

# Why do we give penicillin prophylaxis to children with sickle cell disease?

**Gaston MH et al. Prophylaxis with oral penicillin in children with sickle cell anemia. A randomized trial. N Engl J Med 1986; 314:1593-9.**

**Take Home Message:** Children with sickle cell anemia who are treated with prophylactic penicillin have a markedly decreased incidence of infection from *S. pneumoniae*.

**Highlights:** Given that infection is one of the major causes of death in young children with sickle cell disease, Gaston et al. published the Prophylactic Penicillin Study (PROPS) in 1986,<sup>[i]</sup> investigating the effect of prophylactic penicillin in children with sickle cell anemia. They randomized 215 children aged 3 to 36 months across multiple centers to receive either penicillin twice daily or placebo. The primary outcome was severe infection (bacteremia, meningitis, or pneumonia requiring hospitalization) due to *S. pneumoniae*. The trial was terminated 8 months early, as 13 of the 110 patients in the placebo group and 2 of the 105 patients in the penicillin group developed pneumococcal septicemia, an 84% reduction in incidence. Because early intervention has been shown to be so important, now screening for sickle cell disease is mandated in all states, and all infants found to have sickle cell disease should be given penicillin until at least age 5.

## The Nitty-Gritty:

### Design:

- o Multicenter, randomized, double-blind, placebo-controlled trial

- o N= 215

- § Penicillin group (n= 105)

- § Placebo group (n=110)

- o Setting: 23 centers in the United States

- o Enrollment: 1983-1985

- o Primary outcome: severe infection (bacteremia, meningitis, and pneumonia requiring hospitalization) due to *S. pneumoniae*

#### **Population:**

- o **Inclusion Criteria:**

- § Children aged 3-36 months with an SS hemoglobin pattern on electrophoresis

- § Free from any signs or symptoms of infection

- o **Exclusion Criteria**

- § Receiving long-term antibiotic or transfusion therapy

- § Known allergy to penicillin

- o **Baseline Characteristics** – from the penicillin group; there were no statistically significant differences between groups

§ Mean age: 17.8 months

- 3-5 months: 15.4%
- 6-11 months: 23.1%
- 12-17 months: 14.4%
- 18-23 months: 22.1%
- 24 months: 25.0%

§ Male sex: 48.5%

§ Palpable spleen: 30.8%

§ Received pneumococcal vaccine: 67.0%

§ Previous infection with:

- Pneumonia: 19.2%
- Bacteremia: 5.8%
- Osteomyelitis: 2.9%

§ Mean laboratory findings:

- Hematocrit: 26.1%

- Hemoglobin: 8.8 g/dl
- White-cell count:  $14.6 \times 10^9$ /liter
- Granulocytes: 31.7%

- **Intervention:** children were randomized to receive either penicillin (125 mg BID) or placebo
- **Primary Outcome:** Severe infection due to *S. pneumonia*: 2 patients (2%) in the penicillin group vs. 13 patients (12%) in the placebo group ( $P=0.0025$ ; 84% reduction in incidence of infection)
- **Adverse Events:** none

[1] Gaston MH et al. Prophylaxis with oral penicillin in children with sickle cell anemia. A randomized trial. N Engl J Med 1986; 314:1593-9.