The rights over the lake have recently been purchased by the Palestine Land Development Co. from the Arab owners. The company has employed engineers to estimate the cost of the drainage of the lake and swamp, and is now selling it upon these estimates. Several interested companies are employing their own engineers to check these. Up to the present, no work has been commenced, but it is anticipated that the drainage, which is a simple question, will be completed in 1936 or the following year.

The biological survey of Lake Huleh is in charge of Mr. Roger Washbourn with a botanist, both from the University of Birmingham. The lake is interesting mainly in comparison with Lake Tiberias and other parts of the Rift Valley in Palestine and East Africa. The presence of animals of African affinity was shown by Annandale in 1916, and the biologists are largely concerned with investigating the fauna and flora before the lake ceases to exist. In addition, Huleh lies near the southern boundary of several palæarctic species. The ecology also of a lake with a papyrus swamp in this latitude should prove interesting. Having these objects in view, the zoological part of the work is largely the collection of animals from the varied habitats that the lake and swamp present. To define these accurately, the physical and chemical conditions are being studied, and these are, of course, a prime factor in governing the plankton. The botanist is fully occupied with his study of the swamp and the interrelations of the plants in their different habitats. The difficulty of transport is considerable—and the lake is fever-stricken—but it is hoped that an impression will be secured of the plant and animal life of an area which will soon have ceased to exist.

The Chemotherapy of Malaria*

QUININE was discovered by Pelletier and Caventou in 1820 and was promptly manufactured in France and England in quantities sufficient to permit of its use in the treatment of malaria, in place of crude cinchona bark. This was an early and unconscious application of the principle upon which Ehrlich was to found chemotherapy ninety years later. By that time, thanks to the labours of Hesse, Skraup, Köenigs, von Miller and Rohde and Rabe, constitutional formulæ had been assigned to quinine and the other cinchona alkaloids, which Rabe and his collaborators confirmed in a series of researches culminating in the complete synthesis of dihydroquinine and dihydroquinidine in 1931. Partial syntheses had been effected some years earlier and the methods employed had been extended to the preparation of products allied to the cinchona alkaloids in type, but of simpler structure. In 1891 Grimaux and Arnaud prepared from cupreine a series of homologues of quinine, one of which, ethylcupreine, was tried clinically and found to be somewhat more active than quinine, and this first French experiment in the production of 'modified cinchona alkaloids' led to the preparation of many other substances of this type.

Chemists had in fact accumulated a mass of possible anti-malarials, the therapeutic value of which there was no practical means of testing. This want was supplied when Roehl devised his technique of testing such drugs in bird malaria, using canaries for this purpose. Of the various 'leads' then available for the synthesis of new anti-malarials, Prof. Schulemann and his co-workers, Schonhofer and Wingler, selected methylene blue, which had been shown to have some action in malaria, and from this starting point they evolved plasmoquine in 1924. This was followed by atebrin, discovered by Mauss and Mietzsch in 1930.

These two drugs have one feature in common, a dialkylaminoalkylamino-side-chain, -NH-CHMe-CH_2-CH_2-CH_2-NEt_2, attached at position 8 in 6-methoxyquinoline, in the case of plasmoquine, and at position 5 in 2-chloro-7-methoxyacridine, in the case of atebrin; but as acridine is quinoline with a benzene ring fused on, both drugs can be regarded as derived from 6-methoxyquinoline, a characteristic they share with quinine, which, however, has a different and more complex side-chain. Plasmoquine acts preferentially on the sexual forms (crescents or gametocytes) and atebrin and quinine on the asexual forms (schizonts) of the malaria parasite. Their respective actions in the various types of malaria is not as clear-cut as this brief description implies, but it is permissible now to divide anti-malarial drugs into 'anti-gametocyte', represented by plasmoquine and its allies, and 'anti-schizont', of which quinine and atebrin are types.

These discoveries have led to great activity in the synthesis of such drugs in Great Britain, France, Russia and elsewhere, and Prof. Robinson gave an account of the reactions used in the

* Based on a discussion, introduced by Col. S. P. James, in Section B (Chemistry) of the British Association meeting at Norwich on September 9. Other contributors to the discussion were Prof. W. Schulemann, Prof. R. Robinson, Dr. P. Tate (with Prof. Keilin and Miss M. Vincent), Dr. T. A. Henry, Sir Rickard Christophers and Prof. Warrington Yorke.

preparation of the extensive series of potential anti-malarials made in his laboratory. One of these, in which the side-chain of plasmoquine is replaced by -NH-CH_2-CH_2-CH_2-NH-CH_2-CH_2-CH_2-NH_2, was found to have a chemotherapeutic index 1 : 62 against 1 : 32 for plasmoquine and is, therefore, a promising material for clinical trial. The necessary bird malaria tests on these substances are being made in Prof. Keilin's laboratory at Cambridge by Dr. Tate and Miss Vincent, and the former described the methods used. Inoculation of infected blood provides material for tests on asexual forms of the parasite, and birds infected by bites from mosquitoes are used for tests of activity against gametocytes and sporozoites, and details were given of the results of such investigations of a number of Prof. Robinson's substances.

The bird malaria test has also been applied to a number of other problems. Drs. Buttle and Trevan have shown that the interesting series of alkaloids isolated by Messrs. Goodson and Sharp from ten species of *Alstonia* have no action in bird malaria, and the same is true of the alkaloids of *Picralima klaineana*, though both these drugs have some repute in various tropical countries as remedies for malaria. The same workers made a comparative examination of specially purified specimens of the principal cinchona alkaloids and found that, as an anti-schizont drug in bird malaria, quinine was about twice as active as quinidine or cinchonidine, and possibly five times as active as cinchonine.

These results are of considerable interest in connexion with the use of mixtures of cinchona alkaloids as a cheap substitute for quinine, and justify the action of the Malaria Commission of the League of Nations in providing a standard for such mixtures, which prescribes a minimum content of fifteen per cent of quinine. Much work has also been done, particularly by Giemsa, in assessing the therapeutic value in bird malaria of 'modified cinchona alkaloids'. The results show that, so far, no product of this type is much better than quinine or dihydroquinine; but this work has provided a fund of information as to the influence on anti-malarial activity of modifications in the structure of drugs, which will probably be of great value in the biochemical and biophysical investigations, which are beginning to be made in the hope of ascertaining how and why such drugs exert their specific action. As an example of such work, mention may be made of the paper by Sir Rickard Christophers describing the methods he has used, and some of the results obtained in examining the view that chemotherapeutic effect is a result of some kind of combination between protein substance and the basic side-chains, which are a characteristic feature of effective anti-malarial drugs.

It was particularly appropriate that the discussion should be introduced by Col. James, who has had special opportunities for clinical investigation of the new drugs, plasmoquine and atebrin. He provided a careful survey of their value as true causal prophylactics, as means of avoiding relapses and as preventives of spread of the disease, these being the principal characteristics of their action in which they surpass quinine, for they are to be regarded, not as substitutes for this alkaloid, but as additional weapons in anti-malarial campaigns.

Col. James finally expressed the hope that provision would be made in Great Britain for more intensive chemotherapeutical research. On the same point, Prof. Robinson emphasised the need for the closest co-operation between chemists and biologists in work of this kind, and Prof. Warrington Yorke pointed out that, although in a number of cases, such as sleeping sickness and amœbic dysentery, the first useful chemotherapeutical observation had been made by English workers, we had failed to follow up these observations by systematic pharmacological and chemical work, with the result that the countries of the Empire still had to depend largely on imported synthetic drugs. T. A. H.

Obituary

Mr. J. F. Herd

JAMES FLEMING HERD, senior scientific officer in the Radio Department of the National Physical Laboratory, died on July 22 at the early age of forty-seven years.

Born and educated in Dundee, Herd entered the Post Office, and became a highly skilled officer of the telegraph service. He served in the Royal Flying Corps and Royal Air Force, as an instructor in that part of the service which developed into the Wireless and Electrical School. Retaining the rank of flight lieutenant in the R.A.F. Reserve of Officers, he joined the Meteorological Office as a senior professional assistant, for service at Meteorological Office Radio Station, Aldershot, then engaged in a study of atmospherics in relation to thunderstorm detection. On the formation of the Radio Research Board, that station was taken over by the Department of Scientific and Industrial Research, to which its two scientific officers were seconded, later to become substantive