ticulum could be mistaken for the gallbladder unless all structures are properly identified in three dimensions.

FOOTNOTE

* n-(2,6-dimethylphenylcarbamoylmethyl) iminodiacetic acid, Union Carbide Corp., Tuxedo, NY.

JANET F. BROWN
JULIA W. BUCHANAN
HENRY N. WAGNER, JR.
The Johns Hopkins Medical Institutions
Baltimore, Maryland

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Transient Functional Hyposplenia and Fever

The concept of hyposplenism was established by Dameshek in 1955 (*1*) when he reported a case of nontropical sprue and hyposplenism, first suspected because of the appearance of Howell-Jolly bodies and target cells in the peripheral smear. In 1969 Pearson et al. (*2*) described the inability of an anatomically present spleen to accumulate radioactive colloid in children with sickle cell disease. It became evident subsequently that hyposplenia occurred in other diseases as well (*3-6*).

We describe a case of acquired transient functional hyposplenia associated with a fever of unknown origin.

A 45-year-old black male presented with a 1-wk history of fever and chills. His fever reached 104°F daily and was accompanied by headache and weight loss.

On physical examination, he was in moderately acute distress, with a rectal temperature of 104°F and a heart rate of 105. There was a soft, grade I/VI midsystolic murmur at the left sternal border. Liver was palpable 2 cm below the right costal margin, with a 12-cm span. The spleen was not palpable. The remainder of his examination was unremarkable.

Hemoglobin was 8.8 g/dl, hematocrit 26.6%, and white blood cell count 4,300, with 43% polymorphonuclears, 7% bands, 48% lymphocytes, and 2% monocytes. The platelet count was 198,000. The reticulocyte count was 0.6%. Peripheral smear revealed Burr cells, schistocytes, occasional spherocytes, but no Howell-Jolly bodies. Prothrombin time, partial thromboplastin time, fibrinogen, and thrombin time were normal. Fibrin degradation products were present. Serum haptoglobulin was 160 (normal 60-170 meq%). Direct Coombs test was negative. G6PD was decreased to 69 (normal 140-280 units per billion cells). Hemoglobin electrophoresis revealed 94% of Hb A and 3.3 of Hb A2. The bone marrow aspirate showed decreased cellularity. Chest radiograph and the biochemical profile were normal. LE preparation, RA latex, and ANA were negative. Serum assays for immune complexes were not done.

His temperature continued to spike to 104°F daily and he remained acutely ill. Bacteriologic and serologic studies were unrevealing. On the second hospital day, a Tc-99m sulfur colloid liver-spleen scan revealed minimal hepatomegaly with poor visualization of the spleen. On the fifth hospital day, a splenic flow study was performed. The subsequent static images yielded a spleen that was functional but not of normal intensity (Fig. 1, left).

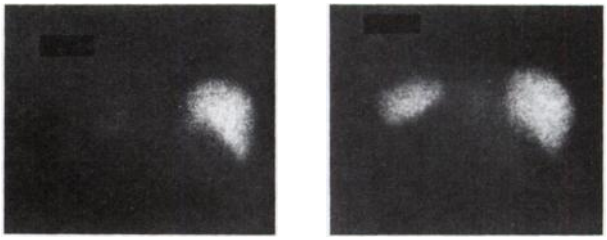

FIG. 1. (Left) Liver-spleen scan, posterior view on Day 5, revealing functional but weak spleen. (Right): Normal liver-spleen scan, posterior view, 6 wk after discharge.

(Although splenic uptake appeared to have increased since the first study, a valid comparison could not be made because of differences in technique.) By the seventh day, the patient was afebrile. Haptoglobulin at this time was decreased to 12. A few Howell-Jolly bodies were noted on the peripheral smear for the first time. By the 12th hospital day, his reticulocyte count increased to 7.3%. His hematocrit rose to 28.1%, and his white blood cell count to 5,200.

Following discharge, he continued to improve symptomatically and his hematocrit rose to 44% three months later. A repeat spleen scan done 6 weeks after discharge was normal (Fig. 1, right).

This patient presented with an acute febrile illness, the cause of which was not determined. His hematological status was noteworthy for the development of anemia and leukopenia. He developed transient functional hyposplenia, manifested by a decreased uptake of technetium sulfur colloid on splenic scan, and by the presence of Howell-Jolly bodies in the peripheral smear.

In 1978, Spencer et al. (*7*) reviewed the world literature and found an incidence of six cases of functional asplenia in over 4,476 consecutive liver scans at three hospitals, from January 1975 to July 1976. He proposed a classification of causes of functional asplenia and divided them into two categories: circulatory disturbances and effects on reticuloendothelial cell function (Table 1).

The functional hyposplenia that occurred in our case does not appear to fit into either of these categories. A transient splenic

TABLE 1. CAUSES OF FUNCTIONAL ASPLENIA

I. Circulatory disturbances
  (a) Gross
    1. Splenic artery blockade
    2. Splenic vein occlusion
    3. Combined vascular occlusion
  (b) Microscopic
    1. Hemoglobin SS
    2. Hemoglobin SC
    3. Thalassemia
    4. Other, such as polycythemia vera
II. Effects on splenic reticuloendothelial (RE) cells
  (a) RE blockade and irradiation (thorotrast loading)
  (b) Combined irradiation and chemotherapy
  (c) Replacement of RE cells by tumor (such as lymphoma, myeloma, or metastases) or by infiltrate such as amyloid
  (d) Cellular damage, as in nutritional deficiency or immunocompetent problems (celiac sprue)
  (e) Possible effects of splenic anoxia

artery obstruction was a possibility but seems very unlikely as there was no suggestion of any vascular embarrassment. It is conceivable that mass hemolysis, possibly related to G6PD deficiency, may have occurred and saturated the splenic macrophages, causing functional hyposplenia. This mechanism has never been previously described.

What seems more likely is that some unidentified antigen-antibody immune complex saturated the RE cells, diminishing the spleen's ability to take up radiocolloid on the scan. There is recent evidence to support such a mechanism. Lockwood et al. (*8*) studied ten patients with vasculitis syndromes who were undergoing plasmapheresis. The investigators used heat-damaged and radionuclide-labeled IgG-coated autologous erythrocytes. These cells are taken up by, and bind to, splenic macrophages. Used in combination, they are felt to be a valid index of basic splenic macrophage function. The investigators found that splenic uptake of the label was markedly depressed before plasmapheresis. It increased up to 60%, however, following plasmapheresis and removal of the immune complexes associated with their primary illnesses. The authors concluded that saturation of splenic macrophages with immune complexes was unblocked by plasmapheresis, which could reverse hyposplenism within 48 hr. They commented that impairment of splenic function may be a common, if not general, phenomenon in patients with fulminating immune-complex disease.

Although immune-complex disease was not specifically identified in our case, it seems likely that some environmental antigen, infectious or otherwise, initiated his febrile illness and by this mechanism caused transient functional hyposplenia.

ROBERT P. FERGUSON
GIAO N. HOANG
Mount Sinai Hospital and
University of Connecticut
School of Medicine
Hartford and Farmington,
Connecticut

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Abnormal False-Positive Response of Exercise Ejection Fraction Due to the ROI: Fixed Compared with Variable

In a recent paper Sorensen et al. (*1*) have reported falsely abnormal ejection-fraction response to exercise in normal volunteers when the fraction is calculated using a fixed region of interest (FROI), compared with a calculation using a variable region of interest (VROI). With the latter, areas of interest are selected separately for end-diastole and end-systole.

Although early in the discussion they consider the response falsely positive when FROI is used, later they offer reasons why the response may be real. We think that most likely the FROI method has produced falsely abnormal results, for the following two reasons:

1. The FROI method as a rule gives a lower value for ejection fraction. This is because systole exposes an area of background that will not be subtracted out if only an end-diastolic ROI is used. The end-systolic count is therefore too high, and EF too low. A separate end-systolic ROI would avoid this error.

2. The left-ventricular region of interest at end-diastole almost always includes some of the lower part of the left atrium, and this will contribute to the ventricular end-systolic count when FROI is used. Increase in ejection fraction with exercise is usually due to increased left-ventricular contractility, which translates into lower end-systolic area, and therefore count. The unwanted atrial contribution (small but significant) therefore becomes proportionately larger during exercise if only the end-diastolic ROI is used.

We reviewed our experience with equilibrium gated blood-pool imaging, performed at rest and during maximal supine bicycle exercise in 21 consecutive unselected patients referred to us for assessment of coronary artery disease. Ejection fraction was calculated using both FROI and VROI. Response to exercise was considered normal if there was greater than 5% rise in ejection fraction at peak exercise using VROI. Nine of the 21 patients reviewed had a normal response to exercise by this criterion. In this group average resting ejection fraction was 0.55 (range 0.48-0.66),

TABLE 1.

		Variable ROI		Fixed ROI	
		average	(range)	average	(range)
Normal response (N = 9)	Rest	0.55	(0.48–0.66)	0.37	(0.27–0.52)
	Exercise	0.68	(0.62–0.75)	0.43	(0.29–0.62)
	Change	+23.6%		+16.2%	
Abnormal response (N = 12)	Rest	0.59	(0.39–0.67)	0.40	(0.26–0.53)
	Exercise	0.53	(0.33–0.69)	0.37	(0.18–0.57)
	Change	−10%		−7.5%	