metabolic action of the agent on bone structure rather than through suppression of growth hormone (179).

Observations of this nature have led to concern over the possible effects of oral contraceptives on bone growth in young women in whom epiphyseal closure has not yet taken place. There is not yet any evidence on which to base this conclusion. First, the use of estrogen even in much larger amounts than those in oral contraceptives is not uniformly successful in inducing epiphyseal closure. Second, there is no evidence that the progestin in oral contraceptives has any effect on bone maturation. Third, in order to be effective at all the estrogen treatment of excessive growth must be started prepuberally, considerably earlier than the age at which oral contraceptives are ordinarily used.

SKIN

Oral contraceptives have been known for some time to produce chloasma, or melasma. Resnick (138) reported an extensive study of 212 patients, a high percentage of which developed melasma with both combination and sequential oral contraceptives. This condition differs from the melasma of pregnancy in that it does not seem to regress completely after medication is stopped. Eighty-seven per cent of Resnick's patients who developed melasma from oral contraceptives had had this condition during pregnancy, suggesting that a history of increased skin pigmentation during pregnancy may be used as an indicator for detecting susceptible individuals.

A more recent case report (155) describes a woman who developed exceptionally marked melasma as well as areas of increased pigmentation of other parts of her body, suggestive of the pigmentation seen in Addison's disease. The authors ruled out this condition to their satisfaction and concluded that the effect was due to activity of melanocyte-stimulating hormone.

It has been known for some time that oral contraceptives decrease sebum production, and that suppression of sebaceous gland activity can be directly correlated with improvement of acne (166).

Erickson and Peterka (52) reported a single case of sensitivity of the skin to sunlight as a result of oral contraceptives; repeated studies in the same patient showed that the effect appeared to be caused by the estrogen. Another effect of these agents on the skin was described by Krane (113), who showed, in rats, that both estrogens and progestins decrease the collagen content of skin and increase its turnover. Progesterone in particular interferes with the generation of cross linkage and the maturation of collagen. Comparable studies have not been carried out in women. Other observations (36) suggest that oral contraceptives may produce a male-type partial alopecia in certain patients. Here again, there is insufficient evidence to confirm this observation (2).

OTHER EFFECTS

Studies of the effects of oral contraceptives on the gastrointestinal tract are limited. Crean (39) reviewed the relation between endocrine secretions and gastric function and described the decrease in severity of peptic ulcer in women during pregnancy and during the administration of estrogens. Whether these effects occur with the administration of oral contraceptives is not known.

A related observation concerns acute colonic lesions in a few women on oral contraceptives (1, 91, 174). The authors postulate that these lesions may result from thromboembolic phenomena.

Goh (63) has reported a significant increase in chromosomal abnormalities, particularly breaks, in the peripheral lymphocytes of women on oral contraceptives. Comparable changes in lymphocytes from male subjects were induced by incubating the lymphocytes with the serum of women on oral contraceptives. These effects disappear on discontinuation of medication. These observations have not yet been confirmed, but they may be related to the findings by Carr (28) of chromosomal abnormalities in abortuses collected from women who became pregnant after taking such agents.

Other clincial phenomena that have been described in association with oral contraceptives include abnormal patency of the Eustachian tube (5), hypertrophic gingivitis (10), myalgia (43), and positive LE cell test without evidence of collagen disorders (151a). Only one isolated report of the possible exacerbation of systemic lupus erythematosus by oral contraceptives (131) has appeared.