A FAMILY STUDY OF HYPOALPHALIPOPROTEINEMIA

C. Vergani\textsuperscript{x}, A. L. Catapano\textsuperscript{xx} and A. Sidoli\textsuperscript{xxx}

\textsuperscript{x}Third Department of Clinical Medicine University of Milan
\textsuperscript{xx}Institute of Pharmacology and Pharmacognosy, University of Milan
\textsuperscript{xxx}Laboratory of Molecular Biology, Farmitalia Carlo Erba

 Milan

In recent years the inverse relationship between HDL cholesterol and the risk of coronary artery disease (CAD) has been supported by a lot of clinical and epidemiological data (1, 2).

However, the mechanisms underlying this relationship are not completely clear yet. It is currently believed that HDL might act as a scavenger of cholesterol from the cells and then deliver it to the liver either directly or via a transfer of cholesterol to other lipoproteins (3). Recent studies in vivo have further substantiated this hypothesis (4, 5).

Several factors are involved in the regulation of HDL plasma levels, its synthesis being modulated by exogenous factors (smoking, overweight, alcohol intake, physical activity, etc.) as well as by genetic ones as supported by studies on relatives of subjects suffering from myocardial infarction and by twin studies (6, 7, 8).

Recently the genes coding for the main components of HDL have been located on chromosome 11 (Apo AI) (9) and 1 (Apo AII) (10).

The gene for Apo CIII has also been mapped on chromosome 11, closely linked to the Apo AI gene (9). Alterations in the Apo AI-CIII gene complex resulted in Apo AI deficiency and premature CAD (11).

The study of conditions with low levels of HDL may help in explaining the role of HDL in relation to CAD. Some years ago we described in a three generation family a syndrome (Familial Hypoalphalipoproteinemia) characterized by a primary reduction of plasma HDL (HDL cholesterol below the 10th percentile of normal population, corresponding to 33 mg/dl) which is not associated to any other lipoprotein alterations (12). This syndrome is coupled with a high incidence of premature myocardial infarction and sudden death and is transmitted as an autosomal dominant trait. We summarize here the clinical, biochemical and genetic data obtained in studying this family.
DESCRIPTION OF THE FAMILY

The three generation family originally described affected by hypoalpha lipoproteinemia lives near Milan. The proband in the second generation had myocardial infarction at age of 37. One brother and one cousin had myocardial infarction at 44 and 48 respectively, two cousins died suddenly at 36 and 51 years of age. Sudden death and deaths caused by myocardial infarction are also reported in some first generation relatives (age of death between 49 and 58). All the subjects in the second generation with CAD are hypoalpha. However, 4 hypoalpha subjects, one fertile woman in the second-generation and one girl and two males in the third-generation are apparently healthy. Coronary angiography in one of these males showed a narrowing of more than 70% of the left anterior descending coronary artery (fig. 1) Hypoalpha members of the family were not overweight (\(\bar{x} = 105\% + 17\) of the ideal body weight), smoked less than 20 cigarettes per day, drank less than 40 g of alcohol per day and had no parenchimal or obstructive liver disease. Neither did they have any of the clinical features observed in other syndromes related to severe HDL deficiency (corneal opacity, planar xantoma, abnormal tonsils, neuropathy, hepatosplenomegaly).

![Fig. 1. Coronary arteriogram of a completely asymptomatic 31 year old subject with hypoalphalipoproteinemia (III-5). A severe stenosis of the left anterior descending coronary artery is observed.](image-url)