## LIVER

As we have already heard from Dr. Corfman, the liver carries on

many functions.

The anatomic structure of the liver in women taking oral contraceptives is difficult to evaluate because of the inaccessibility of the organ. Whereas, Kleiner and his associates, found normal patterns on two biopsies studied with both the light and electron microscope, three more recent reports dealing with 31 women who had liver biopsies performed while they were using oral contraceptives found changes. Although the light microscope could not demonstrate consistent changes, there were structural alterations within the liver cells involving the mitochondria particularly, which were seen with the electron microscope. Whether these alterations existed before the drugs were used, their frequency of occurrence, and whether they are progressive or reversible is not known.

The biochemical effects of the sex hormones on the liver are legion. It is well recognized for example that the liver produces most of the proteins circulating in the blood, and this production is influenced at the cellular level by ovarian hormones. Thus, giving estrogens to animals, including humans, results in an alteration in liver 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 and increases in other fractions. 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 the practicing 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. Kappas and his group demonstrated that estrogens interfered with this liver function and this has also been demonstrated in women taking oral contraceptives. The incidence of this abnormality varies with the dosage of the drug used. 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. 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. It has been shown that approximately one-third of the women who have had jaundice while taking oral contraceptives have also had jaundice or itching while they were pregnant. It is, therefore, important that physicians