

A 16-year-old boy comes to the emergency department for severe left thigh pain. He was diagnosed with sickle cell anemia during childhood. He has had several episodes of unbearable pain in his abdomen, thighs, and lower back that required hospitalization for pain management and intravenous fluids. The patient has been hospitalized 6 times in the past year and has missed several weeks of school. He does not have regular follow-up visits with his physician and sees him "only if required." His temperature is 37 C (98 F), blood pressure is 120/80 mm Hg, pulse is 100/min, and respirations are 16/min. Pulse oximetry shows a saturation of 97%. Examination shows an uncomfortable-appearing boy. The lungs are clear to auscultation. His left thigh is tender to palpation but has no erythema or swelling. He is able to bear weight and has no pain elsewhere. Adequate hydration and analgesics are administered. What is the best intervention to prevent this patient's painful episodes?

- ☐ A. Antibiotics
- ☐ B. Erythropoietin
- ☐ C. Folic acid supplementation
- ☐ D. Hydroxyurea
- ☐ E. Iron supplementation
- ☐ F. Periodic blood transfusions



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- ☐ A. Antibiotics [1%]
- ☐ B. Erythropoietin [0%]
- ☐ C. Folic acid supplementation [1%]
- ☒ D. Hydroxyurea [93%]
- ☐ E. Iron supplementation [0%]
- ☐ F. Periodic blood transfusions [5%]

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Explanation:

User Id: XXXXXXXXXX

Sickle cell anemia	
Pathophysiology	Autosomal recessive inheritance of sickle $\beta$ globin mutation in African & Hispanic populations
Clinical features	<ul style="list-style-type: none"><li>• Hemolytic anemia</li><li>• Dactylitis</li><li>• Acute vasoocclusive pain crises</li></ul>
Laboratory	<ul style="list-style-type: none"><li>• <math>\downarrow</math> Hematocrit, <math>\uparrow</math> reticulocytes, <math>\uparrow</math> serum low-density lipoprotein, <math>\uparrow</math> unconjugated bilirubin</li></ul>



Explanation:

User Id: [REDACTED]

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Laboratory findings	<ul style="list-style-type: none"> <li>• <math>\downarrow</math> Hematocrit, <math>\uparrow</math> reticulocytes, <math>\uparrow</math> serum low-density lipoprotein, <math>\uparrow</math> unconjugated bilirubin</li> <li>• Peripheral smear: Sickled red cells, Howell-Jolly bodies</li> </ul>
Management	<p><b>Maintenance</b></p> <ul style="list-style-type: none"> <li>• Vaccination</li> <li>• Penicillin (until age 5)</li> <li>• Folic acid supplementation</li> <li>• Hydroxyurea (for patients with recurrent vasoocclusive events)</li> </ul> <p><b>Acute pain crises</b></p> <ul style="list-style-type: none"> <li>• Hydration</li> <li>• Analgesia</li> <li>• +/- Transfusion</li> </ul>

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The hallmark of sickle cell anemia (SCA) is recurrent, acute, painful episodes due to vasoocclusion. **Vasoocclusive crises** can be triggered by dehydration, weather change, nocturnal hypoxemia (sleep apnea), infection, and stress, although there is often no identifiable cause. Patients can suffer from severe, unbearable pain involving the chest, abdomen, lower back, thighs, and knees. The affected sites vary with each episode and individual.

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Acute management consists of **hydration** and analgesics along with **nonsteroidal anti-inflammatory agents** and **opioids**. **Hydroxyurea** is indicated in patients with frequent, acute, painful episodes; history of acute chest syndrome; and severe symptomatic anemia. The major effect of hydroxyurea is to **increase fetal hemoglobin** by stimulating erythropoiesis in primitive erythroid precursors. Sickled hemoglobin is therefore proportionally decreased, resulting in reduced polymerization of red blood cells and fewer episodes of vasoocclusion. Hydroxyurea can also decrease the risk of acute chest syndrome and need for blood transfusions.

The primary dose-limiting side effect of hydroxyurea is **myelosuppression** (eg, neutropenia, anemia, thrombocytopenia), but it is otherwise relatively safe.

**(Choice A)** Antibiotics have no role in preventing acute, painful episodes as the primary pathology in most cases involves vasoocclusion, not an infection.

**(Choice B)** Data regarding the benefits of erythropoietin therapy in SCA patients is limited. It is used only when there is inadequate response with hydroxyurea alone.

**(Choice C)** Folic acid supplementation is recommended to replenish the depleted folate stores from ongoing hemolysis. However, it does not significantly decrease the risk of vasoocclusive episodes.

**(Choice E)** Iron supplementation should be avoided as patients with SCA often require frequent transfusions and are therefore at high risk for iron overload and hemosiderosis-related cirrhosis.

**(Choice F)** Periodic blood transfusions are used primarily for treatment (eg, acute stroke, acute chest syndrome, acute multiorgan failure, acute symptomatic anemia, aplastic crisis); transfusions are indicated for stroke prevention. Although transfusions can potentially decrease vasoocclusive episodes by diluting the amount of sickle cells with normal red blood cells, the risk of transfusion reactions, infection, iron overload, and alloimmunization makes this less optimal than hydroxyurea.

#### Educational objective:

Hydroxyurea is indicated in patients with sickle cell anemia who have frequent, acute, painful episodes. It is a relatively safe therapy and works by increasing fetal hemoglobin.



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#### References:

1. [National Institutes of Health Consensus Development Conference statement: hydroxyurea treatment for sickle cell disease.](#)
2. [Systematic review: Hydroxyurea for the treatment of adults with sickle cell disease.](#)
3. [Sickle-cell disease.](#)