BLOOD PRESSURE

Estrogen and other contraceptive steroids are known to alter the concentration of substances thought to be important in the regulation of blood pressure. There are now several reports of hypertension associated with the use of oral contraceptives (97, 171, 183). Increase in plasma angiotensinogen following administration of estrogen was reported several years ago (75). More recently, elevated levels of plasma renin were found in normal pregnancy (24), and estrogen and progestin were found to increase the secretion of aldosterone (104). In addition, oral contraceptives are now known to enhance the reactivity to endogenous renin (97, 98).

It appears, therefore, that susceptible women may experience an increase in blood pressure following administration of contraceptive steroids. Because of the high prevalence of hypertension in the population it is difficult to identify with certainty the women in whom administration of contraceptive steroids has led to an increase in preexisting hypertension or has produced hypertension in previously normal women. Several cases, however, have been reported in which the etiologic relation has been established beyond reasonable doubt (97).

BLOOD CONSTITUENTS

Many studies (6, 7, 22, 29, 95, 102, 120, 135, 137, 158, 160, 173) have been reported describing the effect of contraceptive steroids and allied agents on plasma proteins and their metabolism. Their administration leads to decreases in haptoglobin, albumin, and total serum proteins, and dose-dependent increases have been reported for thyroxine-binding globulin and iodine-binding protein. Increases have also been reported for plasminogen, ceruloplasmin, estrogen-binding proteins, C-reactive protein, renin, factors VII and IX, fibrinogen, beta-glucuronidase and isocitrate dehydrogenase (6, 7, 102, 120, 158, 173). Only a few constituents are decreased by administration of estrogens: lipoprotein lipase, cholinesterase, lactic acid dehydrogenase, and alkaline phosphatase (23).

LIPIDS

Contraceptive steroids are known to increase the concentration of triglycerides and phospholipids, particularly lecithin, in the plasma of women (188). The principal effect is on the lipoproteins of very low and high densities. Hypertriglyceridemia has been consistently found to accompany the use of these agents; the responsible component of the contraceptive preparation appears to be the estrogen rather than the progestin.

According to presently held views, the site of action of estrogens upon triglycerides or lipoprotein synthesis is the liver. Since lipid synthesis requires insulin, it is possible that changes in lipid output are mediated via the effect of estrogens upon plasma concentration of insulin (136). Estrogens have also been implicated in modifying the removal of these lipids from the circulation. It has been demonstrated that the rise in lipolytic activity of plasma brought about by administration of heparin was decreased following administration of estrogens (73a).

Although changes in plasma lipids and lipoproteisn are appreciable following the administration of contraceptive steroids, there is no knowledge of the functional significance of these changes. No specific clinical disturbance has yet been attributed to the alterations in lipid and lipoprotein composition.

SALT AND WATER METABOLISM

The effects of oral contraceptives on water and electrolyte metabolism have not been studied in detail, but it is pertinent to describe the changes produced by individual steroids. For instance, progestin in approximately physiological doses causes a diuresis of sodium followed by retention even while the hormone is administered. The diuretic effect appears to predominate at higher dose levels, but it is not certain whether long-term progestin administration causes diuresis or retention of sodium.

The short-term natriuretic effect of progestin is opposite to that of estradiol-17 beta, which at high doses causes sodium retention. The effect of oral contraceptives on sodium excretion is sensitive to the proportions of its constituents. The overall effect, however, appears to be a decrease of sodium excretion (134).