The Liver Blood Flow after Local X-Irradiation

A suspension of colloidal particles injected intravenously is phagocytized by the reticulo-endothelial cells of the liver and spleen. The blood clearance follows an exponential function of the time $C = C_0 \cdot 10^{-KT}$[1,2]. The constant K is the phagocytic index and is a measure of the phagocytic activity of the RES. K varies inversely with the colloid-concentration in the blood[3]. Below a 'critical dose', the clearance is independent of the colloid concentration. In this range the liver absorbs nearly 100% of the colloids and the clearance is only dependent upon the blood flow through that organ. Under these conditions it is not the phagocytic function of the RE cells which is measured but the liver blood flow. Thus, in this case, the constant K stands for the index of the hepatic blood flow[4]. The critical dose differs dependent upon the species, type, and size of the colloid particles. It can be calculated: ($K \times$ dose injected/maximum value of K)[5]. Before commencing our experiments concerning the liver blood flow, we determined the critical dose to be 8.45 μg of radiogold colloid per 10 g body weight.

The test was performed with 175 male mice weighing 20 $\pm$ 1 g. After an irradiation of the liver region with 500, 1000 or 2000 R (220 kV, 25 mA, 0.5 mm Cu, FHD 50 cm) the clearance of 13.5 μg of colloidal radiogold was measured 1/2, 24, 48, 72, or 96 h later with a γ-scintillation counter over the neck, and K as the index of the hepatic flow was determined. The liver uptake was simultaneously measured with a 1 cm ⌀ collimator directly over the liver region. The animals were then killed and the organ activity of the liver and spleen was determined in a scintillation well-type detector.

Results. The measurement of the γ-activity showed that the clearance of colloidal radiogold was diminished up to 3 days after the irradiation. The constant K indicated no difference whether 500, 1000, or 2000 R were applied (Figure 1). The liver uptake was the same for the irradiated and the control mice, but the maximum was reached later in the case of irradiated animals. The conditions returned to normal 4 days after X-irradiation (Figure 2). The measurement of the organ activity in vitro, 30 min after the injection of radiogold, showed that

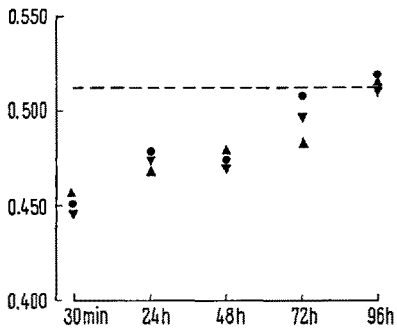

Fig. 1. The index K in normal mice (----) and 1/2, 24, 48, 72, and 96 h after 500 (●), 1000 (▲), and 2000 (▼) R local irradiation.

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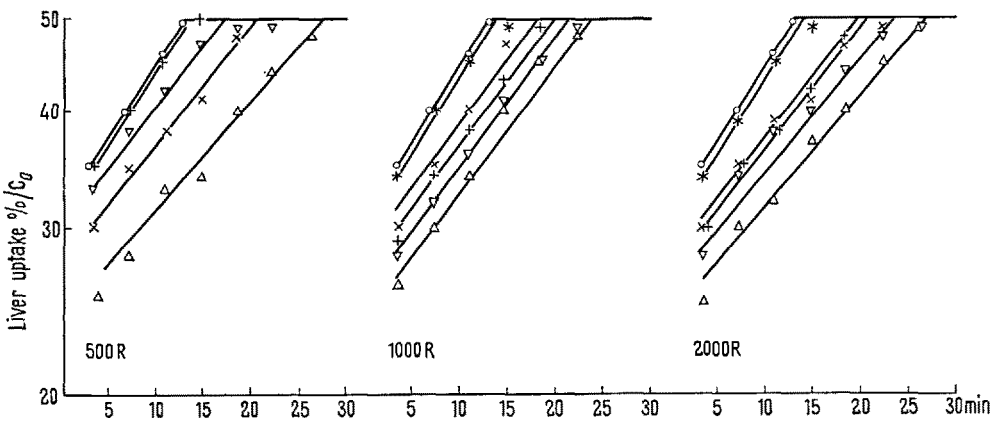

Fig. 2. The radiogold uptake measured directly over the liver region in a 1 cm ⌀ area. Normal conditions (o) 1/2 (△), 24 (▽), 48 (×), 72 (+), and 96 (*) h after 500, 1000, or 2000 R.

Index K, standard deviation, and statistical significance 1/2, 24, 48, 72, and 96 h after local irradiation on the liver region with 500, 1000, and 2000 R

		500 R	P		1000 R	P		2000 R	P
0.512 $\pm$ 0.038	30 min	0.450 $\pm$ 0.060	< 0.01	30 min	0.455 $\pm$ 0.047	< 0.01	30 min	0.447 $\pm$ 0.054	< 0.01
	24 h	0.478 $\pm$ 0.042	< 0.05	24 h	0.467 $\pm$ 0.041	< 0.05	24 h	0.477 $\pm$ 0.041	< 0.05
	48 h	0.474 $\pm$ 0.040	< 0.05	48 h	0.476 $\pm$ 0.059	< 0.05	48 h	0.472 $\pm$ 0.042	< 0.05
	72 h	0.508 $\pm$ 0.047	> 0.10	72 h	0.482 $\pm$ 0.047	< 0.10	72 h	0.497 $\pm$ 0.041	> 0.10
	96 h	0.519 $\pm$ 0.049	> 0.10	96 h	0.516 $\pm$ 0.022	> 0.10	96 h	0.513 $\pm$ 0.040	> 0.10

89.4 ± 5.1% of the injected dose is in the liver and 1.5 ± 0.11% in the spleen, no difference between normal and irradiated mice being seen.

It may be concluded that the hepatic flow is slowed down immediately and up to 4 days after local irradiation. The difference of the liver flow between normal and irradiated mice is statistically significant (Table). The fact that the spleen uptake remained stable whether the liver region was irradiated or not, is proof that the delay clearance is caused by the slowed-down liver blood flow and not by irradiation damaged RES. When the reticuloendothelial cells of the liver are destroyed or blocked, the phagocytosis of the spleen increases compensatorily and the uptake is higher[6].

Our results are confirmed by PIOVELLA et al. who noticed under a transillumination microscope that the blood flow after γ-irradiation of the liver was delayed, with stasis and perivascular microhemorrhages. Conditions returned to normal after a small dose, whereas after a higher dose they were irreversible[7,8].

Zusammenfassung. Mit Hilfe der Clearance von kolloidalem Radiogold, der Leber- und Milzspeicherung wurde die Durchblutung der Leber nach lokaler Bestrahlung der Leberregion bestimmt. Im Anschluss an 500, 1000 oder 2000 R wurde eine Verminderung der Leberdurchblutung festgestellt. Eine Restitutio ad integrum wurde dosisunabhängig 3–4 Tage post irritationem beobachtet.

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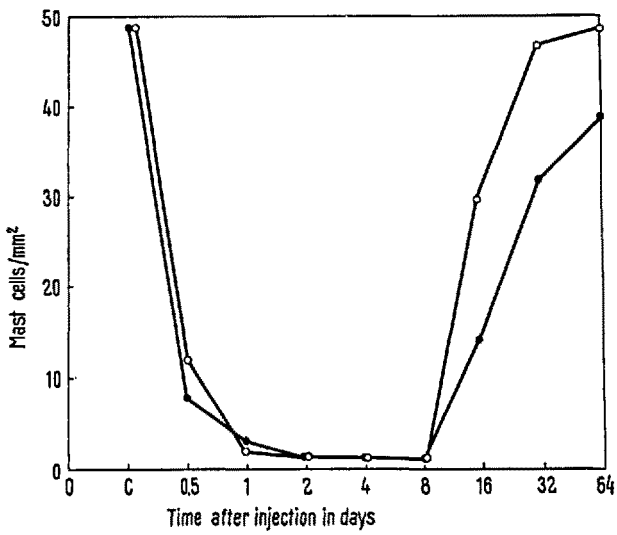
The Histamine and Heparin Content of the Rat's Mesenterial Mast Cells Regenerating after Application of Compound 48/80

The relationship between histamine and heparine in the mast cells is still obscure. The mast cells are a significant source of histamine and heparin, and the release of mast cell granules through experimental means is accompanied by the release of histamine and heparin. RILEY[1] supposes that, on rupture of the tissue mast cell, histamine first spreads rapidly through the tissues, and then a sluggish discharge of heparin follows. WERLE et al.[2] show that the histamine in the mast cells, and also the greatest part of the tissue histamine, forms a complex with heparin. In the complex the histamine acts as heparinate.

It is difficult to develop an experimental procedure making possible separate histamine or heparin release without disruption of the mast cells. SMITH[3], however, found that intraperitoneal administration of low concentrations of toluidine blue, protamine sulfate, or other histamine liberators brought about a significant release of histamine without any disruption of the mast cells in the tissues of the peritoneal cavity. It is, however, a well-known fact that in the majority of experimental conditions the mast cells are extremely sensitive to environmental changes, as well as to irritation or actual injury. Mast cells respond to injury of any kind by liberating substances normally held in their protoplasm. Thus the changes observed in the mast cells immediately after irritation of any kind must be noted with caution.

In this investigation, the appearance of histamine and heparin is examined in mast cells regenerating after previous and complete disruption caused by compound 48/80.

Material and methods. Adult male rats (250–300 g) were injected intraperitoneally with 200 μg compound 48/80 dissolved in 2cm^3 of a 0.9% sodium chloride solution. The control animals were only injected with 2 cm^3 sodium chloride solution. The animals were killed from half a day up to 64 days after the injection. From the mesentery of the lower small intestine, two specimens were taken. One specimen was immediately put into a solution of Reinecke-salt (saturated, filtered solution, diluted with water in the ratio 1:5) for 48 h (SCHAUER and WERLE[4]). The histamine of the mast cells precipitated as 'Reineckat', and, in the unstained translucent preparations of the mesenteries, the granules of the mast cells could clearly be seen. After fixation the mesenterial membrane was carefully – avoiding stretching – placed on a microscope slide. The other specimen was fixed in a 4% basic lead acetate, stained with a 1% aqueous solution of toluidine



Mast cell counts after application of compound 48/80. —●— Reinecke-salt, —○— toluidine blue.

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