

Symposium on Hypocholesteremic Agents

Introduction

A HALF century has passed since various investigators demonstrated that atheromatous deposits appeared in the aortas of rabbits fed pure cholesterol or cholesterol-rich foods. At the time of these experiments little was known about the chemistry or metabolism of cholesterol, and studies of atherosclerosis were oriented in the direction of pathology. In the intervening years the conquest of infectious diseases and improvements in diagnosis and treatment of other diseases have resulted in the establishment of atherosclerotic heart disease as the major cause of death in the Western World. Indeed, in the United States more than 50 per cent of all deaths are attributed to cardiovascular causes. Under these circumstances attention was focused on the role that cholesterol might play in the development of this disease. This question is far from answered, but the general correlation between elevated blood cholesterol levels and atherosclerosis in experimental animals, and the observations that well fed (and usually hypercholesteremic) populations show greater tendencies toward heart disease, has caused much research activity to center about attempts to lower serum cholesterol levels.

Over the years it has been observed that the serum cholesterol level *per se* is far from infallible as a predictor of heart disease. Many attempts have been made to refine this measurement by assaying cholesterol:phospholipid ratios, β -lipoprotein levels or β -lipoprotein

cholesterol levels, to name the most outstanding. Studies in this area are still being pursued vigorously. Preparations which affect serum cholesterol levels are continuously being made available, but none has been spectacularly effective. The elucidation of pathways of cholesterol biosynthesis and degradation have cast new light on the utilization of this sterol. Instead of trying blindly to lower serum cholesterol levels, some workers have been aiming at inhibition of biosynthesis of this compound; others have been investigating means to enhance excretion of cholesterol and its metabolites. The availability of radioisotopes and newer analytic tools such as gas-liquid chromatography have helped to clarify the mechanisms of action of test compounds.

This symposium represents an effort to collate the latest information on three of the newest approaches to lowering cholesterol levels. Thyroid drugs have been tested for many years, but their use has been limited because of side reactions. The current availability of thyroactive compounds, which may separate the effects on cholesterol metabolism from other thyroid effects, has catalyzed research in this area. Nicotinic acid is another compound which has been used extensively in the treatment of hypercholesteremia although its precise mode of action is not yet known. Interference with cholesterol biosynthesis has been suggested as a possible means of lowering



cholesterol levels and a discussion of compounds which affect cholesterol biosynthesis and their mode of action will be presented. The other papers will deal with correlations between cholesterol and atherosclerosis and with methods available for testing of drugs which influ-

ence cholesterol metabolism. These presentations will present, we hope, a survey of current concepts and therapeutic approaches.

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