THE PERSISTENCE OF OESTROGEN PRODUCTION
AFTER ENDOCRINE ABLATION

By

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This paper is a summary of work on the excretion of oestrogens by patients with mammary cancer treated by endocrine ablation. The detailed results are awaiting publication elsewhere.

Huggins (1954) has suggested three factors to account for the failure of oophorectomy and adrenalectomy to cause regression in some cases of metastatic mammary cancer:

i. the removal of the glands may not suppress the production of oestrogenic hormones;
ii. a pituitary factor may be involved;
iii. the cancer may not be hormone sensitive.

We have obtained evidence that oophorectomy and adrenalectomy do not necessarily abolish oestrogen production. Similarly, the production of oestrogen may continue after removal of the pituitary gland.

Oestrone, oestradiol-17β and oestriol have been estimated in the urine of patients with recurrent mammary cancer undergoing the above operations (Brown, 1955).

Removal of the ovaries from menstruating women markedly reduced, but did not abolish oestrogen production. All cases so far examined after a surgical or natural menopause were found to be excreting oestrogen. The mean age of the fourteen patients in this group was 47 years. The mean amounts of oestrogen excreted were:

\[
\begin{align*}
\text{oestrone} & : 2.2 \mu g. \\
\text{oestradiol-17β} & : 1.2 \mu g. \\
\text{oestriol} & : 3.8 \mu g.
\end{align*}
\]

There was considerable day to day variation and occasionally patients excreted four or five times as much oestrogen as the mean figures given above. Conversely, in some specimens of urine, no oestrogen could be detected. In
those post-menopausal women followed before and after oophorectomy the levels were generally unchanged by the operation.

In ten patients it was found that bilateral adrenalectomy (performed some months after oophorectomy) did not permanently reduce oestrogen excretion to zero. The amounts of oestrogen measured varied from day to day and from patient to patient. Oestrone values ranged from 0 to 7 \( \mu g. \); oestradiol-17\( \beta \) from 0 to 10 \( \mu g. \); oestriol from 0 to 17 \( \mu g. \)/24 hours, and the means for this group have little value.

A high proportion of estimations showed no detectable oestrogen in the urine. In only two patients was a consistent absence of oestrogen found during the period under review.

In some of these cases additional evidence for the presence or absence of oestrogen has been obtained by parallel biological and chemical assays. Struthers (1956) found oestrogen-positive vaginal smears in six of seven patients after adrenalectomy.

A second series of patients has been studied after combined oophorectomy and adrenalectomy. Preliminary results indicated that two of eight patients were not excreting detectable amounts of oestrogen. In the remaining six patients very small amounts of oestrogen (1 to 3 \( \mu g. \)) were found intermittently. No tests have been carried out to determine the completeness of adrenalectomy.

Oestrogen estimations before and after hypophysectomy in seven out of nine oophorectomised or post-menopausal women, all with intact adrenal glands, showed an increased production of oestrogen in two cases; no change in three; a slight fall in one, and no oestrogen (after operation) in two. In the remaining case no preoperative specimens of urine were obtained. Oestrogen was found in 26 of 29 urine specimens examined between the 36th and 48th weeks after hypophysectomy. In a man with breast cancer small amounts of oestrogen were found in the urine after castration and hypophysectomy.

Additional evidence for the specificity and accuracy of the chemical analyses when applied to urine from hypophysectomised patients is desirable and the problem is under investigation.

The finding that many patients continue to excrete oestrogen after various forms of endocrine ablation was unexpected. It is apparent that the surgical removal of the gonads, adrenals, or pituitary gland does not necessarily abolish oestrogen excretion and that the hypothesis of oestrogen independence cannot be invoked, when these operations fail to produce a regression, until oestrogen estimations have been carried out.

REFERENCES

