The Influence of Splenomegaly on Red Cell and Plasma Volume

C. D. R. PENGELLY, MD, FRCP, FRCPE

Physician, St Anne’s Hospital, Altrincham, and Trafford Area Hospitals, Manchester

The anaemia of hypersplenism is due to a number of causes, but it is probable that red cell pooling in the enlarged spleen and/or the expansion of plasma volume play a part in the aetiology of the anaemia in every case.

Several studies of red cell and plasma volume in patients with splenomegaly have been done. Fudenberg et al. (1961) described a ‘splenic reservoir’ and their studies showed that pooling of red cells took place in concentrated form in enlarged spleens so that the ratio whole body haematocrit/venous haematocrit (Hb/Hv) rose in proportion to the degree of splenomegaly. Others have not produced such convincing evidence of concentrated red cell pooling, but investigators have generally found increased plasma volumes in patients with enlarged spleens (Bowdler, 1970; Donaldson et al., 1970; Toghill and Green, 1972; Christensen, 1973). The mechanism is not entirely clear, but a recent paper (Hess et al., 1976) suggests that the increase may be a result of the activation of the renin-angiotensin-aldosterone system in these patients.

Bowdler (1970) found evidence of red cell pooling by means of surface counting over the spleen, and again by calculating the difference in red cell volume measured by taking a six minute blood specimen and a 45 minute one after injection of radioactive chromium (51Cr)-labelled red cells. In another study (1969) he examined 28 patients with splenomegaly with surface counting for regional variations in haematocrit and concluded that enlarged spleens had a definite but variable tendency to contain blood with a higher haematocrit value than that of the peripheral venous level. Bowdler concluded that a raised Hb/Hv ratio associated with splenomegaly is more dependent on the concentration of the pool of red cells relative to the venous haematocrit than on the actual volume of pooled red cells and spleen size.

Toghill and Green (1972) found a positive correlation between clinical measurements of spleen size and increased measurements of plasma and total blood volume, but no correlation between spleen size and erythrocyte mass. However, the volume of pooled red cells in the spleen did show significant correlations with the degree of splenic enlargement. They used a three minute initial blood specimen but otherwise their method of estimating the volume of the splenic pool was similar to Bowdler’s.

The present study is an investigation of red cell and plasma volume, Hb/Hv and plasma osmolality in 26 patients with various blood diseases, excluding polycy-
thaemia vera. All had some degree of splenomegaly. The investigations were carried out 28 times in the 26 patients investigated.

PATIENTS INVESTIGATED
These consisted of two with monocytic leukaemia, seven with chronic lymphocytic leukaemia, one with chronic myeloid leukaemia, two with lymphosarcoma, two with Felty's syndrome, five with myelofibrosis, three with hepatic cirrhosis (two portal, one biliary), one with Hodgkin's disease and three with hypersplenism, two of which subsequently developed portal hypertension and hepatic cirrhosis; the third was a presumed case of primary hypersplenism (Table 1).

METHODS
Red cell volume was estimated with radioactive chromium ($^{51}$Cr) and plasma volume with radioactive iodine-labelled human serum albumin ($^{125}$I-HSA), the methods being fundamentally those described by the International Committee for Standardisation in Haematology (1973). The details of the methods used are fully described by Pengelly and McKenzie (1973) and Pengelly (1974). Plasma osmolality was estimated with an Advanced Osmometer (Advanced Instruments Inc., Newton Highlands, Mass., USA).

Spleen size was measured in centimetres, taking the greatest measurement below the costal margin in the anterior axillary line.

RESULTS
The age, sex and diagnosis of each patient, together with the details of splenic size, venous haematocrit corrected for trapped plasma, red cell volume, plasma volume, whole blood volume, body haematocrit/venous haematocrit (Hb/Hv) and plasma osmolality are shown in Table 1. In addition, the mean results of 18 normal subjects are given for comparison (Pengelly, 1974).

The results of plasma volume and whole blood volume plotted against spleen size are shown in Figs 1 and 2. The normal mean plus and minus two standard deviations are shown also. Most of the patients were clinically anaemic, though some of these had higher than normal red cell volumes (Table 1). The results of the red cell volumes were not significantly different on t-testing from those of the normal subjects, but there was significant correlation with the degree of splenic enlargement ($r = +0.8182$, $P < 0.001$). On the other hand, plasma volumes and whole blood volumes were greatly increased in patients with splenomegaly and these increases were highly significant on t-testing compared with the normal values ($P < 0.001$ in both) and there was a highly significant correlation with the degree of splenic enlargement ($r = +0.7847$, and +0.8278 respectively, $P < 0.001$ for both) (Table 1, Figs 1 and 2).

Hb/Hv was not in general significantly increased in the patients with splenomegaly and there was no significant correlation between this value and the
Table 1. Patients investigated and results.

| Case No. | Age | Diagnosis (see key below) | Spleen size (cm) | PCV (1/l) | RCV (ml/kg) | PV (ml/kg) | WBV (ml/kg) | Hb/Hv | Plasma Osmolality (mOsm/kg) |
|----------|-----|---------------------------|------------------|-----------|-------------|------------|-------------|-------|---------------------------|
| 1        | 82  | ML                        | 1                | 0.303     | 19.6        | 53.7       | 73.2        | 0.883 | 295                       |
| 2        | 47  | ML                        | 17               | 0.224     | 25.1        | 72.3       | 97.4        | 1.130 | –                         |
| 3a       | 68  | CLL                       | 10               | 0.294     | 19.9        | 51.0       | 71.0        | 0.956 | 301                       |
| 3b       | 70  | CLL                       | 1                | 0.344     | 17.6        | 39.0       | 58.7        | 0.874 | 297                       |
| 4        | 85  | CLL                       | 8                | 0.360     | 24.5        | 51.5       | 76.0        | 0.893 | 298                       |
| 5        | 46  | CLL                       | 9                | 0.312     | 19.7        | 52.2       | 71.8        | 0.876 | 289                       |
| 6        | 67  | CLL                       | 9                | 0.404     | 24.0        | 47.0       | 70.9        | 0.835 | 292                       |
| 7        | 59  | CLL                       | 11               | 0.351     | 24.3        | 48.4       | 72.6        | 0.951 | 295                       |
| 8        | 75  | CLL                       | 25               | 0.301     | 30.6        | 85.0       | 115.6       | 0.881 | 289                       |
| 9        | 72  | CLL                       | 25+              | 0.330     | 34.3        | 67.9       | 102.2       | 1.017 | 281                       |
| 10       | 52  | CML                       | 20               | 0.426     | 36.1        | 52.7       | 92.7        | 0.913 | 294                       |
| 11       | 51  | LS                        | 1                | 0.366     | 28.3        | 59.8       | 88.1        | 0.896 | 286                       |
| 12       | 63  | LS                        | 10               | 0.391     | 27.5        | 48.9       | 76.4        | 0.923 | 290                       |
| 13       | 46  | FS                        | 9                | 0.376     | 35.0        | 74.4       | 109.5       | 0.851 | 294                       |
| 14       | 65  | FS                        | 14               | 0.227     | 20.4        | 66.4       | 86.8        | 1.037 | –                         |
| 15       | 64  | MF                        | 1                | 0.332     | 20.8        | 57.6       | 78.4        | 0.800 | 290                       |
| 16a      | 53  | MF                        | 9                | 0.294     | 26.9        | 58.1       | 85.0        | 1.077 | 292                       |
| 16b      | 55  | MF                        | 13               | 0.366     | 29.5        | 52.3       | 81.8        | 0.984 | 293                       |
| 17       | 76  | MF                        | 25               | 0.346     | 41.2        | 86.6       | 127.8       | 0.933 | 300                       |
| 18       | 63  | MF                        | 25               | 0.307     | 36.2        | 98.0       | 134.2       | 0.877 | 284                       |
| 19       | 60  | MF                        | 25+              | 0.420     | 41.9        | 79.6       | 121.5       | 0.822 | 283                       |
| 20       | 59  | HC (portal)               | 17               | 0.366     | 25.4        | 58.4       | 83.9        | 0.828 | 293                       |
| 21       | 42  | HC (portal)               | 18               | 0.348     | 31.8        | 55.2       | 87.0        | 1.052 | 293                       |
| 22       | 46  | HC (portal)               | 9                | 0.342     | 24.3        | 55.0       | 79.3        | 0.895 | 286                       |
| 23       | 45  | HD                        | 1                | 0.447     | 28.9        | 40.1       | 68.9        | 0.937 | 299                       |
| 24       | 30  | HS                        | 8                | 0.397     | 34.5        | 60.6       | 95.1        | 0.917 | 285                       |
| 25       | 51  | HS                        | 9                | 0.391     | 25.9        | 42.3       | 68.2        | 0.972 | 293                       |
| 26       | 55  | PH                        | 8                | 0.370     | 19.4        | 35.6       | 55.0        | 0.953 | 293                       |

**Mean**  
0.348  
27.6  
58.9  
86.8  
0.927  
291

**Standard deviation**  
0.052  
6.6  
14.9  
19.6  
0.079  
5

**Normal results (Pengelly, 1974)**  

| Mean | 0.433 | 25.7 | 40.5 | 66.2 | 0.897 | 289 |
|------|-------|------|------|------|-------|-----|
| SD   | 0.020 | 3.6  | 4.7  | 7.5  | 0.029 | 5   |

**Key to abbreviations:**
- **ML** = monocytic leukaemia
- **CLL** = chronic lymphocytic leukaemia
- **CML** = chronic myeloid leukaemia
- **LS** = lymphosarcoma
- **FS** = Felty's syndrome
- **MF** = myelofibrosis
- **HC** = hepatic cirrhosis
- **HD** = Hodgkin's disease
- **HS** = hypersplenism secondary to HC of uncertain aetiology
- **PH** = primary hypersplenism
- **PCV** = packed cell volume (haematocrit)
- **RCV** = red cell volume
- **PV** = plasma volume
- **WBV** = whole blood volume
- **Hb/Hv** = whole body haematocrit/venous haematocrit

**Notes:**
- *a* = first estimation
- *b* = second estimation with different spleen size

Pengelly, 1974
degree of splenic enlargement. Plasma osmolality was not significantly different from the normal on t-testing.

**DISCUSSION**

This study was undertaken to examine the changes in red cell and plasma volume that occur in the presence of splenomegaly and to examine the evidence for red cell pooling in enlarged spleens as indicated by the ratio Hb/Hv. Patients with polycythaemia vera were excluded, as the very high red cell volume in this disease makes the effect of splenomegaly difficult to evaluate. It has been shown that there was a highly significant increase in plasma volume and in whole blood
volume in association with splenomegaly, which correlated well with increasing spleen size. This agrees well with the findings in other investigations (Bowdler, 1970; Toghill and Green, 1972). Red cell volume was often increased in patients with splenomegaly, even in those patients who were clinically anaemic, and the correlation of red cell volume with splenic size was quite definite, even though no overall significant increase in red cell volume was found on t-testing. It is probable that some of these patients had a splenic pool of red cells slowly exchanging with the extra-splenic circulation as demonstrated by Bowdler (1969, 1970) and Toghill and Green (1972). In both these investigations estimations of the pooled red cell volume were made by taking early specimens (six minutes and three minutes respectively) following injection of $^{51}$Cr-labelled red cells, and subtracting the estimated red cell volume from another using a blood specimen taken at 45 minutes. But in the present study the ratio Hb/Hv was used alone as an index of red cell pooling and it is only possible to say that there was a red cell pool of concentrated red cells in the spleen in those patients showing an Hb/Hv ratio significantly greater than the normal value of $0.897 + 0.058$ (i.e. mean + 2S.D.).

Fig. 2. Whole blood volume in patients with splenomegaly.
Bowdler (1969) demonstrated concentrated red cell pooling by means of surface counting in some patients with splenomegaly but it is probable, as found by Bowdler and Toghill and Green, that red cell pooling of average or lower than average haematocrit was present in some of the patients. Fudenberg et al. (1961) found that the red cell pool of concentrated red cells (the splenic reservoir) occurred in every case of splenomegaly and was proportional in amount to the actual degree of splenic enlargement. The reasons for the difference between the findings of Fudenberg et al. and those of Bowdler, Toghill and Green, and myself are not clear.

Plasma osmolality was found to be normal in all but two of the patients in this series and clearly the changes in red cell and plasma volume were not due to alterations in its value (Table 1).

It is concluded that splenomegaly is usually associated with an increased plasma volume and an increased whole blood volume, both of which have a close correlation with the degree of splenic enlargement. Red cell volume is often increased and shows a good correlation with the degree of splenic enlargement but there is no overall significant increase in this value compared with the normal range. Red cell pooling with concentrated red cells is found in some patients as evidenced by the rise in Hb/Hv but it is not constantly present as suggested in a previous study by Fudenberg et al. (1961).

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