[JULY, 1951

Public Health Section

A REPORT ON KALA-AZAR IN ASSAM (concld.)

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The epidemics of kala-azar in Assam and their features

FROM the records of the number of fresh cases of kala-azar in the different districts for the last thirty years (table II and the charts), it will be found that epidemics of kala-azar have occurred in different districts of Assam at intervals of about 7 to 10 years and have lasted for about ten years each time. The charts show two distinct epidemic waves during the last thirty years in Sibsagar, Nowgong, Darrang, Garo Hills and Goalpara districts. Kamrup district had a serious epidemic in the nineteen twenties; since then the incidence of kala-azar has been at a lower level showing slight rises at times. Cachar district shows a fair degree of endemicity without any epidemic outbreaks.

It appears that, after an inter-epidemic period of 7 to 10 years, there is a rise in the number of

cases and this rapidly goes on to the height of the epidemic within a year or two. After the epidemic has reached the peak there is a slight decrease during the next year and again there is a marked increase in the number of cases. The incidence chart shows two or even three rises in the course of the entire epidemic period. The second and the third rise in the number of cases are probably due to the subsidence of an outbreak in some areas followed by epidemics in other areas in the same district. At the end of the epidemic period the number of cases comes down to a level often slightly higher than that previous to the onset of the epidemic. Epidemics have a tendency to increase the extent of endemic area of kala-azar and this is how the disease has progressed up the Brahmaputra valley.

In small isolated communities an epidemic of kala-azar lasts for a much shorter period. This may be illustrated from the following details of an outbreak of kala-azar in a village in Kamrup district :

There was an outbreak of kala-azar in the village Jokhaikona in Gauhati subdivision, served by Barama Dispensary, during 1946–48. There were very few cases of kala-azar in this

TABLE II

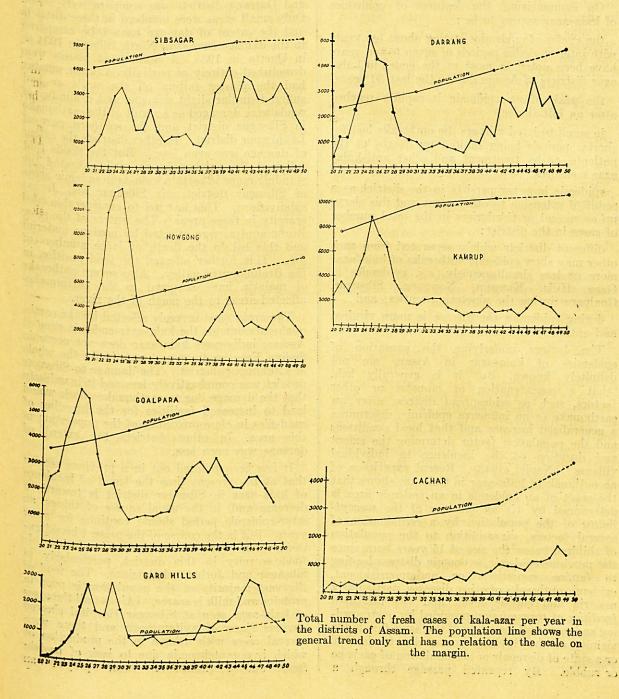
Number of fresh cases of kala-azar treated in the endemic areas in Assam, 1920-49

Year	Goalpara	Garo Hills	Kamrup	Darrang	Nowgong	Sibsagar	Cachar
1920	1,559	49	2,402	387	1.010	050	internet in the second
1921	2,500	84	3,491	1,360	1,816 4,343	659	75
1922	2,731	329	2,700	1,229		875	316
1923	4,176	589	4,098	2,416	5,934	1,307	210
1924	5,016	985	5,780	3,286	$11,847 \\ 13,625$	2,143	352
1925	6,003	1,952	8,758	5,260	13,020	2,929	253
1926	5,671	2,812	7,301	5,262 4,414	13,895	3,285	442
1927	3,495	1,828	6,445	4,414	9,586	2,658	323
1928	2,316	1,690	3,577	4,053 2,228	5,008	1,521	359
1929	2,389	2,905	2,598	1,399	2,614	1,555	394
1930	1,439	1,905	1,814	1,106	2,433	2,387	470
1931	992	882	1,690	942	1,440	1,495	376
1932	1,089	605	2,061	665	1,057	1,095	370
1933	1,159	850	2,223	665 757	1,075	1,269 1,251 1,372	391
1934	1,107	927	2,197	876	1,663	1,201	472
1935	1,245	690	1,465	738	1,726	1,372	529
1936	1,275	793	1,309	636	1,651	938	478
1937	2,046	717	918	514	1,471	864	574
1938	2,541	824	1,189	989	2,317	1,396	445
1939	2,989	808	1 139	861	3,265	3,050	716
1940	3 104	1,346	1,138 1,721	1,491	3,875	3,315	669
1941	3,194 2,761	1,259	2,215	1,128	5,129	4,070	778
1942	3,314	1,496	1,338	2,599	3,593	2,640	1,024
1943	2,639	1,472	1,505	2,393	2,774	3,643	963
1944	2,178	1,722	914	1,860	3,093	3,494	935
1945	2,125	2,484	1,573	2,087	2,758	2,747	805
1946	2,538	3,007	2,286	3,322	2,586	2,629	1,135
1947	2,541	2,809	1,942	2,254	3,552	2,807	1,115
1948	2,121	1,677	1,607	2,586	3,820 3,448	3,354	1,256
1949	1,558	1,433	904	1,796		2,842	1,678
	1,000	-,100	504	1,190	2,807	2,070	1,367

village previous to 1946. The population of the village was 300 and consisted mainly of Kacharis. There were 5 cases in 1946 of which one died during the next year in spite of treatment with urea stibamine. Next year (1947) there were 10 cases of which 9 died in spite of specific treatment with urea stibamine, and in 1948 there were 14 cases of which 4 died and four other patients had to be treated with pentamidine after the failure of urea stibamine in effecting a cure. In December 1948, all infected cases were isolated out of the village and in 1949 no fresh case was seen. Only one case was seen in 1950. During this epidemic

the patients were found to be very ill and had severe anæmia and leucopenia. The diagnosis of kala-azar was confirmed during this outbreak by the aldehyde test and by finding *Leishmania donovani* on sternum puncture.

It will be noted that the total duration of the epidemic was short, possibly cut off by treatment and isolation of the cases, and that kala-azar was not amenable to treatment with urea stibamine at the height of the epidemic. Similar antimony resistance was noticed during the epidemic outbreaks in different parts of Sibsagar district.



From the above account, it will be evident that kala-azar is more antimony resistant during epidemics than during inter-epidemic periods. The death rate is also higher. For example, during 1945–47, 583 cases of kala-azar were admitted into Golaghat Kala-azar Hospital; 85 patients died in spite of specific treatment. During 1949-50, at the end of the epidemic, 187 cases were admitted of which 16 died. The average case mortality was 14.5 during 1945–47 and only 8.5 during 1949-50. The experience of treatment of large number of cases of kala-azar during the recent outbreak of kala-azar in Calcutta was similar.

On summarizing, the features of epidemics of kala-azar appear to be :

the cycles of epidemics lasting about ten years with inter-epidemic periods of seven to ten years have been noted in most of the endemic kalaazar districts of Assam during the last 30 years;

the peak of an epidemic is rapidly reached after an initial rise;

in small isolated villages the outbreaks last for shorter periods being limited by deaths of the patients, or by treatment and other anti-kalaazar measures;

epidemic however persists in the district as a result of extension to other areas and this shows up as second or third rises in the total number of cases in the district;

different districts widely separated from each other may show epidemic outbreaks of kala-azar more or less simultaneously, *e.g.* epidemics in Garo Hills, Kamrup, Nowgong, Sibsagar, Goalpara during the nineteen twenties; and

during epidemics the disease is more virulent and antimony resistant.

The factors underlying the causation of epidemics of kala-azar in Assam are not definitely known. But it is generally held that a concatenation of climatic or other factors, such as widespread distress after an earthquake or an influenza epidemic, determines a generalized increase and that local conditions and the population factor determine the extent and duration of the incidence in individual villages' (Napier, 1943). Recent experience of an outbreak of kala-azar in Calcutta shows that the onset of an epidemic in an endemic area is determined by (i) an increase of the susceptibility of the population by a combination of several factors, viz addition to the population of children below the age of 15 years born since the previous epidemic, economic distress leading to famine conditions or undernourishment, epidemic outbreaks of other diseases, particularly malaria and enteric fever, and (ii) increased facilities of transmission provided by overcrowding and increased breeding of the sand-flies in the vicinity of the dwelling houses due to damage or a state of disrepair or accumulation of garbage By repeated passage through a or rubble.

population thus rendered more susceptible, there is (iii) an increase of virulence of the parasite and the epidemic goes to the peak and continues till interrupted by anti-kala-azar measures or exhaustion of the susceptible material (Sen Gupta, 1947).

The recent earthquake and the incidence of kala-azar in Assam

The recent earthquake caused severe damage in areas to the north of the river Brahmaputra, mainly in Sadiya Frontier tract and North Lakhimpur districts. The damage caused in southern part of Lakhimpur district, Sibsagar and Darrang districts was comparatively small. Only small areas were involved in these districts and the extent of damage cannot be compared to the damage caused in North Bihar in 1934 or in Quetta in 1935. A number of houses were demolished entirely or partially, a larger number had the plaster falling off the walls or had suffered similar slight damage, and a number of roads were damaged as a result of the earthquake in Sibsagar district and the southern part of Lakhimpur district. In other districts the extent of damage was even less. But the floods that followed the earthquake seriously affected the standing crops in certain kala-azar endemic areas of Sibsagar district, viz Sibsagar and Jorhat subdivisions. This has led to considerable food scarcity in these areas. The waters of the river Brahmaputra were affected by noxious material and this led to the death of large numbers of fish. This further affected the food position in the Brahmaputra valley. Also severe outbreaks of malaria have occurred in the earthquakeaffected areas to the north of the river.

The areas most severely affected by the earthquake are outside the kala-azar endemic zone of Assam; indigenous kala-azar does not occur in Sadiya Frontier tract and practically the whole of Lakhimpur district. The damage to Sibsagar district was comparatively less and it is unlikely that the damage due to earthquake shock would lead to increased facilities for the breeding of sand-flies in close proximity of the population in this area. In other districts the extent of damage was even less.

It has been pointed out in a previous section that at the present time the trend of incidence of kala-azar in Sibsagar district is towards a decrease and, in the usual course of things, an inter-epidemic period should continue for some years. But in the course of the present investigations, it has been found that there is considerable food scarcity in this district, particularly in Sibsagar and Jorhat subdivisions. The food of the vast majority of the population is poor in proteins and milk is scarce. (Almost all the cases of kala-azar seen at Sibsagar Hospital showed obvious signs of avitaminosis and there were several cases with ædema in the production of which hypoproteinæmia due to lack of protein and/or kala-azar itself played an food

important part). Rice and green vegetables form the daily food and only occasionally dal, and small fish are eaten. Meat and eggs are not generally taken by poorer class of Hindu population. The other serious problem in Sibsagar district is the presence of a fair number of antimony-resistant cases of kala-azar. These cases may supply a virulent strain of the parasite.

The other kala-azar endemic districts show a tendency to decrease of kala-azar incidence in most of the areas. Increase of kala-azar in these districts as direct result of the earthquake shock is unlikely. But in view of the presence of economic distress and of the drug-resistant cases of kala-azar in Sibsagar district it is desirable to be on the look out for an increase of kala-azar in this district and some parts of Nowgong district (Kathiatoli area).

The problem of drug-resistant kala-azar

In the early days of antimony therapy of Indian kala-azar the impression gained ground that almost all cases could be cured completely with a course of injections of one of the pentavalent antimony compounds, viz urea stibamine or neostibosan. There is no doubt that the results obtained were very good and there were some grounds for such optimism. But even in these early years of successful treatment, careful observers had noted that all cases of kala-azar could not be cured with the best of the antimonials and they had assessed that about 2 to 5 per cent cases proved entirely refractory to treatment. During the last twenty years experience of kala-azar in other endemic areas in the model of kalain the world has shown that the parasite of kalaazar varies in its susceptibility to specific treatment in different countries. Even in India itself recent experience has shown that kala-azar was much more virulent and less amenable to treatment during epidemics than during interepidemic periods. Smith had noted in 1940 that large number of cases of kala-azar proved refractors the outrefractory to urea stibamine during the outbreak at Golaghat in Sibsagar district in Assam. The present investigations also confirm his finding. In Sibsagar district numerous cases of kalo kala-azar had proved antimony resistant during the epidemic of 1938-48 and had died in spite of repeated courses of injections of antimonials. Epidemics elsewhere in Assam have also been at times marked by the presence of similar drugresistant cases and during and after the recent outbreak of kala-azar in Calcutta, large number of such cases were treated at the Hospital for Tropical Diseases of the School of Tropical Medicine.

The drug-resistant cases are generally characterized by either failure to respond satisfactorily or by relapse within a few months after an apparent clinical recovery after an ordinarily efficient course of specific treatment. Some of these cases can be cured with several courses of injections of antimonials or aromatic diamidines. But others relapse repeatedly after some degree of improvement following specific therapy and ultimately these patients die of inter-current infections or the disease itself after several years of suffering.

It is difficult to assess the proportion of resistant cases correctly. It varies in different areas and during different years. In Calcutta, there were 50 'relapsed' cases out of a total of 291 cases of kala-azar diagnosed at the kalaazar out-patients' clinic of the School of Tropical Medicine, in 1950. In Assam there appears to be a fair number of such cases in Sibsagar district even now. The dispensary returns from some of the centres visited show the number of 'relapsed' cases (see under section 'trends of incidence'). There were 96 cases of kala-azar admitted into the Civil Hospital, Sibsagar, during 1950; of these 32 were resistant cases. At the Christian Hospital, Jorhat, there were 8 resistant cases out of a total of 45 cases admitted during 1950. Several other drug-resistant cases from Sibsagar area were seen at the Medical College Hospital, Dibrugarh. The records of five more cases were sent to me from Sibsagar area by the Director of Public Health, Assam. All these cases had been repeatedly treated with urea stibamine and pentamidine; but relapses had occurred invariably. One extremely drugresistant case was sent to the School of Tropical Medicine, Calcutta. This patient was treated with repeated courses of all the most powerful antimony and aromatic diamidine compounds; yet he is not free from kala-azar.

It will be realized that drug resistance in Indian kala-azar is a new and important problem for the medical and public health workers. It renders the treatment of kala-azar less certain and the treatment of resistant cases is time consuming, expensive and not very satisfactory. From the public health point of view, a virulent form of infection persists in the community for several years. As the susceptible population grows in an endemic area, if as a result of several factors there is an outbreak of kala-azar originating from this virulent drug-resistant form of disease, the results may be disastrous. It has already been pointed out that, at the height of epidemics in different areas in Assam, large proportion of the cases have proved drug resistant and relatively large proportion of the affected individuals died in spite of treatment.

Little definite is known about the cause of drug resistance in kala-azar. The resistance may be due to the factors in the parasite or in the host or in both. It is possible that the parasite may be naturally more resistant, e.g. as in Sudan kala-azar, or it may acquire drug resistance like other protozoa (e.g. malaria parasite to proguanil, or trypanosomes to arsenicals) as a result of being subjected to minute fractional doses of specific drugs. It may be pointed out that the use of minute doses of urea stibamine (small fractions of the prescribed doses) is not uncommon in Assam and the attendance of the patients at the treatment centres often rather irregular. This may be an important factor in promoting drug resistance of the parasite in Assam. The possible host factor may be either an inability of the host's reticuloendothelial system to utilize the specific drugs for combating the infection or failure to maintain an effective concentration of the drug in the system.

Control of kala-azar in Assam

Previous to the introduction of specific therapy, the measures for control of kala-azar consisted of isolation of the cases and in the tea estates of Assam, of burning down of the infected 'coolie lines' and building another at least three hundred yards away. The latter led to good immediate results and the number of cases could be brought down very considerably for a few years.

Knowles (1920), after careful assessment of tartar emetic treatment of kala-azar at Shillong, drew attention to the possibility that if as McCombie Young believed 'the reservoir of infection' with kala-azar was man, then the successful treatment of all cases might exterminate the epidemic. Subsequently mass treatment of cases, first with antimonyl tartrates and later with urea stibamine, was adopted as a measure for the control of kala-azar. When the incidence of the disease came down to low levels after the epidemics of the nineteen twenties, it was felt that the treatment campaign was responsible for this lowered incidence and that there were very good chances for the eradication of kala-azar. The Governor of Assam expressed himself in the following words in his farewell speech to the Legislative Council of Assam in 1926 :

> 'We may now say that victory, if not in sight, is assured. The progress in the campaign against kala-azar in Assam has been phenomenally rapid and if it continues at the present rate there is an excellent prospect of this dread scourge being brought under complete control in a few years.'

Study of the incidence of kala-azar in Assam since the inauguration of mass treatment campaign shows that this measure has not prevented the onset of epidemics and has hardly affected their duration. It is conceded that the total number of cases of kala-azar during the outbreak of 1938–48 was less than that during the twenties and that treatment has saved a large number of cases that would otherwise have died. But from the facts collected about the epidemics in small villages, it appears that a large proportion of the cases died at the height of the outbreaks in spite of treatment. Also the problem of drug resistance in kala-azar has assumed important proportions. These facts lead to the conclusion that at present kala-azar can hardly be regarded as under control in Assam.

Recent researches have shown that modern insecticides, viz DDT and allied compounds, are very effective against the sand-fly, the insect vector of kala-azar. It is probable that systematic insecticidal measures may interrupt the cycle of transmission of kala-azar and thus help in its control. Insecticides have not been used to any great extent in Assam for the control of kala-azar. In 1949, however, a number of villages in Nazira area in Sibsagar district were sprayed with DDT in order to control malaria. It may be a coincidence; but since then there has been a distinct drop in the number of cases of kala-azar in this area. It is impossible to be certain whether the decrease was due to natural subsidence of the epidemic at the end of a tenyear period or to the effect of DDT spraying. It will be recalled that the incidence of kala-azar in a group of estates in Sibsagar area (Dr. Burke's practice) is less than that of the neighbouring areas and the district taken as a whole. In these tea estates, pyrethrum-spraying was one of the anti-malarial measures adopted : and it is well known that pyrethrum has a repellent action against the sand-fly as well. The above facts cannot be regarded as conclusive but are suggestive enough to justify the use of insecticides against the sand-fly as well as the mosquito. The measures for the control of kala-azar should consist of thorough treatment of all cases of kala-azar and dermal leishmaniasis (the latter condition is less frequent in Assam than in Bengal) and measures against the insect vector, the sand-fly *Phlebotomus argen-tipes*, using the modern insecticides, DDT and allied compounds.

Conclusions

The present studies on the incidence of kala-azar in Assam have shown that the disease is highly endemic in Cachar, Sibsagar, Nowgong, Darrang, Kamrup, Goalpara and Garo Hills districts. During the ten-year period 1940-49, over 155 thousand fresh cases of kala-azar were recorded and about 1 in 40 people of these districts suffered from the disease. In spite of the fact that mass treatment of kala-azar cases has been in operation for the last 30 years, this measure has failed to prevent the onset of epidemics of this disease in the highly endemic districts. Large number of antimony-resistant cases have been recorded particularly from Sibsagar district during the last ten years and at the height of epidemic of kala-azar in small village communities large proportion of the cases had died in spite of antimony therapy.

The recent earthquake caused severe damage to areas to the north of the river Brahmaputra mainly in non-kala-azar areas. It is unlikely that any outbreak of kala-azar would result in these areas. But in Sibsagar district, though the

extent of devastation has been less severe, destruction of the standing crops as a result of the floods that followed the earthquake has led to marked economic distress and malnourishment. This fact together with the presence of drugresistant virulent kala-azar infection in this area emphasizes the need for close watch and adoption of measures for control.

In view of the fact that mass treatment of cases has failed to control kala-azar in Assam, it is necessary to consider what other measures may be adopted for the purpose. It is well known that insecticides particularly DDT and similar compounds are highly effective against the send for the purpose. If the sand-fly, the insect vector of kala-azar. If DDT spraying of the endemic foci can be adopted, it is highly probable that the cycle of transmission of kala-azar would be interrupted by the destruction of the vector and this measure will help in the control of kala-azar. It will be necessary to continue treatment of all cases of kala-azar and post-kala-azar dermal leishmaniasis (the latter condition is being more frequently seen now) more thoroughly using the most effective pentavalent antimonials and/or aromatic diamidines.

The following words of Knowles (1934) that proved prophetic may rightly be borne in mind at the present time :

The virus is everywhere in endemic areas and a new generation of susceptible persons is growing up. Anything in the way of widespread epidemic disease, famine conditions or such catastrophes as the recent earthquake in North Dil North Bihar may very possibly be followed by a renewed epidemic of kala-azar. The present is not the time to lessen public health activities against the disease; it is rather a period in which vigorous measures should be taken to eradicate all foci '.

The investigations on kala-azar in Assam were undertaken under the auspices of the Indian Council of taken under the auspices of the Indian Council of Medical Research. I am very thankful to the Director of Public Health, Assam, for providing full facilities and help in carrying out the survey and for various epidemiological data. I appreciate the great help I received from the various members of the Public Health Department, Assam, viz Assistant Directors of Public Health, the Medical Officers of Health of the districts and subdivisions and the Medical Officers of districts and subdivisions and the Medical Officers of districts and subdivisions and the Medical Officers of remote dispensaries in the villages, in studying the cases and collecting various data from the dispensaries and departmental offices. My thanks are due to the Inspector-General of Civil Hospitals, Assam, and the staff of the various hospitals and dispensaries under the medical department, to the Principal and the staff of Assam Medical College, Dibrugarh, to the Principal Medical Officers of several groups of tea estates, and mission hospitals and to the Indian Tea Association and the Ross Institute at Cinnamara for help in study of the kala-azar problem in Assam. of the kala-azar problem in Assam.

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PRESENCE OF ARGEMONE MEXICANA SEEDS IN MUSTARD SEEDS GROWN IN BIHAR

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OUTBREAKS of epidemic dropsy have been reported at varying intervals from different parts of this state. In a previous communication (Lal, 1951), details of each outbreak have been described including the severe outbreaks of the disease from various parts of Bihar including Patna the capital town in late 1949 and early 1950. In the course of the steps taken to stop the outbreaks, a large number of oil mills and wholesale mustard seed dealers' godowns were visited. Mustard seeds mixed with argemone seeds were found in only those samples imported. from other states and in none of the indigenous samples. Doubts were raised by some on this observation.

The paper attempts to give the results of an investigation regarding the presence of argemone seeds in mustard seeds grown in this state and the reasons for the seasonal incidence.

Technique of investigation

In early March 1950 a circular letter was sent to all district officers of this state requesting them to collect samples of mustard seeds, through reliable magistrates without giving any prior information to any body,

(i) by actually harvesting a portion of the plant standing in fields,

(ii) from the stock of big oil seed dealers, and

(iii) from the stock of big oil mills engaged in the production of mustard oil.

The letter asked them to report if argemone seeds were available in their respective districts, in large quantities without much trouble and also the harvesting experience of the labourers as to whether argemone seeds were or could possibly be harvested either separately or jointly with mustard seeds.

The district officers got the samples collected between April to June 1950 and sent the same to this laboratory. Each sample was thoroughly examined by the author in bright daylight with