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Relationship between splenic size and splenic function

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SUMMARY The rate of clearance of ^{51}Cr labelled heat-damaged red cells from the circulation has been compared with the dimensions of the posterior scan of the spleen in 79 cases including nine controls. A strong negative correlation was found between the clearance half-time and the parameters of the scan but, as there was a large variation about the regression line, in the assessment of hyposplenism determination of the rate of clearance of heat-damaged red cells cannot be replaced by the easier determination of spleen size by scanning.

Interest in the spleen has increased during the past decade, as it has been possible to assess the function of this organ quantitatively by monitoring the rate of clearance from the circulation of ^{51}Cr labelled heat-damaged red cells. Hyposplenism, a reduction in the ability of the spleen selectively to remove damaged red cells, has been shown to be a surprisingly common complication of many conditions, in particular coeliac disease (Marsh and Stewart, 1970) and ulcerative colitis (Ryan *et al.*, 1974, 1977). The test has also been used to investigate hypersplenism—for example, in patients with cirrhosis of the liver (Holzbach *et al.*, 1964).

An alternative approach to the study of hyposplenism has been to determine whether the spleen has lost its ability to clear intravenously injected colloidal material from the circulation by noting the presence or absence of splenic uptake of ^{99m}Tc sulphur colloid as shown by a scanner or gamma camera (Pearson *et al.*, 1969).

Both of these methods assess the function of the spleen. The size of the organ can be determined from abdominal radiographs or from a scan of accumulated radioactivity within the spleen after the uptake of ^{99m}Tc sulphur colloid, although it must be stressed that the scan defines only the functional size of the spleen (Spencer, 1970). Baker *et al.* (1975) assessed the function of the spleen solely on the basis on the area of the colloid scan, implying a direct correlation between splenic function and splenic size. Does this correlation exist? Holzbach *et al.* (1964) demonstrated such a correlation ($r = 0{\cdot}67$, $P < 0{\cdot}001$) in 12 controls and 19 patients with cirrhosis, 13 of whom were shown to have large spleens. However, Pearson *et al.* (1969) showed that 11 of 12 children with sickle-cell anaemia had no uptake of colloid by the spleen even though this organ was enlarged in nine of the 12 cases. In an attempt further to elucidate any possible correlation, this paper reports the results of combined measurements of the rate of clearance of ^{51}Cr labelled heat-damaged red cells and the functional size of the spleen as measured by scanning in nine controls and 75 patients.

Methods

The nine controls were all healthy male volunteers. The diagnoses of the 75 patients studied are given in Table 1.

Table 1 *Diagnoses of 75 patients studied*

Diagnosis	*Patient (no.)*
Ulcerative colitis	37
Crohn's disease	20
Coeliac disease	4
Iron deficiency anaemia	4
Haemolytic anaemia	3
Pernicious anaemia	1
Lymphocytic lymphoma	1
Bilateral visual failure	1
Meningococcal septicaemia	1
Cholecystitis	1
Granulocytic bone marrow depression	1
Autoimmune disease	1

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Autologous red cells were labelled with ^{51}Cr and damaged by heating for 30 minutes at 49·5° ± 0·5°C. The labelled cells were injected intravenously and nine blood samples were taken during the first 60 minutes to define the rate of clearance from the circulation of the damaged cells. The cells were then haemolysed and the radioactivity counted in an automatic well-scintillation counter. A smooth curve was drawn through the data points using a computer and the clearance half-time, $T_{\frac{1}{2}}$, determined. In the nine controls the $T_{\frac{1}{2}}$ range of 9·0 to 17·5 minutes accorded well with the control range reported by Marsh *et al.* (1966) of 10 to 16 minutes. A posterior rectilinear scan of the spleen was obtained one to two hours after injection using a Picker Nuclear Magnascanner Mark V.

Many authors have demonstrated a direct correlation between the dimensions of the posterior and/or left lateral scans of the spleen with splenic volume. These methods have been reviewed most recently by Aito (1974). In the present study six parameters were measured from each scan—namely, the vertical length of the scan, the maximum length, the horizontal width, the width at right angles to the long axis, the area, and the circumference. Principal component factor analysis was used to derive from these variables three parameters reflecting the size, shape, and orientation of the spleen. Keeling *et al.* (1971), using a similar analysis, had shown that the coefficient of the first principal component correlated well with the splenic volume.

The possible correlations of the clearance half-time with the length of the scan, the area of the scan, and the coefficient of the first principal component were determined.

Results

In the five patients in whom the clearance half-time was greater than 80 minutes the spleen could not be detected by scanning. In one of these patients a very small spleen (5 cm × 2 cm) was found at laparotomy. For the remaining 70 patients and nine controls in whom scans were obtained, Table 2 gives the correlations found using Spearman's rank correlation and Kendall's rank correlation tests for the clearance half-time versus the scan length, the scan area, and the coefficient of the first principal component of the scan. The Figure shows the correlation between the clearance half-time and the scan area. The data are presented on log/log axes and the line of regression was given by

$$\log_e(\text{scan area}) = 4{\cdot}74 - 0{\cdot}232 \times \log_e(T_{\frac{1}{2}}) \quad (1)$$

which can be written as:

$$\text{Scan area} = 114{\cdot}4 \times T_{\frac{1}{2}}^{-0{\cdot}232} \quad (2)$$

Discussion

In a total of 79 cases in whom a scan of the spleen could be obtained, we have demonstrated a very

Table 2 *Correlations found between the three parameters of splenic size and the clearance half-time of heat-damaged red cells*

	Spearman's rank correlation		*Kendall's rank correlation*	
	r_s	P	r_k	P
$T_{\frac{1}{2}}$ vs. scan length	−0·30	<0·005	−0·22	0·002
$T_{\frac{1}{2}}$ vs. scan area	−0·40	<0·001	−0·30	<0·0005
$T_{\frac{1}{2}}$ vs. coeff. of 1st component	−0·37	<0·002	−0·28	<0·0005

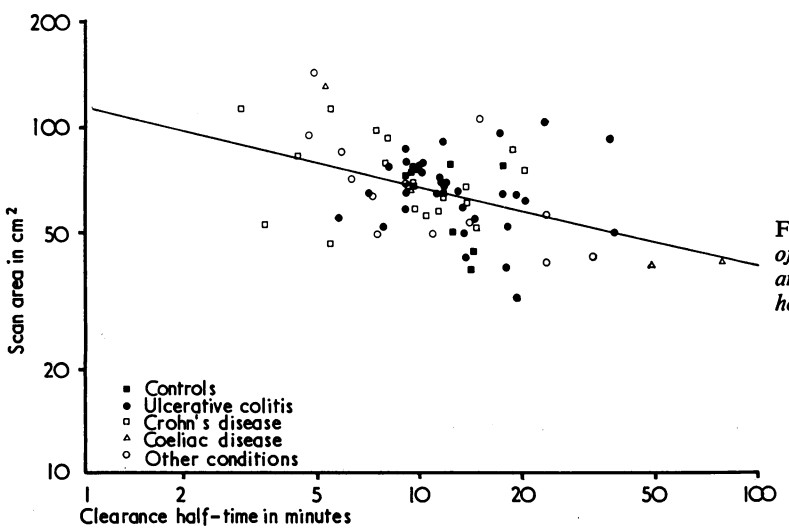

Figure *The correlation between area of the posterior scan of the spleen and the clearance half-time of the heat-damaged red cells.*

significant overall correlation between the rate of clearance of heat-damaged red cells from the circulation and the size of the spleen as assessed by scanning. It was found that the data were best represented as a power function relating the area of the scan to the clearance half-time. The scan area was proportional to $T_{\frac{1}{2}}^{-0.232}$, implying that the area was directly proportional to the clearance rate constant to a positive power. It was not possible to include in the correlation the five patients in whom the clearance half-time was greater than 80 minutes, as no uptake of ^{51}Cr in the spleen could be detected but in the one patient in whom the spleen was examined at laparotomy the spleen was found to measure only 5 cm × 2 cm.

The clearance half-time was used in this study, as it is the clinically most useful parameter that can be derived from the clearance curve. A clearance curve can alternatively be analysed as a sum of two exponential components, the fast clearance representing the selective removal from the circulation by the spleen of the intact but damaged red cells and the slow component representing the removal by the reticuloendothelial system of labelled red cell fragments (Fischer *et al.*, 1971). However, as it is possible in practice to take only a small number of samples, the errors associated with the parameters of the double exponential function are usually large, while the clearance half-time can be obtained more accurately (Smart, 1976). The clearance half-time will of necessity be longer than the half-time of the fast component but, as in the majority of cases the amplitude of the fast component was greater than 70%, the difference between them would not be large.

Pettit *et al.* (1971) found no correlation between the rate of clearance of MHP-damaged ^{81}Rb labelled cells from the circulation and either the size of the spleen as shown by the distribution of ^{81}Rb or the splenic red cell volume measured using ^{11}CO labelled red cells, in patients with myeloproliferative disorders or generalised malignant lymphomas. In these patients the spleens were infiltrated by tumour and the scan area no longer solely reflected the volume of functioning phagocytic tissue. Pearson *et al.* (1969) found that the spleen was visualised using ^{99m}Tc sulphur colloid in only one of 12 children with sickle-cell anaemia, even though the spleen was palpably enlarged in nine of the cases. It was suggested that reticuloendothelial blockade or an abnormality of the splenic circulation caused by the high viscosity of sinusoidal blood containing large numbers of sickled red cells might be responsible for this functional asplenia.

Neither of these situations would apply in the patients studied here with the possible exception of the patient with lymphocytic lymphoma. It must be stressed that, although a strong correlation was found between splenic area and splenic function, in a particular individual the former cannot be used as a measure of the latter. It was found, for example, that the clearance half-times of patients in whom the scan measured 40 cm^2 could fall within the normal range or have values for the $T_{\frac{1}{2}}$ as extreme as 76 minutes. This is further emphasised by examination of the results of G.B., a 41 year old male with ulcerative colitis. When originally tested the $T_{\frac{1}{2}}$ value was 19·2 ± 1·9 minutes and was therefore an equivocal result. The spleen appeared small on the scan, having a length of 6·5 cm and an area of 32·2 cm^2. The investigation was repeated after two years when the patient was in severe relapse. At that time the clearance half-time was 52·9 ± 7·0 minutes but the scan size had not changed. Examination of the scan alone would not have revealed this deterioration in splenic function.

It is possible that the inability of the scan size to predict accurately the function of the spleen reflects the inaccuracy of assessing spleen volume measurements of scan area. Keeling *et al.* (1971) in a study relating the volume of the spleen at splenectomy to the parameters of the radioisotope scan in 32 cases found that, although all the measurements were highly correlated with volume, the 90% confidence limits could differ from the predicted value by as much as a factor of 2. Errors of this magnitude could account for the large variation about the line of regression evident in the Figure.

It is clear, therefore, that in the assessment of hyposplensim, although we have demonstrated a high correlation between splenic size and splenic function, determination of the rate of clearance of heat-denatured red cells cannot be replaced by the technically easier determination of spleen size by scanning.

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