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CHOLESTEROL AND ITS ASSOCIATION WITH ATHEROSCLEROSIS IN HISTORY OF MEDICINE

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INTRODUCTION

Dyslipidaemia reflects one of the numerous disorders related to the metabolism of lipoproteins. It is characterized as hypercholesterolemia, low levels of High Density Lipoproteins (HDL), and hypertriglyceridaemia.[1] Although cholesterol had been isolated as early as 1770, extensive research on its structural ambiguities did not start until twentieth century. [2] Cholesterol playing an important role in the formation of atherosclerotic plaques was first identified by Vogel in 1847 AD.[3] Then, in 1903, a German chemist, Adolf Windaus gave the molecular design of cholesterol, and eventually laid down a detailed structure of cholesterol; an accomplishment that was partially responsible for his earning the 1928 Nobel Prize in the field of chemistry.[2]

The year 1929 proved very remarkable in context of cholesterol, cholesterol ester, and phospholipids as these substances were observed in blood circulation as macromolecular complexes and later on were named as lipoproteins. Michel Macheboeuf, a research fellow at the Pasteur Institute, first elucidated the plasma lipoproteins by utilizing ammonium sulphate of horse serum and separated alpha-lipoproteins, which later on were recognized as high-density lipoprotein (HDL).[4] The role of HDL-C as anti-atherogenic lipoprotein was done by several scientist but it was firmly established by Miller et al.[5]

The creation of the NHLBI at the National Institutes of Health in 1948 was regarded as an advent of contemporary study on atherosclerosis in the U.S. The new institute reorganized Framingham Heart Study in 1949, which proved one of the first major efforts towards the study of chronic diseases.[6]

In 1949, biophysicist John Goffman and his colleagues at the University of California at Berkeley used newly developed ultracentrifuge methods to separate plasma lipoproteins by flotation mechanism. Lipoproteins were isolated by Goffman in his laboratory by analytical ultracentrifuge method but it was too complicated to be applied in clinical practice. Later on, Robert S, Lees, provided a simple method of separating plasma lipoprotein by paper electrophoresis.[4, 7]

But, key role of cholesterol in development of atherosclerosis was recognized in 1950s. [8] In 1951, the American chemist Robert B. Woodward synthesized cholesterol starting with simple compounds; and was awarded the Nobel Prize in chemistry in 1965 for this accomplishment and other work in synthesizing large molecule compounds.[2] In 1951, Russ, Eder and Barr at New York Hospital, Cornell Medical Centre identified higher levels of alpha-lipoprotein in young women than men.[4] Based on Framingham heart study in 1961, the

concept of risk factors of coronary heart disease was established as hypertension and hypercholesterolemia, and the role of cholesterol for causation of atherosclerosis was recognized in the 1950.[9]

The NHLBI launched a program that was termed as the National Cholesterol Education program. On September 1, 1987, Lovastatin became the first statin to be introduced into the market for the treatment of atherosclerosis; a year later the positive results of the primary prevention by Helsinki Heart Study on gemfibrozil was announced.[10] The NHLBI issued its first clinical practice guidelines under the auspices of the NCEP in 1988, again the guidelines were updated in 1993, and "Third Report of NCEP Expert Panel on Detection, Evaluation, and Treatment of High Cholesterol in Adult individual" was issued in 200l.[8]

In 1989, the investigative reporter Thomas Moore wrote a cover story for the Atlantic Monthly Magazine entitled "The Cholesterol Myth" with the tagline of "Lowering Your Cholesterol is next to impossible with diet, often dangerous with drugs, and it would not make you live any longer." [11] Although much advancement has been made in the management of dyslipidaemia, the disease has not been completely evaluated yet as multiple factors plays their role in its causation and progression which ultimately leads to various complications.

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