

Public Health Section

EPIDEMIOLOGICAL OBSERVATIONS ON XK OR MITE-BORNE TYPHUS IN BARRACKPORE, BENGAL

By K. V. KRISHNAN
R. O. A. SMITH
P. N. BOSE
K. N. NEOGY
B. K. GHOSH ROY
and
M. GHOSH

(From the Bengal Typhus Enquiry at the All-India Institute of Hygiene and Public Health, Calcutta, partly financed by the I. R. F. A.)

IN the course of investigations on typhus conducted in the cantonment town of Barrackpore by the Bengal Typhus Enquiry, between 1946 and 1948, certain data relating to the epidemiology of the disease were collected and in this article a brief account of the observations made and conclusions arrived at are presented.

Review of available information on epidemiology of XK typhus in other areas

This disease was first recognized in Japan about 1878. When reports about the disease were published in the medical press, other countries became alive to the possibility of this fever occurring among their people. Between 1909 and 1935 many scattered endemic areas were found in China, Indo-China, Dutch East Indies, Australia, Malaya, Burma, India, and several islands in the Far East. In these areas the disease is now known to be responsible for a fair amount of morbidity and for a variable amount of mortality.

This form of typhus has been variously named by different workers in different countries. In the table below the names are listed :—

Japan :	Tsutsugamushi fever ('tsutsu' = disease and 'mushi' = a mite). Japanese river fever. Flood fever. Kedani fever (Kedani = hairy mite).
Sumatra :	Pseudotyphoid. Mite fever.
Malaya :	Scrub typhus. Tropical typhus. Rural typhus. K form of tropical typhus.
Australia :	Mossman fever. Endemic glandular fever. Coastal fever. Endemic tropical typhus.
New Guinea :	Endemic typhus.
Indo-China :	Le typhus exanthématique. Pseudotyphus of Deli. 'Fievre fluviale d'Extreme Orient.' Tropical typhus.
India :	XK typhus. Mite typhus. Malayan scrub typhus. Tsutsugamushi fever.

Some workers have felt that since the clinical features of the disease in the different geographical areas show variations particularly with regard to the presence of eschar and the fatality rate, one name would not suit all types. At least four names have been suggested, *viz.*, Tsutsugamushi fever, Pseudotyphoid, Mossman fever and Scrub typhus. The characters on which the division into types is based are presented in tabular form below :—

Country	Eschar	Case fatality rate
Japan	.. 'Never lacking'	22 to 68 per cent.
Sumatra	.. 'Always present' in Europeans. In natives less frequently, 40 per cent.	4 to 9 per cent in indigenous population.
Malaya	.. 10 per cent Europeans. 2.5 per cent Asiatic labourers.	14 per cent in severe form.
Australia	.. 'In many cases' eschar found.	Less than 1 per cent.
New Guinea	'Constant feature'	20 per cent.
Indo-China	'Frequently seen' in European cases.	14 per cent.
India	.. Not seen in 'natives'. 35 per cent in outsiders and severe cases. Nil in local inhabitants and mild cases.	Nil in 'natives'. 10 to 15 per cent in outsiders. Nil in local people and mild cases.

It will be seen from the table that the variations do not appear to be greater than what is generally observed in other diseases. Also, as far as the evidence goes, the causal agent, the nature of agglutinins present in the serum of patients and the mode of transmission in all these clinical types are very similar if not identical and as such it seems reasonable to consider them all as one disease. In that case the name tsutsugamushi has precedence over all others and should be adopted.

The causal agent of mite typhus is *Rickettsia orientalis*. The other names for it are *R. nipponica*, *R. tsutsugamushi* and *R. akamushi*. This organism can be grown in tissue culture and in the yolk sac of the developing chick embryo. A study of the various strains of this organism isolated in different countries has shown their close relationship if not absolute identity. All strains are comparatively less infective to guinea-pigs and more infective to white mice; they give rise usually to local necrotic lesions accompanied by fever on intradermal inoculation into monkeys; the serum of convalescent monkeys and guinea-pigs agglutinates proteus OXK antigen (but not OX19 antigen) in the same manner (though in a lower titre) as the sera of humans suffering from mite typhus do,

cross-immunity experiments also support the view that all strains are very closely related.

The epidemiology of the disease as studied in different countries bears a very close similarity. In Japan, the disease is confined to river valleys with sandy soil, generally overgrown with grass and scrub and subject to flooding. Labourers working in such areas contract the disease. In Sumatra, it is found in plantations where workmen are engaged in clearing land overgrown with bush and grass. The disease occurs here during the rainy months. In Malaya, it is a disease of the open scrub country where labourers work for one reason or another or soldiers are camped. In Australia, it occurs among workers in sugarcane plantations, among woodcutters in jungles and among labourers clearing scrub in areas situated near the sea coast having a damp sandy soil. In New Guinea, it occurs among people engaged in clearing virgin bush or in mining. Cases occur throughout the year and have no relationship to rainfall (Blake *et al.*, 1945). In Indo-China, it prevails during the rainy season in plantations located in river valleys subjected to flooding and among labourers engaged in woodcutting or brush and weed clearing.

The animal reservoir of infection is believed to be one or other species of rodents. In Japan, the field rodent *Microtus montebelli* has been shown to be naturally infected with *R. orientalis*. In Sumatra, the house rat *Mus color* and the field rat *Mus diardii* have been suspected. In other areas different species of wild rats and bandicoots have been shown to harbour *R. orientalis* infection in them (Lewthwaite and Savor, 1936; Cook, 1944).

As regards the arthropod vector, the Japanese workers produced evidence between 1907 and 1917 to show that *Trombicula akamushi* was the carrier of tsutsugamushi fever. They were successful in transmitting the disease to a few monkeys through field and laboratory experiments. But their work has never been confirmed. In the other areas of prevalence the mite *T. deliensis* is chiefly suspected. But up to the present no conclusive evidence of its rôle in transmission has been obtained. The disease has not been transmitted to experimental animals or to man by the bites of infected larval mites. In certain endemic areas where other species of mites abound, species other than *T. deliensis* have been suspected to be responsible for transmitting the disease.

If rodents are the reservoirs of infection and larval mites the transmitting agents, the mechanism of transmission based on the available knowledge of the life-cycle and bionomics of the mites would be as follows: Larval mites are parasites of rodents. They acquire infection by feeding on infected rodents. After engorgement with tissue juices of an infected rodent host, they drop off into the soil. The engorged larval mites do not feed again on a

vertebrate host. Hence they cannot transmit the infection to another host, themselves. The engorged mites complete their cycle of development into nymphs and adults in the soil. The nymphs and adults feed only on insect eggs and they are also therefore not responsible for transmission of infection to man or rodents. Eggs laid by infected adult mites give rise to infected larvæ, the infection being transmitted through the ova. These newly emerged infected larvæ attach themselves to rodents or men for a meal and during the act of feeding transmit the infection to their host.

Although this is the alleged mechanism of infection no conclusive proof has yet been obtained to substantiate it. The chief difficulty in the way of obtaining proof has been the inability to breed trombiculid mites in the laboratory in sufficient numbers for conducting transmission experiments.

Nagayo *et al.* (1917) were the first to attempt to rear *Trombicula akamushi* in the laboratory for transmission experiments. They fed nymphs and adults on melon, potatoes and other vegetables and claimed to have obtained one generation but not a second. Using their technique, other workers failed to obtain successful results. During World War II when typhus became a serious problem with the army fighting in the Far Eastern Front, Blake *et al.* tried to obtain proof of mite transmission. But their attempts to carry mites through a complete cycle of development in the laboratory were unsuccessful. Wharton and Carver (1946) in U.S.A. found insect eggs a satisfactory food for nymphs and adults. Using this food they reared *Neoschomgastia indica* in the laboratory. They, however, stated that 'no entirely satisfactory system for culturing trombiculid mites has yet been described'. Michener (1946) and Jenkins (1947) in U.S.A. reared nymphs and adults of certain American chigger mites using mosquito eggs as food. They claimed to have reared two generations. So far as *T. deliensis* is concerned, no one has successfully reared them in the laboratory. The position with regard to typhus transmission at the end of 1947 was that unless a technique was developed for rearing the suspected trombiculid mites in large numbers in the laboratory no solution of the transmission problem could be obtained.

Observations on the epidemiology of XK typhus in Barrackpore

Barrackpore is a small cantonment town situated 14 miles to the north of the city of Calcutta on the banks of the River Hooghly. It has a mixed military and civil population. The total population which was 25,395 in 1931 rose to 32,751 in 1941 and is now estimated at 40 thousand. The Ishapore Rifle Factory, the Calcutta Water Works, a large park, a race course and Government House are located there. There are many barracks and camps for troops

and there is also a small bazaar. Much cultivated and uncultivated land is found all around the town. Some of the land is covered with scrub or grass and some areas are swampy. The soil is alluvial and composed of sand, silt and clay. The months of heavy rainfall are June, July, August and September when about 10 to 12 inches of rainfall are recorded per month and the mean temperature varies from 80° to 90°F. Occasionally heavy downpours are recorded, raising the total monthly rainfall to 25 inches or more. November, December and January are the cold months when the mean rainfall is about 2 inches and temperature between 60° to 75°F. The humidity except during the cold weather is fairly high. The chief febrile diseases prevalent are malaria, kala-azar, enteric fever, typhus and dengue. There are a few hospitals to meet the needs of the civil and military population.

As regards the history of typhus in the province of Bengal in general and in Barrackpore in particular there are no records to show that typhus fevers were prevalent to any appreciable extent prior to 1940. Bradley and Smith (1912) recorded one case of suspected typhus in a British sailor in Barrackpore. Basu (1924) described 15 cases resembling typhus occurring in Calcutta. Boyd (1935) reported 92 cases among soldiers of whom some were alleged to have contracted the disease in Calcutta. These cases were serologically diagnosed and they belonged to all three types XK, X19 and X2. Between 1940 and 1943 the army authorities drew special attention to the occurrence of typhus fevers among troops stationed in several areas in the plains of Bengal (Calcutta, Barrackpore, Jhikargacha, Panagarh, etc.). On the basis of the Weil-Felix reaction these cases belonged to all three types XK, X19 and X2. In 1943-1944 an outbreak of typhus was reported from Darjeeling-Ghoom area. Serological investigation of these cases showed that they belonged mainly to the X19 type. But whether they were of the flea-borne or louse-borne type was not conclusively established. In 1945, Lusk reported 54 cases diagnosed by the Weil-Felix test in an Indian military hospital in Calcutta and among these 42 were XK, 8 X19 and one X2. Roy (1946) reported 10 cases. These cases also belonged to the XK, X2 and X19 types. In the autumn of the same year an unusual increase in fever cases was reported among the civil population of Barrackpore. These cases were suspected by the local doctors to be paratyphoid on clinical grounds and we were asked to investigate the outbreak. Laboratory investigations soon revealed that about 20 per cent of the fever cases admitted into hospitals in the area at the time of the enquiry (during the months of October and November) were definitely typhus. Since then all three kinds of typhus have been shown to be prevalent in Barrackpore with XK typhus as the predominant type. Now cases of typhus are occurring regularly in the area

throughout the year, the maximum incidence being between May and October.

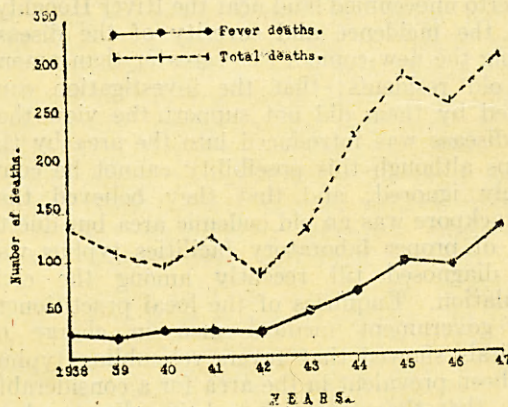
In order to determine whether typhus fever had been occurring in the Barrackpore area in an unrecognized form for a long time previously or whether it was a newly introduced disease, enquiries were made of the military and civil authorities. Enquiries of the military authorities brought out the following facts: that sporadic cases of typhus fever had been occurring since 1905 among the troops resident in the area; that with the stationing of increased numbers of troops during World War II the number of typhus cases increased; that cases occurred mostly in those who were stationed in camps and sheds built close to large open fields and on hitherto unoccupied land near the River Hooghly; that the incidence and severity of the disease among the new-comers were greater than among the old residents; that the investigation conducted by them did not support the view that the disease was introduced into the area by the troops although this possibility cannot be completely ignored; and that they believed that Barrackpore was an old endemic area but due to lack of proper laboratory facilities typhus was not diagnosed till recently among the civil population. Enquiries of the local practitioners and government medical men in charge of hospitals showed that fevers resembling typhus had been prevalent in the area for a considerable time; that these cases were being diagnosed as enteric on clinical grounds—those that lasted for 10 to 12 days being generally diagnosed as paratyphoid and those that lasted for longer periods and were more severe being diagnosed as typhoid; that laboratory aid was seldom sought for diagnosis of cases; that during and shortly after the monsoon months every year fever cases increase; that since the stationing of larger numbers of troops in the area the fever incidence among the civilians had greatly increased; and that in 1946 this fact was brought to the notice of the health authorities. Our own investigation of over 500 fever cases between 1946 and 1948 showed (i) that typhus fevers of the three serological types, viz, XK, X19 and X2, are occurring in the civilian population; (ii) that XK typhus is the predominating type; (iii) that the majority of cases are mild and can readily be mistaken for other fevers such as paratyphoid dengue and influenza; (iv) that diagnosis of these cases on clinical grounds alone is difficult; (v) that laboratory facilities are not available in the area for establishing a correct diagnosis; and (vi) that the adult local population suffer less than adult new-comers. From the evidence collected it seems justifiable to conclude that typhus fevers must have been occurring among civilians for many years past and that Barrackpore must really be considered as an old endemic area. It is hardly feasible that infected rats or trombiculids were carried by troops into the station. The military authorities who had better provision for

laboratory diagnosis of these diseases diagnosed the disease earlier than the civilian authorities and brought to light the prevalence of the disease among the troops as far back as 1905. With the stationing of large numbers of troops and the influx of refugees from all-over the country into the area the incidence of typhus shot up both among the civil and military population.

In chart I the total deaths as well as deaths from fevers for the period 1938 to 1947 among the civilian population are shown.

CHART I

Chart I showing total deaths & fever deaths in Barrackpore



It will be seen that deaths from fevers have gone up enormously in the area. The ratio of fever deaths to total deaths has increased from 1 : 6 in 1938 to 1 : 3 in 1947. While the death rate from fevers was only 70 per 100,000 in 1938, it had reached 320 per 100,000 in 1947. For want of accurate figures total fever cases treated in the hospitals are not shown. But enquiries have revealed that they have risen from a few hundreds to a few thousands (*i.e.* from about 400 to 3,000). Among these about 25 per cent are malaria, 10 per cent enteric, 5 per cent kala-azar, 10 per cent typhus and 50 per cent all other fevers. Out of 538 cases of fever admitted in the civil hospitals during our investigation between October 1946 and October 1948, 102 cases were diagnosed as typhus on the basis of clinical and laboratory findings. It would thus appear that typhus fevers are an important cause of morbidity in the area and their importance is as great as that of enteric fevers which are also prevalent there.

XK typhus occurs in the Barrackpore area in two forms, *viz.* mild and severe. 80 per cent of cases belong to the mild type and 20 per cent to the severe type. The case fatality in the mild type is nil while that in the severe type is 14 per cent. Mild cases are noticed mostly among the local people (children and adults) and the severe cases amongst the new-comers to the area (Indian and European adults).

The age incidence of the disease as noted in over 100 cases is given below :

1 to 5 years	..	Nil.
6 to 10 years	..	8 per cent.
11 to 15 years	..	10 " "
16 to 20 years	..	16 " "
21 to 25 years	..	16 " "
26 to 35 years	..	21 " "
36 to 50 years	..	23 " "
over 50 years	..	6 " "

It will be seen from the table that the majority of cases occurred in adults. The youngest case was 7 years of age and the oldest 56 years.

As regards sex distribution, 19 per cent of cases occurred in females and 81 per cent in males.

The cases belonged in order of importance to the following occupation groups :

Factory labourers residing in camps; water works labourers residing in the fields adjoining the water works.

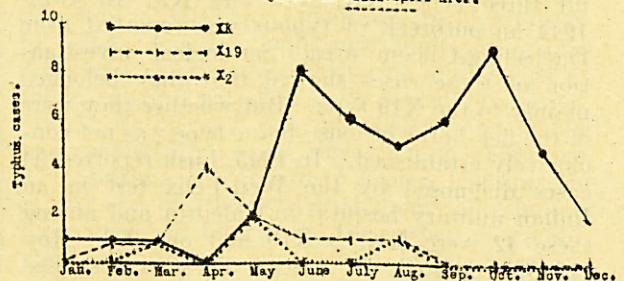
Police constables who are on patrol duty at night; *durwans* who guard cultivated lands, barracks, camps and water works.

Coolies who work in agricultural land and children residing in houses close to uncultivated waste land.

The season of maximum prevalence of typhus was the rainy season beginning in May and ending in November. A few cases occurred in the other months as well. Chart II gives the incidence of typhus per month for 1947 and 1948.

CHART II

Chart II showing incidence of typhus cases by months in Barrackpore area.



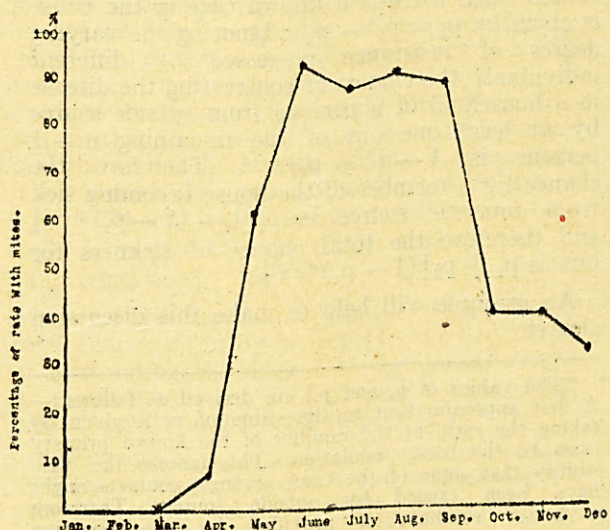
In 14 cases of XK typhus the presence of rickettsia in the blood was demonstrated by intraperitoneal inoculation of washed blood cells into white mice. White mice, which were first demonstrated by us in 1942 to be very susceptible to infection with *R. orientalis*, have been found to be the most suitable for experimentation with this rickettsia. All strains tested produce ascites and enlargement of spleen and death of the mice usually occurs in about 8 to 18 days. The Barrackpore strains are not very pathogenic to guinea-pigs. But after passage through mice, virulence seems to be somewhat increased and inoculation gives rise to fever about 8 to 10 days

later. If the animal is sacrificed slight ascites is found and also rickettsia can be demonstrated in peritoneal and tunica scrapings. If the animal is not sacrificed it almost invariably recovers and the serum of recovered guinea-pigs shows agglutinins for proteus OXK. In a few cases intradermal inoculation into monkeys—*Macacus rhesus*—was tried, but it did not result in the production of a necrotic ulcer. In one monkey a lump formed at the site of inoculation about the size of an almond. No rickettsia was found in the scrapings from this lump but the monkey showed a rise of temperature from which it recovered and its serum showed agglutinins for OXK. Also one* of the workers in the laboratory who accidentally inoculated his finger with rickettsia while injecting an experimental mouse developed an eschar of the papular type with lymphangitis and enlarged glands in about 10 days. This was followed by a severe attack of typhus from which he recovered. His blood showed agglutinins for OXK and rickettsia were demonstrated in animals inoculated with washed blood cells.

During the investigation 1,064 rats were trapped in the area. They belonged to 4 species: *R. rattus*—74 per cent, *Gunomys varius*—13 per cent, *Bandicoota indica*—1 per cent and *Cocidura coerulea*—12 per cent. 32 per cent of the rodents caught were found to harbour mites of one species or more and of the infested ones 72 per cent harboured *T. deliensis*. In rats caught between January and April the rate and intensity of infestation were small (2 to 10 mites per rat) but during the rainy months, May to November,

CHART III

Showing percentage of mite-infested rats with *T. deliensis*.



the rate and intensity of infestation were much higher (50 to 150 mites per rat), *vide* chart III. It was noticed that young rats were seldom infested. This suggests that mites do not

probably breed in nests of rats but that they get attached when the rats emerge for food or water. *Rattus rattus* and shrews were found most frequently and intensely infested with *T. deliensis*. In the others only mild infestations were seen and much less frequently. In shrews the site of election for *T. deliensis* was the outer side of the fore and hind legs, and the base of the tail; they were found less frequently in the ears. In *Rattus rattus* they were found in the ears mostly.

The larval mites found infesting rats were identified. They were found to belong to three genera—*Trombicula*, *Neoschongastia* and *Schongastiella*. Among the trombiculid mites in which our main interest lay several species were found. *T. deliensis*, *T. muris*, *T. munda*, *T. spicia* and two other new species not yet fully studied or named. Of the mites found the predominant species was *T. deliensis*. These were found most frequently in the rainy months which were also the months of maximum prevalence of typhus. Chart III shows the percentage of mite-infested rats showing *T. deliensis*.

A comparison of charts II and III will show the correlation between typhus incidence and prevalence of *T. deliensis*.

Having found that *R. rattus* is more heavily and frequently infested with *T. deliensis* than other rodents, an attempt was made to find out if any of the rats were infected with *R. orientalis*. Since we had found white mice very susceptible to infection with this rickettsia, these animals were inoculated intraperitoneally with 1 cc. of brain emulsion from rats showing heavy infestation with *T. deliensis*. This was done so as to ensure a greater degree of success in isolating the rickettsia. Out of 30 rats examined, 8 were found infected. These 8 strains were tested by mouse inoculation and 6 gave rise to pathological lesions identical with *R. orientalis*, *i.e.* produced ascites and enlarged spleen and also caused death of the mice in 8 to 18 days, average 12 days. These strains, when inoculated into guinea-pigs, behaved like rickettsial strains from human sources and caused fever for a day or two but no death. The serum of recovered guinea-pigs showed OXK agglutinins to a titre of 1 in 125. All these six strains have been provisionally accepted as *R. orientalis*. The other two were considered to be some other strains of rickettsia. From these observations it may be concluded that organisms identical with *R. orientalis* are found in about 20 per cent of *R. rattus* found heavily infested with *T. deliensis*.

In the course of our investigations several attempts were made to rear *T. deliensis* in the laboratory for use in transmission experiments but success was not achieved until we began to use *Culex* eggs as food for the nymphs and adults. Towards the end of 1947, a technique was developed by which successive generations of *T. deliensis* could be reared in the laboratory in large numbers without any difficulty. A

*This is the medical man commented upon by Chaudhuri and Chakravarti, on p. 48.—EDITOR, I.M.G.

separate communication regarding this work is being published. Thus having overcome the main obstacle in the way of transmission experiments, the rôle of *T. deliensis* in the spread of XK typhus was next investigated. The progeny of infected mites bred in the laboratory, on inoculation into mice, gave rise to infection proving transovarian transmission. The progeny of experimentally infected larval mites were fed on clean mice and in five experiments so far the mice contracted infection, thus proving that transmission is through bite of infected *T. deliensis* larvæ. A separate communication on this is being made.

Summary and conclusion

Barrackpore is an endemic area of mite typhus. New-comers to the area suffer from severe disease while the local people suffer from a mild form.

Maximum prevalence is during the rainy season from May to October.

Men working or camping in scrub jungle and fields contract the disease.

24 per cent of *R. rattus* harbour *T. deliensis* larvæ in large numbers and of these 20 per cent show infection with *R. orientalis*.

Several other species of mites found on rats have been identified.

There is a positive correlation between incidence of *T. deliensis* and typhus cases.

T. deliensis have been successfully reared in the laboratory in sufficient numbers for three generations.

Experiments to determine the rôle of *T. deliensis* in the transmission of the disease have yielded positive results. Transovarian transmission of infection from parent mite to its offspring in *T. deliensis* has been demonstrated; and also transmission of infection to white mice through the bite of infected larval mites have been obtained.

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VARIATION IN THE RISK OF SICKNESS FROM CERTAIN COMMON INFECTIOUS DISEASES WITH INCREASE IN THE SIZE OF THE HOUSEHOLD

By R. B. LAL

and

K. K. MATHEW

All-India Institute of Hygiene and Public Health, Calcutta

SICKNESS is the end-result of a succession of complicated processes involving many factors. Any attempt to measure the rôle of any one factor necessarily involves difficulties which are very often insurmountable. However, the influence of some factors may be so dominant that they may be profitably discussed without reference to other factors, though the measure of influence may only be an approximation.

One may reasonably expect that the chances of sickness from an infectious disease would be appreciably higher if there was a domestic source of infection. For additional membership to the household the risk of contracting the disease by an individual may also be expected to increase. In this communication we propose to investigate and roughly measure how this risk in respect of different diseases varies with progressive expansion of the household.

Let p_1 be the chance of a person to contract the disease in question from outside sources and p_1' the total probability of contracting the disease by him when there is one or more patients in the house.* It follows that p_2 the chance of contracting the disease solely from domestic source when there is a known case in the house is given by $p_2 = p_1' - p_1$. Ignoring the varying degree of resistance possessed by different individuals, the chance of contracting the disease in a household of n persons from outside source by at least one out of the remaining $n - 1$ persons is $1 - (1 - p_1)^{n-1}$. Therefore the chance for a member of the house becoming sick from domestic source is $p_2[1 - (1 - p_1)^{n-1}]$ and therefore the total chance of sickness for him is $p_1 + p_2[1 - (1 - p_1)^{n-1}]$.

An example will help to make this discussion clearer.

*The values of p_1 and p_1' are derived as follows:— A first approximation to the value of p_1 is given by taking the ratio of the number of the known primary cases to the total population. This ignores the possibility that some of the cases amongst contacts might have been caused by outside sources. Therefore a better estimate is provided by the equation

$$p_1 = \frac{m}{N - m(n-1)}$$

where m is the number of known primary cases, N is the total population and n is the average size of a family.

p_1' is obtained by taking the ratio of the number of cases amongst family 'contacts' to the total population of infected families excluding the known primary cases.