

was obtained, which was disclosed to be expressed in sum of two exponential components.

Mean transit time for both radiotracers, representing the plasma and erythrocytes respectively, was calculated.

In normals the time was between 8 and 32 seconds and significant difference between both tracer was not observed.

In splenomegalic cirrhosis of the liver and "Baniti's syndrome" the time was evidently

prolonged and especially so for erythrocytes, being three or four times normals and twice or more of that for the plasma.

From the results above described remarkable increase in total splenic flow as well as significant hemoconcentration and stagnation were indicated, in which phenomenon some cause and effect relationship with manifestation of portal hypertension and hypersplenism must be considered.

### **Studies on the Function of REC with $^{51}\text{Cr}$ Labelled Heat Damaged Erythrocytes in the Mice Developed Experimental Hematological Disorders**

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RES function of mice which were induced bone marrow failure by chloramphenicol, splenectomy and sensitization with human gamma globulin and chlorabulin, were studied with sequestrated  $^{51}\text{Cr}$ -labelled heat damaged erythrocytes.

ICR female mice (20 to 24 g of body weight) were used for all experiments. Heparinized iso-erythrocytes were incubated with  $^{51}\text{Cr}$ . at  $37^\circ\text{C}$  for 20 minutes. These tagged erythrocytes were damaged at  $49.5 \pm 0.5^\circ\text{C}$  for 20 minutes, and were injected into mice tail vein.

Half disappearance time of radioactivity in blood, which is called clearance ( $T_{1/2}$ ), was calculated in each mouse. Percent uptake of radioactivity in each organ was observed in decapitated mice on two hours after  $^{51}\text{Cr}$  injection. Five mg of chloramphenicol was administered intraperitoneally two times daily for three consecutive days (CP three days group), or five mg of chloramphenicol was administered intraperitoneally once a day for thirty days (CP 30 days group). One point two five mg of human gamma globulin were administered intraperitoneally three times in each other day (H.G.G. group) or injected with Freund's complete adjuvant for six weeks (H.G.G. & F.C. Adj. group). Splenectomy was done to the mouse aseptically. Splenectomized mice were used for experiments after 10 days (Spx 10 days group), and 20 days (Spx 20

days group).

Normal mice were used for control in each experiment.

Normal mice showed slight changes of  $^{51}\text{Cr}$  organ distributions during 30-120 minutes after administration, and showed 7 times radioactivity per unit of organ weight of spleen than that of liver. The uptake of each organ was decreased in order of liver, spleen and bone marrow in normal mice.

CP 3 days group showed normal range of clearance, decreased uptake of bone marrow, and increased uptake of liver and spleen.

CP 30 days group showed increased uptake of liver and normal range uptake of spleen and bone marrow.

Spx 10 days group showed extremely prolonged clearance ( $T_{1/2}$ ), and increased uptake of liver and bone marrow without a compensation of spleen function. Two splenectomized mice out of four were observed prolonged clearance and two mice showed normal range of clearance following three days CP administrations. Spx 20 days group showed significantly prolonged clearance and increased bone marrow uptake. Their clearance got into a normal range, and increased liver uptake and decreased bone marrow uptake were followed after CP three days administration.

H.G.G. & F.C.Adj. group which were observed ascitic fluids and splenomegaly, showed

shortened clearance, increased uptake of liver (slightly) and spleen (extremely), and decreased uptake of bone marrow.

Chlorabuling group showed increased uptake of liver and spleen, and decreased uptake of bone marrow.

It was concluded from these data that (1) spleen and liver were in the same manner on

the sequestration function of  $^{51}\text{Cr}$ -labelled heat damaged erythrocytes, (2) RES function of bone marrow and that of spleen and liver were observed adverse reactions except splenectomized mice, (3) CP and H.G.G. & F.C.Adj. decreased RES function of bone marrow, and (4) splenectomy increased RES function of bone marrow.

### Fate of Intravenously Administered Damaged Erythrocytes — Whole Body Macro-Autoradiographic Study —

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Whole body macro-autoradiographic studies were carried out in mice to observe organ distribution of heat-denatured  $^{59}\text{Fe}$ -red cells.

$30\mu\text{Ci}$  of  $^{59}\text{Fe Cl}_3$  was injected i.p. to mice for 2 days and after 1 week the blood was obtained from the heart. Such  $^{59}\text{Fe}$ -tagged red cells were treated by heating at  $49\pm 1^\circ\text{C}$  for 45 minutes.  $0.15\text{ ml}$  of heated  $^{59}\text{Fe}$ -red cells was injected into the tail vein of normal and splenectomized mice. At 3, 24, 72 and 168 hours, mice were sacrificed and macro-autoradiography was performed by a modification of Ullberg's technique.

As to the distribution of  $^{59}\text{Fe}$  in normal mice after 3 hours, the splenic activity was predominant followed by the hepatic activity. Activity in the blood was already decreased at this time. Autoradiographic patterns of the liver and kidney were spotty showing the parenchymal structure.

There were no obvious changes in distribution patterns after 24 hours in comparison with those after 3 hours, except that the activity in the blood was decreased still further

and the pattern of the liver was less distinct.

This suggests that  $^{59}\text{Fe}$  released from red cells was taken up by the liver parenchyma.

After 3 days, the activity in the blood was fairly increased over that at 24 hours, and in contrast, the hepatic activity was decreased. Distribution patterns after 7 days were nearly the same as those after 3 days. The activity in the bone marrow showed no obvious change during 7 days.

The organ distribution in splenectomized mice did not suggest any compensatory increase of uptake by the liver and other organs; the blood activity was much higher than the control for at least 24 hours.

These observations clearly demonstrate that the high activity in the blood after 3 days represents reutilization of  $^{59}\text{Fe}$  by the newly formed erythrocytes, and that the spleen has an important role in the uptake of heat-denatured red cells as evidenced by the lack of increase in activity in the liver and bone marrow following splenectomy.