THE EFFECT OF AN OESTROGENIC STEROID ON THE SECONDARY IMMUNE RESPONSE UNDER DIFFERENT HORMONAL ENVIRONMENTS

By

Yasmin M. Thanavala, Shanta S. Rao
and A. N. Thakur

ABSTRACT

The effect of mestranol was studied on the secondary antibody response in mice under different hormonal environments. The results revealed that in the intact and ovariectomized animals treated with the oestrogen, the antibody response was of the parabolic type. In adrenalectomized mice, the administration of the steroid resulted in appreciably elevated levels of anti-tetanus antibodies. The response obtained was similar in animals receiving both the low and high doses of the oestrogen. Removal of both the ovaries and the adrenals resulted in marked increases in the antibody levels.

Thus mestranol exerts an enhancing effect on the secondary antibody response in mice. This enhancement is, however, modified and regulated by the endogenous ovarian and adrenal hormones.

The effect of mestranol on the primary antibody response, in an inbred strain of Swiss mice, to tetanus toxoid has already been reported (Rao et al. 1972). It is an established fact that the antibody response is potentiated after the injection of the second dose of an immunogen. It was therefore of interest to find out the effect of the mestranol administration, under different hormonal environments, on the secondary antibody response in mice to tetanus toxoid.
The materials and methods used were the same as those reported in the previous paper (Rao et al. 1972).

As before, the animals were divided into 4 groups, each consisting of a number of animals as indicated by the figures in brackets.

1. Intact animals (36)
2. Ovariectomized animals (30)
3. Adrenalectomized animals (30)
4. Ovariectomized + adrenalectomized animals (29).

Each of the above groups consisted of 3 subgroups:

a) Solvent group (sesame oil 0.1 ml/animal/day)
b) Low dose mestranol group (0.075 µg in 0.1 ml/animal/day)
c) High dose mestranol group (0.75 µg in 0.1 ml/animal/day).

Unlike the earlier experiments, in which only the primary immune response was studied, in these present experiments a second dose of 1.0 LF tetanus toxoid (simple solution) was injected into the hind foot pads 21 days after the 1st injection. The animals were weighed, anaesthetized and bled to death by cardiac puncture ten days after this second injection.

The sera were analysed for antibody concentrations according to the passive haem-agglutination test.

RESULTS

The results as can be observed in Table 1 indicate that in the intact animals, administration of the low dose of mestranol resulted in an increase in the geometric means of anti-tetanus antibody titers. No difference, however, was observed in animals fed with the high dose of mestranol when compared to the solvent treated animals.

The ovariectomized group of animals, treated with the low dose of mestranol, showed a significant increase in antibody levels as compared to the solvent treated ovariectomized mice. Antibody values were close to those observed in the solvent controls in the ovariectomized animals administered with the high dose of mestranol (Table 1). The antibody levels, in all three groups of ovariectomized animals (solvent, low dose and high dose) when compared to the corresponding groups of intact animals, showed lower geometric mean titers of anti-tetanus antibodies.

Adrenalectomy caused a marked change in the antibody response of the mestranol treated animals (Table 1). These adrenalectomized animals when compared to intact animals also showed elevated antibody levels (Table 2).

In the animals from which both the ovaries and adrenals were removed, treatment with both doses of mestranol gave rise to increased antibody levels (Table 1). All three groups of adrenalectomized + ovariectomized animals showed enormous increases in antibody levels when compared to the corresponding groups of intact animals (Table 2).
Table 1.
Comparisons within the groups.

<table>
<thead>
<tr>
<th></th>
<th>Solvent</th>
<th>Mestranol Low dose</th>
<th>Mestranol High dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intact</td>
<td>3.536</td>
<td>4.454 ( P &lt; 0.05 )</td>
<td>3.536 (N. S.)</td>
</tr>
<tr>
<td>Ovariectomized</td>
<td>2.500</td>
<td>4.353 ( P &lt; 0.05 )</td>
<td>2.680 (N. S.)</td>
</tr>
<tr>
<td>Adrenalectomized</td>
<td>8.204</td>
<td>11.230 ( P &lt; 0.05 )</td>
<td>11.340 ( P = 0.01 )</td>
</tr>
<tr>
<td>Ovariectomized + adrenalectomized</td>
<td>9.330</td>
<td>12.600 ( P &lt; 0.01 )</td>
<td>39.990 ( P &lt; 0.01 )</td>
</tr>
</tbody>
</table>

Values in brackets represent \( P \) values for experimental versus solvent.
N. S.: Not significant.
Antibody titers (IU/ml) calculated as geometric means.

Table 2.
Comparisons between the groups.

<table>
<thead>
<tr>
<th></th>
<th>Intact</th>
<th>Ovariectomized</th>
<th>Adrenalectomized</th>
<th>Ovariectomized + adrenalectomized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solvent</td>
<td>3.536</td>
<td>2.500 (N. S.)</td>
<td>8.204 (N. S.)</td>
<td>9.330 ( P &lt; 0.05 )</td>
</tr>
<tr>
<td>Mestranol Low dose</td>
<td>4.454</td>
<td>4.353 ( P &lt; 0.05 )</td>
<td>11.230 ( P &lt; 0.01 )</td>
<td>12.600 ( P &lt; 0.01 )</td>
</tr>
<tr>
<td>Mestranol High dose</td>
<td>3.536</td>
<td>2.680 (N. S.)</td>
<td>11.340 ( P &lt; 0.01 )</td>
<td>39.990 ( P &lt; 0.01 )</td>
</tr>
</tbody>
</table>

Values in brackets represent \( P \) values for operated versus intact.
N. S.: Not significant.
Antibody titers (IU/ml) calculated as geometric means.

DISCUSSION

Though considerable work has been reported in the literature on the effect of sex steroids on the course of various infections (Weitzner 1941; Von Haam & Rosenfeld 1942; Mankowski 1954; Broome & Lamming 1959; Nicol et al. 1964) no particular effort seems to have been made to study the effect of these hormones on the secondary antibody response.

The results of the present investigation have revealed that in the intact and ovariectomized animals treated with mestranol the secondary antibody response is of a parabolic type. This is in accordance with the observation of Weinstein.
(1939) who reported that small doses of oestrogens protect mice while large doses decrease their resistance to experimental anthrax.

Administration of mestranol to adrenalectomized animals resulted in enhancement of antibody levels well above control values. It was interesting to note, that unlike experiments with intact and ovariectomized animals, the administration of the high dose of mestranol did not lower the antibody response in this group to the level observed in the control animals. The antibody response was in fact maintained at the level observed in animals treated with the low dose of mestranol. Adrenal steroids are known to suppress the immune response (Také & Marine 1923; Char & Kelley 1962; Levine et al. 1962; Heim et al. 1966; Crunkhorn & Meacock 1971). The results of the present investigation using adrenalectomized animals, are in agreement with this concept. The antibody response was observed to become elevated in all the groups of adrenalectomized animals when compared to the corresponding groups of intact animals. The removal of the adrenal corticoids would account for the increased antibody synthesis.

In the groups of animals devoid of both the ovaries and the adrenals, the low as well as the high dose of mestranol induced marked elevation in antibody response when compared to a similar group of animals, receiving solvent alone. Thus, in these animals, the mestranol when given at the high dose did not interfere with the antibody production. Furthermore, striking increases were observed in the geometric mean titers of antibody levels in animals which were ovariectomized in addition to being adrenalectomized as compared to the intact animals.

Thus the results reveal, that the endogenous hormones have a decisive and pronounced effect on the secondary antibody response in the mouse.

ACKNOWLEDGMENTS

The authors gratefully acknowledge the gift of mestranol from N. V. Organon, Holland, and tetanus toxin from Dr. S. Srinivasa Rao, Assistant Director, Haffkine Institute, Bombay. It is a pleasure to thank Mr. J. Rodrigues for his technical assistance.

REFERENCES


Received on August 1st, 1972.