

forests were regarded as mere commercial assets to be exploited commercially. "Forests are now regarded not only as valuable suppliers of timbers for commercial purposes, but as important sources for the supply of fodder for livestock, fuel and small timber for the rural population, apart from their influence on climate, on the conservation of the water-supply, on the flow of streams and rivers and the prevention of erosion of the soil. Bitter experience has taught governments in many parts of the world that without a sound and long range policy of scientific management, irreparable damage might be done to the economic life of a country by the unrestricted destruction of forests. With the growth of population there is constant pressure to bring the more accessible forests under cultivation. Policy had to adjust itself so as to meet legitimate needs without, at the same time, destroying the sources from which those needs can be met."

After considerable discussion the Conference under the Chairmanship of Sir Jagadish Prasad, adopted the following resolutions:

1. (i) This Conference is of opinion that ordinarily there should be only one superior service in each Province, direct recruits to which should receive their training at Dehra Dun.

(ii) That, for the aforesaid training, provision should be made with effect from 1st April 1938 at the Forest Research Institute, Dehra Dun. The instruction should be of the highest standard necessary for Indian requirements.

2. The Conference is in general agreement with the principles of Forest Policy stated in the Government of India Resolution and recommends to Provincial Governments that, in any amendment of the Indian Forest Act or their Forest Manuals that they may undertake, these principles should be maintained.

The Conference also recommends that no proposal for large-scale deforestation should

be approved by a Provincial Government except after the fullest consideration by the Council of Ministers. Where any such proposal is likely to affect another Province or any State, no decision should be taken except after consultation amongst the Governments concerned.

3. The Conference is of the opinion that the advice of the Inspector-General of Forests will continue to be of value to Provincial Governments and that he should, therefore, be allowed to visit Provinces with their consent. He should also be permitted to correspond with Provincial Heads of Forest Departments on technical questions so as to keep in touch with developments in each province.

The Conference elected a Committee to go into the details of the qualifications and the method of the recruitment of candidates to the new Forest College, at Dehra Dun. The Committee which met under the Chairmanship of Mr. L. Mason, President of the Forest Research Institute, Dehra Dun, submitted its report which was adopted by the Conference with minor amendments. Their Excellencies the Viceroy and Lady Linlithgow were at home to the delegates and their ladies at a Tea Party at the Viceroy's House. Sir Jagadish Prasad gave a lunch at his residence in honour of the delegates.

The Conference gave an opportunity to Forest Officers from the different Provinces to meet together and talk over matters of common interest. From these informal conversations, it was evident that the importance of research to Indian Forestry is being increasingly realised. The example of the good work of the Imperial Council of Agricultural Research is proving infectious and opinion seems to favour the organisation of Forestry Research in India on similar lines. In such a scheme, the Dehra Dun Institute may well be the central apex institution co-ordinating and assisting the work of the Provincial Research Centres.

Researches in Chemotherapy.*

THE treatment of disease by chemical substances or chemotherapy, first developed by Paul Ehrlich, originated in his observations on the selective staining of the tissues of a living animal when certain dyestuffs were injected into its body, some of the tissues being intensely stained whilst others remained colour-free. Thus when methylene blue was injected into the blood stream of an animal suffering from malaria, the malarial parasite was found to be strongly coloured and could thus be differentiated from the tissue of the host. Ehrlich was led by these observations to conceive the bold idea of discovering compounds whose chemical affinity for the disease organism would be so great that the organism might be killed without danger to the tissues of the host. The activity of a compound was expressed for purposes of comparison by what Ehrlich called his Chemotherapeutic Index,

viz., the ratio of the minimum curative dose to the maximum tolerated dose of the compound.

Chemotherapeutic research postulates the closest co-operation between the chemist, the biologist and the clinician. The first step is the discovery that some parasite is responsible for a particular disease after which methods have to be found for the isolation, cultivation and study of the pure parasite. This can be done sometimes in the test-tube as with bactericides and amoebicides, while in other cases, the particular disease or one closely allied to it may be produced artificially in animals and studied. The chemical side of research consists mainly in the preparation of compounds structurally related to those drugs which have already been shown to be of clinical benefit in a given disease. Once the chemical constitution of the drug has been ascertained, substances of similar molecular structure are synthesised and tested for their therapeutic properties. A good example is the discovery of Plasmoquin as a result of attempts to prepare compounds allied to quinine and the cinchona

* Summary of the Presidential Address of Dr. F. L. Plyman. F.R.S., Chemistry Section, British Association for the Advancement of Science, Nottingham, 1937.

alkaloids, the medicinal value of which has been known for a long time.

BACTERICIDES.

An early example of research on bactericides was the introduction by Lister in 1867 of phenol to prevent sepsis. Several alkyl phenols were subsequently found to exceed phenol itself in bactericidal value. Thus the Rideal-Walker test for determining the efficiency of a bactericide, which consists in comparing its effect on *B. typhosus* with that of phenol, has shown that thymol- α -methyl-isopropyl phenol—has a phenol coefficient of about 25.

Systematic studies of the homologues of alkyl hydrocupreines by Morgenroth (1911-17), have shown that peak activity is reached with ethyl member (optoquin) for pneumococci, and with the iso-octyl member (Vuzin) for *B. diptheriae*. In actual clinical practice, however, optoquin has failed as a remedy for pneumonia, while vuzin has proved to be useful in the treatment of wounds. More interesting results were obtained from studies in the substituted resorcinol series by the American Chemists Johnson and Lane (1921) and Dohme, Cox and Miller (1926) who were able to demonstrate the profound effect of the length of the side chain on the antiseptic value of the alkyl resorcinol. The maximum effect was observed at 4,*n*-hexyl resorcinol which had a phenol coefficient of 50 while the next lower (*n*-amyl) and higher (*n*-heptyl) member of the series had phenol coefficients of 33 and 30 respectively. An analogous series of experiments carried out by Coulthard, Marshall and Pymman (1930) on the variation of phenol coefficients with increase in the side-chain in the 4,*n*-alkyl phenols, 4,*n*-alkyl guaiacols and 4,*n*-alkyl cresol series has led to the important discovery that the highest phenol coefficient is reached with the *n*-amyl group. 4,*n*-amyl *m*-cresol which has as high a phenol coefficient as 280, has been found to be very suitable for use as an antiseptic in the oral cavity. A dose of 1:10,000 added to 5 c.c. of a mouth washing reduced the bacterial colonies from 4,700 to 4 in 5 minutes and pharmacological experiments showed that it was non-toxic in medicinal doses. It has, therefore, been successfully introduced into medicine as a mouth wash.

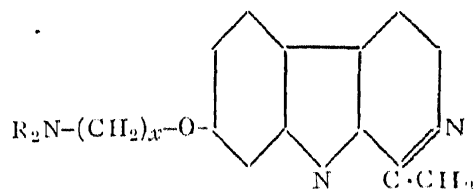
Again, in the case of urinary infections for which phenolic bactericides have given disappointing results and which were formerly treated by giving patients a particular form of diet, known as the ketogenic diet, a study of the bactericidal properties of certain hydroxy-acids by Rosenheim and others has led to the discovery of mandelic acid as a highly potent urinary antiseptic which is non-toxic in therapeutic doses and is not oxidised in the body but is excreted unaltered in the urine. Similarly, for the specific treatment of strepto-coccal infections, certain aromatic sulphonamides have recently been found to give promising results.

AMOEBIKIDES.

Though Emetine has been the principal drug in use in the treatment of amoebic dysentery, its undesirable after effects,—particularly the nauseating effect—have led to a search for similar chemical compounds which would have its beneficial properties but be free from its by-effects.

On the basis of the constitutional formula for Emetine proposed by Brindley and Pymman in 1929, a number of compounds containing two 6:7-dimethoxy-tetra-hydro-*iso*-quinoline nuclei joined through the 1:1'-positions by a chain of methylene groups was prepared and studied. When examined by the technique developed by Laidlaw, Dobell and Bishop for testing amoebicides *in vitro*, they were found to be devoid of any action in dilutions of 1 in 5,000, whereas emetine was effective even in dilutions of 1 in 500,000. Another series of compounds containing what has been termed the reduced benzopyrido-coline ring or a system in which the tertiary N-atom of the *iso*-quinoline is common to two rings, were synthesised by Child and Pymman in 1931, but the most active member of the series was found to be effective in a dilution of 1 in 25,000 only.

Substances like Harmine and Harmaline which are readily accessible in quantity by extraction from *Peganum harmala*, and which were prepared originally with a view to study their anti-malarial properties, have also failed to give promise of a powerful amoebicidal effect. In the homologues of Harmine and Harmaline where the methoxy groups have been replaced by higher alkoxy groups, the bactericidal and amoebicidal activity were found to rise up to a point and then start to fall. Peaks of bactericidal activity were reached at butyl for *B. typhosus* and at amyl for *S. Aureus* while the peak of amoebicidal activity was reached at *n*-amyl harmol. The salts of all these compounds were found to be rather sparingly soluble in water, and hence soluble derivatives had to be prepared by attaching a terminal dialkyl amino-group as in O-X-dimethyl amino-decyl harmol. In this way was made a series of derivatives of Harmol of the following general formula:



in which the size of both R and X was varied.

Among these, the O- λ -di-*n*-butyl amino-undecyl Harmol (R=*n*,butyl and X=11), was found to be many times more active than O-*n*-nonyl Harmol and this led to the suspicion that the dibutyl amino-decyl (or undecyl) group was a more important contributor to the amoebicidal properties of these compounds than the Harmol residue. This anticipation has been confirmed by later experiments. A series of tetra-alkyl diamino paraffins of the general formula $\text{NRR}'(\text{CH}_2)_\mu\text{NRR}'$ was prepared and the minimum amoebicidal concentration under the optimum conditions for emetine was determined. Among these the decane derivatives gave very encouraging results and surpassed in their effects even the dibutyl amino-undecyl harmol referred to above. The peak in the series was reached with the tetra-amyl-diamino-decane which may be referred to for brevity as T.A.D.D. Other compounds were next synthesised in which (a) the hydrocarbon residue was varied keeping the tetra-alkyl group constant, and (b) the tetra-alkyl

group was varied while the hydrocarbon residue was kept constant, but none of these products showed any striking amoebicidal effects. A more detailed study of T.A.D.D. was then undertaken, the conditions of all the amoebicidal tests being those most favourable to emetine, *i.e.*, in a faintly alkaline medium. T.A.D.D. was thus found to be 3 to 5 times as efficient as emetine at a P_H of 6.2 to 6.3. Experiments with mice, again, showed it to possess only one-tenth of the toxicity of emetine when administered orally, and one-sixth on subcutaneous injection. It is therefore clear that its therapeutic index is superior to that of emetine and T.A.D.D. appears now to be an exceptionally promising compound for clinical trial in conditions of ill-health due to infestation with *Entamoeba histolytica*. Clinical examination of the compound by the Trials Committee of the Medical Research Council has, however, shown that the compound when administered

orally, is not sufficiently active to be of real value while its intensely irritating nature has prevented its use intramuscularly, subcutaneously or intravenously.

The foregoing account of investigations in Chemotherapy should give one an idea of the enormous amount of chemical and biological work requiring team-work among groups of chemists, biologists and clinicians, which is involved in attempts to evolve a new drug for the treatment of disease. There are very few private concerns which can provide facilities for such co-operation and it is therefore gratifying to note that lately work of this character is being undertaken under public auspices, such as the work on anti-malarials directed by Prof. Robinson under the Chemotherapy Sub-Committee of the Medical Research Council and that on arsenicals by Sir Gilbert Morgan under the Department of Scientific and Industrial Research.

B. B. DEY.

SCIENCE NOTES.

New Year Honours:—

C.I.E.—Dr. C. W. B. Normand, Director-General of Observatories, Government of India.

Knight Bachelor—Dr. Zia-ud-din Ahmed, Vice-Chancellor, Aligarh Muslim University.

O.B.E.—Mr. R. C. Srivastava, Director, Imperial Institute of Sugar Technology, Cawnpore.—Capt. T. W. Bernard, Director, Bernard Institute of Radiology, Madras.

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Indian Vegetable Oils.—The *Bulletin of Indian Industrial Research*, No. 10 (By N. Brodie, M.Sc., A.I.C., Director, Industrial Research Bureau; Published by the Manager of Publications, Delhi, 1937; pp. 116; As. 6) is a valuable compilation systematically recording the physical, chemical and economic characteristics of about 129 Indian vegetable oils. These have been broadly classified into 24 drying oils, 27 semi-drying oils and 78 non-drying oils, and represent as many as 55 botanical families.

The sources of information have been not only the Governmental publications in the Museum, Agricultural Industries and Forest Departments, but also Journals of the Imperial Institute, Indian Institute of Science, Indian Chemical Society, Indian Institute of Chemistry, and the Society of Chemical Industry. Information has also been drawn from unpublished records of the Government Test House, Alipore, and the Harcourt Butler Institute at Cawnpore.

The review has summarised all fatty work done to the end of 1936, and contains very few errors, omissions or mis-statements. It is well known that, owing to its favourable climate, India is the second largest producer of oil-seeds in the world, and that the oils derived therefrom are in great demand all over the world for a variety of essential, edible, industrial and medical purposes.

The present publication is a valuable handbook of reference to the business man as well as to the chemist, drawing their attention to the lesser

known but abundantly occurring oil-seeds of the country, for their future exploitation for the one or the other of the various uses to which they have been pointed out to be suitable. The thanks of the English-knowing industrial public are due to the author for his thoughtful compilation and to the Government of India for its low price.

All-India Institute of Hygiene and Public Health.—The *Annual Report* of the Institute for the year 1936, recently issued, gives a brief account of its activities and is an impressive record of another year's progress. It may be recalled that the Institute was established from funds (17.87 lakhs) provided by the munificence of the Rockefeller Foundation, New York, U.S.A. The responsibility for its maintenance was undertaken by the Government of India. The Institute provides advanced training for public health workers on an all-India basis.

In the year under report, side by side with basic researches, a number of investigations bearing on public health problems of the country were conducted. One such problem to receive the attention of the research staff was *Cholera*. The causes of epidemicity of cholera in Bengal were investigated and from a statistical analysis of recorded cholera mortality in different parts of Bengal it was found that only certain areas were definitely endemic. The information collected from these areas will be useful in clarifying certain points in regard to the cholera problem. Researches on the chemical constitution of cholera vibrios in relation to the virulence of the organism and simpler methods for determining the chemical constitution of these vibrios will be of help to workers in the field. Statistical studies were carried out with a view to develop a method for forecasting cholera epidemics and so to forewarn public health authorities.

Special attention was paid to the study of epidemic dropsy. The interesting observation that certain supplies of mustard oil when fed to human volunteers, produced symptoms of epidemic dropsy, was made during the year. The