rabbits could be divided into three immunologic groups: first, an immunologic superior ("strong") group, yielding precipitins of a titer of 1:10,000 or more; second, a group of immunologic defectives ("weak"), yielding titers of 1:500 or less; and a few animals occupying an intermediary (or "medium") group. Superior and defective groups were segregated for genetic study.

Several months later, after full convalescence from the first series of injections, the selected groups were bred. Young, born from such union were allowed to attain full adult size (three kilograms) before being tested for antibody production. Briefly summarized, all (100 per cent) of the young born of parents, both of which belonged to the "weak" group, were found to be immunologically defective. Not a single one of these young was able to produce antihuman precipitins of more than 1:500 titer. Young resulting from crossing one "strong" parent with a "weak" mate were 60 per cent immunologically "strong," producing antihuman precipitins of a titer of 1:10,000 or over. This percentage of superior (or "strong") offsprings was increased to 80 per cent by selecting both parents from the "strong" group. Only one atypical litter was an exception to this rule.

Whether or not selective breeding for several generations would increase the percentage of superior offsprings to 100 per cent has not been determined, although a 100 per cent immunologically superior strain of rabbits is predictable. The Polish immunologists quote evidence that the antiserums produced by the "strong" group are not only of exceptionally high titer, but are of superior specific avidity. If this is so, their selective breeding of superior donors of specific antiserums may have an important bearing on future therapeutic methods.

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SYNTHETIC ESTROGENIC HORMONE

Ten years ago Doisy in the United States, Butenandt in Germany, and Marrian in England, independently and almost simultaneously, reported that they had isolated the estrogenic hormone in crystalline form from the urine of pregnancy. During the following years, research by organic chemists revealed that this hormone is closely related to the sterols. Within a short time the constitution of three estrogenic substances was determined: (1) Estron with the empirical formula $C_{18}H_{22}O_2$; (2) Estriol, $C_{18}H_{24}O_3$; (3) Estradiol, $C_{18}H_{24}O_2$.

All these substances had the same biologic effect, producing estrus in the vaginal epithelium of ovariectomized rats or mice, in spite of the fact that they were, chemically, slightly different. After this experience, likewise as interesting for the chemist as for the biologist, the question arose whether it would be possible to synthetize substances with the same biological effect independent of the usual organic source, pregnancy urine.

Starting out with the cyclo-penteno-phenanthrene nucleus found in the natural hormone, English researchers synthetized a large number of chemical bodies and tested them for their estrogenic properties (Dodds and coworkers).[1,2] They succeeded in their efforts, and at the same time were able to prove that the phenanthrene nucleus was not essential for the estrogenic response. The substances first found, however, could not compete with the natural estrogens, since their estrogenic effect was far weaker.

Only recently (1938), Dodds[3] and coworkers could show that a derivative of the chemical substance 4:4 dihydroxystilbene (stilbestrol) produced even a stronger estrogenic effect in animals than the natural hormones.

Clinical trials with this synthetic estrogenic hormone have been carried out in Europe, and about twenty-five publications have appeared in the international literature. The indications in which the synthetic hormone was used were, of course, the same as those in which treatment with natural estrogens would have been advisable. The results obtained by the various clinicians have been surprisingly good so far. Particularly interesting seems the high efficiency of the synthetic hormone when taken in tablet form by mouth. Guldberg,[4,5] in Denmark, was able to produce menstruation in a castrated woman by injection of the synthetic hormone, followed by corpus luteum hormone.

Of course, as frequently happens with the introduction of a new drug, some unpleasant by-effects have been reported, consisting mainly of nausea and fatigue. Toxic changes in liver and adrenals have been demonstrated in animals by Loeser,[6] but only with extremely high doses.

Considering the early stage of development of this synthetic estrogenic hormone, one may expect that further work will lead to its improvement. Should the toxicity prove to be minimal, the potency maximal and the price reasonable (cheap production), this recently synthetized estrogenic hormone will, naturally, be a very valuable addition to the pharmacopeia. Clinical trials by qualified men in this country will doubtless show whether its value is really as high as previously described by European researchers and clinicians.

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1 Cook, Dodds, and Hewett: Nature, 131:56. London, 1933.
2 Cook and Dodds: *Ibid.*, 131:205, 1933.
3 Dodds, Golberg, Lawson, and Robinson: Nature, 141: 247. London, 1938.
4 Guldberg: Zentralbl. f. Gynäk., 2584, 1938.
5 Guldberg: Ugesk. f. laeger, 854, 1938.
6 Loeser: Klin. Wchnschr., 10:346, 1939.

If men gave three times as much attention as they now do to ventilation, ablution, and exercise in the open air, and only one-third as much to eating, luxury, and late hours, the number of doctors, dentists and apothecaries, and the amount of neuralgia, dyspepsia, gout, fever, and consumption, would be changed in a corresponding ratio.—J. F. Clerk.