During the past five years especially we have read a lot about murine typhus as a public health problem. But how much of a problem is it really? How many cases are there? The study reported here suggests that at first the disease was underreported but in recent years there seems to have been some degree of overreporting.

Epidemiologic and Serologic Appraisal of Murine Typhus in the United States, 1948-1951*†

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DURING the last twenty years, varying degrees of reliance have been placed upon the trends of reported typhus morbidity in the United States as a measure of the real prevalence of murine typhus (see Figure 1). During the 1930's, the Weil-Felix agglutination test was made more widely available as the disease became better known to practitioners. Within that decade, reported endemic typhus trebled in two waves. Simultaneously with World War II, there occurred a fivefold increase over 1930, followed in the latter 1940's, by a precipitous decline which has continued to the present. During 1951, the reports were at their lowest ebb within the last two decades. The history of reported murine typhus has been confused with that of the other spotted fevers and there has been extreme variance of opinion as to the reliability of reporting as it may reflect actual incidence. It is the purpose of this paper to present an epidemiologic and serologic appraisal of both reported and unreported typhus since 1948 in order to elucidate this problem of interpretation.

Until about 1946, most investigators [1-4] concluded that murine typhus was an underreported disease. All of their studies were conducted in endemic areas. Since typhus began its rapid decline in 1946, others [5-7] have found it difficult to confirm even half of the reported cases by complement fixation, particularly in areas where the disease has been decreasing.

In 1948, Worcester,[8] collaborating with a county health officer, Dr. A. W. Graham, found that none of 25 reported cases of typhus in Montgomery County, Alabama, was clinically consistent with murine typhus to a degree sufficient to warrant complement-fixation testing. He concluded that this, the nation's largest county outbreak for that year, was the result of misinterpretations of Weil-Felix agglutinations, mostly of low titers.

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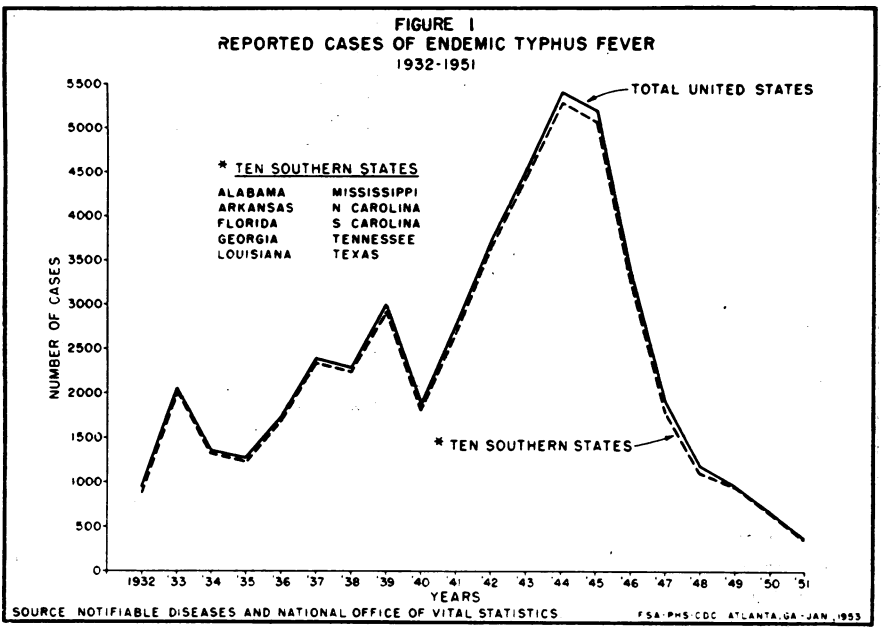

In a presentation before the 1951 Annual Meeting of the Southern Branch of the American Public Health Association the senior author[9] described the initiation of the murine typhus appraisal program and presented preliminary results for 1948 through 1950.

In July of 1947, the Communicable Disease Center instituted a program of appraisal of malaria and other communicable diseases with the collaboration of 5 southern state health departments by assigning medical or nurse epidemiologists to Alabama, Arkansas, Mississippi, South Carolina, and Georgia.[10] Texas was added to the program in 1949. During 1951, similar epidemiologic service was extended to Florida, Tennessee, and Louisiana, thus including 9 of the states in which most of the typhus occurs, omitting only North Carolina and California of those states traditionally endemic for typhus.

The methods and results of the appraisal of malaria have been described previously by the senior author.[11] Although primary emphasis was placed upon the investigation of malaria, secondary emphasis was devoted to typhus. Large groups of supposed typhus cases were studied and appraised in 1947 and 1948, but individual case appraisals were not recorded on cases occurring before 1948.

The objective of the typhus appraisal program was to confirm as many reported typhus cases as possible by clinical and laboratory means. In addition to investigating official reports, all reputed cases, and in some states all significant titers of Weil-Felix were sought out. Cases confirmed by complement fixation were used to select areas for rodent and flea control and to determine the efficacy of the control in terms of trends of murine typhus in human beings.

METHODS OF APPRAISAL

During this study, cases were found to have been reported generally on clinical grounds alone. Rarely was a

case confirmed by complement fixation before it was officially reported. For purposes of this study, an officially reported case is one whose appraisal was made after the interception of the morbidity data anywhere along the channel between the local reporting physician and its ultimate destination in the morbidity tables of the U. S. Public Health Service in Washington, D. C. Throughout the states participating in this study, there was variability in the technics of performance and interpretation of the Weil-Felix test. The states had evaluated the reliability of very few laboratories. Only Florida, Texas, and Tennessee performed complement fixation in their own states. Other states sent their sera to the Communicable Disease Center, Serology Laboratory, Chamblee, Ga.

The identification data of officially reported cases were obtained from the morbidity report card in the state or local health department. Next the clinical and laboratory data were procured from the physician. Since confirmatory serologic tests generally were indicated, this service was offered to the physician as a function of the state health department. On as many cases as possible, the serology was followed for as long as from 3 to 6 months to detect delayed antibody formation. Lastly, the epidemiologic appraiser visited the home and the place of occupation of the patient, and recorded the symptomatology and environmental circumstances of the occurrence of the case. Then, each case was appraised as to its degree of positivity in one of the 5 categories as follows:

Positive—A case has been appraised *positive* if it were clinically consistent with murine typhus and corroborated by complement fixation at least to a 1:4 titer, ideally showing a rise in titer during convalescence.

Presumptive—Cases clinically consistent, in the opinion of the state epidemiologist, but lacking complement-fixation confirmation, were appraised as *presumptive*.

Doubtful—Cases without a clinically consistent history and without complement-fixation confirmation were appraised as *doubtful*.

Not Typhus—When there was corroboratory evidence of some other disease, or strong clinical impression ruling out typhus with negative complement fixation, the appraisal was *not typhus*.

Incomplete—Cases with fragmentary clinical data were appraised as *incomplete* even though they may have been accompanied by negative complement fixation.

Records were made of the exact technic of complement fixation used in the various laboratories. These data were not always obtainable by field personnel. Moreover, in recent years, it is becoming evident that the appearance of complement-fixing antibodies may be delayed by the administration of certain of the newer antibiotics. For this reason, cases treated with antibiotics have been counted as complement fixation tested only if tested 90 or more days after onset, and untreated cases if tested 30 or more days after onset.

Since the various technics of the complement-fixation test varied in sensitivity from laboratory to laboratory and from year to year, according to changing antigens and technics, it has been necessary to adopt a liberal arbitrary level of 1:4 as indicative of typhus when a clinically consistent history was obtained without rickettsial vaccination. Immunized individuals with titers under 1:32 had to show at least a fourfold rise to be called *positive*.

RESULTS

Over the 4-year period, a total of 450 reported and unreported cases were appraised, 351 reported and 99 unreported, in 8 of the 9 states provided with epidemiologic personnel for this purpose. Only Louisiana did not submit appraisals of typhus cases. (See Table 1.)

Of the 351 *reported* cases, it was possible to procure sera sufficiently long after onset from only 230 reports, of which 133, or 58 per cent, were positive to complement fixation and clinically

TABLE 1

Appraisals of Reported and Unreported Murine Typhus Occurring from 1948 Through 1951 in Eight Southern States

	Appraisals	*C.F. Tested*	*No. Pos.*	*Per cent Positive*	*Not Typhus*	*Per cent not Typhus*
Reported	351	230	133	58	57	25
Unreported	99	40	13	33	16	40
Total	450	270	146	54	73	27

consistent. The titers ranged from 1:4 to 1:20,500 with fairly equitable distribution at all levels except the higher ones. Fifty-seven, or 25 per cent, were appraised *not typhus*. Nine cases, however, were confirmed as Rocky Mountain spotted fever. Other misdiagnoses occurred less frequently, such as undulant fever, rat-bite fever, genitourinary infections, tularemia, infectious mononucleosis, etc.

Of the 99 unreported cases, 40 were suitably tested, and 13, or one-third, of the tested cases were serologically and epidemiologically confirmed. Six of the 13 unreported confirmed cases were from Alabama, 6 from Georgia, and 1 from Florida. As would be expected, a larger proportion, 16 or 40 per cent of the unreported tested cases were appraised as *not typhus*. Mostly the differential diagnoses were chronic pyelitis and acute upper respiratory infections; 2 were measles.

DISCUSSION

Published evidence is available from areas of moderate to high endemicity for murine typhus that it has been underreported particularly before 1946. Some of these studies lacked complement-fixation confirmation and are therefore open to some question as to the degree of underreporting.

Since the objective of the appraisal program was to locate and confirm murine typhus, priority of investigation was given to those reports, rumors, and preliminary laboratory results indicating the greatest likelihood of being *bona fide* cases. The percentage of those which would confirm depended on the source of the original lead to the case. The laboratory reports of the Texas State Health Department produced a high rate of confimation when their results were used as original source data.

A special effort was made to detect association of proved cases in time, place, or person, thus defining areas considered as outbreaks. This was successful only as follows:

	Year	*Cases*
Brundidge, Ala.	1950	2
Samson, Ala.	1951	2
Santa Rosa County, Fla.	1951	2
Columbia, S. C.	1951	6

This nation-wide epidemiologic picture of the decline of clinical typhus and lack of association of confirmed cases is a dramatically changed one from the early 1940's when murine typhus was epidemic in many southern cities and counties. Even though cases were followed serologically at least 90 days and frequently longer than a year, it is quite possible that some of the cases which are herein regarded as nonpositive may have been early treated *bona fide* murine typhus. More data will have to be accrued before a valid measure of this factor can be obtained.

However, at least 25 per cent of the reported cases tested were appraised as *not typhus*, indicating that some degree of overreporting exists particularly in the areas of sporadic occurrence of typhus. Many other cases in the *presumptive, doubtful,* and *incomplete* categories could be expected to increase this percentage of overreporting.

In addition to the objective data presented herein, the clinical and epidemiologic impressions of the appraisers, 7 doctors and 6 nurses, are of interest. Cases were originally selected for investigation according to the probability

that they might be confirmed. Many cases, both reported and unreported, went uninvestigated because evidence was not sufficient to support even remotely the clinical impressions formed by the first diagnostician. Certain practitioners were prone to label measles, drug rashes, or some other conditions as murine typhus merely because proved murine typhus was formerly common. Certain of the investigators noted that murine typhus had replaced malaria as a wastebasket diagnosis. Even the lowest titers of Weil-Felix were used as the basis of contention by some physicians that a fever of undetermined origin was due to murine typhus, particularly in the one state which issued Weil-Felix reports which read "Positive for Brill's disease," designating the titer obtained. For these and for many other reasons, not possible to present in a paper of this scope, the epidemiologic investigators were of the opinion that typhus has been an overreported disease in recent years with the possible exception of a few restricted areas in Texas, Alabama, and Georgia.

Whatever the present quantitative relation is between overreporting and underreporting of typhus, it must still be ascertained with more extensive and intensive appraisal of communicable disease reports and a better measure of unreported typhus. If typhus continues its decline since 1946 and its disappearance from previously endemic areas, relatively more overreporting may be anticipated, as has been the case with smallpox, dengue fever, and malaria.

CONCLUSIONS

1. Evidence that typhus has been an underreported disease was collected by previous workers from areas of moderate to high endemicity, principally before 1946.

2. From 1948 through 1951, 351 reported and 99 unreported cases of murine typhus were appraised in 8 southern states. After complement-fixation testing, 58 per cent of the reported cases and 33 per cent of the unreported cases were confirmed.

3. At least 25 per cent of the reported cases tested were appraised as *not typhus*.

4. Some degree of overreporting has been discovered in recent years, especially in areas no longer endemic, where the disease is now only sporadic.

5. The determination of the degree to which areas of underreporting of typhus may tend to balance those of overreporting must await more intensive and extensive communicable disease appraisal.

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