Letters to the Editor

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Gonadotropic Hormones and Cancer

INTEREST in the relations between the anterior pituitary and tumour growth has been considerably stimulated of late by the claim of Zondek, Zondek and Hartoch¹ that the growth rate of the Ehrlich carcinoma in mice is greatly retarded by the administration of large quantities of 'prolan'. In a subsequent paper, Gross² described previous experiments in which he found that administration of 'prolan' had no appreciable effect on the growth of a transplantable sarcoma beyond a doubtful acceleration.

We have carried out some preliminary experiments on the effect of pituitary and pregnancy urine extracts on the growth of the Jensen rat sarcoma implanted in rats of the hooded Reading stock. The tumour strain was kindly given by Dr. J. A. Murray, and we have to thank Dr. S. K. Kon of Reading, and Miss E. Gilroy of Edinburgh, for supplying the animals.

In a group of twenty-four rats, bovine anterior lobe extract—prepared by the ammonia method of Wiesner and Sheard³—was administered before and after tumour inoculation. The present state of the standardisation problem makes it impossible to give any reliable statements regarding the potency of the extract used, but 1.0 c.c. was equivalent to 1.0 gm. of fresh anterior lobe. The experimental animals received six subcutaneous injections of 0.5 c.c. each during the ten days prior to the tumour inoculation and fourteen doses in the fifteen days following. In two animals no tumour resulted; in two others the tumour may have taken, but if so, regression occurred very early; in the remaining animals the tumours grew well. Measurements were taken every three days; the animals were killed on the sixteenth day after implantation and the tumours were removed and weighed. The range of variation was 0–23 gm. if the negative cases are considered, and 4–23 gm. if only the positive cases are considered. If the figures obtained are compared with the standard figures observed in twenty-six animals under equivalent normal conditions (range of variation, 6–25 gm.) it is found that the growth-rate of the tumours in the injected animals differs but slightly from the 'standard' growth-rate. If the negative cases of the pituitary experiment are discarded for comparison of actual weights, it is found that the difference between the normal series and the pituitary series is negligible; the actual difference is 1.04 gm. with a probable error of 1.19.

In a second experiment employing twenty-four rats and conducted by exactly the same technique, we used a gonadotropic preparation of pregnancy urine obtained from a batch of the protein residue which is rejected at one stage when highly purified extracts are prepared by the method of Wiesner and Marshall⁴. Notwithstanding claims made in the literature, it is not possible in the present state of our knowledge to make any exact statement regard-

ing the potency of any extract. As an indication, however, it may be mentioned that in a control experiment it was found that about one two-thousandth of the total given to the tumour rats was sufficient to produce oestrus in rats aged 32 days.

After having received six doses of 0.5 c.c. of the extract during the ten days preceding implantation, and fourteen similar doses during the succeeding fifteen days, the animals were killed and the tumours removed and weighed on the sixteenth day. The tumour weights varied from 13 gm. to 33 gm., the average being 22.46 gm. Comparison with the standard series shows (a) that there is no difference in the incidence of successful implants, and (b) that there is an undoubtedly significant increase in the growth-rate of tumours in the animals treated with gonadotropic hormones from urine. The difference between the respective average weights of treated animals and controls is 8.29 gm. with a standard error of 1.63 gm. The difference of the means is thus 7.54 times the probable error.

This acceleration effect is in accordance with Gross's findings, and one might be inclined to regard the gonadotropic hormones as factors promoting tumour growth. Although their appearance in certain cases of malignancy might be interpreted from this point of view, extreme caution is advisable, and Zondek, Zondek and Hartoch have obtained contradictory results. It therefore seems advisable to refrain from any definite interpretation, but at present it appears that the views of Zondek, Zondek and Hartoch—implying that gonadotropic hormones are secreted in defence against the tumour—are not supported by any data save those supplied by these authors themselves.

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¹ H. Zondek, B. Zondek and W. Hartoch, *Klin. Woch.*, **11**, 1785; 1932.

² L. Gross, *Z. Krebsforsch.*, **38**, 289; 1933.

³ B. P. Wiesner and N. M. Sheard, "Maternal Behaviour in the Rat", Edinburgh, 1933.

⁴ B. P. Wiesner and P. G. Marshall, *Quart. J. Exp. Physiol.*, **21**, 147; 1932.

Accumulation of Ions by Living Cells

THERE appears to be a growing amount of misunderstanding about the different hypotheses so far offered in the endeavour to account for the accumulation of ions by living cells. As an example I quote from a recent paper by Asprey¹: "It is noteworthy that Briggs² has advanced a theory, thermodynamically sound, showing how the accumulation of solutes in the cells of *Valonia* and *Nitella* can be explained . . ." This not only affirms the adequacy of Briggs's explanation, but also accepts his supposed proof that previously proposed theories are thermodynamically unsound. Neither proposition is correct.

Briggs argues that the ionic exchange hypothesis proposed by me³ under the title: "The Accumulation of Ions in Living Cells—a Non-Equilibrium Condition", is invalid because *at equilibrium* it would not account for the accumulation of ions. Argument