are visible. Frequently the addition of more diluent is desirable. When grinding is finished, the pestle is lifted and the additional fluid runs down the stem, thus washing adhering material from the pestle and from the wall of the mortar.

After centrifugation of this tubular mortar the supernate is allowed to run toward the mouth of the tube, where it can be collected in a graduated syringe or pipet.

These pestles and mortars are obviously not interchangeable, so it is desirable that matched parts be suitably numbered. The assembled micromortars may be tubed, and sterilized by dry heat.

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Inhibitory Effect of Implanted Estrogenic Hormone Crystals upon Post-Menopause and Castration Hypophysis of Women.

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It has previously been shown in animals[1-8] that after castration there is an increased secretion of gonadotropic hormone by the pituitary. Similar gonadotropic hyperactivity of the pituitary was shown to occur in humans after castration and after the menopause.[9-14] It

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has furthermore been shown that this hyperactivity can be inhibited by the administration of adequate amounts of estrogens.[15-18] In humans, the inhibition was demonstrated by a decrease or disappearance of the gonadotropic hormone in the urine after estrogen administration. In a previous report[19] it has been shown that by administering estrogens in the form of α-estradiol benzoate crystals implanted under the skin, a therapeutic effect is obtained which is strikingly more prolonged than that which results from a comparable amount of the hormone given intramuscularly in oil. This prolongation of the therapeutic effect was attributed to a retardation of the rate of absorption of the hormone.

The study reported here was undertaken to determine the effect of the implanted crystals of estrogenic hormone on the gonadotropic hormone excretion in surgical castrates and post-menopausal women and to compare the duration of the inhibitory effect upon the hypophysis with that resulting from estrogens administered in oil.

Eight women were selected (5 surgical castrates and 3 spontaneous menopause), all of whom were found to excrete castrate gonadotropic hormone (c.g.h.), the amounts varying from 5 to 28 R.U. per day. Seven of these were implanted subcutaneously with crystalline α-estradiol† or α-estradiol benzoate,† in doses varying from 25 to 50 mg. One patient (a surgical castrate) was given 10 mg daily of α-estradiol benzoate in solution in oil,† intramuscularly, for 6 days. Gonadotropic hormone urine studies were performed on 24- and 48-hour specimens throughout the entire experimental period, which varied from 26 to 92 days.

For the determination of c.g.h. in the urine, a modification of the acetone precipitation method was employed. 600 cc of urine of each specimen were extracted Extracts representing 200 and 100 cc were injected into immature female rats weighing 30 to 35 g, in divided doses, over 3 days. Animals were sacrificed at the end of 96 hours and serial sections made of the ovaries. The smallest amount of extract which induced follicle stimulation (minimum of 3 large

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cystic follicles) or corpora lutea, was considered to contain 1 R.U. A specimen was considered negative for c.g.h. if the equivalent of 200 cc of urine failed to produce microscopic evidence of gonadotropic effect in serial sections of the rat ovaries.

Results. α-Estradiol Crystals. Three cases were implanted with α-estradiol crystals (25, 46.5, and 50 mg, respectively). Castrate gonadotropic hormone disappeared from the urine in all 3 cases 7 days after the implantation. In one case (implanted with 25 mg) c.g.h. did not reappear until 78 days later. In the other 2 cases the urine was still negative for c.g.h. at the end of 58 days.

α-Estradiol Benzoate Crystals. Four cases were implanted with α-estradiol benzoate crystals (26, 37, 27.2, and 30 mg, respectively). Castrate gonadotropic hormone disappeared from the urine 8, 9, 12, and 4 days, respectively, after the implantation. In one case (implanted with 26 mg), the urine remained negative for c.g.h. for 59 days. The remaining 3 cases have remained negative up to the time of the present report (56, 20, and 23 days after the implantation).

The one patient who was injected with 50 mg of α-estradiol in oil began to show signs of pituitary inhibition 5 days after the first injection and the urine remained negative for c.g.h. for 10 days after the last injection. Thereafter, c.g.h. reappeared in the urine.

Summary and Conclusions. It appears from these studies that, by means of the implantation of crystals of α-estradiol and α-estradiol benzoate, it is possible to achieve a strikingly more prolonged inhibition of the hypophysis in post-menopause and ovariectomized women than can be obtained by the injection of comparable amounts of estrogenic hormone in solution in oil. These findings are in accord with the clinical observations of the prolonged therapeutic effect resulting from the implantation of the estrogen crystals.