natural ration. This increase was especially pronounced in the kidneys and livers and is in accord with the hypothesis that excess copper, which is not physiologically effective, may be accumulated when a high level of molybdenum is fed. A dietary level of 1000 p.p.m. of zinc did not appear to have any appreciable effect upon copper metabolism. Growth depression in rats produced by 1000 p.p.m. of added molybdenum to a natural or synthetic ration was not counteracted by the addition of 200 p.p.m. dietary copper. Swine appeared to be more resistant to molybdenum toxicity than did rats. No degenerative changes were observed in the spinal cord, leg joints or muscle tissues of swine fed levels of 1000 p.p.m. of molybdenum or 1000 p.p.m. zinc for a 7-month experimental period. With the criteria of these experiments it appears that dietary zinc was not involved in copper-molybdenum imbalance.

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Fat Storage of an Estrogen in Women Following Orally Administered tri-*p*-anisylchloroethylene. (20688)

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It was reported that tri-*p*-anisylchloroethylene (TACE*) administered orally to ovariectomized rats and monkeys produced estrogenic activity of long duration(1,2). This prolonged action following oral administration resulted from storage of estogenic material in the body fat and its slow release(1,2). Greenblatt and Brown(3) demonstrated estrogenic material in the body fat of human beings given TACE and none in that from patients receiving other synthetic and natural estrogens. Since fat storage of estrogen is of therapeutic significance, further studies extending those of Greenblatt and Brown are reported.

Methods. Fat biopsy specimens† obtained

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TABLE I. Estrogenic Content of Fat Biopsy Specimens Obtained from 14 Women Administered TACE.

Dose/day (mg)	No. days treated	Time from last dose to biopsy	Estrogenic content of fat (mg % TACE equivalent)
48	1	22 hr	.18
192	1	15	0
36	3	18	Trace
48	7	12	.38
72	9	20	.42
72	14	1	.49
72	16	61	.42
24	104	5	.50
24	166	4½	.58
24 48	193 and 103	15	.93
48	111	3½	.80
96	27	4	4.41
24	166	23 days	.2-.4
96	27	34	.25
60	10	15	.50
72	16	15	.54

from omental or subcutaneous tissues were immediately placed in a mixture of equal parts benzene and ethyl alcohol. The tissue, in the solvent, was macerated in a Waring Blender and the homogenate was filtered through cheese cloth. The residue and the cheese cloth were washed twice on a funnel with the solvent; the filtrates were combined and evaporated to drynes over a steam bath. The estrogenic content of the oily residue was estimated by the uterine weight method of Evans, Hines, Varney and Koch(4). The oily residue was administered subcutaneously to the mice either undiluted or diluted with olive oil.

Results. Bioassay results are summarized in Table I. No estrogenic material or only trace amounts were present in the body fat of women who received oral TACE in doses of 48 mg and 192 mg in one day or 36 mg daily for 3 days. Biopsy specimens obtained from patients given 48 or 72 mg of TACE per day for 7-16 days or 24 mg per day for 104 and 166 days, contained estrogenic material equivalent to 0.38-0.58 mg % TACE. Estrogen concentrations of the fat were somewhat greater in 2 patients who received 48 mg for 103 and 111 days. The fat from one patient given twice this daily dose (96 mg) for a shorter period (27 days) contained a considerably greater amount of estrogenic material (4.41 mg % TACE equivalent). From the fifteenth to the thirty-fourth day following TACE withdrawal significant amounts of estrogenic material were recovered from the fat of 4 patients given various doses of TACE for 10 to 166 days. This study suggests that the estrogenic content of fat is dependent upon both the size of the dose and the number of days of TACE administration.

Clinically a single 30-day course of therapy with TACE has frequently controlled menopausal symptoms for prolonged periods(5) and there has been a low incidence of withdrawal bleeding(6). These observations can be related to the fat storage of an estrogenic substance which is slowly and uniformly released.

Summary. The repeated oral administration of TACE to human subjects results in storage of considerable amounts of estrogenic material in the body fat. This material remains in the fat for prolonged periods following cessation of TACE therapy. Results of studies in a limited number of cases suggest that both duration of therapy and the size of the doses are contributing factors governing the level of estrogenic material in the fat.

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