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Effect of Continued Iron Administration on Growth

DURING studies on the effects of repeated parenteral administration of iron to mice, rabbits and guinea pigs, various toxic manifestations were observed¹; but in general there was little effect on growth with either colloidal or diffusible forms of iron. One diffusible iron preparation, namely, 'ferric hydroxide ferrous ascorbate', however, depressed growth markedly. The results obtained with three iron preparations are summarized below.

(a) *Colloidal iron.* When iron in colloidal form is given in repeated sub-lethal doses, a large quantity may accumulate in the body before serious harm results. Mice lived two to three months after twelve weekly intravenous doses of 180 mgm. iron per kgm. of saccharated iron oxide, that is, a total dose of 2.16 gm. iron/kgm. There was no loss of weight in these animals until death supervened. The ultimate cause of death is not clear; but severe damage was noted in the lungs, liver and kidneys. Four one-week old mice injected daily with 40 mgm. iron/kgm. of saccharated iron oxide by the subcutaneous route gained weight normally until they reached adult size (seven weeks), the total dose given being 0.9 gm. iron/kgm. of their final body-weight (20 gm.). Two three-day-old guinea pigs injected daily with 40 mgm. iron/kgm. of the same preparation subcutaneously also continued to gain weight much the same as two control guinea pigs.

(b) *Diffusible iron.* Diffusible iron preparations behave differently both as regards toxicity and fate in the body, the results obtained depending on the nature of the non-ionized whole molecule of the iron compound^{1,2}. Seven young guinea pigs, varying in age from two days to a few weeks and in weight from 75 to 320 gm., were given large doses of diffusible preparations of iron by repeated subcutaneous injections. Four of these received 11.25 mgm. iron/kgm. daily in the form of 'ferric hydroxide ferrous ascorbate', while the remaining three had 30 mgm. iron/kgm. daily in the form of 'ferric chloride caramellate'¹. The latter group grew and gained weight without obvious deviation from the normal, during the whole period of the injections which lasted 63 days, their final weights being 496, 450 and 465 gm. The first four, however, died after 17, 27, 43 and 63 days respectively. Their growth was interfered with appreciably, and although they continued to increase in weight for a while, the rate of increase soon slowed down. In the case of guinea pigs 3 and 4, serious loss of weight was noted in the last few weeks of life, their final weights being 180 and 175 gm. There

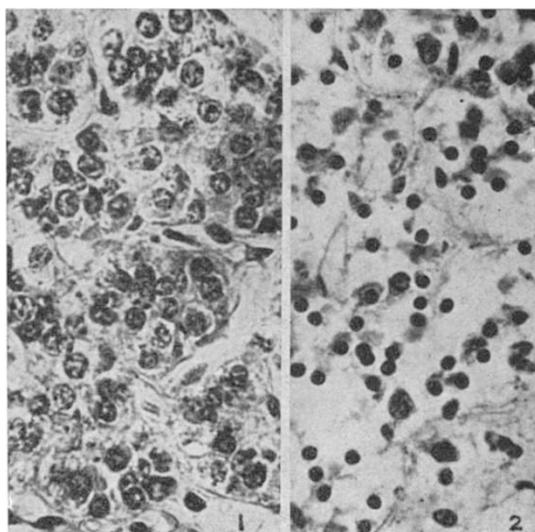


Fig. 1. Anterior pituitary of normal guinea pig showing large vesicular nuclei and abundant cytoplasm. Stained with carmalum. $\times 500$

Fig. 2. Anterior pituitary of guinea pig 4, injected with 'ferric hydroxide ferrous ascorbate'. Section shows numerous pyknotic nuclei and wide spaces between atrophied cytoplasm of cells. Stained with carmalum. $\times 500$

were hæmorrhages in the lungs and histological damage in the adrenals in all four guinea pigs.

Growth retardation after injections of 'ferric hydroxide ferrous ascorbate' may be secondary to adrenal and lung damage, and could be caused through interference with the normal functioning of ascorbic acid. On the other hand, a direct interference with the functions of the pituitary seems likely. Sections of the pituitary in guinea pig 4 revealed iron staining in the cells of the anterior pituitary—a finding which is recorded in the experimental animal for the first time—and there was histological damage with atrophy of cells and pyknosis of nuclei in guinea pigs 3 and 4 (Figs. 1 and 2). Neither iron staining nor histological injury was detected in the pituitaries of animals receiving saccharated iron oxide or 'ferric chloride caramellate'.

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Effect on Lymphocytes of Ionizing Radiation

THE increasing use of radioactive material makes the biological assay of the effects of ionizing radiation of importance. Lymphocytes are agreed to be the most sensitive mammalian cells available for the study of such effects; Trowell¹ has recently published his findings using whole animals and organs. Elsewhere, one of us² has described a method whereby human cells can be maintained alive for periods up to fourteen days without the elaboration of traditional tissue culture technique. All that is needed is 3 per cent agar in distilled water, of which 1 c.c. is added to 2 c.c. of equal parts of human serum