IMPLANTATION and feeding of various synthetic and natural estrogenic hormones, especially diethylstilbestrol, to achieve improved efficiency of feed and better quality of carcass is a common practice among producers of livestock and poultry in this country. Androgenic agents have been used only experimentally to date. The preparations, dosages and techniques employed are regulated by the Food and Drug Administration. Despite their requirement that no detectable residue of estrogenic hormones be present in edible tissues of treated animals offered for sale, some individuals maintain that the use of these hormones should be banned entirely because they believe that controls are inadequate to insure proper usage, and that analytic methods are not sensitive enough to detect minute quantities of hormones, whose repeated ingestion even in trace amounts might prove harmful.

Fortunately, extensive data have been gathered on the physiologic effects of stilbestrol and other estrogenic agents, their therapeutic uses and toxicology. Also, the quantities of estrogenic residues in the tissues of treated animals have been determined.

Greatest concern has been expressed over effects of stilbestrol on reproductive function, on growth, and its possible carcinogenic properties. There is no doubt that stilbestrol can suppress ovulation in women if given in adequate amounts during the proper period of the menstrual cycle; and a relatively large dose (25 mg) may produce temporary impotence, but not sterility, in the male. These effects do not persist, however, when the dosage is discontinued, as the drug is destroyed and excreted in 3 or 4 days.

Relatively little is known about the specific effects of stilbestrol on children since its therapeutic use has concentrated on adults. In one series of young patients treated with 3 mg of stilbestrol daily for a week, no consequences more serious than slight nausea were observed. Unless there exists a placental barrier to stilbestrol and estrogens, it appears that these substances are harmless to the fetus and newborn infant, as extremely high levels of estrogen are characteristic of pregnant women, and no adverse effects were noted in the offspring in two studies of fairly large groups of women given enormous doses of stilbestrol throughout their pregnancies.*

* Recently evidence has appeared that masculinization of female fetuses may occur when stilbestrol is administered in large quantities to human females during pregnancy.
There is substantial evidence that estrogenic substances affect growth, but their action is obscure and authorities disagree on whether they stimulate or suppress skeletal development. Some believe that the result of continuous treatment with estrogens would depend upon the condition of the patient, ultimately bringing him closer to normal size.

Instances of cancer apparently caused by administration of stilbestrol have been reported in various experimental animals. However, attempts to produce cancers by this means have not been uniformly successful, and genetic and species differences undoubtedly exist. The evidence from humans given therapeutic amounts of stilbestrol for long periods is clouded by so many uncontrollable factors that it appears to have little significance.

Even if the claimed recorded cases of mammary cancer in men receiving estrogen therapy actually were caused by stilbestrol, this is an extremely small percentage of all the men and women who have taken stilbestrol for prolonged periods. Furthermore, the consequences of continuous therapy with stilbestrol would appear to bear little relationship to the ingestion of such minute traces of estrogens from "hormonized" meat animals as might conceivably escape detection by sensitive analytic methods, or even the possible occasional consumption of a much higher concentration due to an improperly placed hormone pellet.

Numerous investigators have analyzed the tissues of estrogen-treated poultry, cattle, lambs and pigs for residual hormone activity. A bioassay method, depending on the vaginal or uterine response of rats or mice to the treated tissues, generally is used. Although because of individual variation it is not precisely reproducible, the technique can be made sensitive to as little as 2 parts per billion of residual estrogen. In virtually every instance, even when deliberate overdoses of the hormones were administered, either no residual activity could be detected in the edible parts of "hormonized" animals, or the amounts were negligibly small.

Moreover, it has been demonstrated that tissues of cows slaughtered during pregnancy have far higher concentrations of natural estrogens than tissues of hormone-treated cattle. In addition, such common foods as potatoes, eggs, and milk as well as most commonly-used livestock feeds contain detectable amounts of natural estrogens.

Use of more than the permitted dosages of hormone in poultry and livestock is of no advantage, and feeds containing stilbestrol and the like are supplied by licensed manufacturers, so the possibility of deliberate or accidental over-dosage is remote. Even if an error should occur, stilbestrol is rapidly excreted, and in experiments in which up to 20 times the permitted daily dosage was fed to cattle for as long as 102 days, the residual estrogen in the tissues was still negligible.

Stilbestrol pellets, on the other hand, are absorbed quite slowly; usually several milligrams of stilbestrol remain at the time of slaughter of treated chickens. If properly implanted this pellet residue is discarded with the head and neck, but seizures of lots of poultry containing misplaced pellets have been reported by the Food and Drug Administration. This appears to be the only situation in which there is any likelihood of ingesting an appreciable quantity of estrogen from hormone-treated meat animals, and even here the probability of the same individual receiving such a large dose regularly enough to have any effect is remote.

Federal legislation now in force demands that the residue of estrogens remaining in carcasses destined for human consumption be zero. Since traces of diethylstilbestrol have been detected in the skin and liver, as well as in the neck, of treated chickens of market size and age, it is obvious that the technique for use of this synthetic estrogen will have to be re-evaluated. This problem is receiving scrutiny and study by appropri-
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ate federal agencies and one may safely assume that agricultural practice will be adjusted to meet current legal requirements.

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