surgery. Unfortunately, few upper abdominal cases were encountered, and in these the muscular relaxation was not always perfect. The fault here may well have been due to our inexperience in the use of this new drug.

Fluothane causes a slowing of the pulse rate and a fall in blood pressure in most instances, but these do not appear to be harmful. In fact, the hypotension has often been appreciated by the surgeon, who has remarked on the dry operating field. Excessive falls in blood pressure or pulse rate can quickly be treated by the injection of atropine or methyl amphetamine, or the administration of ether.

The greatest disadvantage exhibited by fluothane is the depression of respiration which occurs not infrequently and may be sufficient to cause cyanosis and CO_2 retention. These undesirable features may be overcome by assisting or controlling respiration, which will also enable greater depths of anaesthesia to be obtained and thereby increase the scope of this agent.

In our opinion, this disadvantage is great enough to warrant limiting the use of the agent to all but skilled anaesthetists until more is known about its properties. It is possible that the disturbances of respiration which we encountered can be avoided by refinements in technique. If this is so, we believe that fluothane may become a valuable anaesthetic agent with a wide variety of uses. By virtue of its non-flammability and the simple method by which it can be administered, it could then attract the general practitioner for use in minor operations, provided he is equipped to treat the respiratory depression which may be encountered. Because of its flexibility it may be preferable to trichlorethylene except in respect of its analgesic properties. Indeed, with the high cardiac safety factor which has been suggested (Johnstone, 1956) fluothane compares advantageously with chloroform.

The pleasant and rapid induction is of particular value in children. A smooth change-over to ether can be effected if required, but when used as the sole anaesthetic agent it provides uniformly good muscular relaxation.

We wish to express our gratitude to Imperial Chemical Industries for the supplies of fluothane; to Dr. H. G. Epstein for his willing help and assistance in matters relating to the inhalers; and to Sir Robert Macintosh for his encouragement and advice.

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The General Council of the Press, at its meeting on October 17, considered a complaint from the Town Clerk of Ayr against the *Sunday Mail* of Glasgow in respect of an article about a visit to the Ayr Welfare Home and Hospital. The ground of the complaint was that the article would create a false impression of the institution. The editor had refused to publish any withdrawal of the allegations and criticism because he was satisfied that the article was fair comment on a matter of public importance. The Council expressed the view that the *Sunday Mail* had approached the matter in a responsible manner and held that the article was fair comment on a matter of public interest.

THE PHYSIOLOGICAL CASTRATION SYNDROME IN BREAST CANCER

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The treatment of metastatic breast cancer is still rather empirical. It can be put finally on a scientific basis only when specific tests for the various factors which influence the growth of breast cancer can be easily performed. At present, however, clinical observation of these cases under treatment can yield valuable information on the course of the disease.

This paper describes clinical observations on a series of cases of metastatic breast cancer treated by a variety of methods. An overall picture of the course of the disease is available, as they are for the most part completed cases.

Introduction

Scowen (1955), in his Langdon-Brown lecture at the Royal College of Physicians in 1955, showed from his experience that the occurrence, either naturally or artificially, of the menopausal state was one of the main factors in regression of tumour growth. This state is manifested by a fall in oestrogen production and change of function of the anterior lobe of the pituitary with a great rise in gonadotrophin activity. It was suggested that the regression probably resulted from a combination of these circumstances rather than a simple oestrogen withdrawal, and that the conception of simple oestrogen dependence could not be fully substantiated.

At some time, from a matter of months to five years, after the menopause the oestrogen level rose and the gonadotrophin fell, giving a pattern similar to the pre-menopausal state. At this stage progress of the growth of metastatic breast cancer occurred, as it did before the menopause. The induction of a further menopausal state by adrenalectomy at this time caused a further regression of the growth.

This sequence of changes is summarized by the accompanying diagram (Scowen, 1955) which shows the classical effect

Diagram showing the commonest menopausal pattern induced by castration or occurring naturally. A further follow-up of this shows a reversal to the pre-menopausal state.

of a castration or the menopause, followed later by a reversal to the pre-menopausal state but without menstrual bleeding. Although true for the majority of cases, there were a few patients who did not follow this pattern.

All the patients in our series developed a carcinoma in the pre-menopausal period. It has been shown by Clemmesen (1948), Clemmesen and Busk (1949), and Anderson *et al.* (1950) that there are two peaks of incidence in breast cancer. They occur roughly in the five-year periods before and after the menopause. It would seem that the fall in incidence of breast cancer at the menopause occurs with the consequent drop in oestrogenic activity at this time. Of course this can influence only those carcinomata which are primarily hormone-dependent, and so generally affects only about 45% of the patients.

In an effort to enhance the results of local treatment by the natural but temporarily beneficial effects of the menopause, radical mastectomy combined with the removal of the ovaries has been tried (Taylor, 1932; Smith and Smith, 1953) in pre-menopausal women. Comparison of these cases with those treated only by radical mastectomy showed that oophorectomy lowers the incidence of metastases developing in the 3-5 years' post-operative period.

Huggins (1954) has shown from an analysis of his patients treated by adrenalectomy that the chance of regression is proportional to the mastectomy-adrenalectomy interval. Where this interval was five years the chance was 60%.

These observations fit in very well with the histories of patients with breast cancer and explain the variability of the progress of the disease.

Present Investigation

Table I summarizes the histories of 19 hormone-dependent tumours treated by removal of ovaries or adrenals, or both.

TABLE I.—*Oestrogen-dependent Tumours*

Case No.	Interval before Menopause		Progress of Secondaries after Menopause or Castration	Duration of Post-menopausal Regression Yrs. Mths.	After Adrenalectomy Secondaries Regressed for Yrs. Mths.	
	Primary Treated Yrs. Mths.	Secondaries Appeared Yrs. Mths.				
1	2 4	7	Regression (C)	3	5	Dead
2	10	3	" (M)	2 6	7	Dead
3	None	1	" (M)	1 1	10	A/W
4	11	3	" (M)	1	11	A/W
5	9	6	" (M)	3 6	8	Dead
6	2 6	9	" (C)	3 9	1 2	A/W
7	2	6	" (M)	1	1	A/W
8	4 2	11	" (C)	4	9	A/W
9	7	2	" (C)	2	6	A/W
10	3 6	1	" (M)	3	8	A/W
11	1	9	" (M)	1 7	1 6	Dead
12	3 8	1 6	" (C)	1 7	4	A/W
13	3	3	" (M)	1 3	2	Dead
14	10	2	" (M)	9	9	Dead
15	1 6	6	" (C)	3	7	A/W
16	1 3	1 3	" (C)	3	5	A/W
17	6	5	" (M)	2	4	A/W
18	10	2	" (M)	4	3	A/W
19	4 2	7	" (C)	4	6	Dead

C=Surgical castration. M=Menopause. A/W=Alive and well.

In order to make the interpretation of the tables clear, Case 1 from Table I will be taken as an example. It shows that the primary growth was treated two years and four months before the menopause. Secondaries appeared seven months before the menopause, which in this case was produced artificially by castration and caused a regression of the secondaries for a further three months; a further regression occurred for five months after adrenalectomy. The patient is now dead.

The time of appearance of the various steps in the history of the cancer process in the patient is related in years to the menopause. This is done rather than giving the patient's age in years, as there is so much variation of the time at which the menopause occurs.

The time of the menopause was obtained from the patient's history. In those which were considerably post-menopausal a single date was given when the periods ceased, and this time was used as the date of the menopause. In the younger ones, however, the usual menopausal history of an episode protracted over some months was given. In these cases the end of that time was taken as the date of the menopause.

The case histories seem to show the following common features: (1) Regression of metastases with the menopause or castration. (2) Reactivation of metastases, from a matter of months up to five years later, which can be controlled by adrenalectomy. In addition, stilboestrol administration sometimes aggravated metastatic growth. If it does so this suggests that a response is likely to be obtained from the removal of ovaries or adrenals.

TABLE II.—*Oestrogen-independent Tumours*

Case No.	Interval before Menopause		Progress of Secondaries after Menopause	Post Menopausal Regression	Progress of Secondaries after Adrenalectomy	
	Primary Treated Yrs. Mths.	Secondaries Appeared Yrs. Mths.				
20	2 7	1 3	No effect (C)	None	No effect	Dead 2/12 after Adx.
21	—	9	" (C)	"	"	Dead 4/12 after Adx.
22	7	5	" (C)	"	"	Dead 3/12 after Adx.
23	1 9	1 2	" (C)	"	"	Dead 7/12 after Adx.
24	1 3	4	" (C)	"	"	Dead 11/12 after Adx.
25	2	6	" (M)	"	"	A/S 4/12 after Adx.
26	3	3	" (M)	"	"	Dead 6/12 after Adx.
27	2 8	7	" (M)	"	"	Dead 11/12 after Adx.
28	3 11	1	" (C)	"	"	Dead 5/12 after Adx.
29	1 10	7	" (C)	"	"	Dead 3/12 after Adx.
30	8	3	" (C)	"	"	A/S 6/12 after Adx.

A/S=Alive with active secondaries. Adx.=Adrenalectomy.

TABLE III.—*Cases With Regression on Stilboestrol Therapy*

Case No.	Interval after Menopause		Results
	Primary Treated Years	Secondaries Appeared Years	
31	9	13	Complete regression for 5 yrs. Now A/W.
32	5	14	Regression for 2 yrs. then reactivation.
33	19	20	Regression of skin secondaries for 2 yrs. then reactivation.
34	8	9	Regression for 2 yrs. followed by reactivation.
35	10	18	Regression for 2 yrs. Now A/W.
36	12	13½	" " 1 2/12. Now A/W.
37	14	26	" " 1½ yrs. Now A/W.

Table II summarizes the histories of eleven hormone-independent tumours. Here again the following common features were present: (1) No effect on metastases with the menopause or castration. (2) No effect obtained by hormone addition or deprivation. (3) Rapid and relentless progression of metastases.

Table III shows some cases in which regression has been produced by stilboestrol. The majority of these were in the ten-year post-menopausal region. The regression was striking, and often lasted for a number of years, but this response appears to be the exception rather than the rule. One may wonder whether these cases are of primary pituitary-dependent nature, the stilboestrol serving to lower the secretion of mammatrophic hormone by the pituitary.

Summary and Conclusion

This paper records clinical observations on a series of cases of metastatic breast cancer treated by various methods.

It is suggested that the behaviour of metastatic breast cancer during a natural or artificial menopause indicates the probability or otherwise of hormone dependence.

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