EPIDEMIOLOGY OF PLAGUE

In 1952 and 1953, the research team of the Institut Pasteur de l'Iran published the results of its work in the inveterate plague focus of Kurdistan. The authors put forward a number of new ideas which, they felt, could be applied in other foci and help solve remaining problems in the epidemiology of the disease.

Investigations of plague epidemiology in eastern Mediterranean countries (Turkey, Syria and Iraq), India, and Java, carried out with the assistance of WHO at the request of the governments concerned, have enabled the research workers of the Institute to test their ideas themselves. A report on these surveys appeared in a recent issue of the Bulletin of the World Health Organization.¹

In the article that follows, Dr M. Balsazard discusses the main points of this report.

The first modern epidemiological studies of natural plague suggested that the disease was due solely to highly susceptible rodent species, because of the spectacular epizootics among these species. The rodents concerned were either domestic ones, headed by the rat, the main cause of human plague, or wild or field species, such as the gerbils in South Africa and the Sciuridae in the Asian or eastern European foci (tarabagans, susliks) and in the Americas (ground squirrels, prairie dogs). It is true that, in these rodent populations, plague always had a tendency to die out because of the very violence of the epizootics. That this disappearance was complete was suggested by the negative results obtained in all investigations of these populations during inter-epizootic periods. However, the continual recrudescence of the disease at the same places in wild foci, and its never-ending persistence in certain rural or urban foci, where the rat was thought to be the only rodent involved, seemed proof of its perpetuation by these highly susceptible species.

A new theory

In 1952, the Institut Pasteur de l'Iran, on the basis of its researches in Kurdistan, introduced the new idea that highly resistant species play a part in plague epidemiology. The research workers of the Institute enunciated the following basic principle: any species exterminated by a disease cannot be the reservoir of this disease, or, in other words, the true reservoir of a disease must be sought not among the most susceptible species but among those whose natural resistance shows them to be the best adapted to the disease. This principle, which may appear self-evident, was in fact directly opposed to accepted ideas, particularly in the case of plague, where resistance to infection had always been considered as a factor limiting its spread.

According to the new theory, the true reservoirs of infection were the highly resistant rodent species and the susceptible species were only temporary victims. Once these susceptible species, and in particular the rat, were regarded as unable to perpetuate the disease, the whole problem of plague epidemiology had to be reconsidered, especially in the case of the so-called "pure murine" foci (India, Java, Madagascar, Kenya, etc.).

Investigations

The new concept found a very wide audience. In Kenya, R. B. Heise was the first to prove that, in one of the most reliably

² Ann. Inst. Pasteur, 1953, 85, 411
established "pure mutation" foci anywhere in the world. Genetic mapping played no part in maintaining the disease and its transmission will reduce these foci, except based on highly resistant strains. In the USA, investigations in the southeast of the country were directed at the Institute of K. F. Mayer, towards species resistant to the infection and rapidly revealed the ability of some of them (M. lastonii, C. festeri). In the USSR, despite the field work performed that mass and C. lastonii activity played a prominent role, a number of workers turned their attention to the resistant species. C. festeri, including species of M. lastonii and the genus B. rubis (B. ovis, C. rhesus, C. lastonii), M. lastonii (M. lastonii and M. rubis) and even A. rubis (C. rhesus) were then investigated. These species, which for the most part had already been recognized in the Soviet Union as being subject to infection and whose resistance was known or that recently has been demonstrated, are now considered to play the principal role in most areas of permanent infection.

Finally, WHO gave the Institut Pasteur de l'Iran an opportunity to extend its investigations by enlisting it into the series of epidemiological surveys conducted by the Governments of India, Iran, Iraq, Syria and Turkey. These surveys took place from 1951 to 1957. In collaboration with national teams, the Institute made possible continuing work in Iran and Khorasan. This group of investigations, in conjunction with the investigations conducted in Khorasan by the Institut Pasteur de l'Iran, under the leadership of Georges Rüdin, covered practically all aspects of plague throughout the world and made it possible to solve a number of important questions relating to the epidemiology of the disease.

Permanence and Focal Point

The Institut Pasteur de l'Iran and its directors were able to realize the great importance of the genera of the Vibrio group in the transmission of plague.

In our experience with the genus M. lastonii, which we have shown experimentally to be highly resistant to plague, the work of our Institute was then to verify the hypothesis that the resistant strains had to be considered as a natural reservoir of the disease, by concluding that "plague is only a disease that affects only the very resistant rodents." Further researches in Khorasan were to show definitively that some strains were resistant or even immune to the classification of the genus M. lastonii, which had already been repeatedly modified by the experts. The Institute undertook the study and classification of the species M. lastonii, with the help of the bacteriologists of the Institute of Khorasan, which was initially conducted for the purpose of determining the species of the genus M. lastonii. The results of these studies revealed pronounced differences between the strains of the genus, especially the species M. lastonii. One of these differences was then confirmed precisely with susceptibility to plague. For example, two species, M. lastonii and M. rubis, possessed the resistance regarded for the time being as the most important for the continued persistence of the disease, that the other species defined in the series of differentiations, M. lastonii, M. rubis and M. rubis, were on the contrary highly susceptible to plague. In the permanent infected focus in Khorasan, there were at least one of the resistant species and at least one of the susceptible species closely mingling in the habitat. While, in the permanent focus in Iran, the resistant species was the only species present, the susceptible species being absent.

In the permanent focus in Iran, the resistant species was the only species present, the susceptible species being absent. The examination of the infective agent showed that the resistance was brought about by several species of host rodent species in the same species. However, the resistant species, and the susceptible rodent complex are the only ones that were detected.

When the term "focal point" was used to describe the presence of resistant species, it was shown that this was not sufficient to ensure itself. The presence of resistant species could bring about only temporary persistence of the endemic plague to occur. It was necessary to have a dense population of highly resistant rodents capable of surviving in the most adverse hygienic and climatic conditions. This permanent persistence existed only in areas where resistant species predominated in large numbers - i.e., in more resistant species, able to the infection in foci, or in large temporary foci with a favorable microclimate.

Transmission of Disease

Transmission is by the sylvatic phase of plague, which is considered to be naturally transmitted in most areas where plague is endemic. The infection is transmitted mainly by ticks, which are found in areas where only highly susceptible species are to be found. It is rapidly transmitted. The disease is spread primarily by direct contact with infected animals, particularly by biting, during the period when they were infected.
The usual routes of plague infection involved direct contact with infected individuals or aboard ships carrying infected goods. However, the plague could also spread through less direct means, such as the bite of a rat flea, which could transmit the bacteria to humans even when there were no visible signs of an infected rodent. The bubonic plague, which was the most common form of the disease, could be characterized by the sudden onset of fever, severe headache, and body aches, followed by the appearance of buboes, or painful swellings, typically in the armpits or groin. The disease could then progress to the pneumonic form, in which the bacteria were released into the air and could be transmitted through coughing or sneezing, leading to respiratory symptoms and often a rapid and fatal outcome.

The historical context of the plague outbreaks in Italy and China during the 14th century is often compared to the modern outbreaks in Asia and Africa. While the causes of the plague may differ, the basic mechanisms of transmission and the human response to the disease remain similar. The effects of the plague on society were profound, with massive death tolls and economic disruptions. The modern world, with its advanced medical knowledge and public health systems, is better equipped to respond to such outbreaks, but the lessons of the past continue to inform our approach to disease control and prevention.
Figs. 2 and 3 show that the disease spread rapidly throughout the world. In the Americas, it reached Mexico in 1665 and then spread through the southern United States. In Europe, it reached the British Isles in 1665 and then spread throughout the continent. In Asia, it reached China in 1665 and then spread throughout the continent.

The death rate was very high, with mortality rates ranging from 30% to 50%. The disease was especially deadly for children and the elderly.

The disease was spread through contact with infected bodily fluids, primarily respiratory droplets. It was also spread through the bite of an infected mosquito.

The disease was treated with quarantine and isolation of infected individuals. In some cases, infected individuals were quarantined in hospital ships or other isolated facilities.

The disease was also treated with various medical interventions, including the use of antiseptics and the administration of medicines. However, these treatments were often ineffective and often caused more harm than good.

The disease eventually ran its course, and the population slowly recovered. However, the toll it took on the global population was significant, with millions of deaths worldwide.
operation the chain of infection from rat to rat, from rat to man, and from man to man. There should be no vaccination, which is too slow and unreliable for immediate prophylaxis, but chemoprophylaxis by means of sulphonamides. There should be no cordon sanitaire or isolation measures, since these are rendered pointless by disinfecting, chemoprophylaxis of contacts, and treatment of patients with sulphonamides or antibiotics.

As regards long-term prophylaxis in infected territory, once it had been demonstrated that wild or field rodents alone play a part in the maintenance and propagation of the infection, it seemed logical to carry out eradication campaigns based on the destruction or at least dissection of field rodents and their burrows. Because of certain prejudices arising from previous failures, public health authorities were at first reluctant to undertake such campaigns, but the success of those carried out in certain invertebrate foci in the USSR showed that they were the only means of obtaining lasting results.

Where long-term prophylaxis at the international level is concerned, certain definitions (as in the case of yellow fever) appear to be called for, i.e., the definition of "receptive areas" as those where *R. rattus* exists side by side with a sufficiently numerous and vulnerable field rodent fauna; of "critical areas" as invertebrate wild foci together with the ports, even if free from infection, situated in their neighbourhood; and, finally, of "immune areas" as areas free from *R. rattus*, together with the neighbouring ports. These definitions might permit the immediate preparation of agreements for international assistance in the event of the invasion of a "receptive area" by plague. In this way the threatened country could be provided with everything necessary to ensure the rapid eradication of the disease before it had time to take root and spread.

An international programme for the detection and delimitation of "critical areas" should be drawn up, making it possible to designate "infective ports" and to plan the eradication of plague in the areas concerned. In the third report of the WHO Expert Committee on Plague, a programme of this type headed the Committee's "Recommendations for co-ordinated research".

(*) Finally, work carried out in the off-season in several villages where murine mortality had been high in the preceding season gave negative results confirming the extreme rapidity with which the infection normally disappears in the case of the rat.

(0) Once Simond had definitely proved the murine origin of human plague by showing the part played by the rat flea in its transmission,...