ABSTRACTS

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IRON


Ferritin from guinea pig liver has been obtained in crystalline form. Intraperitoneal injection of ferric ammonium citrate in guinea pigs was observed to lead to a greatly increased incorporation of labeled leucine or glycine into liver ferritin. Furthermore, eight hours after the injection of iron, a net increase in the protein moiety of liver ferritin was demonstrable. These findings are believed to indicate that iron accelerates the synthesis de novo of the protein moiety of ferritin.

Ferritin consists of a mixture of molecules with the same apoprotein (apoferritin) but different iron contents and different molecular weights. On the basis of these differences it was possible with the ultracentrifuge to separate ferritin into 4 relatively homogeneous fractions. If the assumption is correct that apoferritin is the first compound to be formed in iron-stimulated ferritin synthesis, a tracer dose of glycine should first appear in the iron-free apoferritin and in those “lighter” ferritin molecules containing little iron. In short-term experiments this has been found to be the case. Radioactivity appeared first and in highest concentration in that ferritin fraction which exhibited the lowest iron-to-nitrogen ratio.—R.S.


Sex differences in hemoglobin values and serum iron values in normal and castrated rats were investigated. No sex difference was found in the hemoglobin values of normal rats. Castration produced no significant changes in the hemoglobin values of either male or female rats. The serum iron values of normal female rats were 50 per cent higher than those of normal males. Castration reduced the serum iron values of female rats but caused little change in males. The serum iron values declined with increasing age in normal animals of both sexes, but not in castrated animals. No significant variations of total iron-binding capacity were observed in either male or female rats.—G.C.deG.

The amount of storage iron in the liver and the spleen of rats was increased after prolonged treatment with phenylhydrazine. Under the conditions of the experiment the increased storage of iron could be attributed only to increased absorption of dietary iron. Increased iron absorption was also found in rats fed supplementary dietary iron. It is pointed out that the anemia was almost certainly the factor determining the rate of iron absorption, but the mechanism of its operation was difficult to explain. The significance of these observations in relation to iron therapy in anemia is discussed. It is suggested that anemia markedly increases the absorption of iron from the diet, iron therapy is indicated only in those anemias due to iron deficiency, and that in all other forms of anemia iron therapy is contraindicated because iron is not excreted amid the added iron, if given therapeutically, piles up in the iron stores.—G.C.deG.


In rabbits it was found by use of radioactive iron that the fetus takes up iron from the maternal plasma as ferritin. If there is not enough apoferritin available in the maternal plasma, iron is carried and stored in the fetus as hemosiderin until the formation of ferritin takes place. There is no blocking of iron transport across the placenta when large amounts of iron (40-215 mg. of intravenous Fe within 4 days) are given. The ferritin, hemosiderin, and total iron were measured in 10 human placentas. An attempt has been made to relate these levels to various disease states.—M.H.H.


In this study of extravascular iron loss from the body, four normal individuals were injected intravenously with 5 to 14 mg. of radioiron and the feces were collected for approximately 100 days. The average daily excretion of iron in the feces during the period of study was 0.01 per cent of the dose or 0.4 to 2.0 µg. per day. In three women with iron deficiency the daily fecal excretion was considerably less (0.002 to 0.004 per cent of the dose). In one of two patients with hemolytic anemia the fecal excretion was elevated to 0.07 per cent per day; in the second subject, it was normal. From a ratio of the radioiron to the total body iron, if complete mixing of the iron is assumed, the calculated total fecal excretion of iron in normals was 0.33 to 0.52 mg. per day; in iron deficiency was 0.03 to 0.06 mg. per day and in the one patient with hemolytic anemia was 1.45 mg. per day. The excretion of iron in sweat and in hair was also measured and found to be very small even when copious perspiration was induced. In two dogs, fecal excretion of iron during hemolysis induced by phenylhydrazine, was found to be increased and represented 2.8 to 3.3 per cent of the iron released by hemoglobin destruction.

This work extends observations made by other workers on the excretion of iron from the body. Perhaps of greatest interest is the conclusion that there may exist only a small positive iron balance and that it may be possible to induce iron deficiency in an adult where either absorptive defects or inadequate diets exist for a prolonged period of time.—W.N.J.

Urinary excretion of iron and plasma iron levels were determined in a total of 15 patients during the course of the administration of Ca EDTA. Seven patients with idiopathic hemochromatosis were observed, the remaining 9 patients had various diseases and were used as controls. The control group of patients had urinary excretion values of less than 1 mg. of iron per 24 hours prior to Ca EDTA and showed variable increases in excretion from 1 to 3 mg. after 3 to 4 courses of 1 to 4 Gm. per day of intravenous Ca EDTA. The patients with hemochromatosis had excretions of approximately 1 mg. of urinary iron per day during the control period and had increases in urinary iron excretion of from 1 to 6 mg. per day during the intravenous administration of Ca EDTA. An interesting and constant finding was that the greatest increase in excretion occurred during the first day of Ca EDTA administration. The oral administration of Ca EDTA in dosages of 2 to 9 Gm. per day for a total of 40 Gm. failed to influence the urinary excretions of iron. There was no change in the plasma iron concentration of 4 patients during the administration of Ca EDTA. Routine hematologic analyses failed to show abnormalities during the Ca EDTA therapy. It is appropriately pointed out by these studies that Ca EDTA does not substitute for venesection in the patient with hemochromatosis.—W.N.J.


Until relatively recently it has been thought that total body iron is primarily regulated by the rate of iron absorption from the gastrointestinal tract and that excretion of iron is a minimal factor. Determinations of total body iron as well as rates of iron excretion and absorption were made over a period of months in normal, iron loaded, iron deficient, phenylhydrazine-treated and turpentine-injected mice. Results of these experiments indicate a tenfold range of the rate of iron excretion in the various experimental groups. There was no correlation between the concentration of serum iron and the rate of iron absorption nor between the serum-iron concentration and the rate of iron excretion.—W.N.J.


By means of Wood's biopsy tube the gastric mucosa was examined in 42 patients with iron-deficiency anemia. In 18 of these there was known to have been some blood loss. Samples were also obtained from 31 control patients without alimentary disorders or anemia. The gastric mucosa was histologically abnormal in 74 per cent of patients with iron deficiency anemia and in 29 per cent of controls. In iron deficiency anemia there was superficial gastritis (31%), atrophic gastritis (33%) and gastric atrophy (10%). In controls these figures were, respectively, 6, 10 and 13 per cent.

Histamine-fast achlorhydria was found in 48 per cent of patients and 13 per cent of controls. Of iron-deficient patients only 1 with achlorhydria had normal mucosa whereas 50 per cent of those with free hydrochloric acid had normal mucosa. Of the control series, 82 per cent of patients with free hydrochloric acid had normal mucosa, but all 4 with achlorhydria had gastric atrophy. No relationship was found between the degree of anemia and mucosal changes. Normal mucosa was found with a hemoglobin level of 2.7 Gm. per 100 ml. and atrophic gastritis at 10.4 Gm. per 100 ml. No relation could be established between the changes in gastric mucosa and the presence of glossitis. It is considered that achlorhydria develops after iron deficiency anemia has become established.—R.H.G.


Sections and smears of bone marrow from 23 patients with uncomplicated iron-deficiency anemia were studied. In all cases, the clinical diagnosis had been confirmed by the prompt and adequate response to treatment with iron. The use of bone marrow sections is believed
to be superior to the use of smears because the original relationship between marrow elements is maintained, and because preservation of the reticulum cells permits more reliable estimates to be made of the iron stores. The bone marrows of patients with untreated iron-deficiency anemia were on the average more erythroblastic and more cellular than the marrows of normal controls. The variability in both groups was so great that these histopathologic features could not be considered diagnostic. In contrast, a study of the iron content of the marrow by histochemical methods, clearly distinguishes the iron-deficient from the normal patient. Using the Berlin-blue reaction, iron was demonstrated in all of the control marrows, but in none of the untreated iron-deficient patients. Stainable iron appeared in the marrow rapidly after treatment of iron-deficiency anemia with intravenous saccharated iron oxide but more slowly or not at all after oral administration of iron. Morphologically, the marrow responded to treatment by intensified hyperplasia, roughly proportional to the degree of anemia. Needle biopsies of the liver revealed no constant pathologic changes. After the administration of intravenous saccharated iron oxide, iron storage appeared to take place exclusively in Kupffer cells.—H.R.


Various investigations were carried out on mice, guinea pigs, rabbits, rats and piglets. Iron-dextran was more slowly removed from the blood than was saccharated oxide of iron. The rise in serum iron after a dose of 500 mg. per Kg. of iron corresponds to the theoretic value based on even distribution in the plasma. Sections of lungs from animals receiving doses of saccharated iron oxide equivalent to 150 mg. per Kg. showed heavy iron precipitation and hemorrhages. Doses of iron-dextran up to 500 mg. per Kg. gave only slight iron deposition. The acute toxicity in mice with iron-dextran was only about a third of that with saccharated iron oxide. The urinary and fecal iron excretions were about equal with the two compounds in rabbits. After intramuscular injection, iron-dextran is rapidly absorbed, the iron being taken up by the reticuloendothelial cells. Muscle absorption studies with saccharated iron oxide showed only partial absorption. Anemic piglets utilized 93.5 per cent of the dose of iron-dextran administered, during the first 14 days after the injection.

—R.H.G.


Recently several papers in British journals have dealt with the use of an iron-dextran complex for intramuscular injection. There have been a few reports of reactions, sometimes severe: these may be early or late. A married woman aged 46 was admitted to the hospital for total hysterectomy. After operation she was given intravenous saccharated iron oxide to a total of 680 mg. without trouble and then the intramuscular iron-dextran complex. This was followed by tightness in the chest, nausea, shivering, fever, headache, conjunctivitis, diplopia and blurring of vision. The iron-dextran preparation should be given a more extensive trial before its general use is advocated.—R.H.G.


An iron-dextran complex marketed for intramuscular therapy in man was injected intravenously into white adult male mice in the rather high dosage of 0.5 Gm. per Kg. of body weight weekly and twice weekly. The total amount given was 1, 2 and 3 Gm. per Kg. and the mice were killed up to 10 weeks after the last injection. All the mice developed testicular atrophy. Sections revealed increasing degrees of iron deposition in the interstitial cells and correspondingly increasing damage to the seminiferous tubules with striking effect on spermatogenesis.—R.H.G.
DISTURBANCE OF IRON METABOLISM IN PORPHYRIA CUTANEA TARDA. J. Berman. From the 1st Medical Clinic, Charles University, Praha. Cas. lék. čes. 95: 1361-1363, 1954.

In ten patients suffering from cutaneous form of porphyria, the iron metabolism was studied. In eight the plasma iron was significantly elevated (from 176 to 349 gamma). After administration of 1 Gm. of ferrum hydrogensio reductum, the plasma iron level rose distinctly with little tendency to decline after 7 hours. The author feels that in porphyria, the hepatic regulation of iron metabolism is disturbed and the absorption of iron from the gastrointestinal tract is elevated. There is a close resemblance between the symptomatology of cutaneous porphyria and hemochromatosis: marked pigmentation of the skin, impaired liver function, disturbance of iron and carbohydrate metabolism. The intensity of sideremia has a certain prognostic significance.—M.N.

CLINICAL FEATURES, PATHOLOGY AND THERAPY OF HEMOCHROMATOSIS. M. S. Kleckner, Jr., R. M. Kark, L. A. Baker, A. Z. Chapman, E. Kaplan and T. J. Moore. Department of Medicine, Northwestern University Medical School; Department of Medicine, University of Illinois College of Medicine, and the Medical Service, Veterans Administration Hospital, Hines, Illinois. J.A.M.A. 157: 1471, 1955.

In this interesting discourse on the subject of hemochromatosis, a classification of the disease is proposed wherein three different subtypes of hemochromatosis and four subtypes of hemosiderosis are recognized. Primary hemochromatosis, hereditofamilial hemochromatosis and hemochromatosis associated with a chronic anemia which is unresponsive to therapy are the three types described. Clinical and laboratory data on 35 cases of primary hemochromatosis and 7 cases with hemochromatosis and chronic refractory anemia are presented. In the hemochromatotic patients studied, iron absorption was normal prior to phlebotomy, and following repeated phlebotomies there was a significantly increased absorption of iron. The clinical differences in the various types of hemochromatosis are described, the necessity for diagnosis by liver biopsy is confirmed and a program of therapy is given. It might be added that an attempt to reduce the absorption of iron from the intestine by means of the chronic administration of oral sodium sulfide, such as has been done in patients with Wilson's disease, could be added to the therapeutic program of these patients.—W.N.J.


The authors report a case of hemochromatosis, wherein 40 liters of whole blood were removed over a period of 28 months. There was symptomatic improvement, and the high prephlebotomy serum iron and hepatic iron decreased to the normal range. The patient did not develop anemia or hypoproteinemia although he lost 20 Gm. of iron and 7 Kg. of protein.—W.N.J.

HEMOGLOBIN


In 1951 the author described the spontaneous crystallization of pigeon hemoglobin in the gut of the Triatomata. In this report he describes the crystals obtained with human hemoglobin in several blood-sucking species of Triatoma (T. megista, T. infestans, T. rubrovaris, T. brasiliensis). An hemolysin which can be inhibited by carbon monoxide is present. The hemolyzed hemoglobin loses its solubility by a sudden, rapid loss of the water content of the blood through the intestine of the bug. Under the conditions of breeding and feeding of the Reduvids the hemoglobin crystal of the adult healthy man runs to the same crystallographic form, with three unequal crystallographic axes forming angles of 90° with each other. The crystals belong to the orthorhombic system. Photomicrographs illustrate well the crystals obtained. The author had no cases of sickle-cell anemia.—M.A.J.
ABSTRACTS


With the method described above, the author, using blood-sucking Reduviidae, obtained from the blood of a case of chronic lymphocytic leukemia atypical crystals of hemoglobin, differing in several features from the normal hemoglobin crystals. At least three types of crystals were found, apparently different from the normal orthorhombic system.—M.A.J.


An aniline dye employed to label cloths was the agent of an intoxication with methemoglobinemia in five premature infants. The authors emphasize the need of forbidding aniline dyes for such purposes.—M.A.J.


It has been shown that the blood of mammals with greater body weights has higher oxygen affinities than blood of species with lesser body weights. The oxygen affinities of specific hemoglobins may also be correlated with habits and habitats and bear little relevance to phylogenetic relationships. Therefore, seventeen closely related species were studied by using heart punctures to obtain blood for preparing dilute hemoglobin solutions. Analysis involved visual comparison of the absorption spectrum of the equilibrated sample with that of a standard of known proportions of reduced and oxygenated hemoglobin. The results indicate considerable variations in hemoglobin-oxygen affinity even among species closely related phylogenetically and having similar habits and habitats. Only a rough correlation between body weight and hemoglobin-oxygen affinity was found for the species of mammals studied.—O.P.J.
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