluation. Malaria rapid diagnostic kits are used and interpreted poorly when used for self-diagnosis by laypersons, and they cannot be recommended for a traveler with SCD.

When possible vulnerable travelers should avoid likely mosquito habitat, such as marshy or wet areas, and limit activity after dusk when malaria is most likely to be transmitted. Finally, travel medicine providers should counsel patients with SCD about the symptoms of malaria and advise prompt medical evaluation for febrile illnesses during or after travel.

Other Travel-Associated Infections

There is a wide array of important infections that may affect travelers to developing countries. There is essentially no systematic literature about their relevance to patients with SCD. There have been a few reported cases of *Shigella* bacteremia in SCD patients.[33]A study of 40 patients from Iraq found a higher prevalence of the protozoal intestinal

pathogens *Giardia lamblia* and *Cryptosporidium* species among patients with SCD.[34] *Schistosoma mansoni* infection does not appear to be more common or more severe among patients with hemoglobinopathies.[35] A number of reports describe fatal dengue fever in patients with SCD.[36–38] In aggregate these case reports suggest an association between severe dengue and SCD, however a dedicated case-control study has not been performed. A French study investigated the epidemiological and clinical pattern of tuberculosis in 12 adult patients with SCD. This study found that lymphatic tuberculosis was more common than in otherwise healthy patients with tuberculosis. Interestingly, they also noted that pulmonary tuberculosis in SCD was less frequent than expected.[39]

Vaccination

Routine vaccinations

Individuals with SCD receive all routine childhood immunizations according to the schedule for otherwise healthy children, including live-attenuated vaccinations such as the measles-mumps-rubella and varicella vaccines. In the United States, this vaccine schedule includes a four-dose series of the 13-valent protein conjugate pneumococcal vaccine (PCV13 or Prevnar 13).[40] In contrast with normal children, however, children with SCD should also receive the 23-valent pneumococcal polysaccharide vaccine (PPSV23 or Pneumovax). This vaccine is given to children over 24 months of age at least eight weeks after completing their PCV13 series. A second dose of PPSV23 is recommended 5 years after the first dose for adults aged 19 to 64 years. No additional doses are needed until age 65. Those who receive PPSV23 before age 65 should receive another dose of the vaccine at age 65 years or later if at least 5 years have passed.[41]

Many European countries, including Bulgaria, Germany, Greece, and the Netherlands, recommend a similar four dose series of the pneumococcal vaccine. A three-dose pneumococcal vaccine recommendation is made by the United Kingdom consisting of primary course of two doses at 2 and 4 months of age with a final third dose at 13 months. France, Belgium, and Austria have similar recommendations [41]. Nineteen European countries have specific recommendations for the use of PPSV23 in patients with splenic dysfunction such as those with SCD. These countries include: Austria, Belgium, Czech Republic, Cyprus, Denmark, England, Estonia, Finland, France, Germany, Ireland, Lithuania, Latvia, Luxemburg, Netherlands, Norway, Slovakia, Sweden, and Switzerland [42].

The conjugate vaccine for *Haemophilus influenzae* type B (HiB) is also part of the routine vaccine series for children in the United States. Children receive a primary series of 2 to 3 doses (depending on the formulation) during infancy, followed by a booster at 12 to 15 months.[42] This series is typically sufficient for antibody production so no further boosters are necessary for patients with SCD.

The World Health Organization (WHO) recommends conjugate HiB vaccines in all routine infant immunization programs. By 2009, 47 countries in the WHO European Region had introduced and routinely implemented immunization with HiB-containing vaccines [44]. Most European countries share the US recommendations for a two to three dose series

between the ages of 2 to 6 months followed by a booster at 12 to 15 months. In Estonia, Hungary, Lithuania, Malta, Portugal, and Spain the booster is given at 18 to 24 months [41].

Current immunization recommendations in the United States also include the quadrivalent conjugate meningococcal vaccine (MCV4) for all individuals between 11 and 18 years of age. MCV4 elicits antibodies protective against *Neisseria meningitides* serogroups A, C, Y, and W-135. MCV4 is recommended between ages 2 and 10 for children at increased risk for invasive meningococcal disease.[42] In 2012, a conjugate tetravalent vaccine that can be administered as a single dose from the age of one year was licensed in Europe [44]. Adults with SCD who have not previously received a meningococcal vaccine should strongly consider immunization before travel to areas where epidemic meningococcal disease occurs. [10] This particularly pertains to travel to the Sahel (the semi-desert region immediately south of the Sahara), the Arabian Peninsula, and the Indian subcontinent.

Patients with SCD are at high risk for complications of influenza; these complications include acute chest syndrome, pain crisis, or invasive bacterial infection. Bundy et al analyzed hospitalizations from 4 states in the US (California, Florida, Maryland, and New York) across 2 influenza seasons (2003–2004 and 2004–2005) and found that children with SCD were hospitalized for influenza at 56 times the rate of children without SCD.[43] This study emphasizes the importance of annual influenza vaccinations for individuals with SCD.

Travel vaccinations

Individuals with SCD may receive all age- and destination-appropriate travel vaccinations. Hepatitis A vaccination is now standard for children under 2 years of age in the United States. This is not the case in most European countries. Hepatitis A vaccine is specifically recommended only in Greece and Austria. Cyprus and the Czech Republic recommend hepatitis A vaccine in specific at risk groups [41]. Live vaccines, such as yellow fever vaccination, may be given to SCD patients before travel to endemic areas in Africa or the Americas. Both injectable and oral attenuated typhoid vaccinations are acceptable in SCD patients. There is no evidence that patients with SCD are at particular risk from the oral attenuated typhoid vaccine.

Diarrhea illness and Hypovolemia

Diarrheal illness is a common affliction among travelers to developing countries. Patients with SCD are uniquely susceptible to developing hypovolemia and free water deficits due to chronic microvascular renal disease. [44] One consequence of this is hyposthenuria, the inability to appropriate concentrate urine.[45] This phenomenon has been observed as early as 6–12 months of age. Hypovolemia may be further exacerbated by various factors during travel to tropical regions, such as heat and sun exposure, lack of access to safe drinking water, and diarrheal illnesses such as traveler’s diarrhea. Because erythrocyte sickling is more likely to happen in the setting of a volume deficit, this confluence of risks can predispose travelers with SCD to a vaso-occlusive sickle cell crisis during travel. Of travelers with SCD hospitalized while abroad, 2–68% were hospitalized because of VOC [2,16,60].

Strategies to minimize exposure to enteric pathogens, specifically avoiding potentially contaminated food and water, are crucial for individuals with SCD. There are a variety of strategies for the treatment of drinking water, and for making safe food choices while traveling in developing countries.[46] Oral electrolyte replacement solution (ORS) is widely available both in the United States and abroad, and it would be wise for patients with SCD to procure ORS prior to travel. Patients with SCD may need a lower threshold to seek medical attention for gastroenteritis, especially when accompanied by signs of hypovolemia, inability to tolerate oral fluids, or complications such as fever or signs of dysentery.[46] Presumptive antibiotic treatment of traveler's diarrhea has become the standard of care for healthy travelers; it is certainly advisable in travelers with SCD. Fluoroquinolones are frequently used for empiric treatment of travelers' diarrhea in adults. Azithromycin can be used for this indication in children.[47, 48]

Air Travel and Altitude

Flying in pressurized aircrafts usually poses no problems for sickle cell patients. The most important considerations are to dress warmly, drink plenty of fluids, and to move about the cabin as often as possible.[10] Erythrocyte sickling and therefore SCD complications can be induced by mild hypoxemia, however. Mountain elevations or travel in planes that maintain cabin pressure at approximately 5000 to 7000 feet (1500 to 2100 meters) is associated with a drop in arterial oxygen pressure (PaO_2) that may adversely affect patients with SCD.[49] During air travel VOC may occur in up to 8.7% of patients with HbS. At mountain altitudes, patients with SCD may have a risk for developing VOC as high as 38% [52]. Complications such as splenic infarction have been noted at high altitudes (over 10,000 feet or 3000 meters) even in patients with sickle cell trait – a genotype that is generally asymptomatic. [10, 49]

Prolonged air travel is a well-established risk factor for venous thromboembolism (VTE). [50] SCD itself is a thrombophilic state – in one study the prevalence of pulmonary embolism (PE) in hospitalized SCD patients less than 40 years of age was approximately 3.5 times higher than African-American controls.[51] Current recommendations, however, rely only on individual assessment of thrombotic and bleeding risk factors.[52] Knee-high graduated compression stockings or a single dose of low molecular weight heparin are options to prevent travel-associated VTE in select cases.[50]

Preparedness for Travel and Access to Care while Abroad

Because of the unique travel needs and medical complications for patients with sickle cell disease, it important to know where travelers with SCD can access medical care while abroad. An important resource is the Global Sickle Cell Disease Network (GSCDN), http://www.globalsicklecelldisease.org. This is a worldwide network of researchers and clinicians working in collaboration to help the global SCD community. Their website includes a SCD treatment center map to provide information about location and services of treatment centers all over the world. Prior to travel, families should know the closest center and understand the services available. It is also important to have transportation and financial support available if emergency medical services are needed.

Blood transfusion services available in Africa may be difficult to access. The World Health Organization (WHO) has advocated that countries develop nationally-coordinated blood services which are community-based. These services rely on voluntary non-remunerated blood donors. Despite the recommendation, less than 20% of sub-Saharan African countries have implemented this system.[53] Transfusion practices in most African countries are hospital based and rely on blood donation from patients' family members. Unfortunately, this system does not provide sufficient blood to meet many patients' clinical need. Testing for transfusion-transmissible diseases is also less uniform in the developing world. A sizeable proportion of HIV transmission in Africa has been attributed to blood transfusions.[54] Blood is not routinely tested for malaria, microfilariae, and other blood-borne pathogens.[55] For this reason SCD patients on a chronic transfusion protocol (such as those with a history of stroke) may be encouraged to limit their length of stay to avoid possible transfusion related complications.

All patients with SCD who are planning travel abroad should be evaluated by a trained specialist in travel medicine. Such visits are most productive when scheduled well in advance of travel. Patients should also discuss their plans with their hematologist. All patients should plan to carry a letter from their hematologist explaining diagnosis, treatment plan (including prescription of narcotics and other medications), and complications of disease. This may serve to facilitate appropriate medical care overseas. Patients may also require permission to carry medications on board the aircraft. All medications should be appropriately and clearly labeled. This is particularly true for narcotic pain medications, which many patients with SCD require to manage pain crises. The United States Transportation Security Administration (TSA) states that passengers with medical conditions are not subject to the same restrictions for their liquid medications as are imposed on other liquids.[56] However, if the liquid exceeds the general allowance it must be declared to the TSA agent and help separate from other liquids. Further medication policies vary by airline and specific area of travel. Other countries of origin may have different requirements. It is important for patients to consult their airline for these policies prior to travel. Additionally, patients with SCD are urged to purchase insurance policies for trip cancellation and for medical evacuation / repatriation in the event of a medical emergency overseas.

The rewards of international travel can be substantial for patients with SCD who have experienced a lifetime of chronic illness. International travel may be associated with higher risks and require detailed preparation. However, with advanced planning and involvement of their medical care providers, patients and families can approach their travels safely and well-informed.

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Table 1

Summary of published case series and case reports of travelers with sickle cell disease and their medical complications.

Reference	Cases	Age	Destination	Duration	Complications
Morbidity among child travellers with sickle cell disease visiting tropical areas: an observational study in a French tertiary care centre [16]	39	4.3–11.7 years (median 7.8)	Mali, n=14, Ivory Coast, n=6, Senegal, n=5, Guinea, n=2, Togo, n=2, Niger, n=1, Mauitania, n=1, West Indies, n=4	30–60 days (median 42)	Fever 17.6%, gastrointestinal disorders 17.6%, Vaso-occlusive crisis (VOC) 5%
The risk of going abroad in sickle cell disease[2]	148	18–56 years (median 26.8)	Africa, 49%, Europe, 27%, West Indies, 22%, Asia, 2%	Not reported	VOC 68%, fever 19%, diarrhea 19%, bronchopulmonary symptoms 11%, headaches 8%, vomiting 6%, cutaneous wound 4%
Sickle cell children travelling abroad: primary risk is infection[17]	42	0.2–17.7 years (median 7.6)	Africa, 100% (Mali, West Africa, Madagascar, Moracco)	0.5–3mo (median 1.29 months)	Fever 9.6%, malaria 4.8%, gastrointestinal infection, 4.8%, VOC, 2%, urinary tract infection, 2%
Acute splenic syndrome in an African-American male with sickle cell trait on a commercial airplane flight[61]	1	43 years	San Diego, CA to Newark, NJ on commercial airline	A few hours	Splenic infarction and subsequent splenectomy
Sudden death during long distance air travel in an HbS/C disease patient[62]	1	41 years	Kuala Lampur, Malaysia	2 hours prior to landing	Sudden death from pulmonary thrombo-embolism
Airline travel in sickle cell disease[63]	73	25 years	Between Jamaica and Miami	Not reported	VOC in 1 patient (1.4%)
Risk of altitude exposure in sickle cell disease[52]	45	10–62 years	Commercial airline trips; Reno, NV and Lake Tahoe, CA	Air travel time —1–14 hours, Mountain exposure—not reported	Mountain exposure—splenic crisis (15%), VOC (42%); Air travel—splenic crisis (12.5%), VOC (10%)

Table 2

Summary of recommendations for the travel medicine professional evaluating a traveler with sickle cell disease (SCD)

- Maintenance of routine care
  - Ensure adequate supply of routine medications (e.g. hydroxyurea, penicillin, pain medications)
  - Ensure traveler has identified where he/she can get emergency care
  - For extended travel ensure traveler makes effort to identify a hematologist abroad
- Malaria prevention
  - Individuals with SCD should receive malaria prophylaxis when traveling to destinations where prophylaxis would otherwise be recommended
  - All chemoprophylactic agents are acceptable in individuals with SCD
- Vaccinations
  - Ensure that prior to travel travelers with SCD have received all age-appropriate vaccinations, and vaccinations uniquely recommended to SCD (pneumococcal polysaccharide vaccine, influenza vaccine)
  - All travel vaccinations, including live-attenuated vaccines, are acceptable
- Diarrheal illness and hypovolemia
  - Instruct in preparation of clean drinking water
  - Provide antimicrobials for treatment of traveler's diarrhea
  - Encourage purchase and use of oral rehydration solution
- Travel preparedness
  - Encourage insurance policies for trip cancellation and medical evacuation