

Spleen function and platelet kinetics

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SUMMARY In patients suffering from various platelet abnormalities, quantitative scanning after injection of indium-111 (^{111}In) labelled platelets showed three different patterns of platelet destruction and distribution. In patients with a normal platelet life span but with evidence of increased splenic pooling, the spleen tended to be the main site of destruction. In patients with a moderately reduced platelet life span, the distribution of destruction was similar to normal, uptake occurring approximately equally in spleen and bone marrow. Patients with a severely reduced platelet life span showed abnormal destruction in the spleen and variable destruction in the marrow. However, because of its rapidity this destruction was difficult to quantify, and it was difficult in these cases to distinguish reliably between spleen pool, sequestration, and destruction. Destruction of platelets in the liver appeared to be unimportant in all three groups. ^{111}In , because of its physical characteristics, is preferable to chromium-51 as a platelet label in the assessment of abnormal platelet kinetics.

In patients with chronic idiopathic thrombocytopenic purpura and other platelet abnormalities, surface counting of platelets labelled with chromium-51 has given inconsistent results. There is still considerable uncertainty regarding platelet destruction in these patients; in some cases the liver, and in others the spleen, appears to be the predominant organ of destruction.¹⁻⁴ Heyns *et al.*⁵ and Klonizakis *et al.*⁶ studied the distribution and destruction of indium-111 (^{111}In) labelled platelets in normal subjects using the technique of quantitative scanning. We describe the use of this technique in a study of platelet kinetics in a series of haematological patients with platelet abnormalities.

Material and methods

Patients with a variety of haematological disorders were referred for platelet studies (Table).

Platelets were prepared for incubation with ^{111}In -oxine by one of the three techniques described by Klonizakis *et al.*⁶ In most of the patients, platelets were resuspended in dextrose saline; in some, re-suspension was in plasma saline or plasma. We have previously shown⁶ that the kinetics of platelets are essentially the same by all three techniques. In 15 cases autologous platelets were used; in three patients with very low platelet counts, isologous platelets labelled in plasma were used.

^{111}In -oxine was prepared from ^{111}In chloride (The Radiochemical Centre, Amersham, Bucks) and 8-hydroxyquinoline (BDH) by the method of Thakur *et al.*⁷

Blood samples were obtained at intervals between 15 minutes and nine days after injection of labelled platelets. Whole blood and platelet poor plasma were counted for ^{111}In , and the cell-bound activity was calculated according to the formulae of Goodwin *et al.*⁸ Whole-body scans were performed with a dual detector Ohio scanner (model 84) as early as possible after platelet injection and at intervals thereafter. Spleen and liver ^{111}In were quantified by the technique of Williams *et al.*⁹ The splenic accumulation of effete platelets was estimated by subtraction of the pooled platelet ^{111}In from the total splenic activity, assuming the initial activity to be entirely due to pooling; and the marrow accumulation was estimated by subtraction of the sum of the activities in spleen, liver, and blood from the dose.⁶

Results

The patients were divided into subgroups on the basis of platelet life span: group 1, essentially normal; group 2, moderately reduced; and group 3, severely reduced. Platelet survival curves and estimated spleen and bone marrow accumulation of effete platelets in the three groups are shown in Figures 1 to 3. Patients in group 1 show a decreased marrow uptake relative to splenic uptake; those in

Patients studied after injection of ^{111}In -labelled platelets

Group	Patient	Sex	Age	Diagnosis	Platelet count ($\times 10^9/l$)	Spleen size	T_p (days)
1	△ JH	F	25	Thrombocythaemia	1000	E	4.0
	● JM	M	30	Bacterial endocarditis	130	E	3.0
	○ AB	M	42	Polycythaemia	1200	N	3.9
	□ GP	M	72	Hodgkin's disease	275	E	4.1
	▲ MZ	F	55	Cirrhosis	100	E	3.7
2	◇ JM	M	24	Acute myeloid leukaemia	120	E	2.4
	■ DC	M	14	'Hypersplenism'	40	E*	2.6
	□ YB	M	50	Rheumatoid arthritis	70	N	2.5
	◆ VD	M	75	Multiple myeloma	40	N	2.6
	● PP	M	52	Hodgkin's disease	50	E	2.6
	○ RV	M	7	'Hypersplenism'	60	E*	2.3
	▲ MD	F	75	Chr. lymphatic leukaemia	20	G	2.7
	□ JV	M	28	Myelofibrosis	180	G	2.0
	†△ RD	M	55	ITP	20	N	< 1.0
3	▲ SB	F	45	'Hypersplenism'	40	E	2.0
	†○ KS	F	23	ITP	10	N	< 1.0
	● KW	F	46	ITP	10	E	< 1.0
	†■						< 1.0

'Hypersplenism' = splenic enlargement associated with thrombocytopenia of no definite aetiology.

Spleen size: N = normal; E = enlarged, 15-20 cm (max. diameter); G = enlarged, 20 cm.

*Age taken into account.

†Labelled isologous platelets injected.

T_p = time taken for circulating labelled platelet level to fall to half the 30-minute value.

ITP = Idiopathic thrombocytopenic purpura.

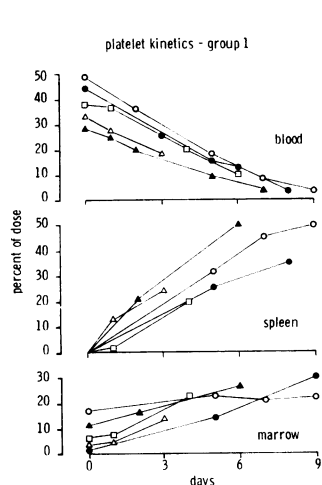


Fig. 1 Platelet survival curves (top), splenic ^{111}In uptake (corrected for pooling; middle) and estimated marrow ^{111}In uptake (bottom) in patients from group 1 (see text) after injection of ^{111}In labelled platelets.

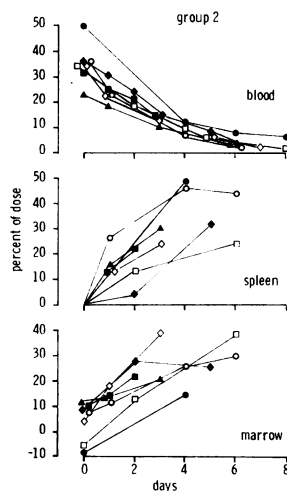


Fig. 2 Parameters shown in Fig. 1 in patients from group 2.

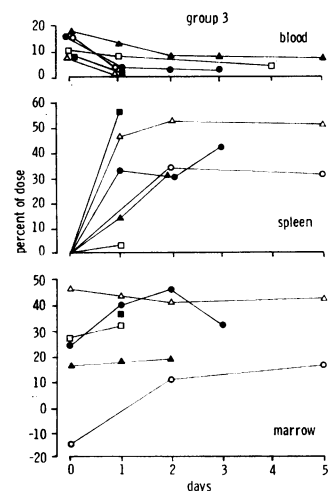


Fig. 3 Parameters shown in Figs 1 and 2 in patients from group 3.

group 2 show approximately equal uptake in marrow and spleen, similar to normals;⁶ and group 3 patients show increased splenic uptake with variable and uncertain marrow uptake.

^{111}In uptake in the liver is shown for all subjects in Figure 4. With the exception of one patient with idiopathic thrombocytopenic purpura, liver ^{111}In uptake was less than in the spleen and rose only slightly during the duration of the platelet life span.

Discussion

In thrombocytopenic patients, the difficulty of incorporating ^{111}In in platelets in sufficient quantity for subsequent external scanning is accentuated because even trace quantities of plasma or anions such as citrate or phosphate compete with the platelets for ^{111}In . The use of dextrose saline as a re-suspending medium overcomes this difficulty to a

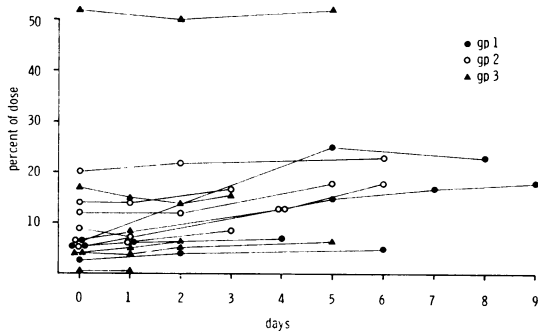


Fig. 4 Hepatic ^{111}In content in all patients after injection of ^{111}In labelled platelets.

great extent and helps to preserve adequate platelet viability.⁶

The patients in group 1 showed abnormal platelet pooling in the spleen, with a low initial blood ^{111}In recovery, a high initial splenic ^{111}In , and a 'flat' survival curve with essentially normal life span; it is reasonable to suppose that the platelets are normal and that the high splenic ^{111}In is a reflection of increased splenic pooling capacity. In these cases the estimated bone marrow platelet destruction seems less than normal, possibly as a result of a shift towards splenic destruction resulting from increased splenic activity; that is, although splenic platelet destruction is increased, total destruction is not, and platelets are not destroyed prematurely. In group 2, on the other hand, bone marrow and splenic destruction appear to be equally accelerated, such that the relative proportion of platelets destroyed at each site remains more or less normal. In these patients, the primary abnormality is presumably in the platelet, as is borne out by the curvilinear shape of the survival curves and the clinical conditions. In group 3, platelet survival is severely reduced, and splenic and marrow accumulation of the effete platelets is markedly abnormal. In this group, the assumption upon which the estimates of splenic and marrow platelet destruction are based is likely to be unjustified. As survival is so short, the distinction between pooling, sequestration (ie, prolonged platelet hold-up), and destruction becomes impossible. Quantification of the bone marrow uptake must be interpreted with caution; the initial sum of blood, spleen, and liver quantities is well below 100% of the dose. Whether this is because bone marrow uptake is very rapid, or because platelet uptake occurs at other, unidentified, sites, is not known. The scan shown in Fig. 5, showing ^{111}In uptake in the kidneys of a patient suffering from thrombotic thrombocytopenic purpura, suggests that such alternative uptake may occur in this disease.

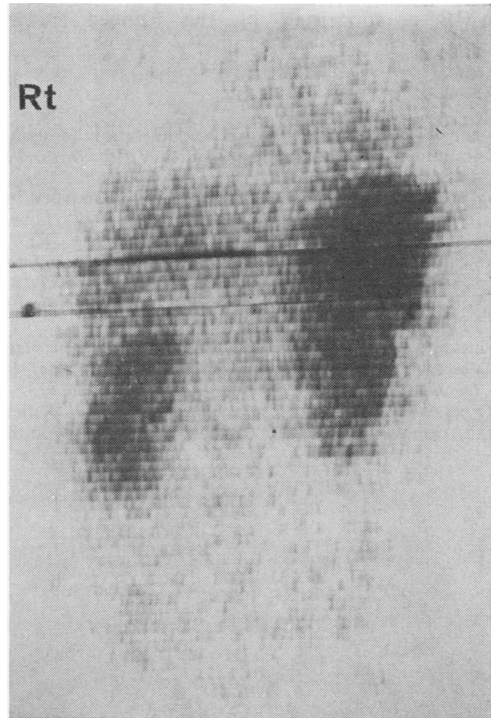


Fig. 5 Scan of patient suffering from thrombotic thrombocytopenic purpura (anterior and posterior abdominal views superimposed) 2 hours after injection of autologous platelets labelled with ^{111}In . Localisation is apparent in spleen, liver, and both kidneys. Abnormal platelet deposition in the kidneys was confirmed post mortem.

Quantification of liver ^{111}In uptake suggests that, even in subjects with abnormal platelet turnover, the liver is not an important organ for platelet destruction. The only patient to show a substantial liver uptake had received isologous platelets. The significance of increased liver uptake is further limited by the likelihood that platelets severely damaged in the labelling procedure are removed rapidly by the liver.⁸

The small series of patients investigated does not allow us to draw many conclusions as to the pathophysiology of platelet destruction, but this study has demonstrated the advantages of ^{111}In labelling, together with sequential quantitative scanning, in obtaining more meaningful information than from surface counting in the interpretation of spleen function in relation to platelet kinetics.

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