Splenic Scintigraphy Using Tc-99m-Labeled Heat-Denatured Red Blood Cells in Pediatric Patients: Concise Communication

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Ten children underwent splenic imaging with heat-denatured red blood cells labeled with technetium-99m (Tc-99m DRBC). The presenting problems included the heterotaxia syndrome, recurrent idiopathic thrombocytopenic purpura following splenectomy, mass in the left posterior hemithorax, and blunt abdominal trauma. In nine patients, the presence or absence of splenic tissue was established. A splenic hematoma was identified in the tenth patient. All patients were initially scanned with Tc-99m sulfur colloid (Tc-99m SC), and were selected for Tc-99m DRBC scintigraphy only after the results of the SC scans failed to establish the clinical problem beyond doubt. The availability of kits containing stannous ions, essential for efficient and stable labeling of red blood cells with Tc-99m and requiring only a small volume of blood, make splenic scintigraphy in children a relatively simple and definitive diagnostic procedure, when identification of splenic tissue is of clinical importance.

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Technetium-99m sulfur colloid (Tc-99m SC) is the most commonly used radiopharmaceutical for imaging of the spleen. Following intravenous administration, it is rapidly removed from the blood by the reticuloendothelial system of the liver, spleen, and (to a much lesser extent) bone marrow. Thus, the spleen is adequately visualized and its image can usually be separated from that of the adjacent liver in patients with normal upper abdominal anatomy. In certain disease entities, however, this is not the case and selective imaging is desirable.

Although splenic imaging with radiolabeled red blood cells (RBCs) has been available for over 20 yr (*1–6*), it is only recently that advances in radiochemical techniques have made it a practical examination.

Chromium-51 was the first radionuclide to be used successfully for the labeling of intact and heat-denatured RBCs for both in vitro and in vivo studies (*2, 7–9*). Chromium-51, however, is an unsatisfactory imaging agent because of its low photon flux, energetic gamma rays (320 keV), and long half-life ($T_{1/2}$ = 27.8 days). Later, technetium-99m was used for the same purpose (*5, 6*). Unfortunately, the binding efficiency of Tc-99m to the RBCs turned out to be less than 25%. The introduction of reductive methods using stannous ions (*10*) led to the development of improved methods for binding Tc-99m to red cells. This technique has been used successfully in several institutions for gated cardiac and gastrointestinal bleeding studies as well as measurements of RBC mass. Heat-denatured red blood cells prepared after labeling with Tc-99m with the same kit have been used for splenic imaging in adults (*11–13*). A problem with that method, as applied to infants, is that it needs 6–8 ml of whole blood. We present our early clinical experience with a modification of the Brookhaven National Laboratory (BNL) method more appropriate for the small blood volumes of neonates and infants.

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MATERIALS AND METHODS

Ten patients were studied. Relevant clinical data are shown on Table 1. All patients were initially imaged

TABLE 1.

Case	Age	Sex	Clinical Diagnosis	H-J Bodies	SC Scan	DRBC Scan
1	11 d premature	M	heterotaxia, r/o asplenia	+	asplenia	polysplenia, RUQ
2	5 mo	M	heterotaxia, r/o asplenia	−	asplenia	polysplenia, RUQ
3	9 d premature	M	heterotaxia, r/o asplenia	+	asplenia	asplenia
4	5 mo	F	heterotaxia, r/o asplenia	+	asplenia	asplenia
5	4¼ mo	F	heterotaxia, r/o asplenia	not done	asplenia	asplenia
6	2½ yr	M	heterotaxia, r/o asplenia	+	asplenia	asplenia
7	2 yr	F	recurrent ITP, postsplenectomy	+	asplenia	asplenia
8	13 yr	F	recurrent ITP, postsplenectomy	+	small splenule	small splenule
9	16 yr	F	r/o splenic hematoma	not applicable	equivocal splenic defect	positive splenic defect
10	21 d	M	left thoracic mass, r/o hepatic or splenic herniation	not applicable	mass is either liver or spleen	mass identified as spleen

Notes: DRBC = heat-denatured red blood cells; H-J = Howell-Jolly; ITP = idiopathic thrombocytopenic purpura; RUQ = right upper quadrant; SC = sulfur colloid; r/o = rule out.

using Tc-99m sulfur colloid (SC). Selective splenic imaging was then performed because the SC scan was inconclusive. Parents or guardians of each patient were informed of the potential risks and benefits of the study.

The method of preparation is outlined in Table 2. The main difference between the adult method and the pediatric version presented here is that only 1 ml of blood is sufficient for the latter. The labeling efficiency with the BNL kit before heat-damaging of the RBCs has been previously reported to be at least 95% (*11*). After heat denaturation, the efficiency drops slightly to 90% (personal communication, P. Richards). Administered dose and absorbed radiation doses to the spleen and whole body are given in Table 3.

Imaging began 30 min after the injection and was

TABLE 2.

Preparation of Tc-99m DRBC for Pediatric Use with the BNL Kit

1. Add 8 ml of normal saline to a BNL kit.
2. Withdraw 2 ml of this solution and inject it into a 3-ml sterile glass tube.
3. Add 1 ml of heparinized whole blood into the 3-ml tube.
4. Gently rotate the tube for 10 min.
5. Centrifuge the tube for 5 min (1200–1500 *g*).
6. Using a long needle, draw the packed RBC into a syringe (do not remove plasma).
7. Add the packed RBC into another tube containing 1 ml of Tc-99m as $NaTcO_4$ (see Table 3 for mCi).
8. Gently agitate the tube for 5 min.
9. Incubate the tube for 12–15 min in constant-temperature bath at 49.5° C.

BNL = Brookhaven National Laboratory;
DRBC = heat-denatured red blood cells.

TABLE 3. RADIATION ABSORBED DOSE FOR Tc-99m SULFUR COLLOID* HEAT-DENATURED RED BLOOD CELLS†

	Newborn	1 yr	5 yr	10 yr	15 yr
	Administered dose (mCi)				
Tc-99m SC	0.4	0.9	1.3	1.8	2.5
Tc-99m DRBC	0.1	0.2	0.3	0.4	0.5
Critical-organ dose (rad)					
Tc-99m SC (liver)	1.8	1.2	1.2	1.0	1.0
Tc-99m DRBC (spleen)	4.0	3.0	2.6	2.4	2.0
Whole-body dose (rad)					
Tc-99m SC	0.059	0.05	0.05	0.049	0.05
Tc-99m DRBC	0.036	0.025	0.019	0.017	0.012

* From Webster EW, Alpert NM, Brownell GL: Radiation doses in pediatric nuclear medicine and diagnostic x-ray procedures. In James AE, Wagner HN Jr., Cooke RE, Eds: *Pediatric Nuclear Medicine*. Philadelphia, W. B. Saunders, 1974, pp 34–58.

† From the Radiopharmaceutical Internal Dosimetry Information Center, Oak Ridge, TN. Assumption: splenic uptake of Tc-99m DRBC is 90% of the injected dose.

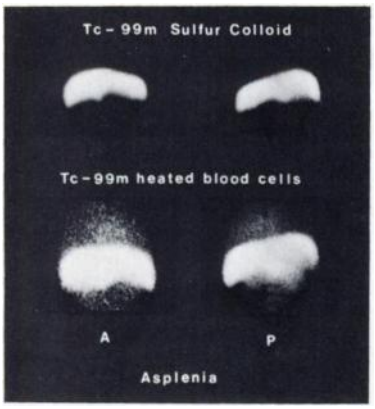

FIG. 1. Heterotaxia with asplenia. Five-month-old female with complex congenital heart disease and midline liver. Sulfur colloid scan (top row) shows no discernible splenic tissue. Heat-treated RBCs (bottom row) confirm absence of selective splenic uptake.

performed with a gamma camera equipped with a high-resolution collimator. Multiple views were always obtained to provide optimal delineation of the anatomy in the upper abdomen. In patients with splenic tissue, its radionuclide uptake was intense and increased with time over a period of 90–120 min. In asplenic patients there was prolonged visualization of the blood pool and liver.

RESULTS

Six patients with the heterotaxia syndrome had no demonstrable splenic tissue on SC scan; two were found to have spleen(s) with the DRBC study (Figs. 1 and 2). Two patients with recurrent idiopathic thrombocytopenic purpura (ITP) were imaged following splenectomy. One of them was asplenic by both methods. The other patient appeared to be asplenic by SC scan immediately following splenectomy, but seven months later, when thrombocytopenia recurred, a repeat SC scan raised the question of a splenule in the left upper quadrant. The DRBC study was then performed in an effort to locate any splenic tissue before a second laparotomy. It clearly demonstrated the presence of one discrete, small spleen (Fig. 3B). At surgery, a splenule 1 cm in diameter was found and removed.

The infant with the left inferoposterior thoracic mass—discovered on a chest radiograph obtained for evaluation of mild respiratory distress—underwent a SC scan. The radiographic abnormality was shown to contain reticuloendothelial system cells, indicating the presence of either hepatic or splenic parenchyma. It was positively identified as the spleen only by the DRBC study (Fig. 4). In the patient sustaining blunt abdominal trauma who had a questionable splenic defect suggesting a hematoma by the SC scan, the DRBC study clearly demonstrated the abnormality.

DISCUSSION

Congenital asplenia and polysplenia are most frequently associated with the heterotaxia syndrome (*14*). In a pathologic study of 51 patients with heterotaxia (*15*), Freedom found asplenia in 32 (63%), polysplenia in 9 (17%), rudimentary spleens in 7 (14%), and normal spleens in 3 (6%). As an autopsy series, the group has more complex lesions with asplenia.

Asplenia, congenital or acquired, is associated with an increased risk of sepsis (*16*), whose incidence increases with the severity of the underlying condition and decreases with age (*17*, *18*). In children splenectomized for trauma, 1–2% develop sepsis (*19*). Of 52 patients with asplenia syndrome seen at the Boston Children's Hospital Medical Center (CHMC) between 1950 and 1975, 12 (23%) died of sepsis (*20*).

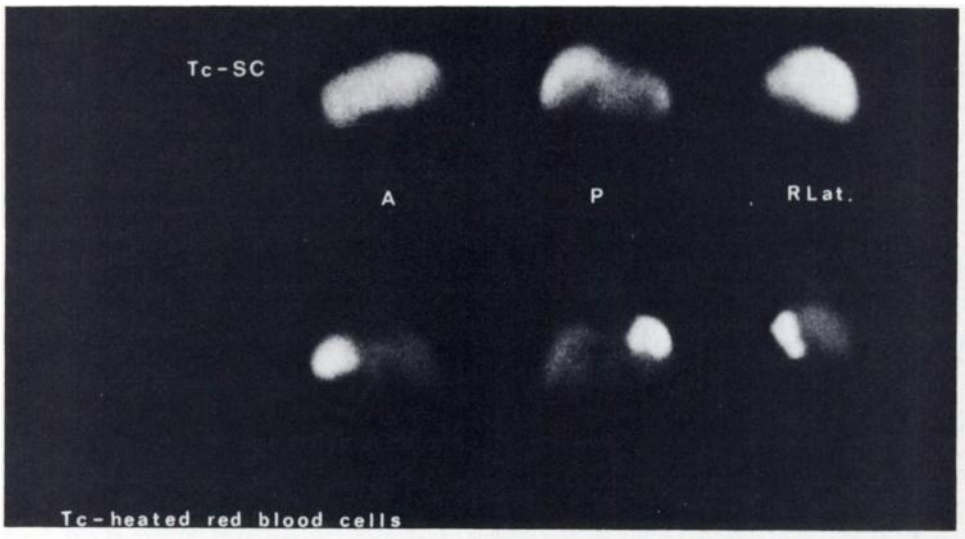

FIG. 2. Heterotaxia with spleen. Eleven-day-old male with dextrocardia and midline liver. Sulfur colloid scan (top row) shows distinct splenic visualization. Heat-treated RBCs (bottom row) demonstrate intense radionuclide uptake by splenic tissue in the right upper quadrant.

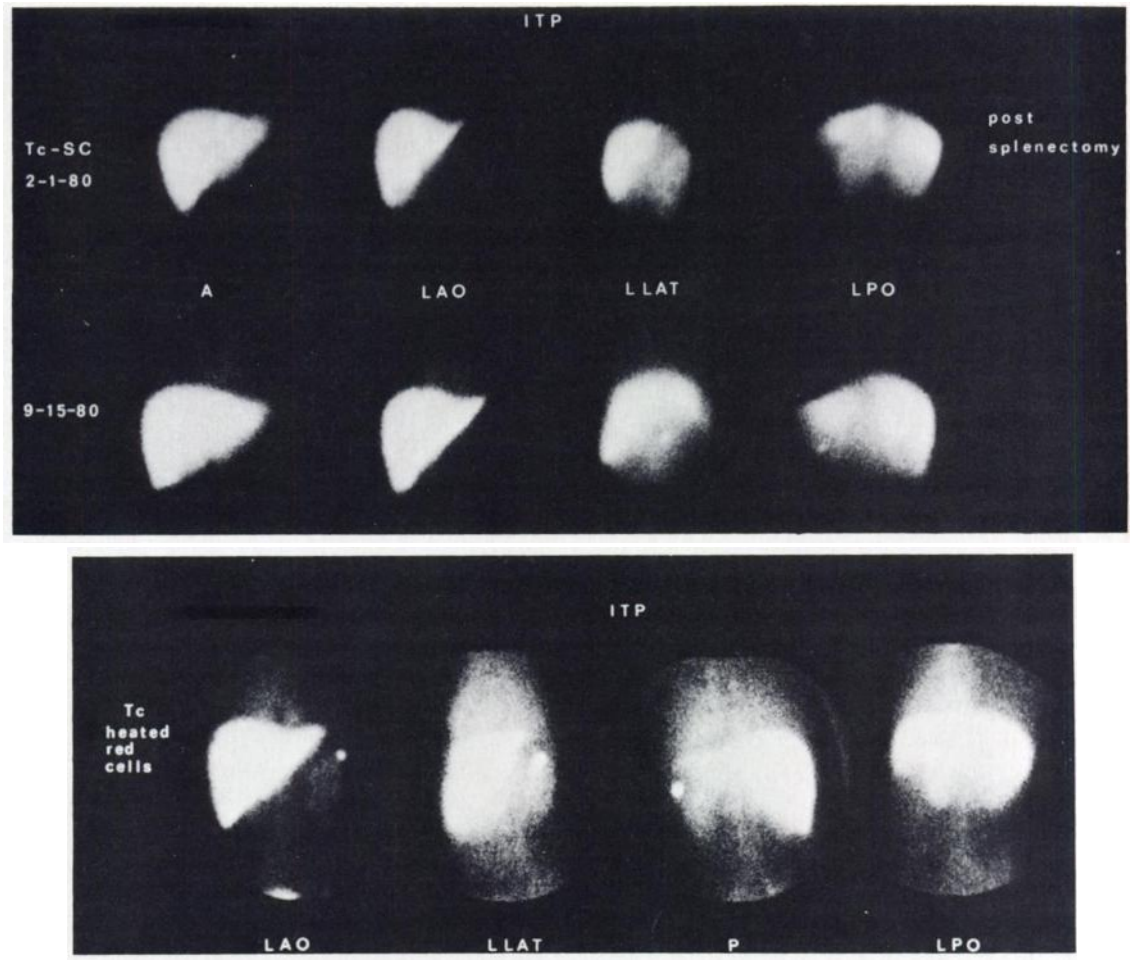

FIG. 3. Recurrent idiopathic thrombocytopenic purpura (ITP) following splenectomy in 13-yr-old female. A: sulfur colloid scan immediately after splenectomy (top row) shows asplenia. Repeat scanning 7½ mo later, after recurrence of symptoms, shows faintly focal accumulation of radionuclide in left upper quadrant, best seen in left lateral and posterior oblique projections. It was suggestive of a splenule. B: heat-treated RBCs clearly show intense focal uptake by splenule, confirmed by a second laparotomy.

Advances in cardiac surgery are increasing not only the survival of children, but also the years at risk for them to develop serious infections. The diagnosis of asplenia is therefore no longer of purely academic interest. Current recommendations for the management of such children include prophylactic antibiotics and pneumococcal vaccination (*16*, *20*).

The diagnosis of asplenia may be strongly suggested by a peripheral-blood smear showing Howell-Jolly bodies. However, these infrequent, intra-erythrocytic nuclear remnants may also be found in peripheral-blood smears of premature, and even full-term, babies with intact spleens (*21*). A more direct approach to complement the clinical and laboratory impression is splenic scintigraphy (*22*). During the past 5 yr, 33 patients with complex congenital heart disease at the CHMC underwent SC scans to rule out asplenia. The spleen was identified in 27 of them (82%) (unpublished data). In the

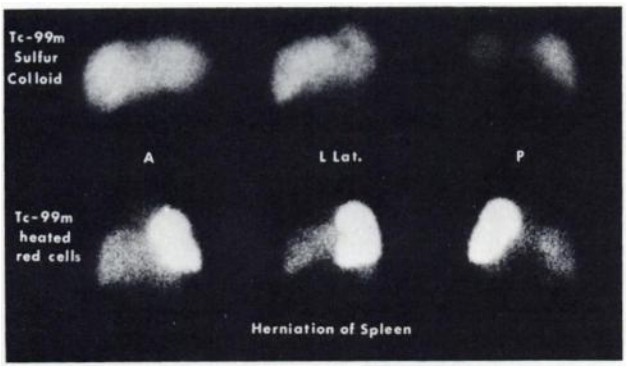

FIG. 4. Left intrathoracic mass in 3-wk-old infant. Sulfur colloid scan shows mass to contain reticuloendothelial system cells. Distinction between liver and spleen is not possible (top row, best seen on left lateral view). Heat-treated RBCs demonstrate intense radionuclide uptake by a partially intrathoracic spleen.

remaining patients some doubt existed even when the SC scan was supplemented with agents selectively imaging the liver, such as I-131 rose bengal. It is in these children that selective scanning of the spleen is advantageous.

The utility of splenic imaging is not limited to the heterotaxia syndrome. The Tc-99m DRBC study may be useful to assist a search for accessory spleens or splenosis in hematologic diseases that require splenectomy (*23*). For instance, nearly 70% of the patients with ITP may benefit from total splenectomy (*24*). Therefore, a DRBC scan may be indicated to facilitate complete removal of splenic tissue. We also anticipate that by the same technique one could locate any splenic tissue left behind or regenerated after an earlier splenectomy.

Furthermore, selective imaging of the spleen is definitely superior to the SC scan when the latter is difficult to interpret owing to masking of the spleen by an overlying left hepatic lobe. This was shown both in the patient with the splenic hematoma and in the infant with the intrathoracic mass.

The requirement of only small amounts of blood for the BNL kit is clearly an advantage with neonates and infants. We recommend this procedure as an imaging method complementary to the SC scan whenever there is reasonable doubt about the latter's ability to establish the presence or absence of splenic tissue.

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