

protein synthesis and consequently in the blood protein levels. Many of these alterations are also demonstrated by pregnant women. During either of these two conditions, estrogen treatment or pregnancy, there is a significant lowering of the total plasma protein level while the component parts show a variety of changes such as decreases in the albumin and gamma globulin levels and elevations of fibrogen, ceruloplasma, plasminogen, transcortin and the thyroid binding globulins (5). The results of these alterations are unknown. Since many clinical laboratory tests used in the diagnosis of disease states depend directly or indirectly upon the blood levels of these proteins, these tests may be "abnormal" in women taking oral contraceptives without an actual disease being present. It is important, therefore, that physicians be aware of (1) which laboratory tests are altered by the oral contraceptives and (2) which patients are taking oral contraceptives, in order that a correct diagnosis can be made.

Another important function of the liver is that of detoxification and excretion. Excretion is dependent upon the transport of blood bile salts to the liver cells and then into the bile ducts. The measurement of this excretory function can be made by injecting dyes such as Sulfobromophthalein (BSP) into the blood and measuring how fast it is removed by the liver. Mueller and Kappas demonstrated that estrogens interfered with this liver function (6) and this has also been demonstrated in women taking oral contraceptives (1, 7). The incidence of this abnormally varies with the dosage of the drug used (8, 9). Since bilirubin is also carried from the blood to the bile in a similar manner, it is not surprising that occasionally abnormally high blood bilirubin levels are reported in women taking oral contraceptives (9, 10). The effects of the oral contraceptives on an existing impaired liver function could result in the clinical manifestations of jaundice. Since pregnancy involves the same hormones, these subclinically abnormal women may also demonstrate jaundice when they are pregnant. Ockner and Davidson reviewed 40 cases where jaundice developed while using the oral contraceptives and 13 of their women (32.5%) also had jaundice while pregnant (11). It is, therefore, important that physicians again recognize the fact that women with liver disease, or women who have jaundice or itching while they are pregnant, are also very prone to develop jaundice if they are given oral contraceptives, and this then represents a clear contraindication to their usage. Fortunately, discontinuing the drug usually rapidly "cures" the patient (12). Finally, it should be pointed out that no deaths have been reported from liver disease in women using oral contraceptives.

It is concluded that several of the metabolic functions of the liver are altered by the steroids of the oral contraceptives, particularly the estrogen portion. The sequelae of these alterations over long term usage is unknown. The immediate effects include the alteration of several of the laboratory tests used in medical diagnoses. Aggravation of existing liver disease, if present, to the point where jaundice may be seen has also been shown. There is no answer to the query of will permanent liver damage result from the use of the oral contraceptives.

B. Lipids

The lipids or fat in the blood are divided into four major groups: (1) free fatty acids; (2) phospholipids; (3) cholesterol; and (4) triglycerides. These individual lipids are bound to plasma proteins (termed lipo-proteins) and carried in the blood. That way they are transported from the site of formation to the site of use. The blood levels of each lipid depends upon a variety of factors including age, diet, weight, sex, and heredity background. In order to meaningfully study any one of these broad groups, each of the variables must be carefully controlled. The importance of the lipids in disease is principally related to the vascular system.

It has been found that there is an elevation of total blood cholesterol and the low density (light) lipo-protein levels in many individuals who demonstrate clinically symptomatic coronary heart disease (13). A major component of this light lipo-protein group is the triglyceride fraction. Thus, cholesterol and triglycerides are suspect to causing vascular disease. It is also known that there is a markedly lower incidence of coronary artery disease in premenopausal women as compared to men of the same age group or postmenopausal women (14). These premenopausal women have ovaries that are producing sex hormones. It has been postulated that (1) the blood lipid levels were altered by ovarian hormones and (2) the lipid levels may be causally related to vascular disease and (3) by altering the ovarian hormone levels in the blood one could prevent or cause serious vascular disease. Accordingly, many investigators