

resulting from the comparison of our total induced activity with that of a preparation of radium-beryllium with known content of radium element) the yields are: < 0.2; 6.8; 19 mgm.

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¹ Bertl, Fürth, Obofil and Sitte, *NATURE*, **139**, 716 (1937).

Androgenic Activity of Ovarian Extracts

It is well known that oestrogenic activity may be shown by extracts of testes and by extracts of urine from the males of certain species. Conversely, androgenic activity can readily be demonstrated in the urine of normal women, and Hill and Gardner¹ have shown that, under certain conditions, the atrophic seminal vesicles of castrated mice can be restored by ovarian grafts. Further, since the comb of the domestic hen atrophies after ovariectomy and responds to male hormone but not to oestrone, its increase in size during the laying season presumably indicates production of androgenic substance by the active ovary.

So far, however, androgenic activity does not seem to have been demonstrated in ovarian extracts, possibly because much larger amounts of male hormone than of oestrone or oestradiol, in terms of crystalline substance, are required to evoke a significant biological reaction. By the use of Fussgänger's highly sensitive modification² of the capon test—direct unction of the comb with the extract—we have now been able to demonstrate androgenic activity in two crude alcohol-acetone-ether extracts of pig ovaries. The first extract was qualitatively tested on the combs of two bantam capons and produced growth (L + H) in five days of 11 mm. and 7 mm., a clear-cut response. The second, quantitatively tested on ten Leghorn capons by the application to each of a total of 0.125 c.c. of the oily extract over five days, produced an average growth of 4 mm., about the same as that given by the similar administration of 2.5 γ androsterone, or 1/40 I.U. The yield of extract was 3.9 gm. per kgm. of fresh tissue, so that the androgenic activity of pig ovaries would seem to be rather less than 1 I.U. per kgm. Suitable control tests with arachis oil solutions of oestrone, oestradiol and oestriol gave negative results, and it is likely therefore that the androgenic activity of the ovarian extracts was due to the presence of substances of the androsterone-testosterone group.

This result is of obvious significance in relation to the origin of the androgenic material in the normal human female. A number of observations suggest that the adrenals are one site of elaboration. Thus Reichstein³ has isolated an androgenic diketone from the adrenal, while, examined by the unction technique, a crude extract of horse adrenal was slightly androgenic, and a highly concentrated discard fraction of pig adrenals, kindly supplied by Dr. Reichstein, gave good growth. Further, Simpson, de Fremery and Macbeth⁴ have shown that very large amounts of androgenic substance may be present in the urine of women with virilism of adrenal origin, and Callow⁵ has isolated as much as 110 mgm. per litre of *trans*-

dehydroandrosterone from the urine of a female child with an adrenal tumour. Finally, in conjunction with Dr. Callow and Dr. Levy Simpson, it has recently been shown that considerable amounts of androgenic material may be found in the urine of ovariectomized women. Nevertheless, the presence of androgenic activity in ovarian extracts shows that the female gonad must also be considered as a possible source of at least a part of the androgenic material found in the normal human female.

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¹ Hill and Gardner, *Anat. Rec.*, **64**, 21 (1936).

² Fussgänger, *Medizin. u. Chem. Z.*, **2**, 194 (1934).

³ Reichstein, *Helv. chim. Acta*, **19**, 223 (1936).

⁴ Simpson, de Fremery and Macbeth, *Endocrinology*, **20**, 363 (1936).

⁵ Callow, *Chem. and Ind.*, **55**, 1030 (1936).

Inactivation of Vaccinia Virus by Ascorbic Acid and Glutathione

JUNGBLUT and his co-workers¹ have shown that the virus of poliomyelitis and diphtheria toxin were inactivated by ascorbic acid. One of us² has shown that addition of ascorbic acid to cultures of *C. diphtheriae* leads to production of relatively atoxic filtrates. Further studies on the nature of this interaction established a reasonable presumption that there was an oxido-reduction between the ascorbic acid and toxophore group of diphtheria toxin.

It occurred to us that if this is the type of reaction involved, other viruses might also be inactivated in the same manner. Experiments conducted with vaccinia virus gave positive results. Relatively small amounts of ascorbic acid inactivated many infective doses of the virus. Similar results were obtained also with glutathione, but this substance proved much less active than ascorbic acid in the same concentration.

The procedure employed was briefly as follows: Vaccinia virus was inoculated into a rabbit testicle. After 3–4 days the testicle was removed, ground with sand, suspended in saline and various decimal dilutions made in saline. These suspensions were mixed with equal volumes of freshly prepared solutions of ascorbic acid. The mixtures were incubated for a half-hour at 37° C. and then kept at icebox temperature. Untreated control suspensions were kept under the same conditions. At various intervals, 0.2 c.c. of the different mixtures were injected intracutaneously into rabbits. A summary of four different experiments is tabulated below:

Vitamin Conc.	Incubation Time	Infective doses inactivated
1:20,000	3 hours	10*
1:2,000	3 "	100
1:200	3 "	1,000
1:20,000	6 "	10
1:2,000	6 "	100
1:20,000	24 "	10
1:2,000	24 "	1,000*
1:200	24 "	10,000

* = incomplete neutralization, that is, delayed reaction and milder lesion. Full number = infective doses completely inactivated.

It will be noted that the ascorbic acid inactivates the virus and that the degree of inactivation depends on the concentration of the vitamin and the time interval during which it is allowed to act.