mouse died after seven weeks of leukaemia with a local tumour in the iliac region. All the untreated controls were dead within 21 days.

In experiment 2, half the animals were given the leukaemia by the subcutaneous route. All five of the treated animals survive and are well but grey. Two untreated control animals also survive: these mice are in all probability sibs, and their failure to "take" the leukaemia can perhaps be ascribed to genetic drift. Of the five animals given the leukaemia intravenously, two treated animals died, one of generalized leukaemia after 19 days and one from an undetermined cause after 45 days; the other three are apparently well. The controls were dead within 17 days.

In experiment 3, homologous as well as isologous marrow was given as restorative treatment. Three of the five animals treated with isologous marrow survive, two having died after 36 and 44 days with generalized leukaemia. Three of the five mice given the homologous marrow from strain A/H mice died between one and two months after treatment. They were wasted and had diarrhoea. These deaths are attributed to complications of the treatment and not to its failure, but the detailed pathological processes are not yet understood. Of the five animals treated with $T_6/+$ bone marrow, three are well and two died within six days of the treatment, death presumably being due to the effects of radiation. Passage of the tissues of one of these to two normal CBA/H mice failed to reveal any leukaemia. All controls died within 26 days.

Discussion

The results show that this particular leukaemia (151/1) of the CBA mouse is not cured by the 950-rad dose of x rays given to the whole body in a single short exposure. When, however, the dose is increased to 1,500 rad and the time extended to 25 hours, in a proportion of cases the leukaemia is eliminated and recovery of the animal from the general radiation syndrome may be effected by treatment with intravenous bone marrow. Previous experience in this laboratory (Barnes and Loutit, 1955) would indicate that for this purpose isologous CBA/H bone marrow would be superior to homologous bone marrow from strain A, and this is borne out by the limited data in experiment 3, where mice given strain A/H bone marrow, though apparently cured of leukaemia, died following chronic diarrhoea. This agrees with other observations, to be published, that homologous bone marrow from strains A, C_3H , and C57 and from the hybrid mice $T_6/+$ given to leukaemic mice after 950 rad of x rays as an acute dose results in death from this same syndrome.

These preliminary experiments are reported because they showed some promise of the successful treatment of murine leukaemia. The results need confirmation with other types of leukaemia in other strains of mice, and different schedules of treatment may well provide more favourable results. If the experiences of several laboratories could be pooled some general laws might be evolved which should help in planning an extrapolation from mouse to man for treatment of those types of leukaemia which are so rapidly fatal as to warrant the use of desperate measures.

Summary

A generalized lymphoid leukaemia (151/1) of the CBA mouse can be transmitted by passage of cells intravenously or subcutaneously. One week after receiving such tissue mice were given x-irradiation to the whole body in doses approximating to the LD_{100} . They were then treated with intravenous injections of isologous (CBA) myeloid tissue and a few with homologous bone marrow from other strains of mice in order to re-colonize haemopoietic and lymphopoietic tissue. Given 950 rads at high intensity (14 minutes), the mice were not cured of leukaemia, but when the dose was 1,500 rads in 25 hours there have been 25 survivors out of 35 after three months.

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ADRENALECTOMY FOR INTRACRANIAL METASTASES FROM CARCINOMA OF THE BREAST

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It is now generally recognized that bilateral gonadectomy with bilateral adrenalectomy often leads to a regression of metastatic carcinoma of the breast and gives results which are well worth while. A course of hormone treatment by androgens (or by oestrogens in the male) should usually precede the operation. There seems, however, to be a widely held opinion (not shared by us) that the presence of cerebral metastases contraindicates surgical treatment because of the poorness of the results, although we could not discover a definite statement to this effect in the literature. Huggins and Dao (1953) describe a series of 53 adrenalectomies (51 females, 2 males) in which only two had cerebral metastases. This may have been due to the fact that such cases were not generally submitted to operation. Neither of these two (one female and one male) responded to operative treatment. Galante *et al.* (1954), however, reported regression of the secondaries in the only case with cerebral metastases (a female) in their series of 31 patients who were submitted to operation. Cade's (1955a, 1955b) series of 100 adrenalectomies (one male) contained no definite example of cerebral metastases, though cases were not excluded for that reason. A few had metastases involving the base of the skull and cranial nerves, and among these there were some satisfactory results (Cade, 1956, personal communication). Similarly, Pyrah and Smiddy (1954), reporting 22 cases (one male), submitted no case with cerebral metastases to operation.

At the Royal Marsden Hospital over 90 adrenalectomies had been done up to the end of 1955. In only two patients were cerebral metastases clinically evident. They are reported here. Both have responded very favourably.

Case 1

In August, 1948, a married woman, then aged 37, had a radical mastectomy done for anaplastic carcinoma of the left breast, not involving the axillary lymph nodes. She was first seen at the Royal Marsden Hospital in January, 1951, with carcinoma of the whole of the right breast, with peau d'orange and a retracted nipple and extensive involvement of the axillary nodes. Bilateral oophorectomy

FIG. 1.—Case 1. Radiograph taken in November, 1954, showing erosion of pituitary fossa associated with cerebral metastases.

FIG. 2.—Case 1. Radiograph taken in May, 1955, six months after bilateral adrenalectomy, showing the healed condition.

was done and a course of x-ray therapy given to the right breast and glandular areas. The local progress of the disease was arrested. Thereafter she attended at irregular intervals and the condition remained unchanged until November 1954. At that time personality changes were very evident, she was unable to sleep, her speech was slow, and she was passing great amounts of urine. Radiographs of the skull showed expansion and destruction of the pituitary fossa, presumably from erosion by growth (Fig. 1). The left lung contained multiple metastases. A large quantity of ascitic fluid was present. Her general condition was very poor and her blood pressure was 95/60.

She was given daily doses of 1,000 mg. of testosterone-propyl-propionate for three days and 50 mg. of cortisone for five days. Her diabetes insipidus was treated with "pitressin." On November 23 it was felt that, although the prognosis was poor, she was as fit for surgery as she would ever be. Both adrenal glands were removed at one operation.

She made a slow but steady recovery. Her mental symptoms cleared up and the diabetes insipidus gradually improved, though she still required small doses of pitressin. In May, 1955, a radiograph showed that the pituitary fossa had almost completely returned to normal (Fig. 2). She has remained reasonably well up to the time of writing (September, 1956), twenty-two months after operation.

Case 2

A married woman had a right radical mastectomy done in March, 1952, when aged 40, for anaplastic carcinoma not involving the axillary lymph nodes. This was followed by a course of x-ray therapy. In August, 1955, she began to have typical attacks of grand mal, four attacks in all.

She was seen at the Royal Marsden Hospital for the first time on September 15. Radiographs revealed large pul-

FIG. 3.—Case 2. Radiograph showing large pulmonary metastases.

FIG. 4.—Case 2. Radiograph taken on January 3, 1956, fourteen days after adrenalectomy, showing regression of pulmonary metastases.

monary metastases (Fig. 3). Treatment was immediately started with testosterone-propyl-propionate (100 mg. twice a week). In November a single attack of petit mal was reported. Early in December she became semiconscious and uncooperative, and was admitted on December 11. Examination revealed an incomplete left hemiplegia, a left upper neurone seventh-nerve paresis, a left eleventh-nerve weakness, and a left twelfth-nerve paresis. The diagnosis of a cerebral metastasis was in no doubt.

On December 13 bilateral oophorectomy and left adrenalectomy was done. No intraperitoneal or hepatic metastases were detected. She rapidly became worse, and the hemiplegia and the coma became complete. On December 20 right adrenalectomy was carried out. After the second stage the patient was desperately ill for two days with pulmonary oedema, but she recovered well. Her neurological state recovered remarkably rapidly and had returned to normal by January 4, 1956. A chest x-ray film (Fig. 4) on January 3 (fourteen days after the second stage of the operation) showed that the pulmonary metastases had almost resolved. She has remained very well up to the time of writing (September, 1956), nine months after operation.

Discussion

Bilateral gonadectomy and adrenalectomy has been done in over 300 patients with metastatic breast cancer in the five series mentioned above. Among all these only five have had involvement of the brain, of which three (including our two cases) have shown a worth-while response. While it would be foolish to draw hard-and-fast conclusions from so small a number, it appears that cerebral metastases may respond to hormone deprivation and will probably do so with the same order of frequency as metastases elsewhere. The special problem of cerebral metastasis is that the condition often becomes urgent. It is a morbid swelling within the rigid skull, and this fact should lead us to submit the patients to early surgery. Often a one-stage operation is to be preferred, as the patient will not improve until the intracranial mass begins to regress in size. We would regard this particular complication of breast cancer as a contraindication to androgen therapy, except perhaps for a short period pre-operatively.

Hypophysectomy or destruction of the hypophysis by radioactive methods, whatever its place may be in the treatment of the other manifestations of metastatic breast cancer, has no place in the palliation of cerebral metastases. R. Luft (1956, personal communication) states that Professor Olivecrona, of Stockholm, does not perform hypophysectomy if intracranial metastases are present.

Conclusions

The operation of bilateral gonadectomy and adrenalectomy is at present the only possible treatment of value for patients with intracranial metastases from cancer of the breast. It should be attempted when possible, because these patients are otherwise doomed. Two successful cases are reported above.

We thank Dr. C. Allan Birch for referring the second patient; and Dr. Stanley Rowbotham and Dr. Christine Ramsay for administering the anaesthetics. We are grateful to Mr. W. P. Greening for advice on the use of androgens and cortisone in Case 1. The photographic department of the Royal Marsden Hospital supplied prints of the x-ray films, which were taken by the diagnostic x-ray department of that hospital.

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POLIOMYELITIS IN SUBURBAN SURREY

CLINICAL AND EPIDEMIOLOGICAL OBSERVATIONS IN THE LIGHT OF VIRUS ISOLATION FROM FAECES

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In recent years the application of tissue-culture techniques on an ever-increasing scale has led to significant advances in our knowledge of virus infections generally, and especially poliomyelitis. The urgent need for more adequate facilities in this country for applying these methods to the clinical and epidemiological problems of poliomyelitis became the subject of much correspondence in the medical press during 1955. Between September 1 and December 31, 1955, virological study of a limited outbreak became possible in part of suburban Surrey. To a clinician and a medical officer of health previously without such assistance the information obtained has been of the greatest value, and it appears opportune to describe the findings.

The comparatively few studies which have been reported in this country relate to an attempt to estimate the value of quarantine in a small outbreak of poliomyelitis in East Anglia (Goffe and Parfitt, 1955), the general distribution of poliomyelitis virus types (Goffe, 1955), and the investigation of atypical disease resembling poliomyelitis (Acheson, 1954; Ramsay and O'Sullivan, 1956; Sumner, 1956).

The most extensive observations, however, have come from the United States and Canada. The value of virus isolation and antibody studies as an aid to clinical diagnosis was shown by workers from the Yale University School of Medicine (Godenne and Riordan, 1955). Detailed epidemiological and virological reports of a small winter outbreak in New York (Melnick *et al.*, 1956) and of a spring outbreak in Toronto (Beale *et al.*, 1956) have appeared. The extent of infection among contacts has been shown (Bodian and Paffenbarger, 1954; Horstmann *et al.*, 1955), and the general status of tissue-culture techniques in the isolation of poliomyelitis and other viruses has been summarized by Melnick (1955), Rhodes *et al.* (1955), and Enders (1955).

The investigation described here was conducted from the Tolworth Paediatric and Communicable Disease Unit of the Kingston Hospital Group, serving mainly the North-Central Division of the Surrey County Council, and virological investigations were carried out in the Virus Research Laboratory of Glaxo Laboratories Ltd., at Sefton Park. The North-Central Division of Surrey is a suburban and residential area with a population of about 200,000, with many of the inhabitants falling into the Registrar-General's social classes I, II, and III. There is a large daily movement of population