the lateral anlage became detached before fusion and that subsequent hyperplasia produced a benign tumour. For many years this theory was accepted, though a few authorities believed that lateral aberrant thyroid tissue represented a secondary deposit from a carcinoma in the homolateral lobe of the thyroid gland (Low, 1903). Crile (1939) thought the condition benign, but later changed his mind and stated that in all his 21 cases a primary carcinoma had been found in the thyroid (Crile, 1947).

It has been suggested that a lateral aberrant thyroid could be either a tumour arising in a laterally placed accessory thyroid or an epithelial inclusion in a lymph node similar to an adenolymphoma of the parotid gland, but it is now agreed that the condition is invariably a secondary carcinoma. The primary is often very small and cannot be detected clinically, but it can always be found by careful examination of the thyroid after surgical removal. The growth is usually papillary and often cystic; it is slow-growing and of a relatively low degree of malignancy. The thyroid often shows abnormal lymphocytic infiltration and areas of calcification. The six cases reported here confirm all of these points. Five patients presented with swellings in the side of the neck which biopsy showed to consist of papillary thyroid tissue. In Case 1 similar tissue was found in a scalene-node biopsy, though no lumps were palpable clinically. All the cases were found to have thyroid carcinomas. The primary growth is usually in the homolateral lobe of the thyroid, but small foci of carcinomatous tissue are quite often found in the opposite lobe (Cases 1 and 3).

The cases reported above have been treated by total thyroidectomy followed by radioactive iodine therapy for the distant metastases. All the patients were subsequently given desiccated thyroid by mouth. Dunhill (1937) described two cases of thyroid carcinoma in young people in whom recurrent growths disappeared on treatment with desiccated thyroid, and it has since been shown that many thyroid carcinomas are hormone-dependent (Crile, 1957). If a patient becomes hypothyroid after treatment for cancer of the thyroid an excess of thyroid-stimulating hormone is produced by the pituitary, and this may stimulate the growth of the carcinoma. It is therefore important that all cases should be given adequate thyroid replacement therapy after thyroidectomy or treatment with radioactive iodine to suppress the production of thyroid-stimulating hormone.

This type of thyroid carcinoma can occur at any age, but it is important to note that it is often found relatively early in life. The age of onset in our cases ranged from 13 to 42 years, but cases have been found in children even younger. The secondary deposits are usually in the related lymph nodes and the growth may spread behind the carotid sheath, involving the recurrent laryngeal nerve. Metastases in the lungs are not uncommon, as in our Cases 1 and 5. Case 1 had received *x*-ray treatment to the thymus gland in infancy, and it has been stated (Winship and Rosvoll, 1961) that a similar history can be obtained in 75–80% of cases of childhood cancer of the thyroid. It is interesting to note that Cases 1 and 5 were thought to be possible cases of sarcoidosis on account of the lung shadows, and Case 5 had been treated previously as nodular tuberculosis of the lungs. Winship and Rosvoll (1961) mention five cases which had been treated as tuberculosis.

Summary

Papillary thyroid tissue in the side of the neck is always a secondary deposit from a thyroid carcinoma, and the term lateral aberrant thyroid can be abandoned. Six cases of this condition, which often occurs in young people, are described. Distant metastases, particularly in the lungs, occur in some cases, but the prognosis is good. Clinically, a diagnosis of pulmonary tuberculosis or sarcoidosis may be made (Cases 1 and 5). After surgical removal of the thyroid or treatment with radioactive iodine it is essential to give full doses of thyroid to prevent the spread of hormone-dependent growths.

Our thanks are due to Dr. H. G. McGregor for permission to publish Cases 1, 2, and 3, and to Mr. P. A. Lane Roberts for Cases 4 and 6; Case 5 is under the care of Mr. Keith Powell.

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Preliminary Communications

Stimulation of Mammary Cancer by Prolactin and the Clinical Response to Hypophysectomy

Hypophysectomy causes objective remission in nearly half the patients with advanced mammary cancer in whom it is undertaken. It does so, presumably, by removing the hormones which support the growth of the tumour. These include follicle-stimulating hormone (which controls the secretion of ovarian oestrogen) and corticotrophin (which controls that of adrenal oestrogen). The roles of growth hormone and of prolactin (mammotrophin) in mammary cancer are uncertain, although they are known to support the development and function of the normal breast.

The fact that the results of hypophysectomy are slightly better than those of adrenalectomy (Atkins *et al.*, 1960) suggests that these or other unknown pituitary factors may be important. Some workers (Pearson and Ray, 1959) have reported that growth hormone stimulates tumour growth, but others (Lipsett and Bergenstal, 1960) have not found any such effect. There is little evidence that prolactin supports the growth of mammary cancer. Hadfield (1957) reported that prolactin was detected in the urine of three patients who subsequently responded favourably to hypophysectomy but not in that of four patients who failed to do so. Others (Baron *et al.*, 1958) have not found any such association. Others again (Segaloff *et al.*, 1951, 1953, 1954) have been unable to find any consistent relationship between the excretion of prolactin and the clinical response to various types of endocrine therapy. Lipsett and Bergenstal (1960) reported that prolactin of ovine origin did not increase the urinary excretion of calcium in patients with metastatic breast cancer.

The purpose of this investigation, which was undertaken between 1958 and 1961, was to discover whether or not ovine prolactin injected into patients with osseous metastases from breast cancer increased the excretion of calcium in the urine. A positive response could be taken as indirect evidence that the metastases had been stimulated (Pearson *et al.*, 1952; Emerson and Jessiman, 1956), and might form the basis of a test for the selection of patients suitable for treatment by hypophysectomy.

METHODS

Nineteen women were studied. Ten were patients about to undergo hypophysectomy for advanced mammary cancer with osseous metastases and nine were control subjects of similar age and without evidence of metabolic or bone disease. They were placed on diets containing 250 mg. of calcium a day for seven days and spent most of their time in bed. Twenty-four-hour collections of urine, but not of faeces, were made from the third to the seventh day. Intramuscular injections of ovine prolactin ("panlitar"), 500 international units a day, were given on days 5, 6, and 7. The calcium content of each 24-hour specimen of urine was estimated by the flame photometer method.

The subsequent clinical response of each patient to hypophysectomy was assessed as "objective remission," "subjective improvement," or "no response" (McCalister *et al.*, 1961).

RESULTS

The mean daily urinary excretion of calcium on days 3 and 4 was regarded as the "basal" level, and the mean of days 5, 6, and 7 as the "stimulated" level. The "stimulated" minus the "basal" level indicated the effect (if any) of prolactin. The results are shown in the Table. The mean daily change in excretion (to the nearest whole number) of the control subjects was +23 mg. and that of all the cancer patients +47 mg. These means are not significantly different (P>0.05). However, the mean of the four cancer patients who failed to respond to hypophysectomy was only −8 mg., while that of the six who did benefit was +84 mg. These means are different (P<0.01) and the ranges do not overlap, although with larger series they would almost certainly do so.

The mean increase in the cancer patients who benefited was greater (P<0.01) than that of the controls, while that of the patients who failed to respond was less, though not significantly so (P>0.05).

Change in Mean Daily Urinary Excretion of Calcium ("Stimulated" Minus "Basal" Level) in mg. per 24 Hours

	Control Subjects	Cancer Patients. Response to Hypophysectomy	
	A	None B	Favourable C
	−19	−27	19
	−6	−16	40
	3	−2	62*
	22	12	113
	22		128
	29		140
	31		
	58		
	65		
No. of subjects ..	9	4	6
Mean (mg.) ..	+22·8	−8·2	+83·7
Standard deviation (mg.)	27·6	16·9	50·1
t	2·48	0·97	4·09
D.F.	8	3	5
P	0·05>P>0·02	0·5>P>0·4	0·01>P>0·001

Comparisons between Group Means

Comparison	Diff. mg.	t	D.F.	P
Cancer patients with no response *v.* favourable response (B–C) ..	−91·9	3·50	8	0·01>P>0·001
Controls *v.* cancer patients with favourable response (C–A) ..	+60·9	3·04	13	0·01>P>0·001
Controls *v.* cancer patients with no response (B–A)	−31·0	2·18	11	0·1>P>0·05

* This patient had subjective improvement (remaining five in group C had objective remission).

DISCUSSION

These results are consistent with the hypothesis that prolactin stimulates the growth of cancer of the breast in some subjects and that this may be the reason for the slight superiority of hypophysectomy over adrenalectomy as a therapeutic procedure. The finding that prolactin increases the urinary excretion of calcium in normal women was unexpected, and there is no obvious explanation for it. Moreover, it complicates the development of a test for the selection of patients for hypophysectomy. Analysis of a larger series of tests will be necessary before precise criteria can be established.

There is no obvious reason for the difference between these findings and those of Lipsett and Bergenstal (1960).

SUMMARY

Injections of ovine prolactin increased the urinary excretion of calcium in normal women. The increase was greater in patients with osseous metastases from breast cancer who subsequently responded favourably to hypophysectomy, but not in those who failed to respond. It is suggested that prolactin may stimulate the growth of breast cancer and that the stimulation of calcium excretion might form the basis of a test for the selection of patients for hypophysectomy.

A. McCalister held the Calvert and Purce Research Fellowships of the Royal Victoria Hospital, Belfast. We thank the management committee of the Royal Victoria Hospital and the Northern Ireland Hospitals Authority for financial assistance; Drs. G. J. A. Edelstyn and J. T. Ward and Sisters K. Speers and S. Lowry for their help; Miss K. Acheson for the special diets; and Mr. D. W. Neill for the urinary calcium estimations. We also thank Professor E. A. Cheeseman for his advice about the statistical analysis.

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