IRON AND HEMOGLOBIN METABOLISM


It has been demonstrated previously that iron absorption normally is regulated by the body's need for iron, despite variations in dietary iron intake. That it is possible under certain dietary conditions, however, to overcome this normal intestinal block to iron absorption is shown in these experiments. Rats receiving a diet of corn grits and lard absorbed large amounts of iron when excessive amounts of ferric citrate were added to the diet. In marked contrast to the three control groups (fed diets of Purina dog chow, Purina dog chow with added ferric citrate, and corn grits and lard without added iron respectively), these rats showed massive deposition of hemosiderin in the tissues, four to six times as much total liver iron, marked elevation in serum iron and nearly complete saturation of the iron-binding protein. None of the animals were anemic during the course of the experiment. The excessive iron deposition could not be attributed to redistribution of body iron associated with large losses in body weight since the control animals on the corn grit diet without additional iron lost a comparable amount of weight with little increase in liver iron.

Although the increased deposition of hemosiderin occurred throughout the reticulo-endothelial system, the most striking finding was the large amount of iron in the liver parenchyma. The dietary factors responsible for this excessive iron absorption have been further analyzed by these investigators in the succeeding paper in this journal. (See the following abstract.)

H. W. B.


Subsequent to the observation (see the preceding abstract) that rats on a corn grit diet with added iron absorbed and deposited large amounts of iron in their livers, various dietary factors possibly involved in this disturbance of the normal regulatory mechanism of iron absorption were investigated.

The effect upon iron absorption of a number of dietary supplements to the corn grit diet, including vitamins, salts, casein and amino acids, indicated that the low phosphorus content of the corn grit-iron diet was primarily responsible for excessive iron absorption. The addition of phosphate salts to this diet effected a significant reduction in iron absorption. Furthermore, it was possible to increase iron absorption in animals receiving a normal diet by adding much larger amounts of iron than previously tried. It was concluded that the amount of iron absorbed is dependent upon both the absolute amounts of iron and phosphorus and upon the iron-phosphorus ratio of the diet. That iron and phosphorus levels are not the sole controlling dietary factors was suggested by the observations made on the effect of casein and of certain amino acid supplements.
ABSTRACTS

Following further investigation of these dietary factors, it would be of interest to determine their influence, if any, on the metabolic defect responsible for increased iron deposition in hemochromatosis.

H. W. B.


Intravenous iron in the form of 'Ferrivenin' was given to 23 patients with rheumatoid arthritis. Twenty of these were observed over a preliminary period of a month, when they had failed to respond to oral iron. Sixteen patients showed a satisfactory response to a course amounting to 1.05 Gm. of 'Ferrivenin.' In these patients, the initial erythrocyte sedimentation rate was low, or only moderately raised, and tended to fall during treatment. The 7 who showed a poor response had high initial erythrocyte sedimentation rate, which remained high. In 2 of these, a second course of 'Ferrivenin' had only slight effect.

S. C.


Globin prepared from hemoglobin by removal of the heme with acid on recombining with heme gives a product differing from the original hemoglobin in such properties as spectral absorption and solubility. This paper describes the preparation of a globin from human red cell hemoglobin which will recombine spontaneously with heme to give a product so closely resembling the original hemoglobin as to suggest that the heme-globin linkages are identical. This makes it at least possible that hemoglobin could be formed in the developing red blood cell by addition of completely formed heme groups to the surfaces of preformed globin molecules.

S. C.


The authors confirm the observations that acidification of urine within the physiologic range will effect a precipitation of hemoglobin by some of the urine samples. Urine which is not modified by the addition of either salts or acids and which is capable of precipitating modified hemoglobin can be obtained from some patients. Healthy individuals existing on an acid-producing diet which is augmented by the oral ingestion of mandelic acid and a limitation of water intake are able to excrete urine which is capable of effecting precipitation of hemoglobin. Urine which precipitates hemoglobin in most instances would appear to possess several variables. In addition to pH and anion concentration studied in this work, it would seem that the known and unknown factors, which are responsible for modification of hemoglobin, play an important role in this system.

G. E. C.


This monograph treats the central problem of myoglobin and its clinical importance. The main part of the work is concerned with biochemical questions and technical problems of determination. The section on myoglobin in clinical medicine may be read with profit also by highly specialized hematologists as the differential diagnosis between hemoglobinuria and myoglobinuria is of considerable importance to them.

The problem that is of special interest for hematologists however is the connection between the metabolism of myo- and hemoglobin.

The author poses the question: May a general iron deficiency become a negative factor for the synthesis not only of hemoglobin but also of myoglobin. The author himself regrets that so few cases of
sideropenia are included in his material. His conclusions are therefore very careful and he seems to leave the solution of this problem to the future. The five most hypochromic cases however showed a low content of myoglobin, possibly indicating difficulties in the synthesis also of this iron-containing pigment. The general discussion of biochemical and physiologic problems connected with myoglobin metabolism are well worth a closer study.

J. W.


The work contains a very complete discussion of our previous knowledge about serum iron and its fluctuations in healthy persons, and also a survey of our knowledge about intravenous iron tolerance tests in normal subjects. Such problems as the interindividual variations of serum iron as well as the variations in the same individual on different occasions were determined. Definite seasonal variations could not be detected. Hypersideremia with values above 200 mg per cent was found in no less than 2.5 per cent of all determinations in normal persons. Nothing indicated that such values were pathologic. As regards the intravenous tolerance test the author was able to confirm the results of previous authors. The "braking" mechanism was found at a level of 400 mg per cent. The author found a certain tendency towards a parallelism between the initial serum iron concentration and the decrease in the serum iron value during the first two hours after the injection. The "braking" mechanism may well be explained by the presence of a specific iron binding component in the serum.

Contrary to the absence of significant seasonal variations of the serum iron, the vitamin C content of the blood was found to vary with the seasons.

Correlations between serum iron and serum ascorbic acid values could not be found. Prolonged oral supply of ascorbic acid increased the vitamin C level of the blood significantly but did not affect the serum iron or the hemoglobin. Three chapters are devoted to iron and vitamin C metabolism in infections. The "braking" mechanism is altered and the later decrease in serum iron during two hours was increased. Nothing indicated the presence of an iron deficiency of the same kind as is seen in essential sideropenia.

Vitamin C in large doses did not influence the altered metabolism of iron.

On the basis of numerous studies the author has confirmed the negative results of previous authors regarding the influence of oral doses of iron or (and) vitamin C. Neither was there found any definite effect of intravenous administration of iron as the preparation "Ferronascin" as regards hemoglobin and R.B.C. values. The serum iron however could be normalized in infections with such treatment.

This monograph contains a wealth of observations both on normal persons and patients with infectious states. The material is treated statistically with a strong critical clinical sense. The book may be read with great profit by all who are interested in these central clinical problems.

J. W.

HEMORRHAGIC DISEASE AND BLOOD COAGULATION


Investigation of the clotting defect in a group of male dogs with an inherited sex-linked bleeding disorder revealed that it is identical to that found in human hemophilia. The dogs were subject to repeated, usually spontaneous and occasionally fatal hemorrhages. Many tissues were involved but hemarthroses were most common. Transfusions with normal whole blood or plasma promptly controlled hemorrhage, temporarily corrected the clotting defect, and made it possible to rear the dogs to maturity; whereas, untreated, few dogs survived a six month's period.

The clotting abnormality, characterized by a prolonged clotting time and delayed prothrombin utilization, could be corrected in vitro by the addition of thromboplastin, normal dog plasma, or protein Fraction I. That the corrective action of the antihemophilic plasma factor requires the presence of platelets was demonstrated.

Only normal whole blood and plasma were effective in vivo. Neither transfusion of aged hemophilic
blood, with a normal clotting time and normal prothrombin consumption, nor transfusions of normal or hemophilic sera were able to correct the clotting defect. It was suggested from these observations that thromboplastin as such was not the corrective factor; that although a source of thromboplastin is available in hemophilic blood, it is too slowly mobilized to be effective at the time the blood is shed; and that the antihemophilic factor in normal blood is consumed during the clotting process.

These experimental animals have greatly increased the investigative possibilities in hemophilia and should add much to our present knowledge of the genetics and nature of the clotting defect in this disorder.

H. W. B.

BOOK REVIEWS


The book is intended as collateral reading for junior and senior medical students, the material presented to be amplified by the presentation of clinics. The preface states: "As compared with the textbook of Medicine, the outlines are not as comprehensive in treatment, and are intended to bring the reader a compact synthesis of what each contributor regards as most important about any given subject." The work is excellently suited for its purpose.

WILLIAM H. CROSBY


This little book contains many diagrams correlating blood and bone marrow findings. Many illustrative cases and seven colored plates are presented.

WILLIAM DAMBISHEK


This is a rather pedantic, old-fashioned work, containing none of the newer work and none of the newer references. It might well have been written twenty years ago. On the other hand, the twenty-four colored plates of blood and marrow are excellently drawn and lithographed.

WILLIAM DAMBISHEK


This monograph is based on the observation of 3 cases, one of congenital afibrinogenemia, one of acquired severe fibrinopenia in a case of carcinoma of the stomach with massive liver metastasis, and one of extreme congenital fibrinopenia. The cases are described in detail and the literature on the subject is revised. The suggestion that excessive fibrinolytic activity might be responsible for cases of acquired fibrinopenia is interesting, even if not supported by experimental findings. The opportunity for a discussion on the role of fibrinogen in capillary response to injury is given by a case of fibrinopenia with prolonged bleeding time. The critical level of fibrinogen for the appearance of hemorrhagic symptoms is also discussed and the final conclusions are in agreement with those of Pinninger and Prunty. Further support is given to the theory that not only the liver but also reticulo-endothelium (spleen, bone marrow, etc.) have an active part in fibrinopoiesis.

A review of the current (1947) conception of the coagulation of blood and a classification of hemorrhagic diseases are offered in the last part of the monograph. Both are based on the findings of American workers in the field. Too much historical and noncontributory material is included in the monograph, although this is understandable in a doctorate thesis. This somewhat overshadows the excellent original material.

M. STEFANINI