ANTAGONISM OF VAGINAL ACTIONS OF OESTROGEN
BY PROGESTERONE AND OTHER STEROIDS

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SUMMARY

The inhibition of the vaginal action of oestradiol and several synthetic oestrogens by progesterone,
and the methyl testosterone and testosterone propionate have been studied quantitatively.
The action of the natural oestrogen is more easily inhibited than that of the synthetic oestrogens.

It is well known that the actions of oestrone and oestradiol on the vagina, i.e. pro-
liferation and cornification, can be inhibited by the simultaneous administration of progesterone, testosterone, and certain other steroids. The quantitative relations for this inhibition have been worked out by Robson [1938a,6].
The purpose of the present investigation was to determine to what extent the action of synthetic oestrogens can be inhibited, and whether the quantitative relations are similar to those obtained with natural oestrogens.

METHODS

The experiments were performed on ovariectomized mice. The oestrogens tested were oestradiol, stilboestrol, triphenyl iodo-ethylene, 7-methylbisdehydrodoisynolic acid and the methyl ether of αα-dimethyl-β-ethyl-allenolic acid. The amounts of the various oestrogens used were such as to give an approximately equivalent oestrogenic effect on the vagina.

Preliminary experiments showed that such effects were produced by the following doses of the oestrogens: oestradiol 0.1 µg., stilboestrol 0.2 µg., triphenyl iodo-ethylene 1 mg., doisynolic acid derivative 5 µg. and allenolic acid derivative 10 µg., when these substances were administered in solution in oil in four injections over a period of 48 hr. The antagonists used were progesterone, methyl testosterone and testosterone propionate.

The experiments were carried out on groups of five mice. In each experiment the following groups were used: (1) a group receiving only the oestrogen (the total dose being given in four injections on the morning and evening of two consecutive days); (2) a group receiving the oestrogen together with the antagonist. Each of these, i.e. the oestrogen and the antagonist, were given in solution in oil on the morning and evening of two consecutive days. The mice were smeared on the evening of the day following the last injection, on the morning and evening of the following day, and on the morning of the day after, i.e. four smears were taken altogether. The effect on the vagina was evaluated in a semi-quantitative manner according to the method de-
scribed by Robson [1938c].
RESULTS

The results are shown in Table 1. The extent of the antagonism produced is shown in a semi-quantitative manner (obtained by comparing the smears obtained in the groups of animals treated with oestrogen and with oestrogen and antagonist respectively). + + + + indicates that the mice had smears similar to those seen in dioestrus,

Table 1. Showing the degree of antagonism (0− + + + +) of the oestrogenic action on the vagina produced by the various antagonists

<table>
<thead>
<tr>
<th>Antagonist</th>
<th>Oestradiol 0-1 µg.</th>
<th>Stilboestrol 0-2 µg.</th>
<th>Doisynolic acid 5 µg.</th>
<th>Allenolic acid 10 µg.</th>
<th>Triphenyl iodo-ethylene 1 mg.</th>
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<td>0</td>
<td>(± slight increase)</td>
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<tr>
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<td>+ + to + + +</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>(± slight increase)</td>
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i.e. there was complete antagonism of the vaginal action of the oestrogen. It will be seen that the vaginal oestrogenic effects of all the oestrogens used can be antagonized.
to some extent by progesterone and methyl testosterone. Testosterone propionate, in a dose of 20 μg., antagonized the effect of oestradiol, but not that of any of the synthetic oestrogens used. It is thus clear that the effects of the natural oestrogen (oestradiol) are rather more easily antagonized by the substances used than that of the synthetic oestrogens.

There was an additional curious finding: though methyl testosterone, in 100 μg. doses, produced some inhibition of the action of the doisynolic and allenolic acid derivatives, 20 μg. methyl testosterone actually appeared to enhance the oestrogenic effect of these two synthetic oestrogens. The significance of this finding is not known.

Among the synthetic oestrogens the effect of stilboestrol and the doisynolic acid derivatives were antagonized to a rather greater extent than that of the allenolic acid derivative and of triphenyl iodo-ethylene.

It might be said, on looking at the formulae shown above, that the less the synthetic oestrogen resembles the natural substance, oestradiol, in chemical structure, the more difficult it is to antagonize its action on the vagina.

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REFERENCES