Role of Radiolabeled Erythrocytes in Evaluation of Splenic Function

The spleen can be viewed as an assemblage of two cell types—lymphoid and reticuloendothelial. To estimate the functions of each of these cell collections requires the use of more than a single technique. Indeed, we now recognize that all splenic functions are not "tightly coupled" and that some activities can be lost without impairing others. From the vantage point of the knowledge gained by many years of work by a number of investigators, we can list some of the major functions of the spleen (Table 1). Evaluation of this array of activities is initially approached by means of the history, physical examination, and a hematologic workup.

Careful study of circulating erythrocytes has a particularly important role to play in the estimation of splenic function. A depressed red cell count is an alerting signal to either impaired production or increased loss or destruction of erythrocytes (as can occur in hypersplenism). Morphology of the RBC also provides further data. Loss of the splenic ability to "pit" intraerythrocytic inclusions results in the circulation of Howell-Jolly bodies in a small portion of the erythrocytes. Recent studies suggest that a more quantitative approach to this splenic function is to count the number of erythrocyte surface pits or indentations (*1,2*). Apparently the spleen normally protects the red cell membrane against such damage. Radionuclides have a role to play in estimating a number of splenic activities.

Splenic erythropoiesis. Production of RBC by the spleen usually ceases at birth, however, the potential for erythropoiesis apparently remains dormant and genetically coded. Thus, during bone marrow failure the spleen can become a site of extramedullary hematopoiesis. Ferrous citrate (Fe-59) has been used to study this phenomenon; however, Fe-59 is far from an ideal radionuclide and other more useful tracers are needed.

Sites of RBC destruction. The key observation was that of Gray and Sterling, who observed that [^{51}Cr] sodium chromate labeled erythrocytes (*3*). This radiochemical formed the basis for determining the distribution of tagged RBCs, the sites of their sequestration, and their apparent survival half-time. Since a portion of the Cr-51 is eluted from erythrocytes, however, the label is not optimum and better tagging agents are necessary. The late Philip Johnson and his coworkers then produced the first "speen specific" radiotracer by using anti-Rh serum to denature Cr-51-labeled RBCs (*4*). After i.v. administration the labeled and denatured red cells accumulated in the spleen. What made the procedure practical, however, was the subsequent demonstration that denaturation of labeled erythrocytes could be accomplished by heating at 50°C. Later Pavel and associates

TABLE 1. A LISTING OF SOME SPLENIC FUNCTIONS

1. Erythrocyte destruction
2. Trapping of foreign particles
3. Hematopoiesis (usually terminates by birth, but the potential remains)
4. Reservoir function for blood elements
5. Culling and pitting (abnormal erythrocytes are removed from the circulation; red cell inclusions such as Howell-Jolly bodies can be removed or "pitted" and the erythrocyte returned to the circulation)
6. Role in platelet and leukocyte removal
7. Possible spenic hormone role in control of hematopoiesis
8. Immunologic functions, such as production of antibodies to intravenously administered foreign particulates

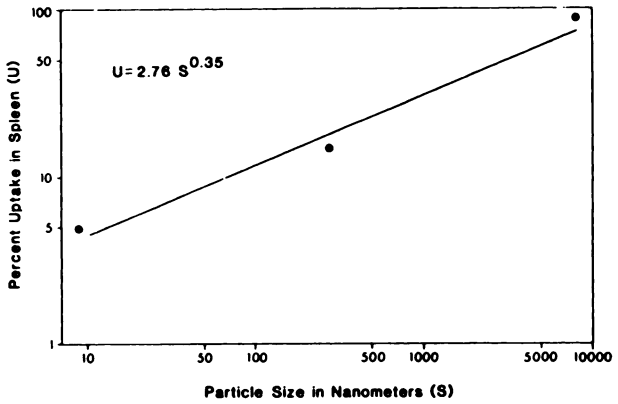

Fig. 1. Log-log plot of percentage uptake of labeled particles by the spleen as function of diameter of particle.

observed that RBCs could be labeled by use of a phosphate and then Tc-99m (*5*), and thus provided the background to the work reported in this issue by Armas and coworkers (*6*).

We can look at the relative uptake of labeled particulates as distributed between liver and spleen. When quite small-sized particles are used (such as Au-198 colloid) there is little extraction by the normal human spleen. With larger particles (the 0.4 μ Tc-99m-sulfur colloid), about 10–15% enter the spleen after i.v. administration. With still larger particulates, such as the denatured 7 μ RBCs, about 90% accumulate in splenic tissue. A plot of such values (Fig. 1) suggests a log-log relationship between percentage uptake in the spleen (U) and the apparent particle size (S, in nanometers). $U = 2.76S^{0.35}$.

This reasoning, however, combines what are undoubtedly two distinct systems. There is compelling evidence that the splenic system for taking up labeled and denatured erythrocytes is distinct from that which accumulates radiocolloid (*7,8*). Data on the disassociation of these two systems in disease states are just beginning to accumulate (*8,9*). Information to be gained by use of the Tc-99m-denatured RBCs in defining the morphology of the spleen may well be minor as compared with data that might emerge on the alteration in splenic RBC trapping in collagen diseases and other disorders. Indeed, our understanding of the uptake process in terms of size, surface charge, and immunologic recognition is still quite rudimentary. Although "functional asplenia" was defined by loss of uptake of Tc-99m sulfur colloid, studies are needed to determine whether the phagocytic function for denatured red blood cells follows a parallel temporal course. Heat-induced damage of RBCs offers a simplicity that is appealing; theoretically, abnormal erythrocytes might lyse. A Tc-99m radiopharmaceutical that binds to red cells and denatures them at the same time may be useful.

RICHARD P. SPENCER
University of Connecticut Health Center
Farmington, Connecticut

ACKNOWLEDGMENT

This research was supported by USPHS Grant No. CA 17802.

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