EDITORIAL

VASCULAR DISEASE IN DIABETES

Only in recent years has it become fairly certain that at least two common types of blood vessel disease exist in diabetes, that these two types may appear together or independently, that they cause different forms of tissue and organ damage, and that they may have different origins. The question of cause is the most obscure, but it cannot be determined until the pathological and clinical entities are better identified than they have been.

Atheromatous and arteriosclerotic vascular disease, with common clinical sequelae such as myocardial infarction, cerebral thrombosis, arteriolar nephrosclerosis and ischemic lesions in the legs and feet, affects diabetic and nondiabetic individuals in much the same manner. Although it is believed that this form of arterial disease occurs earlier, more frequently and in a more rapidly progressive form in diabetics than in nondiabetics, Blumenthal et al.,[1-3] and others[4,5] have presented evidence that this is not so.

A distinctive form of small blood vessel disease, seldom if ever seen in nondiabetics, appears to cause a large number of diabetic lesions formerly considered to be due to atherosclerosis. This form of vascular disease is now known to be responsible for the retinopathy, glomerulosclerosis, and possibly also the neuropathy, which are so devastating in diabetes of long standing. Other less well-established clinical conditions such as diffuse myocardial and localized peripheral skin and bone lesions may also be caused by it. As pointed out by Goldenberg et al.,[6] Bloodworth,[7,8] Yamashito and Becker,[9] Burger,[10] and other students of diabetic vascular pathology, the arterioles, capillaries and venules are the characteristic sites of involvement. The morphology and histochemistry differ from those of atheromatous lesions, chiefly in that endothelial proliferation, basement membrane thickening and accumulations of a hyaline-like mucopolysaccharide substance similar to that which forms the nodules of diabetic glomerulosclerosis contrast with the lipid, fibrotic and calcific lesions of atherosclerosis.

In March 1963, a conference of investigators of various aspects of this problem was organized by the Metabolism Study Section of the National Institutes of Health and held at Airlie House in Warrenton, Virginia. Marvin D. Siperstein, as general chairman, planned the program, had the discussions recorded, and edited the proceedings. Leisurely discussions among fifty invited participants from this country and abroad continued for three days. Disciplines represented were anatomy and ultramicroscopy, pathology, immunology and immunochemistry, biochemistry, genetics, ophthalmology, renal disease and metabolism.

Undoubtedly the most important product of the conference was the insight and stimulation gained by investigators in various fields by free exchange of current ideas and information relating to this puzzling biological problem. Examples of ideas which emerged from the conference are as follows:

Thickening of the capillary and other basement membranes is a consistent early finding in diabetes. This may even antedate the appearance of the overt disorder of metabolism. It certainly antedates the complications seen clinically. It is conceivable that this lesion may cause diabetes by interfering with the release of insulin from the beta cells on demand. The origin of abnormal accumulations of this substance is unknown, but it may well have a metabolic basis. There is evidence that it is a complex glycoprotein, the major protein constituent of which is a collagen-type protein. A retarded basement membrane turnover rate after synthesis could be the reason for the abnormal accumulations in the walls and lumens of arterioles and capillaries, with resulting organ damage. Staining properties, a limited number of chemical studies, and ultramicroscopy all indicate that the thickened basement membrane, the contents of retinal microaneurysms and exudates, endothelial interlacings, hyalinized islets, and other hyaline deposits in epithelial cells, blood vessel walls and elsewhere have a similar composition. Some immunologic studies reveal that this material specifically binds insulin, suggesting that diabetic angiopathies may be associated with an antigen-antibody reaction, with insulin as the responsible antigen.

There were extensive discussions of the vital role of the characteristic small vessel lesions in the production of the disabling complications of long-standing diabetes, particularly retinopathy and glomerulosclerosis, as well as the relationship of the complications to the control of diabetes. Evidence was presented that similar microangiopathy may be seen in diabetes which is not genetic in origin.

The proceedings of this conference have now been published in a 317-page book entitled *Small Blood Vessel Involvement in Diabetes Mellitus*.[11] Twenty-four related papers, freely illustrated, form the body of the volume and serve as the basis for informal discussions which are reproduced in detail.

These authoritative investigations and opinions are the latest and by far the most comprehensive collection of information now available concerning "diabetic microangiopathy," as it is more and more commonly called in the contemporary literature. The conference proceedings are recommended highly for study in depth by all scientists interested in diabetes and the vascular lesions which are seen in it.

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BOOK REVIEWS

JUVENILE DIABETES: ADJUSTMENT AND EMOTIONAL PROBLEMS. Proceedings of a workshop held at Princeton, New Jersey, April 22-23, 1963. *Sponsored by the United States Public Health Service, Diabetes and Arthritis Program; the National Institute of Arthritis and Metabolic Diseases; the Child Guidance Center of Mercer County; and the New Jersey State Department of Health.*

The subject of this conference is important and deserving of attention.

The program began with formal papers by Danowski on the clinical aspects of juvenile diabetes; by Hinkle on the metabolic and renal effects of "arousal" reactions; by Swift on a psychiatric and psychologic analysis of forty diabetic children; and by Opler on the relationship of diabetes to cultural groupings and patterns. These were followed by eight "workshops" and by two further "discussions after workshops." The participants were "drawn from multiple disciplines and included diabetologists, pediatricians, internists, psychiatrists, psychologists and behavioral scientists. Public health officials, educators and clinicians were represented.

Its chief interest is its exemplification of an important current trend, the increasingly rapid growth of specialized groups on the periphery of medicine, particularly those concerned with the psychological and social aspects of illness. These groups tend to concentrate their interest on the so-called personality profile and the social-environmental setting as a background for disease, not only as modifiers of the clinical picture and the therapeutic response but as pathogens in themselves, even in a disease such as diabetes. Thus Dr. Opler includes diabetes "of course" in "the ten somatic disorders usually assigned a psychogenic basis."

To no small extent this trend has been accelerated by the rapidly increasing entry of governmental institutions, welfare and social agencies, teaching and research centers and study projects into the care of the sick. In this setting the patient ceases to be the continuing responsibility of a single physician and becomes a "community responsibility" and material for investigation by the para-medical groups and agencies that dominate these fields. "Multidisciplinary" conferences and reports characterize this approach and reflect strongly a bias toward sociology, psychology and "behavioral science."

Prominent in the mystique of this approach is the assumption that if a large enough "sample" of diabetic children is analyzed for a large enough number of personality and environmental characteristics, there will emerge a "personality profile" distinctive for the child diabetic, perhaps even antedating the onset of the diabetes and predictive of it, and possibly even entering into its pathogenesis.

Dr. Swift studied and rated twenty psychologic and social variables in each of forty diabetic children. Then "a reliability study of the ratings was made using the intraclass correlation, which is essentially an average intercorrelation. Relationships between fifty-five pairs of variables that seemed meaningful in the light of our clinical experience, were studied using the chi square and Yates correction when indicated."