

Amputations in leprosy present a problem, because the skin does not have normal sensibility. Sacrifice of the limb must therefore be considered only when there is no possibility whatever of leaving it *in situ*. D. S. McKenzie (personal communication, 1964), working at the Limb Fitting Centre, Roehampton, has had some success with total-contact sockets for anaesthetic stumps in spina bifida, and, if available, this type of prosthesis might be suitable for lepers, particularly for above-knee amputees. Its value is enhanced by a large bulky stump which is produced by the use of myoplastic flaps.

The guillotine operation is mentioned only to be condemned. It produces very poor scars and stumps, and further amputation is often required (Gillis, 1954).

### Summary and Conclusions

Techniques of proved value for amputations in developing countries are described.

In the lower limb the sites of election are Syme's, below-knee (kneeling-peg), and through the knee, either disarticulation or transcondylar.

In the upper limb as much length as possible should be saved, provided the stump is covered with healthy skin.

Closure of amputation wounds should be either by delayed primary or secondary suture. Immediate closure is often dangerous.

There are virtually no indications for guillotine amputations.

A Long-John-Silver peg-leg prosthesis if sturdily constructed is of great value.

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### REFERENCES

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## CONFERENCES AND MEETINGS

### Recent Research on Burkitt's Tumour : Conference at Kampala, Uganda

[FROM A SPECIAL CORRESPONDENT]

A conference on research into Burkitt's tumour was held at Kampala, Uganda, on 7 January 1966. The conference was sponsored by the Chemotherapy Panel of the International Union Against Cancer. The co-chairmen were Dr. J. H. BURCHENAL (New York) and Mr. DENIS P. BURKITT (Kampala). Delegates attended from Uganda, Kenya, Nigeria, the United States of America, France, Western Germany, Switzerland, Sweden, Australia, and Great Britain. The first session was devoted to a review of the natural history of the disease, and the second to the epidemiology and speculations on the possible aetiology of the disease in relation to its treatment. Chemotherapy was dealt with on the second day; on the third day the question of possible host defences was discussed, and the conference ended with a panel discussion.

#### Unique Histological Appearances

Dr. D. H. WRIGHT (Kampala) emphasized the distinctive morphological characteristics of Burkitt's lymphoma as seen in histological and more particularly in cytological preparations of the tumour. Some still doubted the specific character of this tumour, but he had now studied over 500 cases in Uganda and elsewhere and was impressed by the highly uniform morphological characteristics, which he considered diagnostic. Cytological preparations were made by fixing air-dried tumour imprints in methanol, and staining with May-Grünwald-Giemsa. Burkitt tumour cells also differed from the cells of other forms of lymphosarcoma in their easy growth in short-term tissue culture. Apart from the characteristic cytology the distribution of lesions also differed from that found

in other malignant lymphomata, and leukaemic transformation was extremely rare. Professor R. J. V. PULVERTAFT (Ibadan) described the distinctive growth characteristics of Burkitt tumour cells in short-term cultures, which differed greatly from those of many hundreds of malignant lymphomata he had studied in London.

#### Geographical Distribution

Professor M. S. R. HUTT (Kampala) pointed out that the Burkitt lymphoma was the commonest tumour of childhood in Uganda, comprising 50% of all malignant conditions in endemic areas. In areas where Burkitt lymphoma was especially common the other forms of lymphoma were not necessarily less prevalent. Burkitt lymphoma was therefore an addition to the other forms of lymphoma and did not replace them. The distribution of the common forms of lymphoma in Uganda was simply related to the density of the population, but Burkitt lymphoma had a distinctive distribution in Uganda. Mr. BURKITT said that the disease, though commonest in Africa, had also been described in New Guinea, England, the United States of America, and South Africa. It was, however, common only in the trans-equatorial belt of Africa with a prolongation southwards along the east coast. It appeared to be common in the moist warm lowland areas of New Guinea, but rare in the dry mountainous districts. There was some evidence that it was also common in parts of Brazil. A detailed survey in Uganda showed that in lowland areas along the Nile the tumour was 20 times as common as in the mountainous regions. In the mountains the average age of onset was 16.2 years, whereas in endemic

areas it was 8.1 years. The tumour was extremely rare below the age of 2.

#### Site of Tumour

At the age of 3 all the cases presented with jaw tumours. From 9 to 14 years girls commonly presented with massive bilateral ovarian tumours, and 75% of all girls coming to necropsy were found to have ovarian tumours. After the age of 15 years jaw presentations were rare. The tumour was not uncommon in immigrants to Uganda who had come from the mountainous districts of Rwanda and Burundi, where the disease was almost unknown.

#### Possible Virus Aetiology

Dr. M. C. WILLIAMS (Entebbe) discussed the hypothesis that the tumour might be virus-induced, and that its prevalence in endemic areas could be accounted for by transmission by an insect vector. The hypothesis had arisen from the similarity of the distribution of Burkitt lymphoma with that of the distribution of yellow-fever antibodies in Africa.

Dr. A. J. Haddow, formerly director of the Virus Research Institute at Entebbe, had reasoned that if the hypothesis of a virus aetiology was correct the distribution would indicate a very high rate of infection early in life. The great majority of persons infected would develop immunity, and only a small minority would develop malignant tumours. The rarity of the disease above the age of 15 years in endemic areas except in presumably non-immune immigrants would fit in with the hypothesis. The cumulative age incidence of Burkitt lymphoma in Uganda paralleled the changes in yellow-

fever immunity rates in Uganda. Alternative hypotheses, such as the existence of animal reservoirs, should not be entirely dismissed, since three cases in the West Nile district had occurred within 500 yards of each other. If the arthropod vector hypothesis was correct it was surprising that the disease had not yet been reported from India.

Successful attempts at the isolation of viruses had been made by Dr. T. M. BELL (Entebbe) and Dr. M. A. EPSTEIN (London). The viruses were most easily recovered from cultures of tumour cells, but on a few occasions had been obtained directly from minced tumour tissues.

### Viruses Isolated

Two types of virus had been recovered with some regularity in different cultures and both had been isolated from cultures made from one case. The two viruses were reovirus type 3, a double-stranded ribonucleic acid virus potentially transmissible by insect vectors, and a herpes-like virus, a deoxyribose nucleic acid virus unlikely to be transmissible by insect vectors. Herpes simplex itself had also been isolated on several occasions from minced tumour tissue. In the search for antiviral antibodies the results were significant only in the case of the reovirus type 3, where sera from Burkitt lymphoma patients gave significantly higher titres than sera obtained from controls. Dr. Epstein had established three cultures of Burkitt tumour cells from separate cases. Each of the strains carried a morphologically and biologically similar virus which could be found in developmental stages in both the nucleus and cytoplasm of the tumour cells. A similar virus had been obtained by Dr. Sarah Stewart (U.S.A.) and by Rabson and O'Connor from different cases. Unfortunately this herpes-like virus could not be transmitted to any laboratory animal or tissue culture. One of Dr. Epstein's three strains had recently begun to produce large amounts of the virus, and about 10% of the cells now carried formed virus particles. The significance of these viruses in the aetiology and pathogenesis of the disease remained uncertain.

### Reoviruses

Professor NEVILLE STANLEY (Perth, Australia) said that reoviruses were originally isolated in Australia, where all vertebrate sera contained antisera against one or more of the three common types. The titres increased with age. Reoviruses had also been found in mosquitoes in New Zealand by Dr. J. A. R. MILES. In man reoviruses were found in the respiratory tract and were spread by respiratory discharges and in faeces. Reoviruses injected into newborn mice caused an acute rapidly fatal meningoencephalitis. Acute pancreatic acinar necrosis was also found. Survivors could develop chronic immunological injury. Spleen cells from these mice injected intraperitoneally in newborn animals produced a runting syndrome. Survivors occasionally developed a lymphoma-like disease and a few animals had had jaw tumours. Intranasal administration of virus had produced jaw involvement more often; the tumours were usually unilateral but frequently involved both the maxilla and the mandible.

### Discussion

In the ensuing discussion on the possible viral aetiology of the disease Mr. BURKITT said that the hypothesis of a viral aetiology was supported by the geographical distribution, the age incidence in areas of high and low tumour incidence, the differing clinical manifestations at different ages, and the differing patterns of disease in immigrants from areas of low incidence. Dr. EPSTEIN felt that the occurrence of the tumour outside Africa, and in the areas where insect transmission was unlikely, was not an obstacle to the virus hypothesis. In such areas the virus would pass from case to case by other means. In tropical endemic areas an insect vector would provide the additional factor responsible for the high incidence and characteristic geographical distribution.

### Chemotherapy

Reports on the chemotherapy of Burkitt tumour were presented by Professor D. A. NGU (Ibadan), by Mr. BURKITT, and by Mr. PETER CLIFFORD (Nairobi). The tumour often grew very rapidly, and being painless was frequently allowed to reach enormous proportions before the children were brought to hospital. Many died before any treatment could be given. Fifty-one out of Professor Ngu's 147 patients had died in this way. Professor Ngu had treated 54 patients with cyclophosphamide: 13 had shown complete regression of tumour and 10 had been followed up for up to three years; five of them were symptom-free 1-3 years after treatment.

Mr. BURKITT reported on the treatment of 88 patients with jaw tumours. Seventeen had received methotrexate, 60 cyclophosphamide, and 21 vincristine sulphate. The treatment was usually completed within three weeks. The best responses were obtained in patients who had small tumours. The most important aspect of the results was the possibility of cure, since long remissions had been obtained in patients whose tumours regressed completely. Fifteen had been observed for over a year after treatment. Patients who had had no recurrence after a year seemed likely to have been cured, since 10 were still recurrence-free from three to six years. During the conference Mr. Burkitt demonstrated these 10 children, and two others observed for shorter periods. The children were brought to Kampala specially for the occasion. All the delegates felt they had been witnesses at a unique and perhaps prophetic occasion in the history of cancer therapy.

Mr. CLIFFORD reported on the results of treatment in 59 cases. He had used seven chemotherapeutic agents and found that the most successful were cyclophosphamide, melphalan, and orthomerphalan. Some tumours were very resistant to all agents tried but in sensitive cases even very large tumours had responded. Several courses of treatment had sometimes been necessary before complete regression was obtained, but like Mr. Burkitt he had had several complete regressions, and the patients were free of recurrence for periods of up to three years. Mr. Burkitt had been impressed by the number of complete regressions in patients who had received what he would have regarded as inadequate treatment. He now

felt that the optimal doses may well be far less than those conventionally regarded as desirable in the treatment of malignant disease.

In the discussion that followed several workers noted that the doses of cytotoxic agents tolerated by African children were far higher than could be used in the treatment of malignant disease in European or American children. A possible explanation was that the bone-marrow was hyperactive as a result of chronic malaria and infestation with other parasites, but this could not account for the relative resistance of other tissues such as the buccal mucosa and the gastro-intestinal tract to methotrexate toxicity, or of the hair follicles to cyclophosphamide.

### Host Defences

Mr. BURKITT cited several facts suggesting that host defences played a part in the regression of the tumour. Occasional cases of spontaneous regression had been reported; transient regression had followed the transfusion of serum from convalescent cases, and massive tumours which had failed to respond to energetic chemotherapy had been observed to regress later. Transient regressions had followed vaccination against smallpox. Tumours at some sites often regressed while tumours at other sites were growing. Patients treated with doses far below usually accepted requirements had survived longer than those treated more intensively, suggesting that the latter form of treatment might be damaging some immunological mechanism, thus outweighing the benefits of increased damage to tumour cells.

Professor NGU also reported transient regression following the administration of convalescent serum. Mr. CLIFFORD had observed transient regressions following vaccination against smallpox. He had also tried to use B.C.G. vaccination as a non-specific stimulus of immune responses; he had also injected irradiated autochthonous tumour cells. He agreed with Mr. Burkitt that the difference in response resulted from factors other than chemotherapy and could be a reflection of the immunological competence of the patient. The response to vaccination in some patients suggested that their immunological capacity was impaired, but not that intensive chemotherapy suppressed immunological response.

Dr. EMIL FREI (U.S.A.) also doubted whether intensive chemotherapy suppressed immunological responsiveness. Dr. GEORGE KLEIN (Sweden) reported preliminary results of a study designed to detect specific antibodies against surface antigens present on Burkitt tumour cells. The studies were made on samples of tumour provided by Mr. Clifford. Sera tested included those obtained from normal Swedish adults, from Africans, and from convalescent cases of Burkitt lymphoma. The cells from a panel of patients were incubated with the sera to be tested, and after washing were exposed to a fluorescent antihuman globulin serum. Positively reacting cells had a characteristic fluorescent ring. A very few normal Swedish sera had given positive reactions, but the most strongly reactive sera were those obtained from patients in total regression, many of whom had received intensive chemotherapy.