SPECIAL ARTICLES

ANDROGENS AND TUMOR GROWTH

THE observation of Murray[1] that male mice bearing ovarian grafts developed spontaneous mammary tumors, although normal males do not, and the observation of Lacassagne[2] that the same effect could be produced in males by means of injected estrogens suggested a possible antagonism between male and female sex hormones as regards their carcinogenic properties.[3] Accordingly, in the fall of 1935 experiments were begun on the effects of urinary androgens on the growth and metastasis of the Brown-Pearce epithelioma of the rabbit. Preliminary observations having proved encouraging the experiments have continued to the present, employing over 300 rabbits. In one paper[4] now in press the results with several chemically pure androgens, one estrogen and androgens extracted from human urine are presented in detail. In another[5] some further evidence is presented of the opposite effects on growth of the most active androgen and the most active estrogen available.

Urinary-extract androgens and chemically pure testosterone propionate, both in small doses, quite definitely inhibited the growth of the primary Brown-Pearce tumor implanted in the testicle. For a study of secondary growths (metastasis) four degrees of malignancy were recognized: (1) no secondary growths; (2) few, *i.e.*, less than four scattered small nodules; (3) several, *i.e.*, 3 to 6 sites with multiple nodules; and (4) extensive, *i.e.*, diffuse involvement of 6 or more sites. A summary of the longer-period experiments, running from 89 to 112 days, is given in Table 1. The androgens were injected daily in olive or sesame oil. Controls with and without oil alone showed no material difference in the spread of secondary growths. The average of these two control groups is taken as the unmolested incidence of such growths when the tumor is of average malignancy. Estradiol monobenzoate did not change the percentage of animals having any degree of metastasis or none. The urinary androgens, however, did very positively shift the incidence from the high side of the scale toward the low side. Still greater was the effect of testosterone propionate (10 to 50 I.U. daily) in the same direction. Instead of twenty-nine per cent. (average of the two control groups) having extensive metastases there were none in the group receiving this most potent androgen.

TABLE 1

LONG PERIOD EXPERIMENTS

	No. of rabbits	Degree of Metastases: Extensive No.	Extensive Per cent.	Several No.	Several Per cent.	Few No.	Few Per cent.	None No.	None Per cent.
Control no oil.	25	8	32	7	28	2	8	8	32
Control oil only	35	9	25.8	8	22.8	7	20	11	31.4
Estradiol Monobenzoate	18	5	27.8	5	27.8	3	16.6	5	27.8
Urinary androgens 4.6 to 216 I.U.	55	4	7.3 (−21)	14	25.4 (−1)	13	23.6 (+10)	24	43.6 (+12)
Testosterone 37 & 39 I.U. .	22	9	40.9 (+12)	7	31.8 (+5)	2	9.1 (−5)	4	18.2 (−14)
Testosterone Propionate 10 & 50 I.U...	20	0	0.0	2	10.0	7	35.0	11	55
Total	175		(2−29)		(−16)		(+21)		(+23)

The figures in parentheses represent the changes in percentage from an average of the two control groups. The shift to the low side of the scale of metastases caused by urinary androgens and by testosterone propionate is impressive. The opposite effect of testosterone is not so great.

Conversely, instead of 32 per cent. having no metastases as in the controls there were 55 per cent. having none. Curiously enough, chemically pure testosterone had a moderate effect in the opposite direction.

In experiments which ran to only 60–62 days pure androsterone and dehydroandrosterone, in doses comparable to those used for most of the urinary androgen injections, had no material effect on either the rate of primary growth or the incidence of secondary growths. It is therefore probable that the urinary extracts contain one or more steroids, extractable by the same method as the known androgens, which are responsible for the inhibiting effects noted. Fractionation of such extracts has already been accomplished, and the chemically different groups will be tried soon for anti-carcinogenic properties.

In the short-period experiments also testosterone propionate in doses of 100 and 250 I.U. daily seemed to exacerbate the metastatic process. Dosage therefore is of great importance.

J. R. MURLIN
C. D. KOCHAKIAN
C. L. SPURR
R. A. HARVEY

UNIVERSITY OF ROCHESTER

[1] W. S. Murray, *Jour. Cancer Res.*, 12: 18, 1928.
[2] A. Lacassagne, *Compt. Rend. Acad. Sci.*, 195: 630, 1932.
[3] I. T. Nathanson and H. B. Andervont, *Proc. Soc. Exp. Biol. and Med.*, 40: 421, 1939.
[4] J. R. Murlin, C. D. Kochakian, C. L. Spurr and R. A. Harvey, *Arch. Path.*, in press.
[5] C. D. Kochakian, *Endocrinology*, in press.

EASE OF BODY HEAT LOSS AND RESISTANCE TO INFECTION

WE wish here briefly to report a rather striking dominance exercised over resistance to infection by the ease with which body heat can be lost. White mice