

and his colleagues reported that the free fatty acids were elevated in the blood of women taking oral contraceptives. More recently (1969) they have been unable to confirm this finding. Three other investigators have found normal free fatty acid levels in women taking oral contraceptives.

The second group is the phospholipids. All of the reports demonstrate an elevation of this group. This is a heterogeneous group of many subtypes of phospholipids. The medical meaning of these reported elevations that occur in women taking these oral contraceptives are not known. Recently Bolton and his associates have studied patients with arterial occlusive disease and they have found abnormal blood platelet function (important in blood clotting) which is presumably due to an elevation of the blood phospholipid lecithin. Whether the oral contraceptives elevating this particular lipid make the women susceptible to this vascular clotting is unknown.

The third lipid fraction to be considered is cholesterol. Pincus and his colleagues originally studying this group in Puerto Rico were unable to find any change in cholesterol. More recently, four research teams have found elevated cholesterol levels in their subjects using oral contraceptives. This discrepancy of results can be partially explained on the basis of the different drugs that have been used in these investigations.

There is almost unanimity of opinion among the 10 investigating groups measuring blood triglyceride levels in women taking a variety of different oral contraceptives. All but one of the reports demonstrate a significant elevation of this lipid. Indeed Zorrilla and his group have produced similar elevations by giving women only the estrogen component of the oral contraceptive. Since these lipids are carried on blood proteins, and since we have already described the ability of estrogens to alter the liver's production of blood proteins, these lipid alterations may simply represent a difference in liver function.

Hazzard and associates have been concerned with the mechanism by which the oral contraceptive alters blood lipids. The level of blood triglycerides are dependent upon two processes: First, the production of the liver mediated by insulin and, second, the destruction at fat depots. They have investigated both processes and their results suggest that there is both an increased rate of synthesis or production of triglycerides in the liver as well as a decreased rate of enzyme destruction at fat depots in a woman taking an oral contraceptive. It is apparent that the three metabolic areas under review today (liver, lipids, and carbohydrates) are interrelated, and a primary alteration produced in one may manifest itself in the other two.

Senator NELSON. Have enough studies been made to draw any conclusions about the short- or long-term effects of these alterations?

Dr. SPELLACY. As far as the production of vascular disease is concerned, I do not think there are enough data available at this time to answer that question. It is clear that the blood levels of the lipids are changed but what effect this ultimately will have on a normal population is unknown.

Senator NELSON. And there are no studies that would indicate the effect on the user over a long period of time?

Dr. SPELLACY. Not to my knowledge. I have not reviewed Dr. Wynn's most recent data that he has related to you.