in various organs of the body to which they are carried by the blood stream. Rao et al.[7] recently indicated that aflatoxin B was capable of binding with plasma albumin in vitro. Therefore a possible in vivo transport mechanism for aflatoxin as an albumin complex has been suggested.

The marked increase of glycogen content of the hepatic cells is rather surprising. The result is in contrast to the report of Shank and Wogan[8] who found that liver glycogen was not affected by a 5 daily oral administration of sublethal dose of the toxin to rats. Whether or not this is due to the different routes of administration or the duration of treatment remains to be studied[9].

Zusammenfassung. Nachweis der Absorption von Aflatoxin B_1 durch die Rattenhaut. Die toxische Leberwirkung nach der Hautbepinselung entsprach den von anderen Autoren gefundenen Verhältnissen bei peroraler oder intraperitonealer Verabreichung.

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Enhanced Phagocytic Function in vivo After Whole Body Irradiation

Cells of the reticuloendothelial system (RES) are generally considered to be very radioresistant. They usually shown no morphological damage after even high doses of radiation[1] and little change in phagocytic capacity when tested in vitro[2,3]. The results are far more divergent, however, when the phagocytic activity of the RES as a whole is studied in irradiated animals: depression, no change and increase of activity have been reported[4]. This is probably partly due to differences in species, nature of particles used for measuring phagocytosis, dose of radiation, and time after the exposure, among the different authors. One thing is, however, common to most of these in vivo studies, namely that RES function was tested only within the first few days after irradiation.

Experiments described below were designed to test the phagocytic activity of the RES, with either inert or immunogenic particles, at later times after sublethal or lethal irradiation.

Clearance of colloidal carbon. CBA/H mice, 4–5 months old, were irradiated with 600, 800 or 1000 rads of X-rays[5]. 7 or 14 days later they were injected i.v. with colloidal carbon (16 mg/100 g body wt., Pelikan C11/1431a) and the rate of clearance was measured as described before[5], except that blood samples were obtained from the orbital venous plexus.

Colloidal carbon was cleared exponentially from peripheral blood of all mice, but faster in irradiated than in control ones. At 7 days after 1000 rads and 14 days after 800 rads, carbon disappeared about twice as fast as in unirradiated controls ($T_{0.5}$ = 29.6 and 34.0 min respectively as compared to 60.5 min). The rate of clearance, K (also known as the phagocytic index), was significantly higher in all irradiated groups than in the control group and increased with increase in the radiation dose (Table I).

The rate of clearance of particles from the blood is considered to be a measure of the overall phagocytic activity in vivo in which the liver is known to play a major part[6]. The present results could therefore be interpreted as indicating enhanced phagocytic function of the RES after irradiation. However, in view of the suggested increase in vascular permeability after irradiation[7] it could be argued that faster disappearance of colloidal particles from peripheral blood is a result of general leakage from the vascular system and not necessarily caused by an increased activity of the macrophage system. These 2 possibilities could be distinguished by measuring the uptake of particles by those organs known to play a major role in the removal of particles from the blood stream by RES activity. A general increase in vascular permeability would lead to a reduced uptake in specific organs while an increased uptake in an organ like the liver would suggest greater activity of the macrophage system. In order to study the organ uptake of particles, radioactively labelled bacteria were used in the next experiment.

Clearance and uptake of bacteria. E. coli, strain B/r, were grown to stationary phase, killed by heating to 60 °C for 30 min and labelled with ^{51}Cr (sodium chromate solution, 216 μCi/1 μg Cr, Amersham) as described by Howard et al.[8]. There was less than 3% free ^{51}Cr in the final preparation. CBA/H male mice, about 5 months old,

Table I. Rate of clearance of colloidal carbon from peripheral blood of irradiated and control mice[a]

Radiation dose (rads)	Rate of clearance ($K \times 100$) at times after irradiation[b, c] 7 days	14 days
600	1.46 ± 0.08 (5)	1.32 ± 0.03 (5)
800	1.80 ± 0.11 (15)	2.25 ± 0.17 (20)
1000	2.41 ± 0.13 (9)	–
Controls		1.17 ± 0.03 (32)

[a] All values are means ± standard errors. [b] Number of mice per group is given in brackets. [c] All means are significantly different from the control at 0.05–0.01 level.

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Table II. Rate of clearance from peripheral blood and organ uptake of ^{51}Cr-labelled *E. coli* in irradiated and control mice[a]

Experimental group	Rate of clearance $K \times 100$	% of injected radioactivity					No.
		Liver	Spleen	Lungs	Kidney	Total recovered	of mice
7 days after 1000 rads	14.6 ± 1.1	74.8 ± 0.7[b]	0.47 ± 0.05[b]	2.3 ± 0.2[b]	0.34 ± 0.03[b]	77.9 ± 0.8	6
14 days after 800 rads	15.8 ± 0.9[b]	74.6 ± 1.3[b]	0.74 ± 0.20[b]	2.8 ± 0.3[b]	0.61 ± 0.13	78.7 ± 1.0	8
Controls	11.9 ± 0.2	66.1 ± 0.6	2.64 ± 0.32	6.4 ± 0.3	0.62 ± 0.03	75.7 ± 0.8	8

[a] All values are means ± standard errors. [b] Significantly different from controls at the 0.01 level.

which had been irradiated with 800 and 1000 rads 14 and 7 days earlier respectively, as well as unirradiated control mice, were injected i.v. via a tail vein with 3.2 to 4.2×10^9 organisms. Blood samples were obtained under light ether anaesthesia from the orbital venous plexus 2 and 20 min later, since it had been found in a preliminary experiment that labelled bacteria disappeared exponentially from the circulation for at least 25–30 min after injection. The rate of clearance K was calculated from the equation $C_{t_2} = C_{t_1} e^{-K(t_2 - t_1)}$, where C_{t_1} and C_{t_2} are the concentrations at times t_1 and t_2 (in min) respectively. 40 min after the injection mice were killed by cervial dislocation and liver, spleen, lung and one kidney removed and digested with nitric acid. Radioactivity of blood samples and organ digests was measured by gamma counting in a scintillation well-type counter.

The results are summarized in Table II. In both groups of irradiated mice the rate of clearance of bacteria from the blood was greater than in controls, and so was the uptake of radioactivity by the liver. The uptake by the spleen and lung was reduced in irradiated mice. However, the uptake of radioactivity by the rest of the body other than liver, spleen and lung was not changed, suggesting that increased vascular permeability, if it was present, had little if any effect.

The greater uptake by the liver suggests that the increased rate of clearance of particles from the blood is the result of a greater phagocytic activity of liver RE cells. There is evidence from other experiments indicating that the higher rate of clearance of colloidal particles from the blood of irradiated mice is a consequence of increased intestinal permeability for bacteria and/or their products (ŠLJIVIĆ[9]). These are known to be able to stimulate RES activity[10].

No single explanation can be offered at present for the reduced uptake of radioactivity by spleen and lung. If on the basis of in vitro studies a direct effect of radiation on macrophages is excluded, some indirect effects operating in vivo could be considered. In the whole animal the uptake of particles from the blood stream must be affected by haemodynamic conditions and particularly by the rate of blood flow through specific organs. Greater activity of liver RE cells could reduce the uptake by other organs through competition for a limited number of particles.

Evidence presented here indicates that faster clearance of particles from the blood stream of irradiated mice is the result of greater phagocytic activity of liver RE cells rather than increased vascular permeability. A full account of changes of the rate of clearance of colloidal carbon after irradiation and the mechanisms by which the increased activity of the RES is brought about will be given elsewhere[11].

Résumé. Chez des souris irradiées, le carbone colloidal et les bactéries *E. coli* marquées au ^{51}Cr ont été éliminés plus rapidement de la circulation. En étudiant la distribution de la radioactivité dans les divers organes, on conclut que cette évacuation plus rapide résulte d'une activité phagocytaire plus intense des cellules réticuloendothéliales du foie plutôt que d'une augmentation générale de la perméabilité du système vasculaire.

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Radioprotective Effects of Phytourease

The attempt therapeutically to increase the natural radioresistance of the organism is related to the protection of the individual against harmful effects of ionizing radiation. The natural radioresistance may be increased before irradiation by the administration of radioprotective pharmaceuticals. An important pre-requisite for a favourable action of chemical radioprotectives is their early application, a sufficient concentration in the organism, minimum toxicity and a long-lasting protective effect[1,2].

We have tested in our laboratory in recent years some radioprotective effects of several compounds with antigenic character in experimental animals. KALINA and DIENSTBIER[3] have found the favourable effects of applied human serum albumin in mice and rats before X-irradiation. We have proved, on the one hand, the mechanism of protective effect of HSA and, on the other hand, we have examined some further compounds which appear to be strong antigens in experimental animals[4].

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