CHEMOPROPHYLAXIS IN MALARIA

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MALARIA, the most widespread of all the diseases prevalent in India, causes the greatest amount of morbidity and mortality in the country. The number of individuals that suffer from malaria every year, has been estimated at a minimum of 100,000,000 amongst which *nearly one million die of it per year.* For the interests of public welfare as well as for the general development of the country attention should be directed to the prevention of the disease in individuals. The growth of *Anopheles* mosquito that is responsible for the spread of malarial infection must be checked. This may be done by destroying the breeding centres and by killing the adult stage of the mosquito. Of course, there would take time to materialise. A chemoprophylaxis might then be a better method for controlling the infection throughout the length and breadth of the country.

Quinine is the common antimalarial and is in general use. But it must be taken in doses that would relieve symptoms. Taking this at a minimum of 45 grains, a rough approximation of the annual requirement for India would be (100,000,000 × 45) grains, or, approximately more than 6,00,000 lbs. The average production in India, however, comes to about 90,000 lbs. To this we may add the amount which India imports every year. This on average is found to be 1,10,000 lbs. per year before the war. It thus appears that the consumption of this antimalarial is at best one-third the estimated requirement. From the report of Wilson and Mirchandani on the prospects of cinchona cultivation in India, it may be found that there are enough suitable land in India for cinchona plantation to meet the total requirement of quinine. It is difficult to understand why plantations are still not being started on an extensive scale. The cinchona plants take some years to mature and the maximum content of the alkaloid occurs in trees between the ages of seven and eleven years. In spite of new plantations which might immediately be started, we would have to depend on the imported quinine for years to come. But even then it is difficult to meet the heavy demand of the country with imported quinine from abroad, as the world production of quinine is believed not to exceed 2,000,000 lbs.—Java alone supplying 90 per cent. of the above production. However, when this most valuable remedy in controlling the disease in man, is not yet available in sufficient quantities, we should search for other remedies to eliminate this evil.

It may be noted that in spite of the various measures such as destroying the larval stage of the mosquito by Paris Green or some oil, killing the adults by insecticide, or, protecting the human beings by administration of antimalarials, malaria as a disease is not diminishing to any extent. On the contrary in wartime its fury further increases in virulence. As no immuno-therapy is possible in the treatment of malaria, the most promising line of attack would be by means of chemotherapy. It would have been ideal if a compound would have been available that might have prevented the inception of an infection when a man has been bitten by an infected mosquito. No such compound is yet known and as such a true prophylactic measure cannot be followed.

The next step would be to attack and destroy the malaria parasite in the various stages of development in the human body. Quinine as well as certain synthetic acridine derivatives (Atebrin, Atabrine, Mepacrine or Alecrin) remove schizonts from circulation. But these have no effect on gametes. The drug plasmochin—a quinoline compound is the only gameticide in vogue. Similar other quinoline derivative is also now being found to exert a definite and often better gametocidal action. In spite of treatment with one or other antimalarial drug, some parasites are left in the body mechanism and may reappear in the peripheral circulation causing a relapse at a subsequent interval; *P. falciparum* (tropical malaria) persists after an attack for a year only, the *P. vivax* for two and half years and the *P. malariæ* upto seven years. So the problem in the treatment of malarial patients, would be to find out a therapeutic agent that would destroy the parasites that might have entered into the fixed tissues (probably the reticulo-endothelial cells) and thereby lower down the cause of relapses. Naturally, what is wanted for true chemoprophylaxis is a drug that would act equally on all the above stages of the parasite, or, at least a drug that would prohibit the inception of a malarial infection. It should, of course, be less toxic, more active, readily produced and easily available to the mass. Under these circumstances then, the menace in question be removed or at best checked to a considerable extent.

As it stands at present, there is no drug to prevent infection. Quinine and Atebrin like compounds, however, are *good schizonticides*, and as such, are in heavy demand. The rate of production of quinine and its availability in India, as indicated above, cannot satisfy India's requirements. The only other immediate remedy lies in the production of the synthetic schizonticides. It is now well known how these can be produced. The most important chemicals required, are toluene, benzene, acetone, acetic acid, nitric acid, hydrobromic acid, alkalies, fusel oil, chloroform, benzene, phosphorous oxychloride, thionyl chloride, chlorine, metallic sodium and diethylamino ethanol (or, simple diethylamine). There is no secrecy in the mode of production and every one can produce it. The point is how to obtain the product in quantities to meet India's demands. As 1·5 gram of this antimalarial is required for one course of the treatment, 100,000,000 sufferers in India would require roughly 3,500,000 lbs. To achieve this production our chemical industries would have to supply all the above chemicals costing many

million pounds. Certain of these chemicals, of course, would be easily available, some like toluene, benzene, acetone, fusel oil, etc., are being produced, but on account of Government control their supply is restricted. Metallic sodium, phosphorous oxychloride, thionyl chloride and diethylamino ethyl alcohol are not available at the present moment and have to be imported from abroad. The full requirement for India would necessitate the purchase of 3,150, 4,000, 7,470 and 4,000 cwts. respectively of metallic sodium, phosphorous oxychloride, thionyl chloride, and diethylamino ethyl alcohol approximately. Previously America too synthesized the antimalarial from intermediates imported from Germany. If the start that has already been made in India be encouraged, there is no reason to believe why in very near future India would not be able to satisfy her own requirements by manufacturing all the materials that are necessary within the country itself.

It is quite natural and possible that by producing the synthetic antimalarials and cultivating the cinchona plants wherever possible, we can supply enough materials for suppressing the malarial attack in every part of the country. In the meantime extensive investigations and co-operative research may be carried out throughout the various research institutes to find out a sporozoiticide that would be a true prophylactic, and prevent malarial infection in future.

FORECASTING AND ESTIMATION OF CROP YIELDS

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FORECASTS and estimates of yield of commercial crops like cotton, jute or sugarcane are of considerable importance to the trade and industry, because the availability of raw materials during the season is the basis of all calculations of manufacturing processes. With the increasing emphasis on 'planned' production, a still greater value will come to be attached to reliable estimates of yield, while in an emergency, like the present, arising out of war conditions, accurate forecasts and estimates of production are a paramount need for ensuring sufficiency of food grains and their equitable distribution in different areas. In India, where tax on agricultural land forms the principal source of Government revenue, the Government administration is specially interested in forecasting and estimation of crop yields.

Forecasts or estimates of most probable production are made while the crop is still standing in the field, whereas the actual production is estimated at or soon after harvest. The latter may be treated as a more accurate forecast concerning the movement and arrival of the crop to the market during the season. Estimation of production involves a knowledge both of the average yield per acre and of the total acreage sown with the crop. In England and the United States of America crop forecasts are made by a large number of voluntary reporters who are in close touch with the farming of their respective areas. In America, crop reporters are required to estimate both the yield per acre and the acreage under the crop; but in England acreage figures are obtainable precisely, since compulsory returns for all holdings are made to crop reporters. Except in permanently settled districts, an elaborate Government organization extending to the remotest village looks after crop forecasting in India. Each village has a *patwari* or an accountant who is also the crop reporter. His estimate of seasonal yield is usually expressed as a fraction of the normal yield; a method similar to that adopted in America. Acreage figures are recorded in the village register, which contains a list of all fields in the village, their dimensions and areas sown in each field with different crops each season. Area figures for different crops are consequently known with a high degree of accuracy.

The chief defect of the present methods of forecasting yield in India as well as in other countries is that no objective procedure is employed in arriving at the estimates which are merely opinions of individuals as to what the yield is. The normal yield, which forms the basis, has no precise definition. In America it is understood to represent yield better than the average but less than the maximum. In India, a certain number of crop cutting experiments are conducted on selected plots of land; but a straight average of these experiments is not taken as the normal yield. The figure adopted is based on selected results coupled with local information and opinions of revenue officials. In the absence of accurate estimates of final yield it is usually impossible to judge how closely the forecasts represent true yield. For commercial crops, independent data relating to yield are available through records of arrivals in markets or at factories; but these are ordinarily far too incomplete to provide an effective check on the forecast estimates. For grain crops even this information is lacking. It is frequently argued that the judgment of a skilled and experienced observer regarding average yield cannot be much wrong; but this contention has not been borne out whenever it has been put to a test (Yates, 1936; Irwin, 1938). Yates (1936) has given interesting examples of how forecasts based on a casual inspection of the crop can go badly wrong, and how biased results are produced either by attempting to choose deliberately an average sample or by omitting to follow an objective procedure in sampling. Agreement between different observers is no guarantee that the estimate represents the true average closely. All or majority of them may systematically under or over-estimate it. This bias can be allowed for only if its magnitude and direction can be shown to be fairly constant.

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