

about changes in enzymatic activity during treatment. Acid and alkaline phosphatases and DPN diaphorase, which are clearly hormone-dependent, are greatly reduced (53). Alterations are demonstrable in activity of carbonic anhydrase, uterine peroxidase (170), beta glucuronidase, succinic dehydrogenase, lactic dehydrogenase, and several other enzymes (35). However, accurate appraisal of the changes described must be deferred because of deficiencies in standard values.

Myometrial hypertrophy, dilatation of sinusoids, and edema are recognized effects. Congestion and increased vascularity of tissues are noted during pelvic surgery when oral contraceptives are not discontinued for a sufficient period of time prior to operation (145). Uterine myometrial activity is not significantly changed during treatment, but if medications containing both estrogen and a progestin are used, an increase in contractility is noted on the 8th day after the medication is stopped (15).

Little is known regarding the effects of oral contraceptives on the rate of tubal transport of ova in women. Chang (32, 33) demonstrated that ovum transport was accelerated in animals given progestational agents and that early arrival of ova in the uterus led to failure of fertilization, and to degeneration and expulsion of eggs from the uterus. He noted also that transport and capacitation of sperm were disturbed, but these effects were less pronounced than rapidity of ovum transport in the animals studied. Zanartu (189) found a few motile sperm in the uterus of treated subjects undergoing operations but none in fluid recovered from washings of the fallopian tubes. He therefore suggested that continuous dosage of chlormadinone prevents ascent of spermatozoa.

Suppression of ovulation is one of the most consistent although not invariable effects of steroid contraceptive agents. The ovaries appear grossly small and inactive (145). A few early follicles may be seen beneath the tunica but as a rule no corpora lutea are observed. Ostergaard and Starup (126) reported fresh corpora lutea in six women treated during the cycle in which laparotomy was performed; in most cases these corpora lutea were smaller than normal and they were not associated with elevated pregnandiol levels. Total absence of corpora lutea during treatment is reported in other studies in which culdoscopy was performed (8) and during abdominal operation (145). In Ryan's study (145) focal areas of cortical stromal fibrosis were observed in about half the patients on medication for one year or more. It is of particular concern that in this study thrombi were seen in the ovarian and uterine veins in three of the 27 study cases, but the significance of these observations cannot be assessed until data on control subjects are available.

LIVER

Moderate changes in liver function tests are seen in many symptom-free women on oral contraceptives. BSP (sulfobromophthalein) excretion is diminished with almost all oral contraceptive drugs in up to 40 per cent of women on medication. This effect appears to be dose-dependent (4, 92) and may be related to a fall in serum albumin concentration seen with the use of oral contraceptives (38). Plasma amino acid levels also fall with the use of these agents (37).

BSP is retained in plasma primarily conjugated to albumin, and its retention with oral contraceptives is related to the concomitant alteration in bile transport seen with the use of these agents. Such an effect is produced by all agents that have an alkyl group at the 17-alpha position of the steroid molecule. It is thought to result from inhibition of the glucuronyl transferase system, which participates in the metabolism of bilirubin.

Another commonly observed alteration in liver function is elevation in transaminase values in 20 per cent of patients (50, 100). An increase in SGOT also occurs (99), and in a small proportion of subjects a slight elevation in alkaline phosphatase levels is found. After cessation of treatment, all of these values return to normal over a period of time. These effects are more severe in postmenopausal women. For instance, in two studies BSP retention appeared to occur in most such women on oral contraceptives, and an increase in SGOT was almost universal. In these women, the tests also return to normal after the cessation of treatment.

Jaundice occurs in about one woman in 10,000 on oral contraceptives (124). Many patients have a typical history of nausea, malaise, and itching with