

Significant information derived from the best controlled studies of the effects of oral contraceptives on carbohydrate metabolism is as follows: Glucose tolerance may be reduced during short-term or long-term use of the drugs. In the same subjects plasma insulin levels also rise above normal levels in response to a glucose load. In some cases glucose tolerance returns to normal with continued use of the pill. It is not clear whether or not this is due to the increased amount of circulating insulin. In other cases glucose tolerance remains impaired for several weeks or months after discontinuance of the pill. It then returns to normal if the patient is nondiabetic. Hyperinsulinism appears to persist for longer periods of time than hyperglycemia after the pill is stopped. I do not know the cause for this except as it may relate to the effects of high doses of circulating insulin in reversing the hyperglycemia effect.

Growth hormone is known to have a diabetogenic effect and is also known to be elevated in response to estrogen administration. Increases in this hormone have been noted during oral contraceptive treatment. Lipid metabolism is related to the metabolism of carbohydrates. Blood cholesterol and free fatty acids are not altered significantly by oral contraceptives but the triglycerides are increased and may remain so for several weeks after discontinuance of the pill.

Senator NELSON. May I interrupt a moment?

Dr. CARRINGTON. Yes.

Senator NELSON. Just to refresh my memory, you stated that blood cholesterol and free fatty acids are not altered by oral contraceptives, but cholesterol may be increased. Does that square with Dr. Wynn's study?

Dr. CARRINGTON. Yes, it does. Dr. Wynn's original study showed that blood cholesterol and free fatty acids were mildly increased. His subsequent attempt to reproduce the same effects failed, so that he does not have confirmation of these increases—certainly this is true in free fatty acids, in his free fatty acids study. His triglycerides showed consistent increases and this is his particular concern with respect to the effects upon the vascular system.

Senator NELSON. I had not remembered. I thought he had said blood cholesterol—

Dr. CARRINGTON. This is a very small factor and is pretty hard to document. A number of investigators have worked in this particular area. The increases in free fatty acids have not been reduplicated.

Mr. DUFFY. Excuse me, Dr. Carrington. Did you indicate just a moment ago that Dr. Wynn could not confirm his early findings?

Dr. CARRINGTON. On free fatty acid elevations. On triglycerides, he not only confirmed them, but had an almost 100 percent effect, a very high, a very significant effect in the increases in triglycerides under the therapy. His blood cholesterol was very controversial.

Mr. GORDON. Which are the ones that cause arteriosclerosis?

Dr. CARRINGTON. Blood cholesterol and triglycerides are the main ones here. This is not my particular area of expertise, but I do know that triglycerides are increased and this is of importance to us because lipid metabolism has an effect upon carbohydrate metabolism. I think in the testimony presented to you by Dr. Wynn and by Dr. Spellacy, both of whose work I think is really excellent, will