

## PRELIMINARY NOTE

# Diagnosis of Splenic Involvement in Hodgkin's Disease by Radionuclide Evaluation of Splenic Contraction in Response to Adrenaline

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**Splenic contraction in response to adrenaline was studied by a radionuclidic technique in 33 patients who then underwent exploratory laparotomy and splenectomy. The decrease in splenic size was estimated by the percent diminution of spleen area from the baseline scan, and was found to be significantly less ( $P < 0.001$ ) in the group of patients with Hodgkin's involvement of the spleen. Possible applications of the test for diagnostic purposes are discussed.**

**J Nucl Med 21:384-386, 1980**

Since the introduction of laparotomy and splenectomy as a staging procedure for Hodgkin's disease, clinical evaluation of the spleen has been found incorrect in 30-45% of patients (1,2). Conventional scintigraphic techniques do not provide the degree of resolution required to detect small nodules, and neither moderate degrees of splenic enlargement nor focal filling defects are reliable indicators of splenic involvement (3). Recent reports have suggested that scintigraphy has been useful in studies of changes in splenic size in response to epinephrine and other stimuli (4,5), but no data are available as to whether infiltration of the spleen by Hodgkin's disease alters its ability to change size. The present study was undertaken to determine whether splenic contraction in response to adrenaline as evaluated by scintigraphy, can serve as a diagnostic test in the staging of Hodgkin's disease.

### MATERIALS AND METHODS

The adrenaline test was performed in 33 previously untreated patients with histologically confirmed Hodgkin's disease who afterwards underwent exploratory laparotomy and splenectomy. Hypertensive patients

with organic disease of the cardiovascular system were not given the adrenaline test.

Preoperative clinical evaluation revealed no evidence of supradiaphragmatic disease in 17 of the 33 patients. In 16 patients splenic involvement was suspected on the basis of routine scan evaluation (Fischer's splenic index  $> 5 \times 10^{-3}$ , focal filling defects). In 12 of the 16 patients this was the only manifestation of intra-abdominal involvement, while in four cases positive or equivocal lymphangiograms were also obtained. Laparotomy revealed splenic involvement in eight of the 17 above-described patients, and ruled it out in nine of the 16 patients at risk.

Patients were grouped according to the results of postoperative spleen examination (Table 1). Group 1 included 15 patients with splenic involvement documented by the discovery of Reed-Sternberg cells. Group 2 was composed of 18 patients with normal spleens.

The spleen was visualized by lateral scanning following administration of chromium-51-labeled red blood cells (6). Spleen size was estimated by measuring the scan area with a planimeter, and the extent of splenic contraction was judged by the decrease in projected area as a percentage of the baseline area.

Patients were examined on the day following administration of the tracer, before breakfast. After obtaining the initial scan, a 0.1% solution of adrenaline hydrochloride was injected subcutaneously in a dose of 0.5 ml/m<sup>2</sup> of body surface area. In 25-30 min the scan was repeated, the patient being accurately repositioned.

Received Oct. 23, 1978; revision accepted Nov. 19, 1979.

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TABLE 1. SUMMARY OF FINDINGS FROM PATIENTS (RANGES SHOWN IN PARENTHESES)

	Group 1*	Group 2†
No. of patients	15	18
Age (yr)	29 ± 2.8	24 ± 1.4
Sex distribution: male	9	7
female	6	11
Spleen scan area (baseline)	88 ± 6.3 cm <sup>2</sup> (56–125)	86 ± 5.3 cm <sup>2</sup> (55–134)
Spleen defects on scan	4	3
Mean decrease in spleen size after adrenaline	11 ± 2%	24 ± 2.5%
Change in neutrophils count after adrenaline	67% (11/15 pts)	53% (12/18 pts)
Change in lymphocyte count after adrenaline	240% (11/15 pts)	160% (12/18 pts)

\* Splens found involved at laparotomy.

† Splens normal at laparotomy.

During the procedure pulse and arterial pressure were measured and the intensity of side effects (palpitation, pallor) were noted. In 23 patients total and differential leukocyte counts were made before adrenaline administration and at intervals of 15–30 min. The maximal increase of neutrophils and lymphocytes was calculated.

#### RESULTS

Analysis of the data showed no significant differences in the baseline spleen size between the two groups of patients. Mean initial projected spleen area was 88 ± 6.3 cm<sup>2</sup> in Group 1 and 86 ± 5.3 cm<sup>2</sup> in Group 2 (Table 1).

Figure 1 records the observed splenic responses to adrenaline. Mean decrease in splenic size proved to be less in patients with involved spleen (11 ± 2.0% in Group 1 and 24 ± 2.5% in Group 2;  $P < 0.001$  by Student's *t*-test).

Assessment of the number and size of macroscopic nodules of Hodgkin's disease in the surgical specimens revealed that 12 of 15 patients in Group 1 had multiple nodules < 2 cm in diameter. Decrease in splenic size in these patients ranged from 0 to 19%. In one patient the spleen contained a zone of infiltration spread along the axis of the organ, and in two patients splenic involvement was revealed only by microscopy. Splenic contraction in these three patients was 20–22%. Clinically, signs of reaction to adrenaline were clearly observed in all patients in Group 1.

Examination of the results from Group 2 suggests that contraction of both larger (134 cm<sup>2</sup>) and smaller (65 cm<sup>2</sup>) uninvolved spleens could reach 38%. In 13 of 18 patients, clinical symptoms of reaction to adrenaline were easily observed and decrease in splenic size ranged from 21 to 38% (mean 29 ± 1.9%). In five cases, splenic

contraction was below 14%, and four of the five demonstrated no general symptoms of reaction. This was considered to result from insufficient dosage (two cases) and high tolerance to the drug (two cases). In one patient, general excitement may have caused reduction of the normal spleen size before the baseline scan was obtained.

Analysis of the changes in peripheral blood in 11 patients of Group 1 and 12 patients of Group 2 showed that

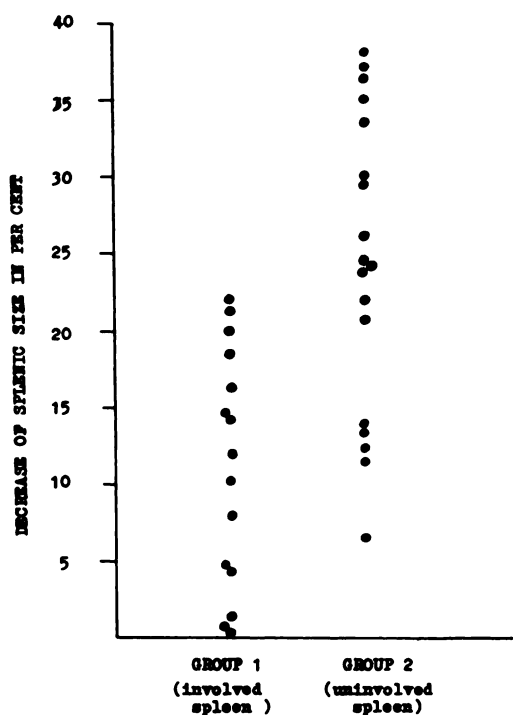


FIG. 1. Scan-documented decrease in splenic size in response to adrenaline administration in 33 patients with Hodgkin's disease. Patients were grouped according to results of postoperative spleen examination.

adrenaline induced similar increases in the neutrophil counts in both groups (67% and 53% over the baseline levels), while lymphocytosis was even more pronounced in Group 1 (240% compared with 160% in Group 2; not significant). However, the difference in the mean decrease in splenic size in these smaller subgroups was found to be significant ( $9.0 \pm 1.9\%$  and  $24.0 \pm 3.4\%$ ;  $P < 0.01$ ).

#### DISCUSSION

Analysis of the changes in peripheral blood was carried out to determine whether differences in the somatic response to adrenaline might account for observed differences in splenic contraction. The data led us to the conclusion that impaired splenic contraction in patients with involved spleens was not an accidental result of feeble vascular reaction but reflected structural changes in the organ. This is thought to be due to a presence of multiple tumor nodules, with development of concomitant sclerotic processes (1,7). The latter may explain the limited contraction in patients whose spleens contained few macroscopically visible lesions.

Since splenic involvement has not been documented in any of the 11 cases in which the decrease in splenic size exceeded 23%, the adrenaline test appears to be particularly useful for ruling out splenic disease. Long-term clinical observation of 17 patients who had demonstrated good splenic contractility (25–50%) supports this opinion, although in them the lack of splenic involvement had not been surgically demonstrated. Still, it is clear that a contraction of 23% or more is highly suggestive of an uninvolved spleen, although the sensitivity of the test is low (seven of 18 in Group 2 showed less than 23%).

Apart from tumor proliferation poor splenic contraction may result also from an individually insufficient dose of adrenaline. It may also be imitated by an inadequately obtained baseline scan, as it was in five of 18 patients. Thus, clinical evaluation of the reaction's intensity is necessary to avoid false-positive results. This

is why five of the above-mentioned patients were excluded from further analysis. With our choice of 23% contraction or less as the indication of splenic involvement, one obtains a sensitivity of 100% (15 out of 15 in Group 1 detected) and a specificity of 85% (two out of 13 in Group 2 included).

Since it has been reported (8,9) that intra-abdominal spread of Hodgkin's disease frequently appears to originate in the spleen and to involve progressively contiguous abdominal lymph nodes, it would be reasonable to use the adrenaline test to refine the indications for laparotomy in Stages I and IIA patients. Since the long-term influence of splenectomy on immunity in surviving patients is not yet clear, the opportunity to spare a proportion of patients from operative staging seems attractive.

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#### ERRATA

In the article entitled "Quantitative Measurement of Skin Perfusion with Xenon-133" by Michael J. Daly and Robert E. Henry, appearing in *J Nucl Med* 21: 156–160, 1980, on p. 157 in the equation, K = slope constant of Xe-133 washout from the intradermal site ( $\text{min}^{-1}$ ), not ( $\text{ml}/\text{min}^{-1}$ )

In the article entitled "False Left-Ventricular Aneurysm: Diagnosis by Noninvasive Means" by Gary Onik et al., appearing in *J Nucl Med* 21: 177–182, 1980, line 13, right column, p. 179 should read: scintigram (40, 43, 50, 65) and true LV aneurysm can also.

In the article "The Deltoid Tuberosity—A Potential Pitfall (The "delta sign") in Bone-Scan Interpretation: Concise Communication" by D. Fink-Bennett and J. Vicuna-Rios appearing in *J Nucl Med* 21:211–212, 1980, the authors' affiliation should read, "William Beaumont Hospital, Royal Oak, Michigan."