

## LETTER TO THE EDITOR

### ON THE PRESENCE OF IRON IN THE BONE

*To the Editor:* In the March, 1965 issue of *DIABETES*, Villanueva and Kelin reported the presence of iron, as detected by the Prussian blue reaction, in the osteoid seams of ribs from diabetic subjects, but were unable to detect iron in the ribs of normal subjects. These provocative observations are, in part, consistent with previous studies, but that Prussian blue formation occurs regularly in osteoid seams of *unfixed* bone from diabetics represents a unique contribution to our knowledge of bone. However, there is information which perhaps accounts for the failure of the above authors to obtain a reaction for iron in bones from nondiabetic subjects.

Early German studies on the presence of iron in bone have been concisely reviewed by Cameron (*J. Path. & Bact.* 33:929, 1930), and in determining the presence of this element in bones he emphasized the necessity of avoiding contamination with iron-containing fixatives. Furthermore, MacCallum has stated that: "... iron in some form is regularly found along the line of ossification and beneath the periosteum in growing bones, and quite as regularly in the border of any area of calcification in other organs." (*A Textbook of Pathology*, W. G. MacCallum, 7th Edit., 1941, pp. 115-116.) Also, he noted that: "The iron must be in some organic combination since it is not at once demonstrable by the ordinary Berlin blue reaction *until the bone has been kept for a time in formalin*, but it is not, as objected by some, due to iron as an impurity in the formalin" (*italics added*). The German workers mentioned above had also noted the importance of fixation of bone to the demonstration of iron.

In an excellent histochemical study of mineral deposits, Bunting (*Arch. Path.* 52:458, 1951) confirmed the presence of iron in subperiosteal bone and in areas of metastatic calcification. He pointed out that in such areas the iron is, at times, *very soluble* and may be removed by thirty minutes of soaking in distilled water. In personal observations on the bones of normal rats and rats rendered rachitic by low calcium or low phosphorus diets (*J. Bone Joint. Surg.* 43A, 419, 1961), iron was regularly demonstrable (in fixed tissues) at the peripheral margin of mineralization in trabecular bone and at the mineralization front of calcified cartilage matrix. Furthermore, sufficient amounts of iron are

present in bones and teeth for precise quantitative analysis (*Biochem. J.* 29:480, 1935) (*Mechanisms of Hard Tissue Destruction*, R. F. Sognnaes, 1963, p. 187).

From the foregoing comments, it would appear that the unique feature of the Villanueva and Kelin study was the detection of iron in *unfixed* bones from diabetic subjects. The Prussian blue reaction occurred in these bones despite underwater preparation of the ground sections and subsequent washing with a detergent. It is not surprising that Villanueva and Kelin were unable to detect iron in bones from normal subjects, but whether the iron in these unfixed sections was removed by prolonged immersion in water, solubilized by the detergent or remained in such firm combination with bone tissue as to be unavailable for reaction with ferrocyanide remains to be determined.

A final point for discussion concerns the principles of the Prussian blue reaction. In tissues, this reaction is dependent on the interaction of ferric ions with added ferrocyanide, the ferric ions being released from combination with tissue components on pre-treatment with acid. That fixation of bone is usually required for consistent demonstration of iron, suggests that in this locus iron ordinarily exists in combination with a rather soluble proteinaceous constituent.

Thus, from available information, one may deduce that iron in bones from diabetics exists in a different form than iron in bones from nondiabetics. However, it remains to be shown that changes in other elements of bone, such as zinc, which may react with ferrocyanide, do not account for the differences in the Prussian blue reaction in the bones of diabetics and nondiabetics. That the reaction for iron does differ in such subjects is a noteworthy observation which will stimulate further inquiry into the role of iron in bone metabolism.

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## BOOK REVIEWS

MODERN NUTRITION IN HEALTH AND DISEASE. *Wohl and Goodhart*. \$20.00, 1282 pages, third edition, ninety illustrations, 186 tables. *Lea and Febiger, Philadelphia, 1964*.

The express purpose of this book is to bridge the gap between the science of nutrition and its application to the everyday problems of public health and clinical medicine. This is the third edition and with each successive appearance, it continues to grow, not only in size, but in quality. The current

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edition contains new chapters on "Inborn Errors of Metabolism," "Nutrition in Alcoholism," and "Nutrition in Neoplastic Diseases." These are all worthwhile additions to the field.

Some highlights are the excellent chapters on body weight, body composition and calorie status, the physiology of the gastrointestinal tract, nutrition in cardiovascular diseases, and the absorption, digestion and metabolism of fats and related lipids. This is not to minimize the expertness expressed in the other chapters, most of which are outstanding and remarkably complete for the space limitations imposed on each of the multiple authors.

This edition, like the previous ones, is divided into three sections: the first on normal nutrition, the second on nutrition in disease, and the third on nutrition in periods of physiologic stress. For the serious student of the subject the section on normal nutrition is well worth studying carefully rather than reading superficially. For the medical student or practicing physician, Part Two presents much of the practical material which he will find of daily use. One is a little disappointed in the section on nutrition in periods of physiologic stress because of the limitation of the subjects handled.

The chapter on nutrition in cardiovascular diseases is exceptionally good; not only is there a good clinical description of the syndromes, but the maturity of understanding of the dietary problems and the metabolic processes involved makes it a must for all medical students in the course of their studies and for physicians to keep on hand as a reference.

An interesting approach to the subject is the uniformity of the chapters. The historic summary in the introduction of each of the phases is extremely interesting. While the summaries are not complete and should not be, they present the highlights of the basic problems discussed.

ON DIABETES MELLITUS. Selected Topics for Students and Clinicians. *W. P. U. Jackson*. \$12.50, 393 pages, *Charles C Thomas, Springfield, Illinois, 1964*.

From Capetown, Union of South Africa, has come a new book on diabetes mellitus. Although the book originated in "a comparative outpost of the medical and scientific world,"

its author, Dr. W. P. U. Jackson, is no stranger to anyone on either side of the Atlantic who is interested in diabetes mellitus. Many workers in the field of diabetes will welcome this compilation of his views on a number of subjects, including some controversial ones. Authors of conventional encyclopedic textbooks may envy Dr. Jackson who has not attempted to discuss all aspects of diabetes mellitus but has emphasized those topics which have been of special interest to him. Relatively more than the usual space is therefore allotted to a consideration of glucose tolerance tests, prediabetes, the infant of the diabetic or prediabetic mother, and pregnancy in the diabetic patient. There is also a section on diabetes in different races, which the author discusses authoritatively as a result of his experiences with the multiracial population of South Africa. However, few aspects of diabetes are ignored entirely and approximately a third of the book deals with the practical management of the diabetic patient.

The book is written in an interesting manner and contains such unusual material as an amusing alliteration regarding large fetuses of prediabetic mothers and some original terms, for example, "diaberg" (diabetic iceberg) to emphasize that diabetes may remain submerged below the level of clinical recognition for many years of the diabetic patient's life. The management of diabetes is presented with a practical, "middle-of-the-road" point of view including the suggestion that one of the special needs of a diabetes clinic is a "repertoire of derogatory phrases" for "obstinate patients who remain fat!"

The chief weakness of this book appears to be the superficial coverage of some subjects with inadequate documentation by references to the literature or by the presentation of quantitative data. Perhaps it would have been better to omit these subjects entirely since the author has not attempted to discuss all aspects of diabetes. There are some apparent deficiencies in editing: at several points where reference is made to another section of the book, the page numbers have not been inserted in the spaces provided; there is confusion in the numbering of figures 44, 45, and 46; figures 44 and 46 are identical and one intended figure has been omitted.

As the author states in his preface, "This is not a textbook." It will therefore be of more interest to workers especially concerned with the aspects of diabetes which Dr. Jackson has emphasized than to physicians in general.