

probably reflect natural variations of the disease. All other patients with clinical and laboratory evidence of malabsorption had a rise in plasma O.D. of less than 0.1.

Summary. Our studies indicate that measurement of changes in plasma optical density after a fatty meal is a simple and reliable screening test for patients with malabsorption syndromes. It is of value in following the course of these diseases and in evaluating response to therapy.

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Effects of Hepatectomy on the Response of the Uterus to Estradiol-17- β .^{*} (24708)

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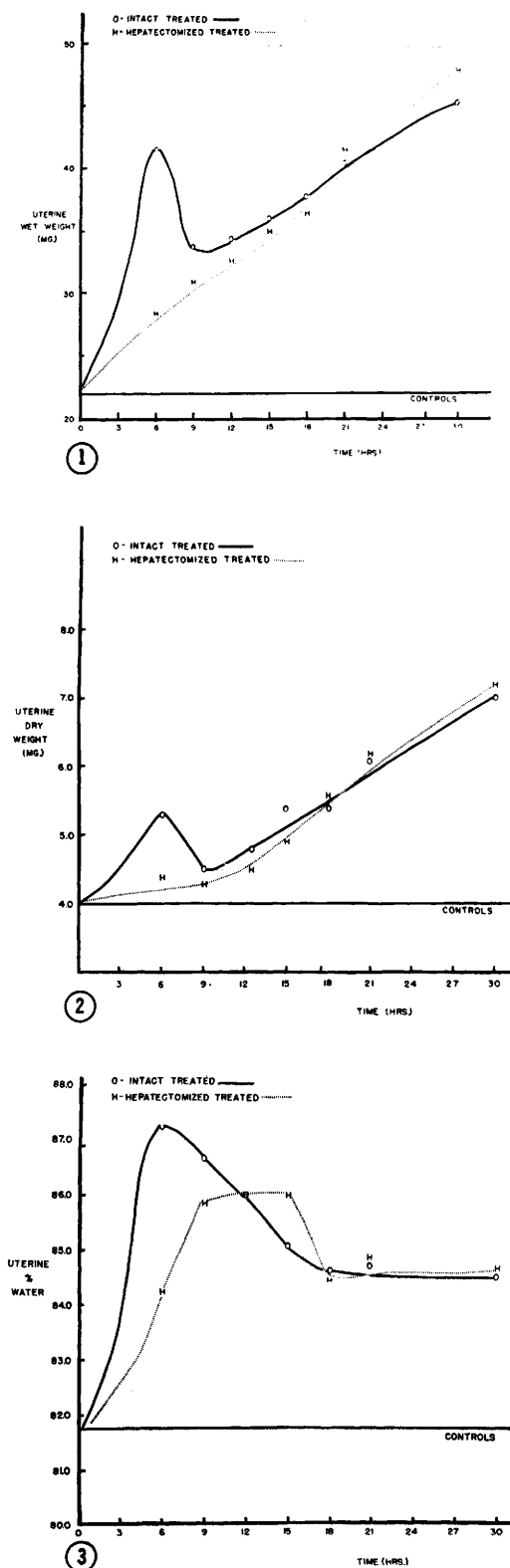
A peak in uterine fluid imbibition in sexually immature rats is reached within 6 hours following estrogen stimulation. This is followed by a period of cellular proliferation and gradual increase in total uterine weight(1). Hechter *et al.*(5) and Kalman(7) showed that early effects were due to a change in capillary permeability. Roberts and Szego(10-12) found that removal of two-thirds of liver greatly reduced early stimulating effect of estradiol on rat uterus. This led them to study of uterine response to estradiol at various intervals after partial hepatectomy and they observed that sensitivity to estrogen was gradually regained. They correlated restoration of estrogen activity with liver regeneration. In the present study, this relationship has been examined by using a slightly different approach and a different interpretation of data is presented.

Materials and methods. The effect of partial hepatectomy on uterine response to estradiol was studied in sexually immature rats by means of methods developed by Astwood (1). Ten animals were used in all control

and experimental groups. Rats (Harvard strain) 24-25 days old and weighing 54 to 60 g were given a single subcutaneous injection of 0.1 μ g estradiol 17- β immediately after 60%-70% of the liver was removed. Uteri and livers of different groups were removed at 6, 9, 12, 15, 18, 21, and 30 hours after treatment. The organs were weighed at autopsy and again after oven-drying 24 hours at 90-100°C, the difference reflecting water content. The technic of partial hepatectomy was based on those reported by Higgins and Anderson(6) and Roberts and Szego(10). The mean value and standard error are presented for key groups.

Results. On the basis of fluid imbibition, partial hepatectomy decreases normal response of uterus to estradiol as seen 6 hours after treatment (intact control, 81.8% $\pm$ 0.02%; intact treated, 87.1% $\pm$ 0.3%; hepatectomized control 81.6% $\pm$ 0.4%; hepatectomized treated, 84.2% $\pm$ 0.6%). However, when uteri were removed at various times later than 6 hours, increases in weight clearly indicate that the effect of partial hepatectomy on accumulation of water in the uterus is one of retardation rather than inhibition (Fig. 1,

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3). The response reached maximum at 9-15 hours, but was not as great as in intact animals at 6 hours. It was previously reported (2) that the peak was reached between 15-18 hours, but 9-15 hours represents a more precise range as determined by larger experimental groups.

Increases in uterine dry weight over controls were used as approximate measure of uterine growth. That this is a valid criterion for growth under these conditions has been shown by correlation between dry weight and increase in total nitrogen. In our experiments, it was found that no significant difference occurred between uterine dry weights of intact treated and partially hepatectomized treated animals from approximately 9 hours to 30 hours after injection of estradiol (Fig. 2). When growth as seen at 30th hour is taken as reference point for comparison, dry weights for both groups are about the same. By this time partial regeneration of liver has occurred, to 50%-60% of normal. When 50%-60% of liver is removed at beginning of experiment, reduction of fluid imbibition and dry weights at 6 hours is approximately the same as that when 70% is removed, thus indicating that the extent by which the response during first 6 hours is decreased, is not closely correlated with amount of liver removed.

Discussion. It is difficult to explain the decreased effect of a single small dose of estradiol, when given at time of partial hepatectomy, on the basis that the liver has an important role in the action of estrogens. This is particularly true for growth phase which becomes pronounced about 9 hours after estrogen is injected. Uterine wet weight, dry weight, and per cent water beyond 15-18 hours are approximately the same for both hepatectomized and control groups, yet at 9-15 hours the liver is only 45% of normal.

Perkinson and Irving(9) report that fol-

FIG. 1. Comparison of physiological effects of estrogen on uterine wet wt in normal and hepatectomized animals treated with 0.1 μ g estradiol 17- β .

FIG. 2. Physiological effects of estrogen on uterine dry wt in normal and hepatectomized animals treated with 0.1 μ g of estradiol- β .

FIG. 3. Estrogen effects on % water in uterus of normal and hepatectomized animals treated with 0.1 μ g of estradiol 17- β .

lowing hepatectomy, liver metabolism does not return to normal for at least 14 days although original weight may be replaced before that time. It has been found(3,6) that the most rapid rate of restoration on third day after removal of 70% of liver. Protein formation in the liver was most rapid during the first 2 days, lipid was incorporated entirely in the first day, and glycogen deposition started on second day(4). That such abnormalities following partial hepatectomy do not cause a significant difference in growth response of the uterus to estrogen gives reason for doubting that the liver is important for estrogenic action under these conditions.

The most striking effects of partial hepatectomy on uterine response to estrogen are evident over the first 9 hours of treatment. Estradiol given immediately after liver removal evoked a maximal increase in uterine water 3-6 hours later than in normal animals. Stress as a result of partial hepatectomy and consequent adrenal stimulation probably plays an important part in retardation of fluid uptake. Kramár(4) observed that rats subjected to various forms of stress showed a decrease in capillary permeability which lasted from 2-4 hours. Interestingly enough, this period is comparable to the time lag in fluid uptake in partially hepatectomized animals, and the decrease in capillary permeability may also account for the level of uterine water not being as high as the normal treated. According to Kramár(8), the immediate capillary stress response also appears in the adrenalectomized animal. This fact, plus the knowledge of effects of adrenal cortical steroids on permeability, suggests a possible explanation for the retardation of fluid imbibition by the uterus in estrogen treated hepatectomized rats.

Summary. When a single subcutaneous injection of 0.1 μ g of estradiol 17- β is administered to immature rats immediately following removal of 60%-70% of liver, fluid imbibition by the uterus is retarded 3-6 hours and at maximum is somewhat less than in normal animals at 6 hours. However, partial hepatectomy does not modify growth response of the uterus to estrogen. There is no significant difference in uterine growth between control and experimental animals from approximately 15th to 30th hour following a single injection of estrogen. Since the effect of partial hepatectomy on fluid imbibition by the uterus is primarily a retardation, and uterine growth is not changed, it seems doubtful that the liver has important influence on the action of estrogen under these conditions.

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