

Letters to the Editor

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NOTES ON POINTS IN SOME OF THIS WEEK'S LETTERS APPEAR ON P. 1071.

CORRESPONDENTS ARE INVITED TO ATTACH SIMILAR SUMMARIES TO THEIR COMMUNICATIONS.

Multiple Activities of Anhydro-oxy-progesterone

THE introduction of anhydro-oxy-progesterone (pregneninolone, ethinyl-testosterone) by Inhoffen and Hohlweg¹ and Ruzicka, Hofmann and Meldahl², and the demonstration by the former authors of its high progesterone-like activity when given by mouth, opens up the possibility of an important advance in endocrine therapy (see, for example, Zondek and Rozin³); but its multiple biological properties also make the substance of considerable theoretical interest.

In our experience, anhydro-oxy-progesterone, tested as described by McPhail⁴, is equally active by mouth and by injection in producing progestational proliferation in rabbits. A total of 5 mgm. in propylene glycol produced the same average response, when given by either route, equal to that given by about 0.5 mgm. of progesterone injected in oil solution. In addition to this strictly progesterone-like activity, the compound, unlike progesterone, will cause growth of the uterus of the immature or ovariectomized rat or mouse without previous treatment with oestrone, that is, it shows metrotrophic activity similar to that of oestrone or testosterone. Thus, injection to the spayed rat causes a mixed oestrone-like and progesterone-like effect. The capacity to produce an increase in uterine weight is about the same whether the substance is given orally or by injection, but there is evidence that oral administration results in progestational proliferation of the endometrium less complicated by oestrous changes than does injection.

In addition to the rather generalized gynaecogenic property of causing growth of the uterus of the immature or ovariectomized animal, anhydro-oxy-progesterone also seems to be oestrogenic in the strict sense that it will cause cornification of the vaginal epithelium of the ovariectomized rat or mouse. Fully cornified vaginal smears were produced by the injection of 2-4 mgm. to spayed rats, and 0.8 mgm. to spayed mice. When the substance is given orally, however, its activity on the vagina is lower, since 4 mgm. produced only a little cornification in the presence of leucocytes in some rats, while 1.6 mgm. did not cornify the vagina of the mouse. Vaginal opening in the rat was also less frequent in animals receiving oral doses than in those receiving equal amounts by injection.

In the capon comb-growth test, anhydro-oxy-progesterone shows weak androgenic activity. Tested on groups of five Brown Leghorn capons, 30 mgm. by mouth produced an average increase in length plus height of 3.5 mm.; 30 mgm. by injection produced an increase of 4.6 mm., equal to that produced by about 0.5 mgm. (5 I.U.) of androsterone. By injection on to the comb, 0.15 mgm. produced an average increase of 2.2 mm.

Of the activities of anhydro-oxy-progesterone investigated, therefore, only its effects on the rodent vagina appear to be less when the substance is given orally than when it is given by injection. In addition to this remarkable activity by mouth, anhydro-oxy-progesterone seems to be the only compound so far described which possesses progesterone-like, metrotrophic, androgenic and oestrogenic properties.

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¹ Inhoffen, H. H., and Hohlweg, W., *Naturwiss.*, **28**, 96 (1938).

² Ruzicka, L., Hofmann, K., and Meldahl, H. F., *Helv. chim. Acta*, **21**, 372 (1938).

³ Zondek, B., and Rozin, S., *Lancet*, **i**, 504, No. 9 (1939).

⁴ McPhail, M. K., *J. Physiol.*, **82**, 145 (1934).

Nicotinic Acid Requirements of Insects: a Biological Test for Nicotinic Acid

THE importance of vitamin B for the growth and development of insects has been stressed by several investigators. But very little is known of the ingredients of the vitamin B complex which are actually required by the insects.

We have found that the moth *Galleria melonella* can be cultivated on a medium containing one part of yeast and two parts of wax. It was noted that purification of the wax and autoclaving of the yeast in a strongly alkaline solution at 130° during a lapse of time which is sufficient to destroy both the vitamins B₁ and B₂ (riboflavin) does not impair the normal development of the insect. However, its development is stopped if the autoclaved yeast is thoroughly washed with water and alcohol. Upon addition of the aqueous or alcohol yeast extract the development is resumed.

It follows from our experiments that nicotinic acid exerts the same favourable effect as the yeast extract. Nicotinic acid can thus be identified with the vitamin B-component which is indispensable for the development of *Galleria*. This does not certainly imply that vitamins B₁ and B₂ have no influence whatever¹. Since our experiments were not carried out in sterile conditions, the possibility remains open as to the production of these vitamins by some micro-organisms. Anyway, as a matter of fact, no development did take place in the absence of nicotinic acid.

Further experiments have shown that as small a dose as 5-10 γ nicotinic acid per 100 gm. of the medium lacking vitamin was sufficient to produce the above effect. After 8-10 days there were no living larvæ left in the medium lacking nicotinic acid, whereas big, well-developed larvæ were creeping about