An epidemic of tropical sprue in southern India
II: Epidemiology

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Tropical sprue is usually thought of as being an endemic disease. However Hilary (1759) describes the disease in what may have been an epidemic form in Barbados, and since the nineteenth century a number of epidemics have been described from the Indian subcontinent (Baker and Mathan, 1968).

In Tamilnadu (formerly Madras State) in southern India, endemic sprue has probably been present for many years (Baker, 1957). In this area between 1960 and 1962, there was a widespread epidemic of diarrhoea in which a number of the affected individuals had symptoms persisting for months and in some cases for years. Clinical and laboratory investigation of affected individuals showed them to be suffering from tropical sprue (Mathan and Baker, 1970). This communication reports the results of an epidemiological study of this outbreak. A brief preliminary report of this epidemic has been published previously (Baker et al., 1962).

METHODS

Five villages ("K", "M", "N", "P" and "T") and the eastern part of a town ("W"), all within a radius of five miles in North Arcot District of Tamilnadu (fig. 1), were chosen for a detailed study which was begun in August 1961 (the "detailed survey"). In the five villages every house, and in the town, every fifth house, was visited. As far as possible every person in the house was interviewed by one or more members of a team of doctors and health visitors. Detailed information regarding occupation, family and individual income, housing, diet, water supply, sanitation, the presence of cattle and other animals, the incidence of other diseases, and the individual's bowel habits, was recorded on a standard proforma. Individuals were considered to have diarrhoea when they had noticed a change in bowel habit and were passing three or more unformed or semiformal stools per day. When diarrhoea was, or had been present, a full clinical history was obtained. All people who had diarrhoea for ten days or longer during the previous year were included in the analysis. When people had died of the disease before the arrival of the team, information was obtained from the nearest available relative. The same area was kept under surveillance until 1969 and each affected person was followed-up.

The area affected by the epidemic was determined both by spot surveys carried out by the same team and by information from the State Public Health Department and Medical Service. In addition, in an endeavour to study the geographical distribution of the disease

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in greater detail, a more rapid and less-detailed survey of 248 villages, with a total population of 204,161, was carried out over a strip some 15 miles wide and 50 miles long, along the northern border of the epidemic area (the 'rapid survey').

**Fig. 1.** Part of Tamilnadu (Madras State) showing the elevation above mean sea level, and the main rivers. The approximate area affected by the epidemic is shown by the dotted line. The rectangle shows the position of the villages and town studied in the intensive survey.

**GENERAL DESCRIPTION**

The area in which the epidemic occurred is about 50 miles wide and 80 miles long, in North and South Arcot Districts of Tamilnadu (fig. 1). The area is traversed from west to east by three large rivers. For most of the year these rivers are dry, but at the time of the monsoons they contain water. Scattered all over the region are innumerable wells and tanks or dams, varying in size up to several square miles in area. These tanks are shallow and often dry-up during summer, but are full during the rainy season.

The total population of North and South Arcot Districts in 1960 was 62 million. The majority of people live in villages which vary in size from about 200–5000 population. In these villages the people usually live in streets, or areas, according to their caste or religion. Most villages have a hamlet for the Harijans, separated from the main village by a distance which may be from a few hundred yards to a mile or more.

In the villages, the majority of houses have earthen walls and floors and thatched roofs, but there are usually some houses, belonging to the more wealthy, made of baked brick,
with tiled roofs and cement floors. In the towns a higher proportion of houses are made of brick. For the purposes of this study one ‘household’ is defined as those people eating from one kitchen. The number of individuals in one household ranged from 1 to 21 with a mean of 5±2. The larger household units are ‘joint families’ consisting of members of three or more generations.

The majority of the houses are infested with rats, bugs, lice and cockroaches. Flies and mosquitoes are also plentiful. Mosquitoes of all varieties are most numerous in the months October–December. The most prevalent species are *Culex virophthalmi*, *C. fuscocephalus*, *C. bitaeniorynchus*, *Anopheles subpictus*, and *A. hyrcanus*.

During the wet season many houses are damp. In the villages there are no latrines, the adjoining fields serving for this purpose. Garbage is either thrown away indiscriminately, or is collected in a pit near the house and transferred at intervals to the fields. In the towns the authorities make arrangements for the regular collection and disposal of nightsoil and garbage, but these facilities are not always utilized.

The area receives its rainfall both from the south-west and the north-east monsoons, the larger part falling in the period September–December. In 1960 the rainfall was exceptionally heavy and had been equalled only four times in the previous thirty years.

Most of the population are vegetarians either by economic necessity or religious practice. A detailed nutritional survey and dietary analysis of a similar population has been reported by Rao and Rao (1958 a, b, c). Drinking water is usually obtained from surface tanks or unprotected wells, and is never boiled before use.

The vast majority of people in the area are Hindus, but there are also small groups of Jains, Muslims, and Christians. Among the Hindus there are a large number of different groups, but for the purposes of this study they may be divided broadly into Brahmins, non-Brahmins, or caste Hindus, and Harijans. The Brahmins are the traditional priestly caste. Economically they range from the very wealthy to the relatively poor. In the area studied in the intensive survey there were Brahmins in two of the villages (‘N’ and ‘T’). They all lived in fairly well kept brick houses. Unlike other communities, washing forms an important part of their religious ritual, and they are generally cleaner in their personal habits. The caste Hindus form the bulk of the population in the main villages, and are usually employed in agriculture. The Harijans are the community which were previously considered to be ‘out-castes’. They work as labourers in the fields, as sweepers, or in various handicrafts such as cobbbling or mat weaving. Many of them are very poor, their diet is correspondingly less adequate and their housing is of a lower standard.

**THE EPIDEMIC**

*Time of Onset*

In each of the villages and the town covered by the detailed survey, the pattern of onset of new cases was similar. Till August 1960 there was only a very occasional case of diarrhoea, but in September more cases began to occur, reaching a maximum in November of that year (fig. 2).

*Virus Research Center, Poona, unpublished data, 1965.*
In the rapid survey, the month of peak incidence varied, apparently in a random fashion, in different villages, from October 1960 to December 1961. In each village the basic pattern of onset was similar to that shown in fig. 2. The combined data of the incidence for all the villages (9,177 cases) in the rapid survey shows a peak incidence in November 1960 and again in November 1961 (fig. 3).

**Village Incidence**

The percentage of the population affected varied widely from village to village. In some villages within the epidemic area there were no cases, while in other nearby villages 20 to 40 per cent. of the population were affected. Near the edge of the epidemic area the proportion of the villages that were affected decreased, and the percentage attack rate in the affected villages also tended to decrease. A rough estimate suggests that probably in the whole area 100,000 people were affected.
Fig. 4. The age-sex specific attack rate, in ten-year age groups, per hundred of the population, in the detailed survey.

Open columns = males  shaded columns = females

Fig. 5. The age specific attack rate, in two-year age groups, in children, per hundred of the population, in the detailed survey.

The age-sex specific attack rate per hundred of the population in each ten-year age group, in the detailed survey, is shown in fig. 4. In general the attack rate increases significantly with age ($P < 0.001$). However in children (under 12 years) the attack rate was highest in the first four years of life (fig. 5) ($P < 0.001$). The overall attack rate in the two sexes was equal (19 per cent.). There was an increased incidence in females of child-bearing age, and a
decreased incidence in females over forty, however these differences are not statistically significant.

During the first two months of the epidemic, the attack rate in the under-20 years age group was relatively low, but in the subsequent months the attack rate in the younger age groups increased. The mean age of the patients affected in the first two months of the epidemic was 43 years, but by the period May to December 1961 it had fallen to 31.4 years (see Table).

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<td>Mean age</td>
<td>43.5</td>
<td>43.9</td>
<td>39.8</td>
<td>37.5</td>
<td>35.3</td>
<td>33.0</td>
<td>34.8</td>
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<td>Standard error of mean</td>
<td>8.5</td>
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Analysis of variance shows these differences to be statistically significant at the 0.1 per cent. level. In the rapid survey, the overall attack rate was lower, but the same pattern was present with respect to age and sex incidence.

**Incidence in Households**

More than one case frequently occurred in one household, the greatest number encountered being 10. Occasionally several members of a household would fall ill on the same day, but more often one person would first fall ill, followed after an interval of a few days to a

![Fig. 6. The interval, in months, elapsing between the time of onset of one case and the next in a given household, in the first year of the epidemic.](image-url)
number of weeks by another, and so on. During the first year of the epidemic the interval between one case in a household and the next in that household was a month or less in 55 per cent. of such pairs (fig. 6).

**Effect of Diet**

The diet eaten by people within the epidemic area was identical with that eaten by people in unaffected surrounding areas. Foodstuffs, such as pulses, which were not grown locally, or which were grown in insufficient quantity, were imported from the same sources as supplied the rest of the state. Careful enquiry regarding the dietary habits of the affected and unaffected households showed no detectable difference between the two, and no consistent association between the consumption of any one dietary item and the incidence of the illness.

In view of the suggested aetiological role of rancid fats (French, 1955), particular attention was paid to the types and sources of cooking oil. No evidence could be obtained to suggest that they were in any way connected with the illness. The possibility of aflatoxin from ground nuts playing a part in the illness was also considered. However the epidemic started before the ground nut harvest and had a similar incidence among those who ate ground nuts and those who did not. The cereal 'varagu' (*Paspalum scrobiculatum*), if improperly prepared, is said to produce a brief watery diarrhoea, but there was no relation between varagu consumption and the disease. No insecticides had been widely used on crops in the area during the preceding year.

There was no difference in the incidence of the disease in those who obtained their drinking water from surface tanks, from unprotected or from semiprotected wells.

**Incidence According to Socio-Economic Factors**

In the detailed survey the incidence was similar in all religious groups, except the Brahmins, among whom it was only 1 per cent. The incidence among non-Brahmins was the same in those with an estimated family income of less than Rs.100 per month and those with an income of more than this. The incidence also bore no relation to the type, size and value of the house, the type of roofing, the type of walls and floors, or the proximity of the surrounding houses.

Among the non-Brahmin groups there was a slightly higher incidence among agricultural labourers and a slightly lower incidence among landlords, but these differences are not statistically significant.

**Spread within the Village**

The spread of the epidemic through the villages usually followed a similar pattern. This is illustrated in figure 7 (a-d) which shows the occurrence of cases in village 'P'. The village had a total of 69 houses, five of which were vacant. In the remaining 64 there were family units varying in size from one to twenty people. The index cases were in two houses in September 1960 (fig. 7a) and gradually the epidemic spread over most of the village. It will be seen that in some houses all the cases occurred within one month whereas, in others, there were new cases occurring over a period of several months. At the end of 1961 thirteen
Fig. 7. (a - d) Diagrammatic plan of village 'P' showing the spread of the epidemic. Each square represents a house. Open circles (o) represent unaffected persons, closed circles (●) represent new cases occurring during the given period and circles with a cross (●) represent cases that had occurred before this period. (Figs. c and d see opposite).

of the houses remained unaffected, even though at times these unaffected houses were very near heavily affected ones (e.g. the south-east corner of the village). No other significant differences could be detected between the affected and unaffected houses.

In village 'N' there were 88 inhabited houses, 24 of which were in a section of the village occupied by Brahmans and 64 in the rest of the village occupied by caste Hindus.
(fig. 8). No one in the Brahmin houses developed the disease, whereas in the rest of the village 35 houses were affected, and the pattern of spread through this part of the village was similar to that seen in the other villages. In village 'T' there was also a localized Brahmin community of 27 households only one of which was affected, whereas in the rest of the village occupied by caste Hindus, 62 out of 283 households were affected.

In all villages there were schools. In villages 'N' and 'T' these were attended by children from all communities including the Brahmins. During school hours the children mixed freely and shared the same drinking water. A number of the affected children from the non-Brahmin communities attended school while suffering from the disease, but none of the Brahmin children became ill.
Fig. 9. Time of death in months from onset of disease up to two years.

Mortality

Fig. 8. Diagrammatic plan of village 'N' showing affected and unaffected houses, and the distribution of Brahmins' houses.

Of the 940 cases in the original survey 276 (29.4 per cent.) died within seven years of the onset. Twenty-three per cent. of the total deaths occurred within the first month (fig. 9), and from the descriptions, appear to have been related largely to fluid and electrolyte losses. Of the deaths after the first month, some appear to have been due also to fluid and electrolyte disturbances, others were associated with varying degrees of hypoproteinaemia, anaemia and secondary infection.

The percentage of affected individuals who died varied significantly in the different age groups (fig. 10). The highest case mortality rate was in the age groups over 60 and under 10. As might be expected, the case mortality rate in children was highest in the first four years of life. The overall case mortality was slightly higher among the affected females.
(26.8 per cent.) than among the males (22 per cent.) \((P<0.05)\). The rate among Harijans and among non-Harijans was identical.

![Bar chart showing age groups and case mortality rate](image)

**Fig. 10.** Case mortality rate in ten-year age groups in detailed survey.

Open columns = males  shaded columns = females

*Incubation period*

In two cases, individuals who lived outside the epidemic area came to stay with relatives in the epidemic area. Both developed diarrhoea, one within five days and one within six days, of their arrival in the area. In both cases, subsequent investigation showed them to have the classical features of tropical sprue.

**DISCUSSION**

Detailed clinical study of patients from the epidemic proved them to be suffering from persisting intestinal malabsorption identical with that found in cases of endemic tropical sprue (Mathan and Baker, 1970). Since the cases had a temporal and spatial relationship to each other it may be concluded that all the affected people were suffering from a similar illness, and that this epidemic was, in fact, an epidemic of tropical sprue.

Epidemics of tropical sprue are by no means new. Hillary (1759) described a disease in Barbados which was probably tropical sprue, and stated that it reached epidemic proportions, but he gives no further details. Sheehy et al., (1965) describe an occurrence of the disease in a military housing area in Puerto Rico, which could be considered a small epidemic. All other recorded epidemics have been in India, Pakistan or Burma (Baker and Mathan, 1968). Many of the recorded epidemics occurred under war-time conditions, where detailed study was not possible, and where the population studied, or at risk, was a very selected group. It is therefore often difficult to make meaningful comparisons with the present study.

Several studies record a seasonal incidence with a peak incidence in June (Crombie,
1880; Leishman, 1945; Keele and Bound, 1946; Elder, 1947; Ayrey, 1948), at 'the end of the monsoon' (Girdwood, 1948) and during October and November (Stefanini, 1948). In this study, although a peak incidence was found in November in some villages (fig. 2), data from the rapid survey showed that there was no consistent seasonal pattern in the peak incidence in individual villages. Several authors have suggested a relationship with the rainfall (Stefanini, 1948; Girdwood, 1948) and the present epidemic began towards the end of a year of exceptionally heavy rainfall. However, there was no history of a similar epidemic in earlier years of high rainfall, and although the epidemic made a big impression throughout the area, no one could recall anything like this in living memory.

It is of interest that reported epidemics have occurred in places with altitudes differing from just above sea level to 8,000 ft. (Crombie, 1880), so that if all these epidemics are of the same aetiology, their occurrence does not seem to be influenced by altitude as such. In the epidemic reported here, the disease did not appear to spread into the scattered villages in the hills to the west of the epidemic area, nor to the east below 250 ft. above sea level. However, this may have been fortuitous.

There was no apparent connection between the temporal spread of the epidemic and the geographical relationship of villages to each other, to the means of communication, or to waterways. There was also no detectable reason to explain why some villages were heavily affected, whereas other nearby villages were only lightly affected or unaffected.

The reported attack rate of the disease has varied widely in different epidemics. Crombie (1880) reported that between 50 per cent. and 75 per cent. of the adult population of Simla were attacked, as evidenced, for example, by the fact that of twenty-two persons invited to a dinner party on Wednesday, the 16th June, only six were in a condition to take their place at table, and 'a cricket match ... fell through, because only eight of the two elefants put in an appearance'. Leishman (1945) reports that in some units of British troops as many as 50 per cent. developed the disease, while among the Italian prisoners of war the incidence was 8.5 per cent. (Stefanini, 1948). In this epidemic the incidence ranged widely, in different villages, from less than 1 per cent. up to 40 per cent. of the total population.

The lower overall attack rate in the rapid survey, as compared with that in the detailed survey, is partly due to the fact that there were many lightly or unaffected villages in the former. Also the rapid survey was more retrospective and it is probable that many individuals had forgotten illnesses of short duration.

In many of the reported epidemics there were no children at risk. Crombie (1880) noted that there were only very few cases in children and it has usually been thought that tropical sprue is rare in children (Fairley, 1939; Manson-Bahr, 1965). However, a recent study showed that the disease occurs in children, although in the epidemic form the attack rate is lower than it is in adults (Mathan et al., 1969). This lower attack rate in children, and the demonstrated lowering of the age-specific attack rate as the epidemic progresses, is an unusual finding for an epidemic disease. Burnett (1959) has suggested that such a pattern might be expected in an infectious disease in a non-immune population.

Several investigators have stressed the apparent importance of previous dietary deficiency in the incidence of the disease, suggesting that the less adequate the diet the greater the incidence (Walters, 1947; Stefanini, 1948; Ayrey, 1948; Girdwood, 1948). In this epidemic the incidence among Harijans and caste Hindus was equal, although the diet of the former was less adequate. By western standards, the majority of the population
were suffering from subnutrition, and this may have contributed to the evolution of the epidemic, but there is no evidence on this point. It is also possible that some specific dietary deficiency, or some dietary toxin, might have been responsible, but this study does not provide any positive evidence in favour of either of these hypotheses. In any diarrhoeal illness the water supply is always suspect, but there was no discernible relation to the sources of drinking water.

Within a given household the pattern of spread varied widely, though most often the occurrence of new cases was spread out over a period of weeks, with the earlier cases being in the older people. A similar pattern of intrafamily spread was observed in an isolated family epidemic of sprue (Mathan et al., 1966).

Within a given village, although there appeared to be clustering of cases in space and time, no satisfactory explanation was found to account for the pattern of spread. None of the environmental factors studied appeared to have any influence on the spread of the disease and no satisfactory explanation could be given as to why some houses were affected while others remained free.

The almost complete absence of the disease in the Brahmin communities in villages ‘N’ and ‘T’ is striking. The adult Brahmins did not associate closely with other adults in the village, but the children mixed freely, even with children from the Harijan community, during school hours. In general the Brahmins were wealthier than the average non-Brahmins, and their houses and diet were therefore slightly better. The Brahmins also tended to be cleaner in their personal habits and to have cleaner houses than the rest of the village. However diet and wealth had no effect on the incidence among the non-Brahmins, and there were other groups of houses in villages ‘N’ and ‘T’ which were identical with those in the rest of the village but which were unaffected. The freedom from attack of these houses and of the Brahmins remain unexplained findings. The apparent failure of the disease to spread to the Brahmin children within the schools in villages ‘N’ and ‘T’ would seem to make a direct faecal-oral or respiratory transmission of an ‘infectious agent’ an unlikely possibility.

Other reported epidemics of sprue have had a much lower case mortality rate than this epidemic. The main reason for the large number of deaths was the failure of patients to make use of existing medical facilities, aggravated by the traditional practice of restricting fluid intake in people with diarrhoea. In a recent epidemic where simple medical care was utilized from the first few weeks of onset, and adequate fluid intake encouraged, the case mortality rate was reduced to less than 2 per cent.

Temporary malabsorption has been reported after acute bacterial enteritis (King and Joske, 1956), after cholera (Lindenbaum, 1955), and after a Reo virus infection (Subin, 1956) and it is possible that in certain people classical sprue may develop after similar infections. However stool examinations and stool cultures in this epidemic showed that the affected individuals were not suffering from cholera, from infection with usually recognised bacterial pathogens, or from infestation with parasites known to produce malabsorption (Mathan and Baker, 1970). Unfortunately at the time of the epidemic facilities for virological studies were not available. It should also be emphasized that at least two epidemics of diarrhoea, in a similar population, did not result in tropical sprue (Mathan and Baker, 1968), so that not every type of intestinal damage will produce tropical sprue.

It is of interest that the team investigating the epidemic (6–12 people) lived in town ‘W’
for a period of six months during the latter part of the epidemic. They ate locally obtained food and spent all day in surrounding villages, but none of them developed the disease. On the other hand one group from the Medical College drove through the affected area, slept on the roadside near a farm house at the southern border of the area and next morning breakfasted in a nearby town. Five days later seven out of ten of this group became ill with fever, abdominal distension, and diarrhoea and one went on to develop what appeared to be typical tropical sprue, though no laboratory tests were available.

Certain features of this epidemic such as the pattern of incidence, the short 'incubation period', the age specific attack rate and the occurrence of fever in 25 per cent. of cases (Mathan and Baker, 1970) tend to support the suggestion that the epidemic may have been caused by an as yet unidentified infective agent. Stefanini (1948) also records fever at the beginning of the illness in 12 per cent. of cases, and Ayrey (1948) found fever at the onset in 10 out of 25 cases in one outbreak. A number of authors have postulated that sprue may be an infectious disease (Galloway, 1955; Bahr, 1915; Marason-Bahr, 1957; Leinman, 1945; Woodruff, 1949) but until at least one infectious agent is isolated this remains an unconfirmed, though plausible, hypothesis.

The value of this study was limited by its retrospective nature, nevertheless a distinctive epidemiological pattern was present. Further studies of epidemics, during their course, are needed to determine whether this pattern is consistent. The application of modern epidemiological, bacteriological and virological techniques to epidemics of sprue may help to solve the problem of the aetiology of this disease.

SUMMARY

A large epidemic of tropical sprue occurred in southern India in 1960–62. There were an estimated 100,000 cases and a case mortality rate of about 30 per cent. The epidemiological features of the disease are described. The attack rate increased with increasing age. Sex, wealth, housing, diet and the source of drinking water had no apparent bearing on the incidence of the disease. The Brahmin community was relatively unaffected. Mortality was highest in the under 10 and over 60 age groups. The possible aetiology of the disease is discussed. The features of the epidemic are compared with previously reported epidemics.

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