



EDITORIAL

NEWER CONCEPTS OF ATHEROSCLEROSIS

Atherosclerosis, by far the most important form of arteriosclerosis, is characterized by the formation of fatty and fibrous plaques in the intima of the larger arteries. It is the number one killer among nondiabetics as well as diabetics, but the incidence of aberrations of carbohydrate metabolism among persons with severe atherosclerosis is extraordinarily high.¹

Research on this most important disease of civilized man has, in recent years, been devoted so overwhelmingly to the study of the blood lipids that one might almost say that a formula had been evolved: too much of some kind of lipid in the diet, hence too much in the blood, hence too much in the vessel wall. That such simplification is probably far from the truth is emphasized in a recent lucid and balanced review.²

Recently there seems to have been a welcome reawakening of interest in the anatomy and physiology of the arterial wall³ and in some of the nonlipid constituents of the atheromatous plaque. In relation to the latter, two lines of thought which have been given scant attention in this country have appeared lately in the foreign literature.

The first of these, which has been set forth chiefly by Duguid,^{4,5} has come to be called the thrombogenic theory and holds that mural thrombi may become incorporated into the lining of the artery in such a way that eventually a typical fibrous or fatty atheromatous plaque results. It does not necessarily follow that all plaques arise in this way, but evidence is increasing that many do. The theory is being broadened by the demonstration of small quantities of fibrin in very small, and presumably early lesions by the fluorescent antibody technic⁶ and other methods,⁷ and by application of

dynamic concepts of a balance between the deposition of fibrin and fibrinolysis.⁸ Also, it is being recognized that such deposits of fibrin may be related to, or result from, extravasations of blood in the intima.⁹ The lack of attention given to the thrombogenic theory in American textbooks and symposia on atherosclerosis (with the outstanding exception of the Princeton conference⁸) is all the more surprising when one realizes that many of Duguid's conclusions were anticipated, not only by Rokitansky,¹⁰ but also by the careful observations of Clark, Graef and Chasis¹¹ and of Horn and Finkelstein.¹²

The second line of investigation, which, so far as the present writer is aware, has not even been mentioned in the American literature, is that of Randerath and Diezel.^{13,14} These authors, using special dyes and polarized light, and studying the muscular arteries rather than the aorta, claim to have demonstrated fibrillar, highly polymerized mucopolysaccharides in greater abundance in diabetics than in nondiabetics. Such lesions are so characteristic that they have dubbed them "MPS plaques," and have postulated that, as a result of insulin deficiency, protein-bound hexoses and hexosamines of the blood accumulate in the intima of the artery and eventually become transformed from slightly polymerized to highly polymerized compounds. Thus the metabolic disturbance in diabetes is tied directly to the atheromatous plaque (perhaps successfully, for the first time). It is, of course, possible that these deposits may be secondary, as suggested by some experimental work¹⁵ and even that they may tend, by their anticoagulant properties, to prevent further thrombi in such loci.¹⁶ However, if confirmed, the work of Randerath and Diezel should be of special value in contributing toward a unifying concept of the pathogenesis of the so-called complications of diabetes.

It is possible that neither of these two approaches to the study of atherosclerosis will prove, in the years ahead, to have great validity or significance. On the other hand, they may provide, temporarily, refreshing relief from the current preoccupation with cholesterol and lipoproteins.

REFERENCES

- 1 Waddell, W. R., and Field, R. A.: Carbohydrate metabolism in atherosclerosis. *Metabolism* 9:800, 1960.
- 2 Hilditch, T. P., and Jaspersen, H.: *Lipids in Relation to Arterial Disease*, Distributed by J. Bibby and Sons, Ltd., 1959. Liverpool, England.
- 3 Lansing, A. I. (ed.): *The Arterial Wall*. Baltimore, Williams and Wilkins, 1959.
- 4 Duguid, J. B.: Thrombosis as a factor in the pathogenesis of coronary atherosclerosis. *J. Path. & Bact.* 58:207, 1946.

⁵ Duguid, J. B.: Chapter 22 in Cowdry's Arteriosclerosis, ed. by H. T. Blumenthal. 1961 (in preparation).

⁶ Woolf, N., and Crawford, T.: Fatty streaks in the aortic intima studied by an immuno-histochemical technique. *J. Path. & Bact.* 80:405, 1960.

⁷ More, R. H., and Haust, M. D.: Atherogenesis and plasma constituents. *Am. J. Path.* 38:527, 1961.

⁸ Astrup, T.: Rôle of blood coagulation and fibrinolysis in the pathogenesis of arteriosclerosis. In Conference on Connective Tissue, Thrombosis and Atherosclerosis, held in Princeton, N. J. Ed. by I. H. Page. New York, Academic Press, 1959.

⁹ Leading article. Intimal haemorrhage. *Brit. M. J.* 1:961, 1959.

¹⁰ Rokitsky, C.: A Manual of Pathological Anatomy. Translated from the German by C. W. Moore. Philadelphia, Blanchard-Lea, 1855, vol. 4, p. 200.

¹¹ Clark, E., Graef, I., and Chasis, H.: Thrombosis of the aorta and coronary arteries, with special reference to the "fibrinoid" lesions. *Arch. Path.* 22:183, 1936.

¹² Horn, H., and Finkelstein, L. E.: Arteriosclerosis of the coronary arteries and the mechanism of their occlusion. *Am. Heart J.* 19:655, 1940.

¹³ Randerath, E., and Diezel, P. B.: Morphologische Pathologie der extrarenalen Angiopathie beim Diabetes mellitus. Proceedings of the Third Congress of the International Diabetes Federation, Dusseldorf, 1958. Stuttgart, Geo. Thieme, 1959, p. 54.

¹⁴ Randerath, E., and Diezel, P. B.: Vergleichende histochemische Untersuchungen der Arteriosklerose bei Diabetes mellitus und ohne Diabetes mellitus. *Deutsches Arch. f. klin. Med.* 205:523, 1959.

¹⁵ Bollet, A. J., Wang, C., and Adlersberg, D.: Experimental atheromatosis: acid mucopolysaccharide content of the aorta. *Circulation Res.* 8:88, 1960.

¹⁶ Gore, I., and Larkey, B. J.: Functional activity of aortic mucopolysaccharides. *J. Lab. & Clin. Med.* 56:839, 1960.

PHILIP M. LE COMPTE, M.D.
Boston

BOOK REVIEWS

DIABETES MELLITUS: A HANDBOOK FOR NURSES. By Marguerite M. Martin, R.N. \$3.50, pp. 167, W. B. Saunders, Co., Philadelphia and London, 1960.

The author has written a handbook for nurses which touches upon all phases of diabetes. In this endeavor she has had a unique advantage and stimulus in that her husband has had diabetes for over thirty years. She has carefully and comprehensively outlined the opportunities, duties and problems confronting nurses in the management of diabetes.

Nurses should know the symptoms of diabetes so well that they are able to recognize the condition quickly. It is necessary for them to know all new drugs in general use. The nurse should understand that because a diabetic individual falls into a certain age group, or patient type this does not necessarily indicate that he will respond to treatment with the oral agent usually applicable to his group. Moreover, nurses need to be familiar with possible side effects of the oral hypoglycemic

drugs as well as insulin, so that they will be able to call them promptly to the physician's attention. Very close surveillance of postoperative diabetic patients by the nurse is necessary.

In accordance with modern broad concepts, nurses must recognize their responsibility to the community in teaching prevention, and detection. They can assist in the detection drives conducted by the American Diabetes Association each November. Industrial nurses in particular have an opportunity to play a part of inestimable value in the detection of unknown diabetics. Because of the confidence and affection engendered in employees over a period of years, the industrial nurse is able to assist, teach, and encourage diabetic workers who are concerned or confused about their condition or its management.

As pointed out in this publication a great deal of education in diabetes should be assigned to nurses in their various capacities. Although there are numerous handbooks for diabetic patients written in simplified language, this book is very suitable for background material for the nurse who is concerned with education since it is the product of a nurse experienced in this area.

AN OUTLINE OF CHEMICAL GENETICS. By Bernard S. Strauss, Ph.D. \$5.00, pp. 188, W. B. Saunders, Philadelphia & London, 1960.

This excellent book summarizes the chief developments in the rapidly advancing field of chemical genetics. Dr. Strauss cites the evidence for deoxyribonucleic acid (DNA) being the code-carrying material that is transmitted in heredity. He gives a concise picture of the helical structure and chemical constitution of the DNA molecule, with evidence in support of the Watson-Crick model and its proposed mechanism of replication. There is a good description of what may constitute a gene from the operational and chemical standpoint, and how it may carry the hereditary code and transmit it. Also well described are the template relationships between DNA and RNA (ribonucleic acid) and the proposed mechanisms by which the arrangement of purine and pyrimidine bases in these structures may order the sequence of amino acids that regulate and determine which protein is synthesized. An entire chapter is devoted to current concepts of the mechanism of protein and hence enzyme synthesis. Mutations and their possible mechanisms of production at the chemical or gene level are described.

There is a short chapter only on the biochemical genetics of man; but there is a concise review of three well-chosen examples of inborn errors of metabolism or human genetic disease about which most is known concerning the precise enzymatic defects or alteration in protein structure, which illustrates well the concept of molecular disease. This gives insight into the manner by which a single gene—enzyme or gene—polypeptide defect can produce a multiplicity of apparently unrelated symptoms and signs (pleiotrophy) in a specific disease.

The subject matter covered here lays a groundwork for understanding much of the recent progress in human genetics and medical genetics, accomplishments that, coupled with those that have been achieved in human cytogenetics, are providing a fresh approach to the causation and pathogenesis of many diseases. In other instances they give us new insight into the mechanisms underlying many of the variable responses, both beneficial and toxic, that occur with drug therapy.