Book Reviews

Insulin Anniversary

Impact of Insulin on Metabolic Pathways. A symposium, Jerusalem, Oct. 1971. ELEAZAR SHAFRIR, Ed. Academic Press, New York, 1972. viii, 570 pp., illus. $13.50.

The International Symposium on the Impact of Insulin on Metabolic Pathways was one of a number of such events that were held around the world in 1971 to commemorate the 50th anniversary of Banting and Best's discovery of insulin. The symposium was planned to attract a forum of prominent contributors and to present the results of research done locally. It was attended by 550 participants and included 40 lectures, 3 panel discussions, and approximately 120 short communications, which form the basis of this book.

Notwithstanding the title, a wide range of topics related to diabetes is discussed. The lectures deal with factors affecting insulin secretion, pancreatic beta cell function in prediabetes, the relationship of growth hormone and insulin, the effect of insulin on metabolic pathways and enzyme regulation, and hormonal control of adipose tissue metabolism. The panel discussions, which are reported in their entirety, consider questions related to the indications for use of oral hypoglycemic agents, complications in diabetics and their management, and future trends in diabetes research. The short communications highlight the multidisciplinary approach of investigative endeavor in this area, since aspects of physiology, biochemistry, pharmacology, genetics, nutrition, anatomy, and pathology related to insulin and diabetes are presented.

I particularly enjoyed the strong historical flavor that permeates the book. The foreword by Best is a beautifully constructed, concise statement of events leading up to the momentous discovery in 1921. The economy of words and modest approach of his account of the crucial experiments that he and Banting performed only serve to increase one's admiration for their achievement. The chapters by J. O. Leibowitz and J. J. Groen deal objectively with the concept of diabetes in historical perspective, whereas those by L. Nelken and R. Carrasco-Formiguera are highly personal accounts of the historical events and climate in the pre-insulin era and the impact that the isolation and availability of this hormone had on physicians, scientists, and patients. The controversial matter of the role of the Romanian scientist N. Paulesco in the discovery of insulin is discussed by Pavel and his colleagues, and a reply to the Romanian Academy of Sciences by Tiselius, director of the Nobel Institute, included in their paper makes interesting reading, as does the subsequent discussion of this topic by the symposium participants.

As one might expect in a book of this nature, there is a great deal of variability in the scope and quality of the scientific papers, but most provide useful reviews of their authors' work. The chapter by Renold and his colleagues from Geneva dealing with the endocrine-metabolic abnormalities in rodents with hyperglycemic syndromes is of particular interest. For many years research related to diabetes has been hampered by the lack of a suitable animal model. Renold describes a variety of hyperglycemic states, some of which parallel the human disease closely, in ten species and strains of mice, rats, and hamsters. The development of thickened glomerular capillary basement membranes in the spiny mouse, *Acomys cahirinus,* and the presence of ocular lesions including saccular retinal aneurysms, loss of retinal capillary endothelial and mural cells, and changes in the ultrastructure of the capillary basement membrane in rats rendered chronically diabetic with streptozotocin are provocative findings of great significance. New information concerning the molecular events that occur when a rising glucose concentration stimulates both the secretion and biosynthesis of insulin is presented by Kipnis and Permutt, and Fajans and his co-workers review their extensive investigations into the mechanisms whereby amino acids effect insulin release in vivo. Stimulation of insulin release by synthetic nonmetabolizable amino acids such as 2-amino-bicyclo-(2,2,1)-heptane-2-carboxylic acid and 4-amino-1-guanyl-piperidine-4-carboxylic acid indicate that under certain conditions this process may be activated by the transport of these amino acids across the beta cell membrane or by interaction with a membrane receptor site. The studies on cerebral edema in diabetic coma by Kleeman are of considerable interest, and the panel discussion entitled "Insulin and metabolism: forecast of trends in research" provides a useful overview of the many unresolved basic and clinical problems in this field.

In summary, this book is a convenient source of information and ideas in the study of insulin action and diabetes. Although there are a number of other recently published symposia covering similar topics, its rapid publication and detailed and well-edited discussions make this one worthwhile reading.

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The Other Hormone

Glucagon. Molecular Physiology, Clinical and Therapeutic Implications. PIERRE J. LEFEBVRE and ROGER H. UNGER, Eds. Pergamon, New York, 1972. xiv, 370 pp., illus. $37.50.

For 50 years now, glucagon has been overshadowed by insulin. Since it is not likely that we will see TV specials in 1973 celebrating the golden anniversary of glucagon's discovery, this handsome monograph is timely. It does an admirable job of summarizing what is known and suspected thus far about glucagon. Its 27 authors by and large constitute the membership of the international and somewhat exclusive "Glucagon Club."

The book is actually a conglomerate of 22 independent reviews (several with multiple authorship), of which some are telegraphic in style and others are exhaustingly detailed. Here, the women excel: not only are they better writers but they also seem more scientifically cautious and critical than a few of their confreres. Ann Lawrence's guarded chapter on the role of glucagon in causing or contributing to human disease other than diabetes is exceptionally interesting, lucid, and provocative. Lise Heding, writing on the

immunology of glucagon, carefully expresses persistent doubts about the specificity of the antibodies currently in use for the glucagon radioimmunoassay.

Another noteworthy contribution is that of Roger Assan ("In vivo metabolism of glucagon"), who has received less than due recognition on this side of the Atlantic for his enormous amount of work on glucagon.

The two most important chapters in the book should be the one on the physiology of glucagon and the one on immunoassays for glucagon. The latter, by Alfred Luyckx, is both scholarly and satisfying in its fine details of this recondite art. The former, however, is disquieting, largely because of textual errors. As in several earlier publications from Unger's group, its statistics are occasionally enigmatic (for example, the "glucagon" curve in the graph on page 239). Another disturbing feature is repetition of the oft-quoted statement that hyperglucagonemia is characteristic of "severe" diabetic ketoacidosis, when that conclusion is based on defining *severity* by the amount of insulin subsequently administered rather than by the magnitude of metabolic derangements at the beginning of treatment.

There are some other jarring notes in the monograph. They begin with the dust jacket, which, I suppose for "artistic" reasons, bears the nonsensical peptide fragment (residues 16–29) from glucagon as well as the complete (1–29) sequence. The editors would do a service by providing their readers with an erratum sheet, which should include the following: the legend to the photomicrograph on page 14 should read ". . . nerves (N) are present to the *left* of the A-cell"; the photomicrograph on page 22 is upside down; the glucagon-degrading enzyme ("glucagonase") cleaves the N-terminal *di*peptide His-Ser from the chain and not a *tri*peptide (page 48); glucagon and secretin share 14 (not 13) common amino acids at identical positions in the two chains (page 199); ". . . glucagon secretion during starvation is essential to the prevention of fasting *hypo*glycemia . . ." and not *hyper*glycemia (page 219); the last sentence on page 227 is incomprehensible unless the authors mean "glucose" rather than "glucagon"; and the term "biohormonal response" on page 238 is meaningless unless the authors intended "bihormonal," referring to both glucagon and insulin (and even this term I would eschew). References in the texts of chapters 6 and 15 badly need to be corrected (including an undeserved umlaut for Murlin, the codiscoverer of glucagon); and the credit to "Dexter and Allen" on page 264 is omitted from the references of chapter 17.

One thing is clear from the monograph: now that we can distinguish between pancreatic and gut glucagon-like activity in plasma, there is promise that much of the confusion of the 1960's about the physiologic role of glucagon during acute flux of metabolic fuels may be dispelled. As Unger himself points out, it is time now for investigators outside of Dallas to attempt to corroborate his observations. Another exciting field to follow is the developing understanding of peptide hormone-membrane receptor interaction, which Rodbell describes in his chapter.

There is something in this monograph for chemists, biochemists, physiologists, immunologists, pharmacologists, internists, and cardiologists. The book is particularly useful for its 1400 references, and it should be made available to research fellows, house staff, and medical students. They probably won't be able to afford it for themselves. If that is your problem, too, then watch for Piero Foà's excellent paper "Glucagon: an incomplete and biased review with selected references," which should appear soon in the journal of the American Society of Zoologists (the *American Zoologist*).

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Wild and Captive Animals

Behaviour of Wolves, Dogs and Related Canids. MICHAEL W. FOX. Harper and Row, New York, 1972. 220 pp., illus. $10.

In this monograph many aspects of the behavior and social organization of hand-reared wolves and other canids (mainly foxes, coyotes, jackals, and domestic dogs) are outlined, compared, and contrasted, with the aim of providing an understanding of behavioral evolution and some of the consequences of domestication. The author hopes in this way to provide a stimulus for further studies.

An adequate classification of canids is provided in the first chapter, but little is given on the evolution of behavior, and I was disappointed that the account of canine ancestry stops with *Tomarctus*, the forerunner of wolves, foxes, and dogs, since the subsequent evolutionary development, though its details can only be conjectured, is most instructive.

The most important section of the book is an account of the comparative aspects of behavior in several canids, with in addition an illuminating comparison of facial expression in canids and primates. This difficult subject is well presented in an easy, flowing style with superb photographs which enable the reader to judge the significance of visual signals (shoulder stripes, cheek spots, and the like) much more easily than would be possible from line drawings.

I found the description of events leading to the formation of a wolf pack in a four-acre enclosure the most stimulating passage of the book. This account vividly illustrates how studies of captive animals can assist in the understanding of wild animal behavior that is normally difficult to observe.

The chapters dealing with some of the finer points of canine social behavior (sexual and filial bonds, socialization, predation, and so on) are interesting, but are basically brief summaries of earlier works by the author and others and provide little new information. Apart from the section on predation, studies of the wolf dominate these chapters, which is annoying since one would hope to read more about the related canids as the title promises. Possibly more reference could have been made to ecological studies and behavioral field observations, and although the author clearly emphasizes in the preface that much of his description of behavior is derived from captive animals this is not always obvious in the text.

Possibly the worst segment of the book is the account of the relationships between canids and other species. It is poorly documented by field observations, and little is said about the implications of such relationships. Its inclusion detracts from the other chapters.

The final chapter deals with differences and similarities between domestic dogs and several other canids as well as briefly considering the effects of domestication. Several statements here are misleading. It cannot be unequivocally stated, for example, that wolves and foxes acquire information about the population density of like-species