ing. A tablet with a 4% incidence has a modified early secretory phase from days 8 to 12, while one with 40% incidence of break-through bleeding may be secretory from days 10 to 20.

(*a*) *Containing 0.05–0.09 mg. Ethinyloestradiol:* An intermediate picture was seen in this group with a gradual decrease in alkaline phosphatase and early increase in acid phosphatase activity (Fig. 1, IV). The post-secretory low columnar or cuboidal glands showed a weak, moderate, or strong monoamine oxidase activity from day 17 onwards.

(*b*) *Containing 0.075–0.1 mg. Mestranol:* Alkaline phosphatase was stronger and acid phosphatase weaker during the cycle than with the corresponding ethinyloestradiol tablets. Though most specimens were from Ovulen and Lyndiol 2.5 (break-through bleeding 4%) which produce a post-secretory atrophic endometrium from day 13 onwards, only two biopsies showed a strong monoamine oxidase activity (Fig. 1, V). The day 24 specimen giving a strong reaction was from the Ovulen-treated endometrium of a woman complaining of loss of libido. The other strong reaction was given after several months' continuous therapy with Lyndiol 2.5, when the patient was complaining of depression and abdominal distension: cyclic therapy, discontinued because of menstrual headaches, was then restarted at the patient's request.

DISCUSSION

In the normal cycle there is a dramatic rise in the monoamine oxidase activity of the endometrium in the late secretory phase. At this time endogenous oestrogen levels fall and premenstrual tension is common, especially among older women. With a strongly progestogenic combined oral contraceptive tablet the rise in endometrial monoamine oxidase occurs early in the cycle at day 12, at which time the woman is receiving constant amounts of exogenous oestrogen. If the amount of oestrogen is low some women may notice a depressant effect on mood or libido. Though a strongly progestogenic combined tablet such as Lyndiol has strong monoamine oxidase activity early in the cycle, the high dose of oestrogen in the tablet seems to protect against the depressant effect. However, Ferin (1966, personal communication) found that some ovariectomized women taking Lyndiol became depressed and treated them with monoamine oxidase inhibitors. With the strongly oestrogenic sequential regimens the amount of oestrogen is high, the monoamine oxidase activity low, and fewer women complain of depression. With the intermediate compounds monoamine oxidase varies in activity and may even be weak in post-secretory glands.

It is interesting, in view of our finding in women, that Michael *et al.* (1967) showed that progesterone inhibited sexual receptivity in female rhesus monkeys. As the endometrium is especially sensitive to variations in oestrogens and progestogens the changes in monoamine oxidase activity may reflect similar changes occurring in other sensitive areas of the body such as the hypothalamus. Cyclic changes in the rat hypothalamus have been reported by Kuwabara *et al.* (1967), who found that monamine oxidase and biogenic amine activity reached a maximum at pro-oestrus. In women, plasma monoamine oxidase has been found to double at the end of the cycle, and significantly higher values were recorded in amenorrhoeic women (Klaiber *et al.*, 1967). These findings support the hypothesis that progestogenic stimulation causes generalized changes in monoamine oxidase metabolism which may be a factor in the occurrence of depression and loss of libido in susceptible women.

Kane *et al.* (1967) described mood and behavioural disturbances in women who were using a variety of oral contraceptives, while Daly *et al.* (1967) reported two cases of psychosis associated with the use of sequential regimens. In our series many women had mood disturbances and vascular side-effects at the same time. It seems possible that susceptibility to mood changes may be affected by vascular reactivity (Grant, 1968).

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