HORMONAL EFFECTS ON SEBACEOUS GLANDS IN THE WHITE RAT

III. EVIDENCE FOR THE PRESENCE OF A PITUITARY SEBACEOUS GLAND TROPIC FACTOR*

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In a previous paper (1) we reported that in ovariectomized mature white rats, pituitectomy results in sebaceous gland atrophy which cannot be counteracted by progesterone. Progesterone in similar rats without pituitectomy is a potent hyperplasia-inducing factor for sebaceous glands (1, 2). The sebaceous gland stimulating effect of testosterone in similar rats is, in parallel fashion to the progesterone effect, greatly reduced by pituitectomy although in this case not entirely abolished (1).

In the current report on our studies aimed at better understanding endocrine influences on sebaceous glands, we present evidence for the existence of a pituitary sebaceous gland tropic factor which probably will prove to be a hitherto unrecognized anterior pituitary hormone.

MATERIAL AND METHODS

Groups of five to ten similarly treated mature female Sprague-Dawley rats both ovariectomized and pituitectomized were used for testing the ability of various pituitary and analogous factors to restore sebaceous gland responsiveness to progesterone and testosterone stimulation. The technic for evaluating sebaceous gland volume responses in these animals to the various endocrine regimens used was as previously described (1, 2). Briefly, two biopsies were taken from symmetrical sites on the dorsal region of individual rats—one was taken before hormone administration and the other after daily administration by subcutaneous injections of various hormones for three weeks. After preparation of routine hematoxylin and eosin stained serial sections of uniform thickness, these were projected on a screen to provide one thousandfold magnification. Individual sebaceous gland alveoli were then followed throughout their entirety in the serial sections and tracings were made of their outlines as they appeared in consecutive sections. Cross-sectional areas were determined by planimetry. From the cross-sectional area and known thickness of the section the volume of that part of the gland in each section could be calculated. From these volumes, by addition, the approximate volume of the entire individual gland could be derived. Then, from the volumes of six randomly selected individual glands in each biopsy, the average sebaceous gland volume was calculated. The effect of particular hormone

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TABLE I

Types of standard hormones used and their dosage bases

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Commercial Preparation and Manufacturer</th>
<th>Dosage Basis</th>
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<tbody>
<tr>
<td>Progesterone (in sesame oil)</td>
<td>Progesterone, in Oil (Eli Lilly &amp; Co.)</td>
<td>Mgms.</td>
</tr>
<tr>
<td>Testosterone propionate (in sesame oil)</td>
<td>Oreton (Schering Corp.)</td>
<td>Mgms.</td>
</tr>
<tr>
<td>Prolactin</td>
<td>Luteotrophin (E. R. Squibb &amp; Sons)</td>
<td>International unit</td>
</tr>
<tr>
<td>ACTH</td>
<td>Purified Corticotropin-Gel (Wilson &amp; Co.)</td>
<td>U.S.P. unit</td>
</tr>
<tr>
<td>Pituitrin (oxytocin plus other posterior pituitary activities)</td>
<td>Pituitrin-S (Parke-Davis &amp; Co.)</td>
<td>International unit</td>
</tr>
<tr>
<td>Pitressin (vasopressin plus antidiuretic activities)</td>
<td>Pitressin (Parke-Davis &amp; Co.)</td>
<td>Pressor unit</td>
</tr>
<tr>
<td>Chorionic gonadotropin (from human pregnancy urine)</td>
<td>A.P.L. (Ayerst, McKenna &amp; Harrison, Ltd.)</td>
<td>International unit</td>
</tr>
<tr>
<td>Gonadotropin (from pregnant mare serum)</td>
<td>Gonadogen (Upjohn Co.)</td>
<td>Cortland-Nelson unit (equal to 20 international units)</td>
</tr>
<tr>
<td>Gonadotropin (mixture from pituitary and pregnancy urine sources)</td>
<td>Synapoidin (Parke-Davis &amp; Co.)</td>
<td>Synergy rat unit</td>
</tr>
</tbody>
</table>

regimens in individual animals could then be expressed as percent change in average sebaceous gland volume in the post-treatment biopsy specimen as compared with the pretreatment specimen. From the average volume changes in individual animals the average change in sebaceous gland volume within each group of five to ten similarly treated animals was determined. These group averages are indicated by bars in the figures along with the endocrine regimens that were used for each group.

The various standard hormone preparations used in these experiments are tabulated in Table I together with their sources and types of dosage units.

RESULTS AND DISCUSSION

Figure 1 summarizes the results of the first series of experiments from which it is evident that both ACTH and highly purified growth hormone (STH)* not only failed to prevent progressive sebaceous gland atrophy induced by pituitectomy but also failed to restore the loss of responsiveness of these glands to progesterone stimulation even though the high dose of 10 mgms. daily of the latter was given. The dosages of growth hormone and ACTH given were active doses as judged respectively from growth stimulation or gross adrenal hyperplasia in the animals over the experimental period. These two pituitary preparations of course also contain two other closely-linked potent hormone activities—namely,

* Kindly supplied by Dr. S. W. Hier of the Wilson Laboratories. A daily dose of 0.1 mgm. led to a weight increase of one gram daily in our experiments.
intermedin or melanocyte stimulating hormone activity associated with ACTH and diabetogenic activity associated with growth hormone.

In the next series of experiments summarized in Figure 2, several gonadotropic substances and posterior pituitary hormones were similarly tested for their ability to counteract the effects of pituitectomy on sebaceous glands. The first two sets of bar graphs illustrate 1. the stimulating effect of testosterone as well as that of progesterone on rat sebaceous glands and 2. the atrophy and loss or great reduction in responsiveness of these glands to steroid hormonal stimulation after pituitectomy. From the rest of the figure it can be seen that pituitrin and

![Graph showing changes in average sebaceous gland volume during the three week period of injections in first series of experiments.](image-url)
pitressin, prolactin, chorionic gonadotropin (APL), and purified follicle stimulating hormone (FSH)* (3) generally failed to counteract the sebaceous gland effects of pituitectomy whereas, by way of contrast, Synapoidin and Gonadogen were for the most part active in restoring sebaceous gland responsiveness to progesterone or testosterone stimulation. Synapoidin is a mixture of chorionic gonadotropin extracted from pregnancy urine and gonadotropins extracted from pituitaries while Gonadogen is a pregnant mare serum gonadotropin whose actions closely mimic those of pituitary gonadotropins.

In order to further characterize the nature of the pituitary sebaceous gland tropic factor present in Synapoidin and Gonadogen, representatives of Wilson and Co. were asked to prepare for us several crude fractions from hog anterior pituitaries which might contain the active principle. They kindly consented to do

* Kindly supplied by Dr. S. L. Steelman of the Armour Laboratories—dosage in terms of Armour units (4).
this and of several preparations submitted for testing, we found that two ("Pit. I" and "Pit. II") contained the sebaceous gland tropic factor. The gonadotropic activities of these two fractions in Cortland-Nelson units were 0.110 u/cc. for Pit. I and 0.036 u/cc. for Pit. II. The sebaceous gland tropic potencies of these fractions as compared with that of Gonadogen are shown in Figure 3. In this figure it should be noted that Pit. II, which had but little gonadotropic activity, nevertheless was more potent even than Gonadogen in restoring sebaceous gland responsiveness to progesterone. Thus, sebaceous gland tropic effect appears to vary independently of gonadotropic effect. Furthermore, pituitary fraction II

![Figure 3](image_url)

**Fig. 3.** Average sebaceous gland volume changes induced by pituitary fractions as compared with change produced by Gonadogen.
produced no gross effects of growth hormone, ACTH or thyrotropin in these experiments. Currently experiments are in progress to purify and further characterize the sebaceous gland tropic factor present in Pit. II. Details of its preparation and nature will be published later.

Although admittedly premature, several interesting speculations suggest themselves should these experiments be applicable to man. First, we would have explanations for the seborrhoeas associated with some types of midbrain damage if connected with pituitary stimulation, and could better understand the complexity of endocrine influences associated with the seborrhoea in acne vulgaris. And second, if it should be feasible, the administration of this pituitary factor together with progesterone in order to stimulate oily seborrhoea would promise therapeutic usefulness in conditions such as tinea capitis caused by *M. audouini*, asteatosis and perhaps other dermatoses complicated by dryness of the skin.

**SUMMARY**

In ovariecetomized mature white rats, pituitectomy results in sebaceous gland atrophy and loss or greatly diminished responsiveness of these glands to growth stimulation by progesterone and testosterone. Various pituitary and analogous factors were tested for their ability to counteract these effects of pituitectomy on sebaceous glands. Of these preparations, ACTH, growth hormone, follicle stimulating hormone, prolactin, pituitrin, pitressin, and chorionic gonadotropin all failed to restore sebaceous gland responsiveness to progesterone stimulation. However, pregnant mare serum gonadotropin and crude pituitary gonadotropin preparations did restore such sebaceous gland responsiveness. Evidence is further presented that this pituitary sebaceous gland tropic factor, although contained in some gonadotrophic fractions, varies independently of gonadotropic activity.

**REFERENCES**


**DISCUSSION**

Miss Nancy Lasher, B.A. (in closing): In the absence of more complete and controlled clinical data, the similarity of progesterone action in the rat and in man must necessarily be inferential. It must be kept in mind that all animals used in our experiments are ovariecetomized. This prevents the additional complica-
tion of pituitary-gonadal interaction which might tend toward inhibition of the progesterone effect in order to re-establish equilibrium.

The experiments clearly indicate the complexity of endocrine factors involved so that interpretation of pregnancy effects is difficult. The inhibition and production of estrogens—a depressant of sebaceous gland activity—is another complicating effect.

It is clear that there is a need for clinical experimentation on hypogonadal individuals before the role of progesterone can be truly evaluated. It is similar to the situation involving the role of testosterone before the work of Hamilton on its acne producing effects on eunuchs and eunuchoids.

Dr. Stephen Rothman (in closing): We did not give grams but milligrams, and in our first publication we have shown that the progesterone effect can be obtained with as little as one microgram daily. Indeed such dosage cannot be called astronomical.

To my knowledge, so far no studies were done to determine whether progesterone can elicit seborrhea in man. I believe it is highly improbable that different mammalian species would act differently in this respect.

It is highly controversial whether progesterone is beneficial in acne but even if it were, there is a possibility that large doses of progesterone suppresses the pituitary factor we are talking about.