OF LICE AND MEN
By G. B. MATHEWS

In recent months, typhus has claimed widespread attention. News reports from Europe have mentioned that the German armies in Poland and Russia, territories notoriously infested with typhus, have kept this scourge well under control by new methods of diagnosis and prophylaxis. Here in Shanghai there have also been a number of typhus cases which have come to the notice of the public, thus increasing the interest in prophylactic measures.

There are several institutions in East Asia occupied with the preparation of typhus vaccine. Among them, the Fu Jen University of Peking can probably claim the longest experience and most accurate statistics of the efficiency of the vaccine, since it has been preparing it for more than a decade.

The author was born in Germany. He studied philosophy and natural sciences at St. Augustin near Bonn, as well as in Chicago, Rome, and Harvard; and theology in Rome. Later on, he undertook special studies at the Zoological Station at Naples, at the Robert Koch Institute in Berlin, with Hans Zinsser, the great typhus authority of Harvard Medical School, and with H. R. Cox at the Rocky Mountain Laboratory of the US Public Health Service. Since 1934 he has been Professor of General Biology, Plant Pathology, and Paleobotany at the Fu Jen University of Peking.—K.M.

IN 1528 the army of Charles V was besieged at Naples by the French under Francis I. The battle was to decide the struggle for hegemony in Europe between the two rulers. Charles' army, reduced to less than 11,000 men, was encircled by the French, some 28,000 strong. The situation seemed hopeless for the besieged, until the French had to raise the siege. Their 28,000 men had dwindled to 4,000, who could easily be disposed of, and in 1530 Charles was crowned ruler of the Holy Roman Empire. Typhus had been his biggest aid in obtaining the throne. This was one of the earliest and, at the same time, most effective strokes dealt by typhus that history records.

In 1566, Emperor Maximilian II with 80,000 men set out to battle Sultan Soliman in Hungary. Disease, undoubtedly typhus, ravaged his army to such a degree that he was forced to give up his campaign against the Turks. In 1632, King Gustavus Adolphus of Sweden had to raise the siege of Nuremberg owing to a typhus epidemic among his soldiers. Instances abound in history where typhus held the trump card in political affairs. It is still a powerful factor in our own century. In 1915, typhus broke out in Serbia, and in less than six months 150,000 soldiers died, among them some 30,000 Austrian prisoners of war. The mortality rate of this epidemic was about 60 to 70 per cent. According to Tarrassowitch's estimate, there were 30 million cases of typhus and 3 million deaths in European Russia alone between 1917 and 1923. The Serbian and Russian epidemics show beyond
a doubt that typhus has not lost its vitality and power since it laid low the army of Francis I in 1528. Here in China, where typhus statistics among foreign missionaries are accurate, the mortality rate is staggering.

CATCHING TYPHUS

But how does one get typhus? First of all, typhus should be distinguished from typhoid fever. The latter is essentially an intestinal disease due to *Bacterium typhi*. Typhus belongs to the Rickettsial diseases, and the realm of its work is the blood system, especially the small capillaries, and the nervous system. It is due to the presence of *Rickettsia prowazekii*, a microbe whose citizenship in the animal or plant kingdom is still an open question. The agent is called *Rickettsia prowazeki* after H. T. Ricketts and S. von Prowazek, both of whom died victims to the disease the eradicated. The microbe enters the human body through the bite of a typhus-infected louse. The disease may also be caught when infected, crushed lice-material or feces of infected lice come into contact with delicate tissues, such as mucous membranes. Both the body louse and the head louse may be carriers. A single bite of a louse may suffice to inject so many microbes into the human organism that the body cannot immediately neutralize the invaders. A battle ensues, fever follows and, if the heart can stand it, the microbes are conquered.

Typhus is an acute fever which does not always conform to the conventional manner of fevers. Its usual behavior is as follows. After a ten- to fifteen-day period of incubation, the disease breaks out. The onset may be gradual or extremely abrupt, closely resembling a heavy cold or influenza. The temperature rises to 39 or 40 degrees centigrade (103 or 104 degrees Fahrenheit). The patient complains of chills, great depression, weakness, and pains in the head and limbs. Eruptions appear on the fourth or fifth day after the onset and last for five to seven days, sometimes even longer. When there is no epidemic, the diagnosis is very difficult in the pre-eruptive stage. The rash usually breaks out on the shoulders, spreads over the body, and extends to the hands and feet. The spots (*petechiae*) do not, as a rule, spread over the face and forehead. At first they are pink, then turn to purplish, and finally become reddish-brown and brown. In the latter stages, the spots do not lose their color under pressure. The names of the disease were taken from these *petechiae*: *Tabardiglio y puntos*, De Toro, 1574; *Fevres queim lenticularis vel punctelas vocant*, Fracastorius, 1546; *Fièvre exanthémateuse*; spotted fever; *Flecker presumably*. A severe headache is a symptom of considerable importance. The typhus crisis sets in between the thirteenth and fifteenth day.

Since it is not easy to diagnose typhus, the inexperienced may easily mistake it for another disease. Without the rash and the epidemic, many a typhus case goes unrecognized. Besides, there are few places where the only safe diagnosis, that by microagglutination, can be made.

METHODS OF COMBAT

Many attempts have been made all over the world to combat this dreadful disease, either by preventing its outbreak in case of an unnoticed infection (prophylactic), or by curing the patient by administering a typical medicine (therapeutic). Experiments made with the serum from convalescent patients or from immunized animals can be interpreted as helpful or useless as the special conditions are interpreted. All the prophylactic methods have the same aim: to stimulate the production of antigens by an artificial disease on a small scale. Several methods have been tried out, and their inventors have claimed a more or less absolute protection against typhus. There are two currents of thought relative to the production of immunity: one group uses the living virus, the other the dead virus for injections.

LIVING "RICKETTSIAE" INJECTIONS

There are two main types of typhus. The first is the murine typhus, sometimes called "Mexican" or "Manchurian ty-
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phus,” caused by Rickettsia mooseri with the rat-flea-man cycle, hence often called “flea-borne typhus.” The second is the classical typhus, also called “European typhus,” caused by Rickettsia prowazeki with the louse-man cycle, hence often called “louse-borne typhus.”

In North Africa, injections were occasionally made with subinfective doses of living virus. This is an extremely dangerous procedure, since the amount of virus cannot be determined accurately, and the infective material may lead to an outbreak of the disease. So another method was employed. The virulence of the living virus was weakened by adding egg yolk and olive oil to the infective emulsion. However, this type of injection cannot be recommended, since the egg yolk and the olive-oil emulsion may kill the virus, in which case either the number of virus will not be sufficient to guarantee the desired effect, or the infective material will remain in the body. One instance will show the errors that can be made: in South America, 800 persons were vaccinated against murine typhus with the living, weakened virus according to the Blanc method, a method generally used among the natives of Morocco. Twenty-three per cent of the 800 people became sick of typhus, and five of them even died.

Although only a very small amount of Rickettsiae is required in the use of living virus, it is much better, and perhaps it is the only safe method, to use dead microbes in the form of a vaccine. Rocha-Lima was the first to experiment with the infected intestines of lice as a prophylactic vaccine. After the Great War, Weigl developed in Lemberg the method which bears his name. He made systematic and successful researches in the preparation of a vaccine from infected lice. When the Polish Government stopped financing his experiments, he was forced to stop his research. But whenever anyone approached Weigl about the production of the vaccine, he conducted the operations and gave a visual demonstration as to how the vaccine could be produced. This was very wise, since everyone knows from experience the difference between reading a cookbook recipe and then applying the directions successfully. The Weigl method has also been used in China and Ethiopia.

FU JEN’S “LOUSE INSTITUTE”

How, then, is this vaccine prepared? Let us go to the Microbiological Institute at the Fu Jen University in Peking and observe the various stages in its preparation. The Microbiological Institute has been preparing the Weigl typhus vaccine for the last twelve years.

At Fu Jen we use the Weigl method and the Cox method. For the Weigl method, a large number of lice and a large number of Rickettsiae are required. It is true that the virus grows in many mammals, but in mammals the Rickettsiae cannot be stained, which means that they can be neither seen nor counted as is necessary for standardizing the vaccine. Thus we need a large number of lice which must be free of other diseases, such as trench fever, relapsing fever, and Volhynian fever.

A LOUSY STORY

Let us start with the preparation. As soon as we can diagnose that a person has classical typhus, we know that the Rickettsiae prowazeki are in his organism and blood serum. We therefore take a few cubic centimeters of his infected blood (Fig. 1) and inject it intraperitoneally into a guinea pig (Fig. 2). This
guinea pig is then isolated and its temperature taken regularly. It soon shows signs of the disease, and when it registers a high temperature, from 102 degrees Fahrenheit normal to 106 degrees, we know that the fever is at its height, which happens anywhere from three to twenty days after the infection. The guinea pig is very suitable for our purpose because, when it gets typhus, the Rickettsiae multiply in all its organs, especially in the brain, which show histological lesions. The fever is a sign of the fight between the organism and the invaders. At the height of the fever, the guinea pig is anesthetized, and a portion of the brain (Fig. 3) is taken out aseptically, while the other remains are burned at once. The small portion of the brain is then pulverized and dissolved in saline solution for further use.

Now the lice enter upon the scene. The brain emulsion with the living Rickettsiae is injected into each louse intrarectally. Since the louse is only about four millimeters long, this enema has to be given under a binocular microscope, which not only enlarges the appearance of the louse but also gives a plastic view of the tiny animal (Figs. 4 & 10). Our technicians can administer about 250 enemas in an hour without a single miss.

With each injection, millions of man-borne, guinea-pig-reared virus are transferred to a new host. The Rickettsiae are extremely small, measuring 0.0008 by 0.0004 millimeters. Here they settle down and thrive in the cells lining the stomach and intestinal walls and appear in large numbers in the feces. In a few days, the number of Rickettsiae increases tremendously, and from eight to ten days after the injection the louse would succumb to typhus. From this fact it is clear that, from the point of view of the history of typhus, the louse is not the natural host of typhus but that the louse caught the microbes relatively recently. In another thousand years or so, the Rickettsiae prowazeki may be absolutely harmless for lice, just as Rickettsia rochrimae has already become.

**BIOGRAPHY OF A LOUSE**

You will naturally wonder: how do we manage to get all the lice necessary for the production of the vaccine? How do we feed them, since their natural food is human blood? We have in the Microbiological Institute our own stock of lice. They are securely kept in small wooden boxes, one side of which consists of a fine silk screen. There are about two hundred lice in each box. For feeding, they use the silk side of the box (Fig. 6)
Fig. 5. The living reservoir of *Rickettsia prowazekii,* the microbes that cause typhus: guinea pigs at Fu Jen University, Peking

Fig. 6. A louse compartment (approximately natural size). Note the felt border which makes sure that no louse escapes. On the left, the cover, there is a louse. On the right, on the silk bottom of the compartment, there is a felt pad covered with louse eggs.

Fig. 7. Enlarged section of the felt pad in Fig. 6. Note two lice on the eggs.

Fig. 8. Lunch time for the lice. The human wet nurse feeds about 5,000 lice at once.
MEN AGAINST TYPHUS

Fig. 9. Four laboratory assistants at Fu Jen University, Peking, at their delicate work

Fig. 10. Male (above) and female (below) body louse under the microscope. Note the "thumb"-like opposable inner claw which enables the louse to get a good grip on hairs and fibers

Fig. 11. One year's guarantee against death from typhus: Dr. D. J. Tehang of the Microbiological Institute of the Fu Jen University giving a typhus-vaccine injection
and lay their eggs on a small felt pad (Fig. 7). Every day the felt pad is taken out. Thus from our hundred boxes we collect these pads and start a new box of lice, all with the same birthday.

After four or five days at body temperature the eggs hatch. If the temperature is lower, the eggs may not hatch for more than a month. In hatching out, the larva shows an extraordinary sense of engineering. First it opens a little lid at the end of the egg. But the opening is too small for it to crawl out; it must squeeze itself out. How does it do this? It swallows air in front and ejects it from behind. Finally the air-pressure at the rear is strong enough to pop it out into a new phase of its life. Now it feeds, or sucks, until its birthday garment becomes too tight, and it changes to a new one, molting. This happens three times. After the third molting, i.e., after two weeks, the louse becomes sexually mature. The female soon begins to lay eggs, about five every day, and continues to do so for about a month. This means that she produces about 150 eggs in her span of life. In laying the eggs, the mother lousefastens them with a sticky cement to hair or to the fibers of clothes or felt pads.

The lice, whether almost transparent youngsters or gray adults, have no trouble finding their nutrition if they are on a host. They sink their hollow stylet into the tender human skin, pierce a vein, and suck the blood until they are gorged. Some saliva flows into the tiny borehole, and if the saliva contains some *Rickettsiaceae*, as may be the case in an infected louse, one bite may be sufficient to cause a fatal sickness. From this you may wonder how we manage to feed our several thousands of small guests.

At about this stage in our sight-seeing tour of the Microbiological Institute, our visitors begin to feel itchy and are obsessed with the fear that perhaps they have become involuntary hosts to a few stray lice. Our louse doctor, D. J. Tchang, who prepares the vaccine, has not been vaccinated for more than two years and, though he spends several hours in the laboratory every day, he has never been ill with typhus. Dr. Tchang confidently assures visitors that there is no danger of infection from a stray louse in the laboratory.

But what do the lice eat, and how are they fed? We are lucky. One of the four assistants tells us that it is lunch time for the lice. He goes to the incubator, which is always kept at body temperature, and takes out all the boxes with their inmates. The boxes are securely closed. These boxes are then strapped to the legs of human wet nurses (Fig. 8). They remain there for about twenty minutes, during which time the lice sink their proboscies through the silk side of the box into a vein and suck blood. It is quite clear that the wet nurses must have had typhus before, or that they must have been vaccinated, and that they must not harbor other microbes or disease germs. That is easily determined in our laboratory. Our lice are quite aristocratic. Their apartments are cleaned every day and heated to body temperature; they (the lice) are served two full meals of fresh, healthy human blood a day. It may be lousy business, but it is worth while.

**The Utility of Lice**

After eight days of this high life, the lice are killed. The laboratory assistants, like undertakers, remove their entrails, intestines, stomach, and esophagus, all of which are studded with billions of *Rickettsiaceae*. This process is done under the microscope. The parts extracted are sterilized with carbolic acid. Several hundreds of the digestive tracts are then pulverized, the larger remnants of the intestinal walls being removed by centrifuging. A microscopical test determines the number of *Rickettsiaceae*; a physiological test ascertains the virulence of this particular lot of intestines.

After this, the material is prepared for the ampules, a set of three (Fig. 12). The
first shot should contain the intestines of seven lice, the second that of fourteen, and the third that of twenty-one—altogether about forty or fifty intestines. The ampules are then ready for anyone who wants the shots. Who are the people who want this vaccine? In the first place, missionaries and physicians who, by nature of their occupations, often come in contact with patients suffering or dying from typhus. They have to be vaccinated every year (Fig. 11).

VALUE OF PROPHYLACTIC VACCINATION

The value of prophylactic vaccination can best be judged from facts. In Poland, 2,755 persons received the triple injection up to 1933. The results were carefully tabulated. Not one person got typhus, though physicians and employees of hospitals were constantly exposed to infection. An interesting incident happened in Weigl’s laboratory, which, though unintentional, was of value. One of the male wet nurses of the lice let his wife feed the infected lice. His wife had been vaccinated in 1930; this incident took place in October 1931. She was immediately forbidden to continue the feeding. However, no aftereffects were noticed. Vaccination had prevented her from contracting typhus.

STATISTICS IN CHINA

The statistics for China, compiled by the Rev. J. Rutten are most satisfactory. The Scheut Fathers, whose Superior General Father Rutten was, have a difficult mission territory in North China and maintain a personnel of 165 to 220 missionaries. In the period of twenty-five years from 1905 to 1930, there were 130 deaths in their mission district. Out of these 130 missionaries, 88 died of typhus. Of these 88, 47 had not reached the age of thirty-six and only 6 were over fifty. In 1930, Father Rutten made vaccination compulsory for his missionaries in that district and established the Microbiological Institute in Peking. During the ten years from 1930 to 1940, not a single missionary died of typhus; they had all been vaccinated. The number of deaths occurring in the years 1931 to 1935 was 7, a mortality rate that is not surprising. From 1936 to 1940, 18 deaths occurred; out of these 5 were over seventy years of age, one being eighty-six and another eighty-eight; 7 were over fifty; 3 were under thirty-six (one of them having been murdered). Thus, during a period of twelve years, when vaccination was obligatory, no deaths were due to typhus. This warrants the conclusion that the vaccine gives one-hundred-percent immunity against typhus. Some might argue that better hygienic conditions removed the danger of typhus. This is not the case. Several of the missionaries contracted typhus during the last twelve years, but owing to the vaccination the disease was never fatal.

Statistics on the vaccinations made among the Chinese do not, in my opinion, warrant any conclusions concerning the usefulness of this or that vaccine against typhus. The Chinese may, without knowing it, have survived a benign case of typhus in childhood. It is also possible that their genetic constitution is different from that of foreigners. From history we know that foreign armies and explorers were laid low by diseases to which indigenous people were not susceptible.

OTHER METHODS OF VACCINE PREPARATION

We may also mention some other methods of vaccine preparation from dead virus. Zinsser and his co-workers prepared vaccine against murine typhus from rats and mice. Another method consists of growing the Rickettsiae in tissue cultures on agar-agar. Cox recently developed a method by growing Rickettsiae of the Rocky Mountain spotted fever in chicken eggs. At Fu Jen we
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tried this method for *Rickettsiae prowazeki* and discovered that the *Rickettsiae* grew in large numbers in the embryo-sac membrane. On an average, one egg yielded from ten to fifteen doses, i.e., forty-five injections. One egg was so prolific in *Rickettsiae* that it yielded eighty-five doses of vaccine. This method is now used exclusively in the Chemotherapeutical Institute of Frankfurt am Main.

We have seen that typhus can be chained, and the aim of the various governments of the world should be to localize the endemic centers as much as possible. This must go hand in hand with hygienic improvements, i.e., the eradication of lice. It will probably be some time before, in some countries, bathing is not considered revolutionary, the changing of clothes in winter time becomes frequent and regular, and a bathtub is found in every home. On the other hand, however, we know the enemy, we know his malicious tactics. We can successfully forge the weapons by which we hope to conquer typhus until the time comes when mankind knows typhus only from history.

### The Neurosurgeon

Working like linemen on a far-flung telephone network, surgeons now operate on the nervous system itself—daring, delicate, miraculously effective surgery—to check the pain of incurable disease or block the effects of hidden ills that cannot be treated at their source. Pain of incurable disease can be such unending, unbearable torture that victims look forward to death for merciful relief. Doctors used to administer drugs which interrupt the agony with spells of stupor.

Today the neurosurgeon declares that victims of incurable disease can live out their days without drugs or suffering. Every pain impulse, wherever it originates, must travel up the main spinal trunkline to the brain. When the pain cannot be eliminated at the source, the surgeon offers his recourse: interrupt the pathway of pain. This operation is performed at the point just before the nerves of the painful part enter the spinal column. Only a small incision is made in the nerve cable and great care must be taken to cut only the sensory nerve and not the motor nerve. The patient is deprived of nothing but his sense of pain and temperature in that part of the body. His tactile sense, or feeling, is left whole. Thousands of these pain-conquering operations have already been performed successfully.