derived from man with those of bacilli derived from the experimental infections. Unfortunately there are few such characteristics available for study in an organism that cannot be cultivated, though the antigenic structure is one. Until recently little progress had been made on the antigenic structure of mycobacteria. Now G. Castelnuovo and her colleagues[6] have shown that immuno-electrophoretic methods can be used to define more precisely the antigenic structure of mycobacteria sufficiently to distinguish species differences, and these may be applicable to the human leprosy bacillus. While it is essential to clear up these fundamental points studies on the present experimental infections should be pursued. Because the foot-pad type of infection, unlike the infection established in hybrid black mice, can be initiated without subsequent serial passage, it is more directly applicable to studies on the human leprosy bacillus. Already it has been used successfully as a screening test for anti-leprosy drugs.[7] So far the experimental infections have been established only with the bacilli from patients with lepromatous-type leprosy. Similar experiments should now be undertaken with bacilli obtained from patients with other types of leprosy. This might help to show whether different types of leprosy in man are determined by differences in the bacilli (perhaps with differences in virulence) or by different degrees of resistance in man. Occasionally patients relapse after several years of improvement on continuous treatment with diaminodiphenyl sulphone or other anti-leprosy drugs. The relapses may be due to the development of drug resistance by the bacillus, but it has not been possible to test this because the organisms cannot be cultivated. Now for the first time it should be possible to determine whether relapse is due to drug resistance of the bacilli by using the foot-pad infection in mice. Thus these advances in the transmission of leprosy to experimental animals are likely to be of practical value as well as putting leprosy research on a firmer experimental basis.

IMPERIAL CANCER RESEARCH FUND

Just over 60 years ago the research work of the Imperial Cancer Research Fund began under Dr. Bashford in two small rooms in the old Examination Hall on the Victoria Embankment. Last August the fund moved most of its 200 scientific workers and technicians to the impressive new laboratories in Lincoln's Inn Fields next door to the Royal College of Surgeons. Much can be learned about the Fund's growth and expanding influence from the report which Sir Cecil Wakeley, chairman of council, presented at the annual general meeting last week. In the main part of the report Dr. G. P. Marrian, F.R.S., outlines some of the more important projects which are now in hand. Much of the work on breast cancer is concerned with endocrinological aspects of this disease, and the report refers to the "Guernsey Project," the purpose of which is to investigate the possibility that abnormalities in the urinary excretion of androgen metabolites and 17-hydroxycorticosteroids of the type that have been found in patients with early and advanced breast cancer might conceivably precede the appearance of clinical symptoms of the disease. So far the research workers have secured the co-operation of 2,000 out of the 5,000 women on the Island of Guernsey whom they hope eventually to enrol as volunteers.

The Fund is also investigating the connexion between viruses and tumours, leukaemia, and prostatic cancer.

The financing of these and many other projects is a heavy responsibility. Mr. A. Dickson Wright, the Fund's honorary treasurer, was able to report that in 1962 the income from all sources for the first time exceeded £1m. More than half of this went directly to the building fund. The new laboratories cost £2½m. and only £400,000 of this is still outstanding. The fund's income from investments is about £80,000, but Mr. Dickson Wright estimates the annual cost of running the laboratories will be well over half a million pounds. Thus the work of the fund is completely dependent on donations and legacies. Few similar organizations can have more willing or more able helpers in the matter of raising funds. They can see for themselves the splendid results of their efforts in the completion of the new laboratories, which, they will be glad to learn, the Queen and the Duke of Edinburgh are to visit in June.

[1] Imperial Cancer Research Fund, *Sixtieth Annual Report and Accounts 1961-1962*, 1963. Lincoln's Inn Fields, London W.C.2.

RELAPSING TYPHOID

The antibiotic chloramphenicol is the drug to-day universally employed for the specific treatment of typhoid fever. The dosage now given is smaller than formerly because large doses may precipitate toxic crises of the disease, sometimes severe. For a case of average severity a dosage of 0.5 g. of chloramphenicol by mouth six-hourly is generally agreed to control the infection adequately and to produce a satisfactory clinical response, with decline of the fever after delay of at least two days. The problem of relapse after control of the initial attack remains,[1] and rare complications such as typhoid osteomyelitis—a case of which is described by Dr. G. A. H. Miller and his colleagues at p. 1068—still occur.

Some further data on relapses in typhoid are to be found in a recent paper from the Philippines.[2] Of 408 cases of typhoid, the subject of this report, 251 were treated with chloramphenicol, while the remaining 157 treated palliatively served as controls. The chloramphenicol was given orally in doses of 0.25 to 0.5 g. according to age and body weight every six hours until fever ceased—an average period of 4.81 days—and thereafter every eight hours for about five days. The average duration of treatment in these cases was just under 10 days and the average dosage of chloramphenicol about 18 g. Twenty (8%) of the 251 patients on chloramphenicol died, most of them on the fourth day; 28 (11% of the total in this group) suffered recurrence of the disease on average about 14 days after subsidence of the initial fever; all of these 28 recovered. Of the 157 control patients 36 (23%) died; but only 6 (4%) suffered recurrence of the disease, and the relapses in this control group developed on average some nine days after subsidence of the initial fever. Again none of the relapses caused death. The relapse rate in this series

therefore proved to be about three times as great among the chloramphenicol-treated patients, despite their lower mortality, as among those not so treated. Widal tests in samples of each of the two groups of patients, treated and untreated, gave supporting evidence that specific treatment of the disease with chloramphenicol inhibits the development of immunity to the causative infection, and so increases the relapse rate.

In his recent monograph on the disease R. L. Huckstep,[3] from study of a very large series of patients in East Africa, agrees with previous workers that inadequate treatment with chloramphenicol is followed by a high relapse rate. Chloramphenicol treatment should be continued over at least 14 days when possible to reduce the relapse rate to the minimum, but it cannot entirely eliminate the risk of relapse. In Huckstep's series of untreated patients with typhoid relapses occurred in 14%; in those treated with chloramphenicol for 10 days or less it rose to 41%; and in those given it for half as long again the figure fell to 28%. This last figure was more than halved when a single dose (0.25–0.5 ml.) of T.A.B. vaccine was injected towards the conclusion of the chloramphenicol treatment; but T.A.B. vaccine must not be given unless the patient's general condition is reasonably good and he is free from complications of the disease.

MALIGNANT LYMPHOMA IN CHILDREN IN AFRICA

The distribution of different types of cancer in the temperate zones and in the tropics presents many challenging problems. Now the malignant lymphomas seen commonly in children in Africa have recently had fresh light shed on them.[1] An earlier report from New Guinea[2] described a similar condition in a man of 22 years and a woman of 55. Lymphomas are regarded as allied to lymphocytic leukaemia, and indeed the histological picture in the lymph nodes may be identical; it is only the changes in the peripheral blood which characterize the leukaemia.

The most frequent and characteristic presenting feature of this condition is a tumour of one or more quadrants of the jaws and of other sites, including the kidneys, adrenals, ovaries, testes, salivary glands, liver, spleen, thyroid, heart, intestine, retro-peritoneum, extradural space in the spinal canal, and the orbit apart from the eye. Though the tumour appears to spread through the cardiovascular circulation it is notable that lungs, lymph nodes, and spleen are rarely involved. Of all malignant tumours in African children in Uganda 50% are these peculiar forms of lymphosarcoma,[3] and of these half occur as multicentric tumours in the maxillae and mandibles. It is the commonest childhood tumour not only of the jaw but of the sites previously mentioned. The disease runs a rapidly fatal course.

In a series of recent articles D. P. Burkitt[4–6] has shown that the geographical limits of this disease in Africa coincide with those areas where the mean temperature falls below 60° F. (15.5° C.) and where the mean rainfall of the year is below 30 in. (76 cm.). The field surveys showed that the tumour appears to be dependent on altitude because it is dependent on temperature, and to be dependent on humidity because it is dependent on vegetation. On this evidence J. N. P. Davies suggested that the tumours might be transmitted by a vector and induced by a virus. This possibility undoubtedly requires full investigation, and a team of research workers sent to Entebbe by the Imperial Cancer Research Fund is attempting to isolate virus from material obtained by tumour biopsy. A short account of the research is given in the Fund's latest annual report[7] (see annotation on p. 1041).

Another aspect of this problem might well be mentioned. In 1949 Davies[8] discussed the "sex hormone upset in Africans" and postulated that Africans are more subjected to oestrogens than Europeans because their livers, damaged from malnutrition and chronic infections, are unable to inactivate these hormones. Urinary excretion of oestrogen has since been studied in Johannesburg by I. Bersohn[9] in 21 Bantu males aged 20–45 years and in 21 European males aged 20–48 years, and this study suggested that the Bantu males excreted unduly high amounts of oestrogen and oestradiol. This was believed to reflect decreased inactivation in the liver owing to some dysfunction.

More recently the work of A. W. Greenwood[10] has raised some interesting problems which may be relevant to human cancer. By keeping female domestic fowls at a constant temperature of 65° F. (18.3° C.) and relative humidity of 60% and giving them 12 hours of fluorescent light and 12 hours darkness per 24 hours, he found that all the hens in the constant environment finally succumbed to an adenocarcinomatous type of cancer primarily involving the reproductive system, while none of the birds in the uncontrolled environment suffered this disease over a comparable period. Greenwood considers that the elimination of normal seasonal moulting caused by the environment may lead to endocrine disturbance, and he is carrying out further experiments in climatic chambers to elucidate this phenomenon. It would seem to show that environment alone can lead to changes which are associated with cancer, since there was no question of infection in this experiment. But cases of lymphoma are rare outside the demarcated zone wherein the postulated arthropod-borne virus would be expected to be present. High excretion of oestrogen was seen in the Union of South Africa, which lies outside the area, and thus the two zones do not coincide. Studies to elucidate these two problems might well lead to fundamental advances in our understanding of cancer.

Sir Charles Dodds, F.R.S., was re-elected President of the Royal College of Physicians of London on April 8.

[1] *Brit. med. J.*, 1962, **1**, 41.
[2] Lantin, P. T., Geronimo, A., and Calilong, V., *Amer. J. med. Sci.*, 1963, **245**, 293.
[3] Huckstep, R. L., *Typhoid Fever and other Salmonella Infections*, 1962. Edinburgh and London.
[1] See *Brit. med. J.*, 1962, **1**, 855.
[2] Saave, J. J., *Med. J. Aust.*, 1955, **1**, 358.
[3] Davies, J. N. P., *E. Afr. med. J.*, 1961, **38**, 486.
[4] Burkitt, D. P., ibid. 1961, **38**, 511.
[5] —— *Brit. J. Cancer*, 1962, **16**, 379.
[6] —— *Brit. med. J.*, 1962, **2**, 1019.
[7] Imperial Cancer Research Fund, *Sixtieth Annual Report and Accounts 1961-1962*, Lincoln's Inn Fields, London W.C.2.
[8] Davies, J. N. P., *Brit. med. J.*, 1949, **2**, 676.
[9] Bersohn, I., *S. Afr. med. J.*, 1957, **31**, 1172.
[10] Greenwood, A. W., *Animal Production*, 1962, **4**, 80.