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Pearson H A, Spencer R P & Cornelius E A. Functional asplenia in sickle-cell anemia. *N. Engl. J. Med.* 281:923-6, 1969.
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Decreased splenic reticuloendothelial uptake of radiocolloid (^{99m}Tc) in young children with sickle cell anemia who had clinical splenomegaly was designated "functional asplenia." This defect is the probable basis for the high mortality from pneumococcal sepsis that these children experience in the first years of life. [The *SCI*® indicates that this paper has been cited in over 245 publications.]

Functional Hyposplenia in Young Sickle Cell Children

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In the late 1960s, a number of case reports described infants and young children with sickle cell anemia who had died of fulminant pneumococcal meningitis and sepsis. Their clinical courses were similar to the severe sepsis seen after surgical splenectomy, and yet we knew that most young patients with sickle cell anemia had clinical enlargement of their spleens. I remember examining the blood of a two-year-old boy with sickle cell anemia who had developed, and fortunately recovered from, severe pneumococcal sepsis. On his blood smear, Howell Jolly bodies were easily noted. These intraerythrocyte particles are normally "pitted" and removed from the circulating red cells by the spleen; but, paradoxically, this child had an enlarged spleen that could be palpated below his umbilicus.

At the time, my colleague and old Dartmouth classmate, Richard P. Spencer, told me about procedures for reticuloendothelial imaging using sulfur colloid tagged with the short-lived radionuclide ^{99m}Tc. A spleen scan was done on the sickle cell child, and there was no uptake of the radiocolloid by his clinically enlarged spleen. Study of a number of other young sickle cell patients showed that their enlarged spleens also failed to take up the radiocolloid. The term *functional asplenia* (perhaps better functional hyposplenia) was coined to describe the phagocytic hypoactivity of the enlarged spleens of young children with sickle cell anemia. Functional asplenia was contrasted with the anatomic asplenia that occurs in these patients during the second decade of life as a consequence of autoinfarction.

Functional hyposplenism was found to be temporarily reversible by blood transfusions in sickle cell children less than six years of age; however, it was irreversible in older children. Functional hyposplenism was not congenital but rather an acquired defect, developing between 4 and 12 months of age as the level of fetal hemoglobin decreased after birth.[1] It was later demonstrated that functional hyposplenism could be more easily diagnosed by enumerating the percentage of circulating vesiculated or "pocked" red blood cells using interference phase contrast microscopy.[2]

These studies helped to provide insights into the pathophysiologic basis of the severe sepsis that until recently killed 10-20 percent of infants with sickle cell anemia. This inordinate mortality can be markedly reduced by early institution of penicillin prophylaxis, for penicillin appears to protect the hyposplenic infant.[3] Because neonatal testing for hemoglobinopathies coupled with early penicillin prophylaxis of affected infants can significantly reduce mortality, a National Institutes of Health Consensus Development Conference has recommended that testing for sickle hemoglobinopathies be made part of standard neonatal screening programs.[4-6] As of June 1989, 30 states have mandated such programs.

Studies of the spleen in our laboratories continue as we learn more about Galen's *misterii plenum organum*.

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3. **Gaston M H, Verter J I, Woods G, Pegelow C, Kelleher J, Presbury G, Zarkowsky H, Vichinsky E, Iyer R, Lobel J S, Diamond S, Tate Holbrook C, Gill F M, Ritchey K & Falletta J M.** Prophylaxis with oral penicillin in children with sickle cell anemia: a randomized trial. *N. Engl. J. Med.* 314:1593-9, 1986. (Cited 35 times.)
4. **NIH Consensus Development Conference.** Statement. Newborn screening for sickle cell disease and other hemoglobinopathies. *JAMA—J. Am. Med. Assn.* 258:1205-9, 1987.
5. **Wethers D, Pearson H & Gaston M,** eds. Newborn screening for sickle cell disease and other hemoglobinopathies. *Pediatrics* 83(Supp.):813-913, 1989.
6. **Pearson H A.** A neonatal program for sickle cell anemia. *Advan. Pediat.* 33:381-400, 1986.

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