BOOK REVIEW

THE DIABETIC FOOT, *edited by Marvin E. Levin, M.D., and Lawrence W. O'Neal, M.D., with twelve contributors, $25.50, 262 pages, 249 illustrations. St. Louis, C. V. Mosby, 1973.*

The editors have compiled ten chapters, written by many authors, of comprehensive information concerning the various aspects of foot problems as they occur in the diabetic patient. Dr. Levin has contributed one chapter on the medical aspects; Dr. O'Neal has written a chapter relating to the anatomy and the surgical pathology and their correlations with the clinical picture.

An extensive review of the literature related to diabetic neuropathy (Eliasson), vascular disease (Williamson, Kilo and Crespin) and bacteriology (Little) is presented. These authors may be credited with providing the most worthwhile source material for medical students and physicians who wish to study this problem in depth. However, the information is presented in such a fashion that virtually every study or observation is given nearly equal weight. Thus, the authors are on the one hand objective and thorough in their presentation, but on the other provide little positive guidance for the average physician. For example, in the chapter on "Neuropathy," Eliasson states, "everyone agrees that strict control of the diabetic state offers no protection against the occurrence of diabetic neuropathy". Whether or not such is true, practicing physicians are provided with little encouragement to be enthusiastic in their efforts to improve control of the metabolic aspects of the diabetes. Nonetheless, excellent descriptions of the pathogenesis, clinical manifestations, and general principles of therapy can be found in these presentations.

A fine chapter by Staple concerning "Roentgenography of the Diabetic Foot" provides excellent correlation of the clinical picture and course with the x-ray findings, including a description of specific arteriographic procedures.

Walker's descriptions of procedures for peripheral arterial surgery are excellent, and they are buttressed with sufficient diagrams to clarify the material in the text. Also, a section on "Debridement and Amputations" by Bradley is well illustrated, as is a follow-up chapter by Badger covering the "Rehabilitation of the Diabetic Amputee".

The role of the podiatrist is well described in general terms and in specific, with regard to prevention and care. In this chapter, the podiatrist has stayed away from the increasingly controversial area of how much prophylactic surgery should be carried out by the podiatrist and/or surgeon to correct some of the structural deformities in the feet that might lead to a significant foot problem later.

Over-all, "The Diabetic Foot" appears to be the most comprehensive compilation of available information concerning this subject. It is well illustrated and contains appropriate recommendations. The problems with the book relate to the presentation of a number of facts and procedures without sufficient emphasis on a cohesive plan of action for a given problem, such that the average physician can be guided away from errors of either omission or commission. This defect is always inherent in multiauthored texts and might be overcome by specific case presentations, both failures and successes, so that treatment described in the text could be related to a specific foot problem as it presents itself.

ABSTRACTS

Artini, D.; Abbiati, R.; Orsini, G.; Parenti, M. A.; Bloch, D.; Daturi, S.; and Mandelli, V. (Carlo Erba Res. Inst., Milan, Italy): PHARMACODYNAMIC ASPECTS OF TWO SULPHONYLUREA DERIVATIVES GLIPIZIDE AND GLIBENCLAMIDE. Diabetologia 9(Suppl.):311-16, 1973.

Verbatim summary. The results of experiments in dogs with and without two glucose loads and in the isolated pancreas to compare the pharmacodynamics of two low-dosage aryl-sulphonylureas, glipizide and glibenclamide, are described and discussed.

The results agree with those obtained by other authors confirming that glibenclamide shows delayed but prolonged activity on both plasma insulin and glucose levels. Moreover glibenclamide counteracts the hyperglycaemia induced by the second glucose load less efficiently. Glipizide acts faster on insulin and glucose levels, which return quickly to normal. When a second glucose load was given it was still more active in reducing plasma glucose levels. The dynamics of insulin secretion following glipizide more closely resembles tolbutamide than glibenclamide.

Balasse, E. O.; and Neef, M. A. (Metabolic Unit & Lab. of Experimental Med., Univ. of Brussels, Brussels, Belgium): INFLUENCE OF NICOTINIC ACID ON THE RATES OF TURNOVER AND OXIDATION OF PLASMA GLUCOSE IN MAN. Metabolism *22*:1193-1204, September 1973.

The effects of antilipolysis induced by nicotinic acid (N.A.) on the turnover rates of oxidation of plasma glucose were examined in normal and obese subjects using labeled glucose infusions. Changes induced by N.A. were similar after an overnight fast or in starved subjects. Plasma FFA and blood levels of glycerol and ketones decreased by 60 per cent; plasma glucose remained constant but hepatic glucose output and the plasma removal rate of glucose both increased. The fraction of glucose taken up by tissues and the fraction of expired CO_2 derived from glucose were increased. Augmented glucose utilization occurred despite a slight

decrease in plasma IRI, indicating that N.A. increased sensitivity to insulin. The data indicate that the effects of N.A. may be partly mediated through changes in plasma FFA concentration and are consistent with the hypothesis that the glucose-fatty acid cycle proposed by Randle plays a significant role in the control of glucose metabolism in man. C.S.

Betteridge, A.; and Wallis, M. (Schl. of Biological Sciences, Univ. of Sussex, Falmer, Brighton, United Kingdom): BIOSYNTHESIS OF GROWTH HORMONE IN THE RAT ANTERIOR PITUITARY GLAND: STIMULATION OF BIOSYNTHESIS IN VITRO BY INSULIN. Biochem. J. *134*:1103-13, August 1973.

The effect of insulin on the incorporation of radioactive leucine into growth hormone was investigated by using rat anterior pituitary glands incubated in vitro. A 50 per cent stimulation over control values was observed with insulin concentrations above 2 μM. (280 mU./ml.). The effect was specific for growth hormone biosynthesis over the range of 1 to 5 μM. of insulin. Lower, more physiologic concentrations had no significant effect on the system. Above 10 μM. of insulin, total protein synthesis was also increased. The stimulation of growth hormone synthesis could be partially blocked by the addition of actinomycin-D, suggesting that RNA synthesis was involved. Insulin was found to stimulate the rate of glucose utilization in a similar way to growth hormone synthesis. 2-deoxyglucose and phloridzin, both of which prevented insulin from stimulating glucose utilization, also prevented the effect of insulin on growth hormone synthesis. If glucose was replaced by fructose in the media, the effect of insulin on growth hormone synthesis was significantly decreased. The authors conclude that the rate of utilization of glucose may be an important step in mediating the effect of insulin on growth hormone synthesis. T.J.M.

Blum, J. W.; Wilson, R. B.; and Kronfeld, D. S. (Univ. of Penn. Sch. of Vet. Med. and MIT, Cambridge, Mass.): PRAPARTUALE HYPERINSULINAMIE UND KALZIUMABHANGIGE INSULINSEKRETION BEI DER KUH. Schweiz. Med. Wochenschr. *103*:849-52, 1973.

Insulin secretion was studied on pregnant cows a few days ante- and postpartum. The expected antepartum hyperinsulinemia was confirmed. The observed serum insulin levels were compared to blood sugar and serum calcium concentrations. No correlation between glucose and insulin was found antepartum, while postpartum a positive correlation was observed. In the initial phase after delivery severe hypocalcemia was often observed. During this period no correlation between glucose and insulin could be demonstrated. However, there was a significant correlation between calcium and insulin concentrations ($r = 0.419$, $P < 0.020$). These data indicate that a normal calcium concentration is needed, even in vivo, in order to elicit an adequate glucose-induced insulin secretion. N.K.

Chlouverakis, C.; Bernardis, L. L.; and Hojnicki, D. (E.J. Meyer Mem. Hosp., Buffalo, N.Y.): VENTROMEDIAL HYPOTHALAMIC LESIONS IN OBESE-HYPERGLYCAEMIC MICE (obob). Diabetologia 9:391-95, 1973.

Verbatim summary. Bilateral electrolytic lesions were placed in the ventromedial nucleus (VMN) of lean and obese-hyperglycaemic mice (obob). The body weight of lean mice increased markedly and body composition studies revealed an increase in the percentage of body fat and a decrease of body water. Both serum insulin and glucose were increased. However, the body weight of obese-hyperglycaemic mice (obob) with bilateral VMN lesions failed to increase, though their body fat showed a small increase and their body water decreased. These data suggest that the VMN of obese-hyperglycaemic mice is functional. The small increase in the adiposity of *obob* with bilateral VMN lesions might be due to the size of the lesion, which appeared to be smaller in the *obob* than in the lean mice.

De Leeuw, I.; De Baere, H.; Decraene, P.; Lemmens, P.; and Verhaegen, H. (Antwerp Diabetes Study Group, Merksem, Belgium): AN OPEN COMPARATIVE STUDY OF THE EFFICACY AND TOLERANCE OF A NEW ANTIDIABETIC AGENT: GLIPIZIDE. Diabetologia 9(Suppl.):364-66, 1973.

Verbatim summary. Glipizide is a sulfocyclohexylurea with proven antidiabetic properties. Glipizide treated patients have been compared during an initial period of three months with three groups of comparable patients receiving single agent therapy viz. glibenclamide, chlorpropamide, or phenformin. The drug seems to be an easy-to-handle antidiabetic agent, active in a dosage from 2.5 to 20 mg. in patients with maturity-onset diabetes who are not satisfactorily controlled by diet alone. The frequency of primary failures are slightly higher than with glibenclamide and chlorpropamide, but on the contrary the tolerance was better and the side effects negligible.

Pappenheimer, J. R.; and Setchell, B. P. (Dept. of Biochemistry and Inst. of Animal Physiol., Cambridge, Dept. of Physiol., Harvard Med. Sch., Boston, Mass.): CEREBRAL GLUCOSE TRANSPORT AND OXYGEN CONSUMPTION IN SHEEP AND RABBITS. J. Physiol. *233*:529-51, September 1973.

This is an intriguing study in which the authors investigate the mechanisms responsible for the ability of ruminants to tolerate severe hypoglycemia. Anesthetized sheep and rabbits were compared with respect to cerebral glucose transport and oxygen consumption as a function of glucose concentration in cerebral extracellular fluids. Glucose in plasma was decreased by insulin or increased by intravenous infusion. Measurements were made of cerebral blood flow, arterial venous concentration differences of glucose, oxygen and the concentration of glucose in cerebral spinal fluid. Equations for carrier-mediated transport accurately describe steady state glucose flux across the blood vein barrier as plasma concentration of glucose was varied from 0.2 to 30 mM. The transport of glucose across the blood brain barrier of rabbits was as efficient as that in sheep and in both species Tm was ten to fifteen times greater than normal rates of glucose utilization. During hypoglycemia the concentration of glucose in cerebral spinal fluid was less in sheep than in rabbits. Steady state utilization of glucose by sheep brain decreased to 50 per cent of normal when steady state concentration of glucose in cerebral spinal fluid fell to .1 μM./ml.$^{-1}$. In rabbits the corresponding concentration was 0.7 μM./ml.$^{-1}$.

The authors suggest that the transport capacity of membranes separating cerebral spinal interstitial fluid from the site of glucose phosphorylation is greater in sheep than in rabbits, and that this may be a principle adaptation which enables ruminants to withstand severe hypoglycemia. T.J.M.