psoriasis of the scalp. Patients found it cosmetically superior to ointments and creams, and the preparation was effective compared with the inert base.

NOTE.—Since this work began Hagerman (1965) has reported the successful use of an alcoholic solution of triamcinolone in psoriasis of the scalp. The preparation he used contained salicylic acid and benzalkonium chloride in

addition to the steroid, and his patients used an occlusive dressing on the head at night.

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Preliminary Communications

Host Defences to Burkitt Tumour

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The possibility that host factors or immunological agents play a part in the results achieved in the treatment of the Burkitt tumour has long been suspected. Thus Burkitt (1962), in East Africa, showed that adults living in regions where this lymphoma was prevalent did not suffer from the tumour, whereas adults who had come from non-endemic regions were apt to contract the lesion. Moreover, the overall long-term survivals achieved in the treatment of the Burkitt lymphoma are much better than those achieved with other lymphomas (Chemotherapy of Burkitt Tumour, 1966) even with small doses of drugs. Regressions of the Burkitt lymphoma have even occurred when treatment was abandoned or refused (Burkitt *et al.*, 1965).

Ngu (1965) suggested that if host factors were involved in some of the remissions seen such factors would theoretically be easier to detect in those who had had long remissions than in those who had succumbed early to their tumour. Such early deaths might be taken as presumptive evidence of failure or inadequacy of host defence factors, whatever the reasons for this failure might be. Hence it was decided to search for a humoral factor in patients with long remissions.

MATERIAL AND METHOD

Blood was donated by two Burkitt tumour patients with uninterrupted remissions of over two and a half years who had not received cytotoxic drugs in the preceding year. Control blood was donated by a young healthy English doctor who had spent nine months at Ibadan and a healthy young American scientist who had spent only 72 hours in Nigeria. Two factors were taken into account in the design of the trial. Firstly, it was thought prudent to exclude from the donors of immune plasma patients with remissions of less than two years, since recurrences of the tumour after nearly a year's remission had been seen. With a further year of remission the risk of infusing live tumour cells or whatever their causative agents might be was minimized. Secondly, plasma was preferred to serum because it avoided waste in separating serum from the small volumes of blood donated by children. Moreover, as the recipients were themselves generally anaemic, it was always possible that they might need the red cells as well. The donated blood was thus stored as whole blood, but the plasma was separated and stored frozen shortly before its expiry date.

"Immune" Plasma Donor I.—A 10-year-old girl (blood-group O, Rh-positive) was first seen in February 1962, at the age

of 6, weighing 41 lb. (18.6 kg.) with a lymphoma (Burkitt tumour) of the right cheek, confirmed by x-ray and histological examination. She received 5.5 mg. of mustine hydrochloride into the right external carotid artery and a further dose of 6.2 mg. into the arch of the aorta via a femoral artery catheter. Six weeks later regression of the tumour was rapid, and she has remained completely symptom-free to the present time with no evidence of tumour anywhere in the body.

"Immune" Plasma Donor II.—A boy (blood group B, Rh-positive), now aged 14, was first seen in December 1962 with Burkitt tumour of the right maxilla and was treated by intravenous cyclophosphamide (490 mg. daily $\times$ 7). The response of the tumour was good, but because of persistent bony deformity he was started six weeks later on a maintenance course of 50 mg. of cyclophosphamide by mouth daily. This was continued intermittently for a year and then stopped. There is now no evidence of disease on clinical and radiological examination.

CASE 1

A 4-year-old boy (blood group B, Rh-positive) was admitted to hospital on 2 September 1965, with a 20-day history of swelling of the left cheek and right upper eyelid and some respiratory difficulty. On examination he was a very ill child weighing 22 lb. (10 kg.) with bilateral involvement of both maxillae and both mandibles by tumour masses. The maxillary tumour had ulcerated into the nostrils, from which a moderate amount of bleeding was observed. Nasal obstruction and extension of tumour into the mouth had rendered normal breathing difficult. A tracheostomy was therefore established on admission. The periorbital tissues were involved by tumour, more extensively on the right side than on the left. The rest of the physical examination did not reveal obvious tumour masses elsewhere in the body.

X-ray examination of the facial bones showed extensive destruction of both maxillae and mandibles with displacement of the teeth (anarchie dentaire). There was a loss of dental lamina dura.

Biopsy examination of the tumour on the left cheek showed the presence of Burkitt tumour cells.

On 3 September 150 ml. of immune plasma I was transfused into the child. Next day he looked infinitely better, though he had a temperature of 102° F. (38.9° C.). The patient's general condition remained satisfactory, but his temperature continued to swing until 12 September, when it settled. Because of occasional epistaxes, however, and a haemoglobin of 6.9 g./100 ml. (47%), he was transfused with 350 ml. of whole blood obtained from a local adult Nigerian who had not suffered from Burkitt tumour. On 12 September it was noticed that the jaw tumour was regressing fairly rapidly, and next day the serum uric acid had risen to 9.6 mg./100 ml. Throughout this period no cytotoxic drug had been given.

He remained well until 26 September, about three weeks after the plasma infusion, when it was noticed that the tumour in the left cheek had recurred. A week later it was 3 cm. in diameter, and intravenous cyclophosphamide (10 mg./kg. body weight) was started,

being continued for five days, with complete regression of the tumour. He was discharged home on 29 October in reasonable health but having lost about 4 lb. (1.8 kg.) in weight.

A week later he was readmitted with a history of vomiting and listlessness. Examination showed a thin dehydrated child with a bed sore over the sacrum, moderate neck stiffness, paralysis of the third, fourth, sixth, and seventh cranial nerves, and a flaccid paraplegia of both legs. At lumbar puncture the pressure was raised, and when examined by phase contrast microscopy and tissue culture his C.S.F. was found to contain viable Burkitt tumour cells in large numbers. X-ray examination of the spine showed a small paravertebral mass in the lower thoracic region. He was again treated with intravenous cyclophosphamide for 10 days without any change in his clinical condition, and he died on 5 December.

Necropsy showed only scars of healed lesions in the maxillae and renal cortex, where tumour masses had been. Viable tumour was present within the meninges and involved the cranial nerves at the base of the skull; histology showed only a Burkitt-cell "meningitis and encephalitis."

CASE 2

A 4-year-old girl (blood group O, Rh-positive) was admitted to hospital on 19 January 1966 with a two-month history of swelling of the right cheek. She had a classical Burkitt tumour of the right maxilla and mandible, with extension of tumour into the parotid and right submental regions. She also had an enlarged lymph node in the right posterior triangle. A specimen of bone marrow from the right iliac crest showed gross invasion by Burkitt tumour cells; an x-ray film of facial bones showed destructive changes typical of Burkitt tumour; an intravenous pyelography revealed displacement of calices by an intrarenal deposit; and biopsy of the tumour disclosed Burkitt tumour cells.

On 20 January, after immune plasma II (group B, Rh-positive) was found compatible with the patient's red cells (group O, Rh-positive), she was given an infusion of 100 ml. of the immune plasma. She was also started on prophylactic tetracycline, given for two weeks. On the fifth day after this she developed a swinging fever of up to 102° F. (38.9° C.), which persisted until the 14th day. Coinciding with the onset of the fever, the jaw tumour appeared to be somewhat larger and then became softer and more cystic in consistency. When the fever began to subside on the 14th day the tumour had become smaller and its cystic consistency more evident. The serum uric acid was at this time 17.9 g./100 ml. (4.9 g./100 ml. on admission).

When tumour regression had ceased, two weeks after the plasma infusion, a pint (500 ml.) of fresh compatible blood from an adult Nigerian was transfused without any effect on the rest of the tumour. Cyclophosphamide (10 mg./kg. intravenously daily) was also started. Further regression of the tumour was observed, as well as a continued general improvement in the clinical status of the patient. On the fifth day of chemotherapy she suddenly collapsed and died. Necropsy did not show any haemorrhages. Partly necrotic tumour tissue was present in the right cheek, lower cervical lymph nodes, and right femur. Histology of the cheek tumour showed few viable tumour cells, but an increase in the number of histiocytes. No satisfactory anatomical cause of death was found, and it was thought to have been due to hyperuricaemia consequent upon the drug-induced tumour destruction.

CONTROL CASES

Two control patients were treated.

The first, a girl of 9, had a five-month history of swelling of the left jaw. She had the clinical features of Burkitt tumour, which was confirmed by radiological examination of the facial bones. Because she was slightly anaemic, whole blood was given instead of plasma, and 1 pint (500 ml.) of group O, Rh-positive blood donated by an English doctor who had spent nine months in Ibadan was transfused. She remained well with a low-grade pyrexia until two weeks later, when it was evident that the tumour had continued to grow, measuring 17.5 cm. compared with 13 cm. on admission. She was given a single dose of intravenous cyclophosphamide at 30 mg./kg. (total dose 400 mg.), and the response to this was good.

The second patient was a 10-year-old boy who gave a three-month history of bleeding gums, loose teeth, and swelling of the left cheek, followed by swelling of the right mandible. He had typical Burkitt tumour swellings affecting the left maxilla and right mandible. There was some ulceration and infection of the intraoral parts of the tumour. He was given 200 ml. of compatible plasma donated by a young adult visiting American scientist. Eleven days after the plasma infusion the facial masses had increased in size. It was thought that the plasma had had no effect, and the child received a single dose of cyclophosphamide (35 mg./kg. intravenously) with good regression of the tumour.

DISCUSSION

Four conclusions may be drawn from these studies. Firstly, the "immune plasma" had a marked anti-tumour effect in Case 1 and a moderate effect in Case 2. Secondly, the two patients receiving immune plasma had a moderate fever for which no satisfactory cause could be found (and which was refractory to antibiotics and antimalarial drugs). Thirdly, the remission of these fevers coincided with the onset of tumour regression. Fourthly, during the tumour regression the serum uric acid level was markedly raised in Case 2 and slightly raised in Case 1. In contrast, the control plasma had no anti-tumour effect and its recipients did not have a persistent fever similar to that seen after the infusion of immune plasma. These observations suggest that the immune plasma had a specific anti-tumour factor missing from the control plasma.

The action of isoagglutinins in Case 1 contributed to the fall of the haemoglobin levels, but it is uncertain if isoagglutinins have any anti-tumour activity. Studies in tissue culture of the Burkitt tumour have not shown that the blood group of the sera used plays any part in the growth or destruction of the tumour cells (B. O. Oshunkoya, personal communication, 1965).

The possibility that the immune plasma contained oncolytic viruses was considered. Nevertheless, it is difficult to see why such viruses, if they existed, should be confined to these donors. Their presence in others, including other Burkitt tumour patients, might lead to spontaneous tumour regression in some such patients, or after blood transfusions a similar spontaneous regression might be observed. Neither of these events has been seen. It should be pointed out that if such tumour regression occurs without the direct isolation of oncolytic viruses it would be difficult to exclude immunological causes for the regressions.

By exclusion we are left with the possibility that "immune" factors were present in the plasma transfused. The clinical course of the disease in the donors of the immune plasma, themselves with long remissions after relatively small doses of cytotoxic drugs, suggests an immunological agent or host factors in them. However, the anti-tumour effects of the "immune plasma" on Cases 1 and 2 are in themselves strong evidence for the existence of such factors in the donors. Finally, the recurrence of the tumour in Case 1 about three weeks after the infusion of immune plasma is within the period when passively transfused immunity might be expected to last.

These preliminary observations require further confirmation, and the possibilities of their therapeutic application remain to be explored. They are of interest and importance, since they provide objective evidence for the existence of host factors to the Burkitt tumour.

Further, the importance of demonstrating the existence of immunological factors lies in the possible identification of the antigens to which they have been formed. It is evident that since the anti-tumour effect of the "immune" plasma is directed at the tumour cells, the antigens are in some way related to these cells. It is tempting but probably incorrect to conclude that the tumour cells are the sole antigens. They probably merely represent the visible or target part of the antigen, with an invisible and possibly a more important part in close relation with the tumour cells. The identification of these invisible

antigens, believed by many to be viral, should receive considerable encouragement from the knowledge that immunity to them exists. In any case, the detailed characterization of these immunological factors themselves, and the possible isolation of specific immunoglobins and their use in future studies, may assist us in finally identifying the causative agent of the Burkitt tumour.

I should like to thank the patients for their willing co-operation in these studies, also the expatriate donors of blood. Dr. L. Luzzato assisted with the preparation of the plasma. I am grateful to the various members of the hospital staff whose assistance and co-operation were invaluable. Mr. M. O. Olumakin did useful secretarial work. This survey was supported in part by the Ella Lyman Cabot Trust and by a Senate Research Grant of the

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Medical Memoranda

Peripheral Mercury Embolization Occurring during Arterial Blood Sampling

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The collection of peripheral arterial blood by an anaerobic technique is essential to many clinical procedures. Generally the blood is collected into heparinized syringes in which some inert fluid is placed to fill the dead space; mercury has been used as the inert fluid and cases of embolism of this mercury have been reported in America (Lathem *et al.*, 1954; Buxton *et al.*, 1965). We report here a further example of this misadventure occurring in Great Britain.

CASE REPORT

The patient, a 32-year-old physiologist, was taking part in an experiment which entailed collecting samples of arterial blood at

15-minute intervals over a two-hour period. In order to do this a Courmand needle was introduced into the left brachial artery in the antecubital fossa. Blood was collected in syringes with eccentric nozzles, the dead space in the syringe, about 0.3 ml., being filled with metallic mercury.

The needle was introduced without incident at 15.30 hours on 28 January 1966, and blood sampling began almost immediately. Throughout the experiment the subject was sitting upright with his left arm and the needle in it hanging by his side. During the experiment some "mechanical thrills" were felt in the left hand and fingers; these were presumed to be due to minor embolic episodes, and as this sort of phenomenon had been noticed in previous experiments no particular significance was attached to them.

After the experiment the subject noticed a rash developing on the dorsum of his hand, and at the same time the hand and the ulnar side three fingers became painful. The pain increased in intensity, and an x-ray film taken then revealed deposits of metallic mercury in the soft tissues of the middle, ring, and little fingers, the hypothenar muscles, and the medullary cavity of the proximal phalanx of the middle finger of the left hand, and in the soft tissues of the forearm (Fig. 1).

The patient was admitted to St. Thomas's Hospital on 29 January. He was then fully conscious but in considerable pain, and com-

FIG. 1.—X-ray film of left hand taken 20 hours after the accident. Metallic mercury is shown in the small blood-vessels.