EFFECT OF THYROID DISEASES ON LIPIDS AND APOLIPOPROTEINS IN BLOOD

Thesis

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By

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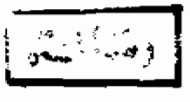

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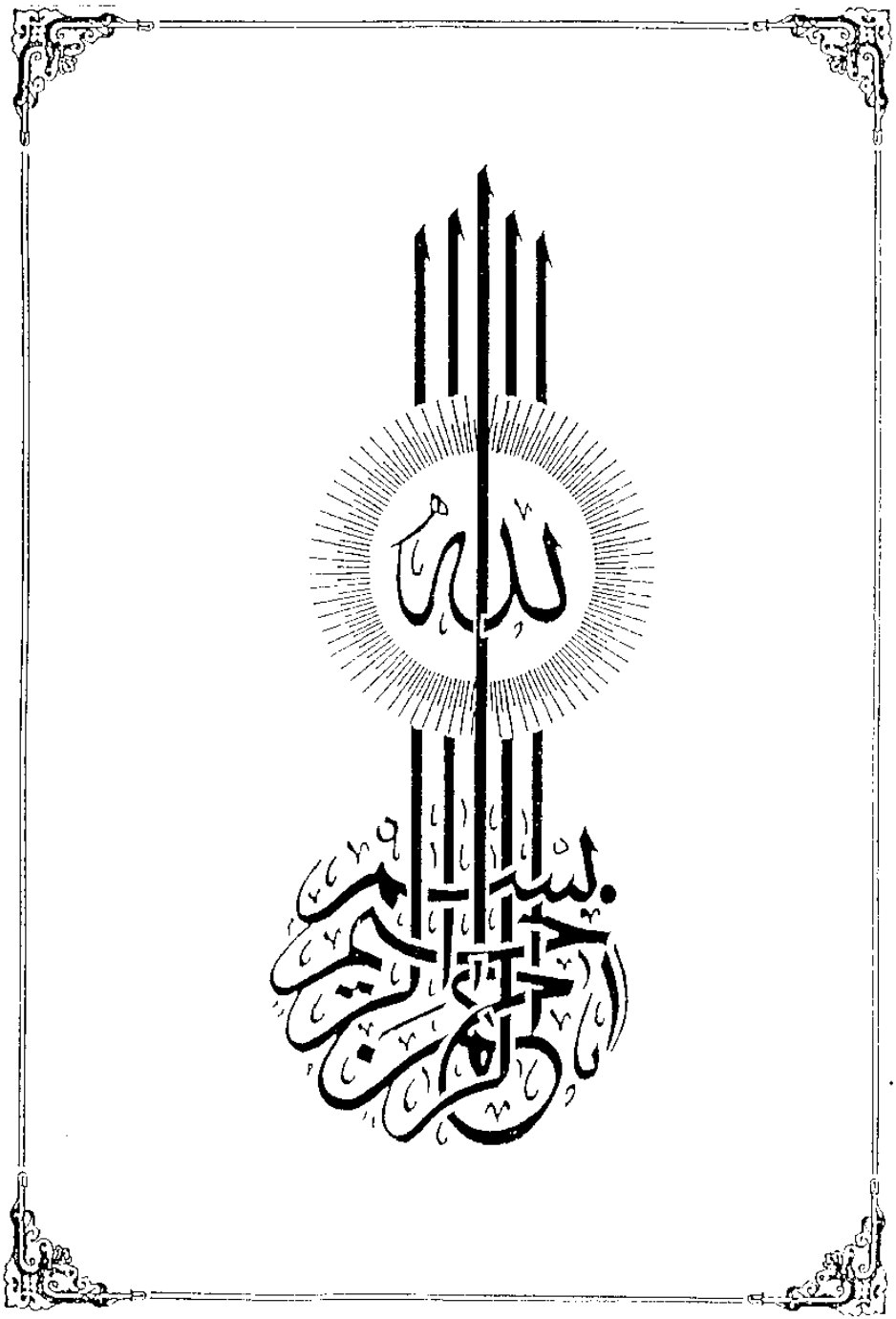

To my mother and to the

spirit of my father

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INTRODUCTION

I- INTRODUCTION AND AIM OF THE WORK

A- Introduction

During the past three decades, considerable studies have been done, concerning the role of plasma lipoproteins in the development of atherosclerosis and subsequently coronary artery disease (CAD).

It is now well established that plasma lipids mainly total cholesterol and triglycerides are one of the major risk factors for CAD. Low density, very low density lipoproteins and apoprotein B are directly correlated with CAD incidence (Gofman et al., 1966). The high density lipoproteins and apoprotein A are inversely correlated with CAD and are considered protective against atherosclerosis (Miller and Miller, 1975).

One of the factors, which play a major role in the metabolism of lipoproteins, is the thyroid gland. Thyroid hormones (T_3 and T_4) affect the synthesis, mobilization and catabolism of lipoproteins (Walton et al., 1965). Therefore, thyroid dysfunction has a major influence on the level and distribution of various lipoproteins in the serum (Abrams et al., 1981).

B- Aim of the work:

The aim of this work is to investigate the effect of both hyperthyroidism and hypothyroidism on the concentration of various lipids and apoproteins in the patient's sera.

REVIEW OF LITERATURE

II- REVIEW OF LITERATURE

A- Lipoproteins:

Since lipids account for much of the energy expenditure of the body, the problem is presented of transporting a large quantity of hydrophobic material (lipid) in an aqueous environment (blood plasma). This is solved by associating the more insoluble lipids, (triacylglycerols and cholesteryl esters) with more polar ones (phospholipids and cholesterol) and then combining them with protein to form a hydrophilic lipoprotein complex (Havel et al., 1955).

The lipoprotein transport pathway can be divided into exogenous and endogenous systems, that transport lipids of dietary and hepatic origin, respectively. Both systems begin with the secretion of triacylglycerol rich lipoproteins. These are intestinal chylomicrons in the exogenous system and hepatic very low density lipoproteins (VLDL) in the endogenous system (Kane et al., 1980).

1- Structure of lipoproteins:

Lipoprotein particles are formed of a hydrophobic core of triacylglycerols and cholesteryl esters, surrounded by a surface monolayer of polar phospholipids. The surface coat also contains small amounts of unesterified cholesterol together with proteins called apoproteins (Eisenberg, 1979 and Scanu et al., 1980). Through interactions with enzymes and cell surface receptors, the apoproteins direct each lipoprotein to its site of metabolism.

The binding of lipids to the protein is weak enough to allow for ready exchange of lipids among serum lipoproteins and tissues. However, this link is strong enough to allow for separation by several physical and chemical techniques (Levy et al., 1971).

2- Classification:

The lipoproteins are classified according to density, chemical composition and particle size into chylomicrons, very low density lipoproteins (VLDL), low density lipoproteins (LDL) and high density lipoproteins (HDL) (Havel et al., 1955 and Nelson, 1972).

a- Chylomicrons:

Chylomicrons are lipoproteins of density less than 0.95 gm/ml, which are synthesized in the intestine during active fat absorption. Therefore, they carry triglycerides of exogenous origin (Zilversmit, 1969).

These chylomicrons are huge lipoproteins, varying in diameter between 800 A° to 1 micron, and of molecular weight from 100 to 1000 million daltons. They are very rich in triglycerides, which constitute more than 90% of the molecule. Total cholesterol content is about 2 to 5%, phospholipids are 3 to 6%, while proteins are 1 to 2% (Kostner and Holasek 1972). They contain apo B_{48}, apo A, apo C and apo E (Schwartz et al., 1978).

Their light scattering properties cause the blood and plasma to appear cloudy or milky and they float to the top of a test tube within 12 to 24 hours, forming a creamy layer. Chylomicrons do not migrate on agarose or cellulose acetate electrophoresis strips and are found at the line of sample application, i.e. origin (Fredrickson and Levy, 1972). The presence of chylomicrons in plasma, after an over night fast, is pathological.

b- Very low density lipoproteins (VLDL):

Very low density lipoproteins occupy a density range of 0.95 to 1.006 gm/ml. Their diameter varies between 300 to 800 A°, and the molecular weight is from 5 to 130 million daltons (Lindgren et al., 1972). As observed through the electron microscope, they are surrounded by a halo which may represent a surface coat (Hamilton, 1968).

They do not float to the top of a test tube on standing, but, when present in plasma in excessive amounts, will cause the plasma to appear cloudy or even milky. VLDL migrate in most electrophoretic media towards the anode with prebeta (α 2) mobility and are frequently referred to as "Prebetalipoproteins". They are composed mainly of triglycerides from 45 to 65%, free cholesterol 4 to 8%, esterified cholesterol 16 to 22%, phospholipids 15 to 20% and protein from 6 to 10%. The protein is mostly apo B_{100} with some apolipoprotein C and apo E (Skipsi, 1972).

They are formed in the liver and transport the bulk of endogenous triglycerides. In the absence of chylomicrons or during the fasting state, this

lipoprotein class correlates closely with the triglyceride level in plasma (Levy et al., 1972). The interaction between VLDL and lipoprotein lipase enzyme (LPL) result in smaller triglyceride and surface material depleted remnant particles, referred to as intermediate density lipoproteins (IDL).

c- Intermediate density lipoproteins (IDL):

Intermediate density lipoproteins occupy a density range of 1.006 to 1.019 gm/ml. They are present in the absence of metabolic disease only in very low concentration. They are thought to be metabolic products of VLDL, or precursor particles of LDL.

d- Low density lipoproteins (LDL):

Low density lipoproteins are defined as lipoproteins of density 1.019 to 1.063 gm/ml. The diameter of these lipoproteins varies between 200 to 250 A° (Lindgren et al., 1972). They do not cause turbidity of plasma even when present in excessive amounts. LDLs migrate in electrophoretic media with B-globulins and are referred to as beta lipoproteins.

Cholesterol accounts for about half of the LDL mass, most of it is esterified. LDL contains about 45 to 50% esterified cholesterol, 6 to 8% free