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Cigarette Smoke-Induced Depression in LCAT Activity

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The effect of acute inhalation of cigarette smoke on plasma cholesterol esterification by lecithin–cholesterol acyltransferase (LCAT) in atherosclerosis-susceptible White Carneau pigeons was examined. Pigeons were assigned to four treatment groups. (1) Shelf Control fed a chow diet and not exposed to smoke products. (2) Sham pigeons fed a cholesterol-saturated fat diet and exposed to fresh air by the Lorillard smoking machine. (3) low nicotine–low carbon monoxide (LoLo) animals also fed the cholesterol diet and exposed to low concentrations of these cigarette smoke products; and (4) high nicotine–high carbon monoxide (HiHi) birds fed the cholesterol diet and subjected to high concentrations of these inhalants. Both Control and Sham birds had significantly higher LCAT activity (percentage esterification per minute) than HiHi pigeons. Experiments designed to determine whether altered enzyme and/or substrate were responsible for depressed activity revealed no smoke-related modification in substrate efficiency. In addition, Sham and HiHi pigeons had similar concentrations of plasma-free cholesterol, high density lipoprotein (HDL) cholesterol, cholesteryl ester and phospholipid, and similar HDL phospholipid and cholesteryl ester fatty acid profiles. However, reduced LCAT activity in HiHi pigeons can be explained by (1) impairment of enzyme efficiency as estimated by *in vitro* analysis, and (2) *in vivo* reduction in levels of LCAT cofactor, HDL apoprotein A-I.

INTRODUCTION

Lecithin–cholesterol acyltransferase (LCAT) (EC 2.3.1.43) is a plasma enzyme which catalyzes esterification of cholesterol on high-density lipoproteins (HDL) by transferring a fatty acid from the C-2 position of phosphatidyl choline to free cholesterol (Glomset, 1968). HDL apoprotein A-I is an important cofactor in this reaction (Fielding and Fielding, 1971; Soutar *et al.*, 1975). Although the metabolic significance of the LCAT reaction has not been completely elucidated, Glomset (1979) has postulated that LCAT may be involved in the removal of excess phospholipid and free cholesterol from lipoprotein remnants and may participate in the mobilization of cholesterol from peripheral cell membranes and its subsequent transport to the liver.

HDL serves as the lipoprotein substrate for LCAT and may also have antiatherogenic properties related to its ability to remove cholesterol from extrahepatic tissue (Glomset and Norum, 1973; Glomset, 1979). Numerous epidemiological studies have demonstrated a strong inverse relationship between HDL cholesterol concentration and the incidence of coronary heart disease (Gordon *et al.*, 1977; Castelli *et al.*, 1977). A similar correlation also exists between coronary heart disease and HDL's major protein component, apoprotein A-I (Berg *et al.*, 1976). Much recent attention has focused on HDL levels and established heart disease risk factors such as cigarette smoking (Enger *et al.*, 1977; Hulley *et al.*, 1979; Berg *et al.*, 1979; Garrison *et al.*, 1978). Results from these studies show that smoking reduces HDL cholesterol (Enger *et al.*, 1977; Hulley *et al.*, 1979; Garrison *et al.*, 1978) and apoprotein A-I and A-II levels (Berg *et al.*, 1979).

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