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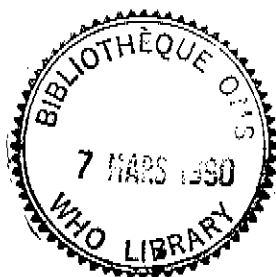
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WHO CONSULTATION ON PLAGUE

(New Delhi, India, 11 to 15 September 1989)



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A WHO Consultation on Plague was held in New Delhi from 11 to 15 September 1989. The purpose of the Consultation was to review the trends of plague in different geographical areas and practical implication of plague surveillance in its natural foci, to evaluate the diagnostic and preventive technologies available and to advise WHO on further strategies and specific projects related to plague prevention and control.

## 1. INTRODUCTION

The WHO Consultation was inaugurated on 11 September 1989 by Dr U Ko Ko, Regional Director, South-East Asia Region. Dr Ko Ko emphasized that even though human plague is no longer a problem in many of the countries of the world, the persistent natural foci of sylvatic plague and continued sporadic outbreaks in various parts of the world pose a threat of resurgence of human plague and thus still require constant attention of the health authorities in the endemic countries. Dr N.K. Shah, Director, Prevention and Control of Diseases, outlined the scope and objectives of the Consultation. Dr (Mrs) S. Sehgal was nominated Chairman, Dr Hou Pei-sen, Vice-Chairman and Dr A. Barnes, Rapporteur.

The present global situation regarding plague, the latest trends in epidemiology, control programmes and laboratory diagnosis were presented and the recommendations made at the Inter-Country Seminar on the Epidemiology of Plague (Rangoon, 2-6 December 1985) have been endorsed.<sup>1</sup> In addition, country papers on plague were presented by the participants. The participants were divided into two working groups. One group was assigned to work on the epidemiological aspects of plague and to prepare guidelines for surveillance and control taking into consideration the recent trends in the use of insecticides and rodenticides. The other group prepared guidelines for the role of the laboratory in the detection and surveillance of the disease.

The participants also visited the National Institute of Communicable Diseases where they witnessed the activities for flea and rodent identification and laboratory tests carried out by the Institute on plague.

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<sup>1</sup> SEA/Plague/15

## 2. REVIEW OF THE GLOBAL PLAGUE SITUATION

The following table shows the number of cases of plague and the number of deaths which have been notified to WHO over the last eight years, i.e. since the Informal Consultation on Plague Surveillance and Control in 1979.<sup>1</sup>

NUMBER OF CASES OF PLAGUE NOTIFIED TO WHO 1980-1987<sup>2</sup>

|                    | 1980       | 1981       | 1982       | 1983        | 1984        | 1985       | 1986        | 1987        |
|--------------------|------------|------------|------------|-------------|-------------|------------|-------------|-------------|
| <u>AFRICA</u>      |            |            |            |             |             |            |             |             |
| Angola             | 21         | 6          |            |             |             |            |             |             |
| Kenya              | 5          |            |            |             |             |            |             |             |
| Libya              |            |            |            |             | 8           |            |             |             |
| Madagascar         | 11         | 44         | 38         | 24          | 39          | 85         | 29          | 23          |
| South Africa       |            |            | 19         |             |             |            |             |             |
| Uganda             |            |            | 153        |             |             |            | 340         |             |
| Tanzania           | 49         | 9          | 76         | 569         | 603         | 129        | 360         | 356         |
| Zaire              |            |            | 1          |             |             |            |             | 474         |
| Zimbabwe           |            |            | 3          | 1           |             | 1          |             |             |
| <u>AMERICAS</u>    |            |            |            |             |             |            |             |             |
| Bolivia            | 26         | 21         | 1          | 21          | 12          |            | 94          | 2           |
| Brazil             | 98         | 59         | 151        | 82          | 37          | 64         | 58          | 43          |
| Ecuador            |            | 8          |            | 65          | 7           | 3          |             |             |
| Peru               |            | 27         | 11         | 17          | 413         | 44         |             | 31          |
| USA                | 18         | 13         | 19         | 40          | 31          | 17         | 10          | 12          |
| <u>ASIA</u>        |            |            |            |             |             |            |             |             |
| China              | 30         | 1          |            | 25          |             | 6          | 8           | 7           |
| Myanmar            | 73         | 1          | 165        | 96          |             |            |             |             |
| Viet Nam           | 180        | 11         | 116        | 127         | 196         | 137        | 104         | 107         |
| <b>WORLD TOTAL</b> | <b>511</b> | <b>200</b> | <b>753</b> | <b>1067</b> | <b>1346</b> | <b>486</b> | <b>1003</b> | <b>1055</b> |

It is estimated that the above numbers represent only a portion of the actual number of cases which have occurred and may not, in fact, even represent all of the known, active enzootic foci in the world.

Europe: Natural foci of plague in Europe still exist only in fringe areas of the Caspian depression and the eastern slopes of the Caucasus.

Eurasian land mass: The north-western boundary of the natural plague foci goes slightly beyond the limits of the desert zone, continuing a short distance into the desert steppe, i.e. the area between the Volga, the Don rivers and the Ural river. The main focus of natural plague in the eastern part of the continent lies in the steppe region. The foci extend as far as the northern and eastern limits of the steppes and penetrate widely into the forest steppe zone.

<sup>1</sup> WHO/BD/PL/79.71

<sup>2</sup> WHO Wkly Epidem. Rec., No. 47, 1988, 360-362

Asia: Natural foci in Asia stretch in an uninterrupted chain across the desert and steppe regions from the foothills of the Caucasus, eastern Turkey and north-east Iran in the west as far as Liao-Ho to north-east China. The southern boundary of the plague area passes to the north of Mukden and through Chifeng to Kaigan. Nowhere do the Asian foci reach the coast of the Pacific. Foci are found in China, Mongolia, Viet Nam, Cambodia, Myanmar, India, Nepal, Indonesia, Iran and the south of the Arabian peninsula, the Yemen Saudi Arabian border and in Saudi Arabia.

Africa: Natural foci of plague are known to exist in broad areas of Africa; these include areas in the Union of South Africa, Namibia, Lesotho, Kenya, Tanzania, Mozambique, Madagascar, Uganda, Zaire, Senegal, Mauritania, Libya and probably Egypt.

Americas: Natural foci of plague occur in 15 western States of the USA, in south-west Canada on the border with the USA and in northern Mexico in North America while foci have been recorded in Argentina, Bolivia, Brazil, Ecuador, Peru and Venezuela in south America.

### Summary

It will be noted from the above table that the incidence of human plague is relatively stable and has, indeed, declined compared to the 1970s. The much larger number of cases at that time was mainly due to the number being reported from Viet Nam. More recently, the number of cases notified annually from Tanzania accounting for some 30% of the total number of known cases, has influenced the global epidemiological situation. However, rodent plague activity continues to occur in most, if not all, existing foci, presenting a threat of new outbreaks at any time in presently quiescent areas.

## 3. REVIEW OF PLAGUE SITUATION IN THE PARTICIPATING COUNTRIES

The present situation of plague, the current status of control measures, the problems and constraints in China, India, Indonesia, Madagascar, Myanmar, Nepal, USA, USSR and Viet Nam were reviewed and thoroughly discussed. The following are the summaries of country presentations.

### 3.1 China

Plague is still a public health problem in China. During the ten years from 1979 to 1988, 100 persons were affected by plague in the provinces of Qinghai, Yunnan, Gansu as well as the autonomous regions of Tibet, Inner Mongolia and Xianjiang. The mortality was 56 per cent. Most of the cases were scattered. Of the 100 cases, 61% were infected by hunting, skinning and eating marmots or other infected animals; 38% of patients suffered from bubonic plague, 39% of pulmonary and 18% of septicaemic plague.

Plague foci are distributed in 197 districts of 17 provinces and autonomous regions in China. They are divided into ten types according to their main reservoirs and their land forms. Fifty-four species of vertebrates and 41 species of arthropods have been found naturally infected. Among them, 11 species of rodents and 11 species of fleas have been identified as the primary reservoirs and vectors of plague respectively. According to surveillance data, epizootics have been active in recent years. From 1981 to 1988, the epizootics were detected in nine out of ten types of natural foci. Active natural foci were detected in Inner Mongolia, Ningxia, Shanxi, Gansu, Qinghai, Xingjiang, Tibet and Yunnan provinces. In the south and south-east coastal provinces, the epizootics have been controlled since the late 1950s, but serologically positive results have occasionally appeared during surveillance even after 30 years. Further surveillance and study are needed to find out if natural foci continue to exist in these regions.

At present, the general practice of plague control in China depends mainly on taking comprehensive measures suited to the various foci, preventing human cases and taking strict precautions against outbreaks. The measures successful in China are due to the establishment of a preventive network, management organization, and the relevant regulations.

Research on plague in China includes development of methods for reducing the threat of plague in natural foci, studying the mechanisms of persistence of Yersinia pestis in the natural foci, improvement of plague diagnosis and development of a vaccination programme in selected areas.

### 3.2 India

Plague is a disease of great antiquity in India and was responsible for tremendous mortality until 1950. The disease is estimated to have caused 12.5 million deaths between 1889-1950. The last human case in India was reported in 1966 from Karnataka State. Since 1966, a few suspected outbreaks have occurred, especially in the historic plague endemic areas of south India and Himachal province in north India. However, none of these could be confirmed to be plague. One of these outbreaks in Himachal in 1983 was very similar to pneumonic plague and of the 22 cases, 17 died.

Different species of rodents are prevalent in different geographical regions in India. Ratfalls continue to occur in endemic areas. Of the 44 ratfalls that were investigated during 1978-89, none was found to be due to plague. Under the plague surveillance activities, rodents were trapped and examined for bacteriological evidence up until 1980. Since then only sero-surveillance is in progress and except for 13 sera (Tatera indica) in 1979 and three (T. indica) in 1989, none of 188,025 rodent sera and 16,061 dog sera tested up until September 1989 revealed plague activity.

Xenopsylla cheopis and X. astia are the major species of rat-fleas in India. While the former is predominant amongst domestic rodents (specific flea index = 4.93), the latter shows a high specific flea index (12.72) amongst the wild rodents. Periodic assessment of susceptibility of rat-fleas have shown resistance to DDT and dieldrin.

The National Institute of Communicable Diseases acts as the nodal centre for surveillance and control of plague in India.

### 3.3 Indonesia

Plague was first detected in Surabaya, the capital of east Java in 1910. From there the disease spread widely through east, central and west Java with a total of 239,407 cases. Of these cases 17.6% occurred in east Java, 51.5% in central Java and 30.9% in west Java. By the end of the 1950s, plague was reported only in two mountainous zones (Boyolali and Wonogiri). After 1957, two outbreaks occurred in Boyolali, in 1968 and 1970 respectively.

At present there are two active natural foci of plague: 1) in the district of Boyolali, central Java; 2) in the district of Pasaruan, east Java. Both natural foci exist on mountain slopes between 1,000 and 1,500 meters above sea level. The important reservoirs of plague are Rattus rattus diardi and Rattus exulans (in central Java) while Hylomys suillus has also been confirmed to be the reservoir of plague in east Java rather than R.r. diardi and R. exulans.

The species of fleas which play a role as a vector in the transmission of plague are X. cheopis and Stivalius cognatus. Plague outbreaks usually occur during the rainy season.

Human, rodent and flea surveillance has been carried out in the endemic areas since 1968. There are two kinds of human surveillance: 1) active human surveillance which is carried out by plague personnel who look for fever cases with lymphadenopathy or fever cases with bloody sputum. 2) passive human surveillance is carried out by health centres and the local hospital. Rodent and flea surveillance has also been carried out in the natural foci since 1968 by trapping rodents, collecting fleas and running serological tests on rat sera. Attempts to isolate Y. pestis are done only from the organs of the sick or dead rodents and from their fleas.

Since 1967, instead of the flea index, Geometric Mean Positive Titre has been selected as the barometer of the plague situation in the plague endemic areas.

In the prevention and control of plague several steps have been taken:

1. Health education;
2. Sanitation to reduce rodent food and harbourage;
3. Flea control using DDT and other insecticides;
4. Treatment of all suspected cases and contact persons with tetracycline and streptomycin;
5. Active immunization if there is an outbreak.

The plague surveillance and control programme is limited by its very low priority in the Ministry of Health and by lack of appropriate reagents for laboratory tests and flea susceptibility test kits. There is also a need for training of laboratory personnel in plague diagnosis.

The epizootic sources of human infection in Indonesian plague foci (R.r. diardi and X. cheopis) and the peridomestic bridge between the maintenance and epizootic cycles (R. exulans and S. cognatus fleas) are known. With the information available, it has been possible to improve the surveillance system for early detection of plague activity. Before outbreaks can be anticipated and prevented, research is needed to identify the maintenance cycle in terms of its components and the ecological relationships that enable plague to persist in its natural foci.

#### 3.4 Madagascar

Plague appeared for the first time in 1898, but only in the ports. In 1921 it then appeared on the high plateau (above 700 metres) and has persisted there ever since. In the 1930s, plague killed more than 3,000 people every year. The situation improved from 1936 onwards with the introduction of mass EV vaccination. After 1950, the number of cases and deaths declined sharply with the use of DDT against fleas and the treatment of patients with streptomycin.

Human plague cases occur the year round but most of them occur during the hot wet season (October to March). One thousand four hundred and fifty cases of human plague were recorded from 1956 to 1988, of which 91% were bubonic plague with 32% mortality and 9% were pulmonary plague with 60% mortality. The capital, Antananarivo, which had no plague from 1950 to 1980, had a small epidemic from 1981 to 1987.

The Yersinia bacillus in Madagascar is of the oriental variety. The fleas which transmit plague are: X. cheopis in the towns and villages and Synopsyllus fonquerniei in the countryside. The only rodents involved in the plague cycle in Madagascar are R. rattus (R. norvegicus has appeared in Antananarivo only in the last few years).

Surveillance, control and prophylaxis are the responsibility of the Plague Division of the Communicable Disease Control Service (Ministry of Health). This Division has a central health laboratory at the Pasteur Institute, Madagascar.

The usual methods are used to identify and isolate Y. pestis. However, it must be pointed out that most of the strains are obtained by intraperitoneal inoculation of white mice immunodepressed with cyclophosphamide.

Resistance of plague-vector fleas to organochlorine, organophosphorus and carbamate insecticides in three high plateau regions has been reported.

### 3.5 Myanmar

Plague was first reported in Myanmar in 1898, appearing first in cities in the south, then spreading by routes of transportation to central and upper parts of the country by 1905. During subsequent decades the incidence of plague diminished in lower Myanmar and by 1956-1965 was almost non-existent there. Cases and outbreaks continued to occur in central Myanmar where the disease appears to be firmly established in rodent and flea populations. In 1967 plague spread once more across the country, eventually involving every state and division except Chin State, Ayeryawaddy Division, and Taninthary Division.

With the passage of time, plague morbidity and mortality have shown a downward trend; however, it still remains a public health problem of significant importance. Some of the reasons for its persistence in the country are the emergence of resistance to insecticides (DDT) in rat-fleas, ignorance and indifference of the community towards reporting of epizootics in their houses as well as in the fields. The common species of rodents involved in plague are R. exulans, R. rattus, Bandicota bengalensis, Mus musculus and Suncus murinus in domestic surroundings and R. rattus, B. savilei, M. booduga, M. cervicolor, Millardia sp. in rural areas. The flea vectors are X. cheopis and X. astia.

To improve control, the country required reinforcement and improvement in all aspects of laboratory diagnosis, predictive surveillance activities and research to develop effective methods for the prevention and control of plague.

### 3.6 Nepal

Plague was not reported until 1960 in Nepal. In 1960-62, 150 cases of suspected plague were reported from two districts in the Terai plain region bordering Bihar and Uttar Pradesh States of India. The epidemiological details of these plague cases were not determined. The first known outbreak of plague occurred in one district of the far-western mountainous region of Nepal. This district, called Bajhang, lies near the Uttar Pradesh border of India at an elevation of 8,500 feet. The epidemic took place over a period of eight weeks during which 26 persons fell ill and 18 died. The attack rate was calculated as 3.1% and case fatality rate was 69 per cent. About six months later another outbreak was reported in the same area during February 1968. Information on this report was however not available. Since then no case of plague has been reported in Nepal. Whether or not a natural focus exists in Nepal is not known. However, due to cyclic nature of the disease, surveillance is necessary. It is suggested that a Plague Unit be established under the Zoonotic Disease Section at the central level with trained manpower to initiate plague surveillance as soon as possible.

### 3.7 United States of America

Plague is enzootic among native wild rodents and their fleas in much of the United States from the Pacific Coast eastward to about the 97th meridian. The disease in animals is characterized by sporadic or periodic epizootics among susceptible rodent populations. Human cases result from chance encounters with plague-infected fleas or infected animals during epizootics and typically occur as single, isolated events or as small case clusters. During the past decade there has been an average of about 19 cases per year in the United States. Most occur in either the south-western states or the Pacific Coast states. The disease occurs predominantly in young persons: 21% of cases occurred in the 0-9 year age group and 25% in the 10-19 year age group. However, cases occurred in people ranging from one week to 82 years of age. The case fatality rate until recently has averaged about 18% with the greatest percentage of deaths (33%) in the elderly (> 50 years) and among males in the 20-29 year age group. Secondary plague pneumonia is a common development and occurred in 22% of all cases from 1975-1980, however, the incidence of pneumonic complications has more recently declined to <10% of cases. No human-to-human transmission has occurred in the United States since 1924. Nevertheless, at least four and possibly five cases of pneumonia plague have occurred in recent years, all acquired by close contact with plague infected pet animals, (particularly cats) that had developed secondary pneumonia plague.

Plague surveillance and control in the United States is multifaceted and involves a wide range of local, state and national agencies as cooperators. Persons involved in this network of observers report unusual events in animal populations, collect and submit specimens for testing and may participate in control actions in areas where humans are at risk. Trends in the incidence of plague in animal population is also supported by the collection and testing of sera for Y. pestis antibodies of wild carnivore and domestic dog populations. These sero-surveys, used as a broad measurement of plague activity, enable to locate and focus attention on rodent plague activity with greater precision.

Plague control is carried out only in areas of high human risk, using insecticides for flea control and both rodenticides and environmental management for rodent control.

### 3.8 USSR

The natural foci are spread over the territory from central Caucasus and Transcaucasus in the west to the desert and semi-desert areas of central Asia and Kazakhstan, and further to the east to the boundary areas between the USSR (Siberia) and Mongolia.

The current classification of the USSR natural plague foci grouped by rodent species of reservoirs is as follows: suslik and marmot (Citellus and Marmota) foci (north-west Caspian steppe focus, central Caucasus focus, Tuva focus, Transbaikal focus, Tien-Shan focus, Altai focus, Talass focus). Gerbil (Rhombomys and Meriones) foci (Transcaucasus plain and foothill focus, central Asia plain/desert focus, Volga-Ural plain focus, Araks plain focus). Vole (Microtus) foci (Dagestan mountain focus, Transcaucasus highland focus, Altai mountain focus). Pika (Ochotona pricei) focus (Gissar mountain focus).

The north-west Caspian steppe focus, central Asia desert focus, central Caucasus focus and Transcaucasus highland focus are constantly active. Sporadic plague epizootics in rodents are noted in Tuva, Altai, Gissar and Dagestan foci. In all other foci there is little activity and epizootics have not been detected there for a long time.

In the 1980s, plague epizootics occurred in central Caucasus and Transcaucasus highland foci, the north-west Caspian steppe and central Asia desert foci, and in particular the Mujunkum, Aral and Balkash mesofoci.

### 3.9 Viet Nam

Human plague cases usually occur during the dry season with a peak in April, May and June. Bubonic plague occurs in 95-97% of the cases. Primary septicaemia and pulmonary plague are rare. The case fatality rate is commonly 2.5 to 3.5 per cent. Streptomycin, tetracycline and other aminoglycosides are effective in treating human cases. Good results are also achieved if sulfonamide is taken in correct doses during the first 1-2 days of disease, but is advised only in mild cases or for chemoprophylaxis of case contacts.

Y. pestis and/or F1 antibodies have been found in 12 species of rodents, one insectivore (S. murinus) and has even been reported from one species of herbivores.

Epizootic plague is spread primarily in domestic rats, particularly in rural areas. The distribution of reservoir rodents and their roles in plague epidemiology differ in accordance with the biocoenoses involved. R. norvegicus prevails in the cities, plains and coastal areas where less intensive epidemic/outbreaks occur. In the rural and mountainous areas where intensive and long lasting epidemics/epizootics occur, R. exulans is found to be the major plague reservoir. The main plague vector identified in Viet Nam is X. cheopis. The favourable factors for the persistence of plague in Viet Nam are a temperature from 21-26°C, the presence of R. exulans and the absence of floods.

The application of a national programme of plague control has given encouraging results. The number of plague foci is decreasing. The average morbidity and mortality rates in the country are low, particularly in urban areas. However, the natural foci of plague have not been properly investigated. Because of socio-economic problems being experienced by the country, there are difficulties in the implementation of the appropriate preventive and control measures on a much larger scale.

## 4. PREVENTION AND CONTROL OF PLAGUE

### 4.1 Prevention

When the location of natural foci is known and their characteristics understood, there are a number of measures that can be taken to prevent the occurrence and risk of possible spread of plague. The first step is to ensure that there is an adequate knowledge of the epizootiology of plague in the particular focus being considered, i.e., the species of small mammal reservoirs present in the focus, the extent to which infection is found in the different species, the species of fleas present on different hosts within the focus, the degree of susceptibility or resistance to infection of the small mammal population in the areas, and the vectorial capacity of the various flea species. Information on the normal seasonal variations in population density is essential as a basis for detecting any abnormal changes such as a sudden decline or increase in the populations which may be a sign of an epizootic. If it is anticipated that vector control measures may have to be carried out with insecticides, the baseline susceptibility for the insecticides most likely to be used should be established. The most important measure thereafter will be the establishment of an effective surveillance system which will be adequate to detect unusual plague activity in a focus, a subject which will be dealt with separately.

### 4.2 Surveillance

Surveillance on the international, national and local levels is of utmost importance in developing a comprehensive understanding of global and focal trends of plague activity and in the development of programmes capable of preventing the spread of plague, of controlling outbreaks and of preventing human exposure.

#### 4.3 International surveillance

Human case surveillance is an essential first element in plague surveillance. In recent years there has been an unfortunate tendency for countries to under-report the occurrence of plague or to fail to report it altogether in fear of having quarantine measure applied against them by countries or in concern that the country may be avoided by tourists or other visitors. By such failures to report, information on plague important to the international community is lost and possibilities for obtaining assistance in combating an outbreak may also be lost. It must be emphasized that any country reporting plague should be able to do so without penalty.

#### 4.4 National surveillance

Surveillance is indispensable as an early warning system in those regions or countries where plague foci are known to exist or in which there are rodent/flea populations susceptible to the introduction and establishment of plague.

It is essential that specially trained personnel be available in each country or region to carry out surveillance and undertake the measures necessary to control or prevent an outbreak. The staff should have the ability to recognize the overt signs of plague in animal populations, collect appropriate specimens for diagnostic testing at a central laboratory and be able to conduct epizootiological or epidemiological investigations at least on a preliminary basis. They should be familiar with the ecological components of the known and suspected foci in their countries and the factors and components that may lead to human exposure. They should be able to assess the need for control measures and be able to select, plan and implement those which are appropriate to prevent human exposure or extension of epizootics.

#### 4.5 Development of a phased surveillance and control programme

The 1979 WHO Informal Consultation on Plague held in Geneva<sup>1</sup> produced a four-phase programme which was later confirmed at the Rangoon Inter-country Seminar in 1985<sup>2</sup> in which basic and immediate steps to be taken in the event of a plague outbreak were outlined as well as progressive measures to be taken for the development of a predictive surveillance and preventive control programme. This scheme is useful regardless of the resources available in a given country or the status of its health programme or the degree of knowledge available concerning the focus in question.

The activities in the various phases may be briefly described as follows.

##### Phase I. Case recognition and medical intervention

- A. Assure clinical diagnosis, isolation and tentative identification of Y. pestis, and treatment of patient(s).
- B. Assure identification of Y. pestis (regional laboratory).
- C. Assure confirmation of Y. pestis at the central laboratory.

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<sup>1</sup> WHO/BD/PL/79.71

<sup>2</sup> SEA/Plague/15

- D. Perform preliminary epidemiological investigations:
- determine by epidemiological histories the locations where infection(s) might have been acquired;
  - locate, observe and/or treat case contacts (when the pulmonary form is suspected and persons have been exposed to a suspect source of infection);
  - determine the potential animal or human sources of infection.
- E. Inform the general medical community, the health authorities, and the public of the problem, using all available public health channels and news media.
- F. Consider and evaluate the utility of a vaccination campaign among selected population groups.

Phase II. Epidemiological/epizootiological investigation and emergency control

- A. Locate specific sites at which infections were acquired.
- B. Determine animal and vector species potentially involved, using field observations, collections and general knowledge supported by laboratory tests.
- C. Locate and define vector and rodent populations in contact with people and potentially hazardous to them.
- D. Identify ecological parameters of significance for the development of control strategies.
- E. Determine or estimate by rapid surveys the geographical extent of the epidemic/epizootic.
- F. Commence emergency vector control operations immediately following "A" and "B", extending outwards as indicated by data from "C", "D" and "E".

Phase III. Predictive surveillance and preventive control

- A. Conduct research necessary for the establishment of a predictive surveillance system and control programme suited to the focus.
- B. Develop preventive control strategies based on surveillance data, landscape characteristics, and host/vector ecology.
- C. Implement research to develop environmental control measures against rodent reservoir species.
- D. Provide a continuing and unfailing public information and health education programme on plague.

#### Phase IV. Management

- A. Continue surveillance in plague enzootic and epizootic areas.
- B. Undertake pre-emptive control measures on the basis of the predictive surveillance programme.
- C. Conduct environmental management to maintain reduced populations of commensal rodents and key wild rodent reservoir species.
- D. Continue community education and exchange of information among agencies and institutions concerned with plague research, surveillance and control.
- E. Continue research and development in the areas of diagnosis, microbiology, therapy, ecology and control of plague.

#### 4.6 Plague laboratory

The existence and availability of a central plague laboratory is essential for the successful conduct of plague surveillance and control programmes. The predominant clinical features of the disease in humans, e.g., high fever and lymphadenopathy, are also major manifestations of many other infectious diseases which must be ruled out by specific laboratory tests before plague can be accurately identified or confirmed. The conduct of a plague surveillance programme also requires that fleas, animal tissues, and serum specimens be examined for evidence of plague infection.

Preliminary diagnostic tests to identify plague, such as staining to determine the presence of bipolar organisms, may be done in the field to determine immediate courses of action pending confirmation. Other tests, such as biochemical analysis, culture, and the fluorescent antibody test (if reagents are available) may be performed in a laboratory equipped and staffed to undertake basic bacteriological work. The results of these tests should be considered either as suspect or, at best, presumptive, identification of plague or evidence of plague activity. Further and more comprehensive testing should be performed in a central laboratory with the facilities and personnel skills to positively confirm or rule out the suspect or presumptive findings. Confirmatory tests in addition to those already mentioned include mouse or guinea pig inoculation and subsequent recovery of *Y. pestis*, lysis of cultured organisms by specific bacteriophage at both 28°C and 37°C, and/or four-fold rise (or fall) in antibody titre by the passive haemagglutination test plus the passive haemagglutination inhibition test.

Newer tests, especially the various enzyme linked immunoabsorbent assays (ELISA) have been developed for the detection of plague antigens as well as plague antibodies, but await evaluation, standardization, and simplification before they can be recommended for widespread use in the field. Recent research on these and other, newer, tests such as biotin based DNA probes suggest the possibility of field kits for the specific identification of *Y. pestis* antigens in animal tissues and flea vectors. Such tests would vastly simplify the logistics of plague surveillance and move the identification of plague nearer the source, thus saving considerable time in identifying human cases and animal epizootics.

There remains a strong need for the maintenance or establishment of central plague laboratories in endemic or recently endemic regions or countries. The primary functions of such laboratories would be:

- Confirm laboratory diagnoses made by local laboratories.
- Report human and rat plague to WHO through appropriate channels.
- Support epidemiological and epizootiological investigations.
- Conduct research on the epidemiology, ecology, diagnosis, therapy and control appropriate to the country and the specific foci concerned.

#### 4.7 Treatment

The most effective drug against plague is streptomycin. Other effective drugs include kanamycin, chloramphenicol, the tetracyclines and sulfonamides (e.g., sulfadiazine) any of which might be the drug of choice, depending on the age and condition of the patient, the circumstances of the case, and the availability of the drugs. Gentamicin has been successful in treating human patients and in animal trials, but because of greater experience, streptomycin remains the drug of choice. The sulfonamides cannot be recommended when more effective and safer alternatives are available. Streptomycin is rapidly lethal to *Y. pestis* and must be used judiciously to prevent the rapid release of endotoxin followed by shock in the patient. Dosage levels and administration of the drug chosen should follow WHO recommendations. The penicillins are not effective for the treatment of plague.

Antimicrobial therapy should be started promptly, without waiting for laboratory confirmation, but after specimens have been taken for diagnosis. Because secondary pneumonia may already have developed, plague patients should be hospitalized and, if possible, isolated for the first 48 hours after specific therapy has begun.

All contacts of patients with possible pulmonary involvement should be quarantined and given either tetracycline (30 mg/kg body weight daily, orally in four equal doses) or trisulphapyrimidines (60-75 mg/kg daily in four equal doses at 6 hour intervals) for 10 days. Chemoprophylaxis is generally not indicated for contacts of patients with bubonic plague unless the hazard of a common source of infection persists. All case contacts and community associates of bubonic plague patients should be kept under surveillance and treated if symptoms develop. Care should be taken that patients on chemoprophylaxis receive the drugs and for the whole period prescribed.

#### 4.8 Transmission control

The transmission of plague either from one reservoir to another or to man can be most rapidly effected by control of the flea vector; only after this has been achieved should rodent control measures be considered. Though it may be quite feasible to achieve a very high level of rodent control in a plague focus, whether rural or urban, the death of many plague infected rodents would be likely to cause the introduction into the environment of large numbers of flea ectoparasites leaving the bodies of their dead rodent hosts and many of these fleas may be infected with plague. These hungry fleas will avidly seek another host thus leading to a greater spread of the disease than would have been likely had the rodent hosts not been killed. It is for this reason that the first step in controlling an outbreak of plague and interrupting its transmission is the control of the vector flea.

#### 4.9 Control of plague vectors

Generally speaking, experience has shown that the most effective manner of controlling flea vectors is through the application of insecticides formulated as dusts into burrows or on areas where the rodent hosts are likely to cross (such as rat runways) taking up the dust onto their fur and bringing it back to the burrows where the fleas will be killed by it. While dusts are certainly the formulation of choice, this formulation may not be readily available. A liquid insecticide spray can be applied, if necessary, especially to control fleas on indoor rodent populations. If a residual spray formulation is applied, greater attention will have to be placed on spraying floors and into rodent burrows than would normally be done when carrying out a residual spray application for malaria vector control.

The choice of insecticide and the formulation as well as the method of application can be guided by consulting the copious literature on this subject, and several recent reviews are available on request from WHO. However, prior to selecting an insecticide for use in a plague flea vector control programme, it is essential to carry out insecticide susceptibility tests to determine whether the local flea population has developed a resistance to any of the insecticides which may be considered for use in their control. Susceptibility test kits for this purpose are available through the WHO Regional Offices or the Division of Vector Biology and Control at WHO headquarters.

#### 4.10 Rodent reservoir control

Once an effective control programme has reduced flea indices and hence the likelihood of transmission, attention can be given to the reduction of rodent population densities. By ensuring that actual or potential reservoir populations are kept at a low level not only is the possibility for further outbreaks of human plague reduced, but there may be a collateral economic benefit if the target rodent populations are also causing damage to crops and stored food. In many endemic countries, there is little appreciation of the complexity of an effective rodent population reduction programme and the "rat" killing methods employed often have relatively little impact on rodent densities and may, in fact, lead to eventual increases in rodent population densities through the temporary reduction of population competition. Efforts need to be made to ensure that rodent control personnel are trained in modern methods and have available to them newer generations of rodenticides which are generally more effective and safer for man, his domestic animals, and harmless wildlife.

### 5. CONCLUSIONS AND RECOMMENDATIONS

#### 5.1 Epidemiological surveillance

It is felt that the international surveillance of plague is still not entirely satisfactory. Many outbreaks of plague go unreported for a variety of reasons and it was recommended that epidemiological surveillance be improved and timely notification be made of zoonotic and human outbreaks and that the exchange of information on all aspects of the epidemiology, prevention and control of plague be improved.

The countries should be encouraged to develop an effective, early warning system for the predictive surveillance and control of plague, supported by timely and accurate laboratory diagnosis of both human and animal specimens.

## 5.2 Community participation in surveillance and control

Every effort should be made by national and regional laboratories to enlist the participation of the community in the surveillance of plague and in its control by measures appropriate for use by the community itself with special emphasis on environmental measures that would reduce rodent densities and hence man-vector contact.

Continuous awareness should be created amongst the medical and veterinary personnel regarding the utility and availability of the plague laboratory in the diagnosis and surveillance of plague, and the epidemiological investigation of outbreaks.

## 5.3 Chemotherapy

Early institution of specific chemotherapy in appropriate dosage is essential to reduce the morbidity and mortality especially so in pneumonic plague. Tetracyclines, streptomycin and chloramphenicol have been widely used. These drugs should be used in dosage as recommended by WHO. Since many new antibiotics are now available, studies should be undertaken to assess their efficacy. The contacts or family members of a plague case should be placed under medical surveillance or treated with prophylactic doses of antibiotics or sulfa according to the situation and degree of actual or potential exposure.

## 5.4 Vaccination

Both live and inactivated vaccines against plague are available. Observations on the result of their use in the field indicate that they appear to have reduced morbidity and mortality to some extent in outbreaks of bubonic but not pneumonic plague. The immunity which they provide is, however, of short duration and a revaccination is necessary to maintain the level of immunity. Adverse side effects following revaccination are common. In the light of the restraints, vaccination is recommended only for high risk groups such as laboratory personnel working on plague or field workers in endemic areas. Vaccination should be used only for the prevention of plague and should not be used as a means of control during outbreaks.

## 5.5 Strengthening of laboratories

Fully staffed and properly equipped laboratories should form an integral and essential part of plague surveillance and control. The number of such laboratories in a country should be according to the endemic/epizootic area and/or magnitude of the problem. These laboratories should be capable of undertaking bacteriological and serological studies and should function under the guidance and supervision of a national laboratory which should perform activities pertaining to detection and confirmation of Y. pestis, relevant studies on mammology, entomology, immunology, studies on vaccines, vector susceptibility to insecticides, maintenance and characterization of Y. pestis strains, study of its sensitivity to newer antibiotics, use of animal models for isolation and characterization of local strains and establishing liaison with regional/WHO collaborating centres.

## 5.6 Training of laboratory staff

Regional laboratories should be set up which will act as regional reference centres to support national laboratories to train manpower, to develop educational material and to maintain and characterize strains. These laboratories should be encouraged and strengthened to produce diagnostic reagents for use in countries and their regions.

Training courses should be organized in collaborating centres on laboratory techniques in plague for scientists from different countries who should, in turn, act as trainers for laboratory workers in their respective countries.

### 5.7 Supply of reagents

Until indigenous production of reagents commences, the WHO collaborating centres should continue to supply the test kits.

### 5.8 Evaluation of test kits

Multicentric studies should be undertaken to evaluate the test kits currently being produced. The protocol for such study should be prepared by a country currently not involved in production.

### 5.9 Training and cooperation

There is a great need to train plague workers at all levels from paramedical personnel and community health workers through physicians, epidemiologists, microbiologists, ecologists and entomologists. A programme of continuing education is necessary to ensure that personnel keep abreast of new developments. For example, advantage should be taken of the WHO supported MSC courses in medical entomology and vector control to provide professionals with additional training in the epidemiology and control of rodent-borne diseases.

Training can be carried out in existing centres or laboratories. As suggested by the group, a more productive approach might be to train trainers at existing centres who could then train others in dispersed locations.

There is an urgent and continuing need for the development and support of regional laboratories to assist national laboratories in establishing surveillance and control programmes, organize training courses and seminars, and to maintain liaison with reference laboratories. Such regional laboratories in cooperation with WHO collaborating centres and in close liaison with national reference centres should play a key role in developing and improving national and international early warning surveillance systems, establishing standards for responses and actions.

### 5.10 Cost-effective measures

In many areas of the world rodent species which are reservoirs of plague as well as other diseases of public health importance may also be major agricultural pests, causing serious crop losses, while in urban areas, towns and villages, commensal species can cause huge losses in stored foodstuff.

As has been stated elsewhere in the report, in plague endemic areas rodent control measures should be carried out only after flea populations have been reduced through dustings. Afterwards, efforts should be made to keep rodent populations at the lowest possible levels. Whenever possible, particularly in urban areas, this should be done by denying food and harbourage to rodents through improved sanitation. Where such an approach is not deemed feasible, rodent control can be achieved through careful and assiduous use of rodenticide baits. Studies should be encouraged in each country to determine what are the most acceptable local baits and toxicants available for use in the control of each important species

### 5.11 Study of other rodent-borne diseases

Plague remains a threat in many countries with established natural foci of the disease. However, with the suppression and reduction in the number of human cases in a country, there may be some pressure to disband centres where responsibility is restricted only to the study and control of plague. It would therefore seem prudent for centres with a reduced work load concerned with plague, to use their expertise to begin studies

of other important rodent-borne diseases. Among these should be such diseases of virtually global distribution such as leptospirosis, murine typhus, haemorrhagic fever with renal syndrome (HFRS), etc. The expertise of the plague laboratories in studies of rodent and ectoparasite-borne diseases represents a valuable resource for the countries.

#### 5.12 Research

Regional laboratories should be supported and encouraged to undertake both basic and applied research on better elucidation of plague epidemiology, ecology and control, the basic molecular biology of the plague organism, and the development of rapid and accurate field tests for the identification of plague in humans, animals and flea vectors, such as DNA probes, ELISA antigen and/or antibody capture methods.

#### 5.13 Updating of the Plague Manual

The existing WHO Manual on Plague should be updated to incorporate newer tests and methodologies in laboratory aspects of plague, for new developments in vector and reservoir control and additional epidemiological information, including an updated plague distribution map.

#### 5.14 International cooperation and assistance

The international agencies and WHO collaborating centres should provide assistance and coordination for the development of manpower in the field of bacteriology, entomology, mammology, epidemiology and clinical aspects; for the supply of reagents and test kits; for strengthening of existing centres, national control activities and dissemination of technical information as well as results of research undertaken in different parts of the world. To develop and strengthen national plague activities, consultants may be provided by international agencies to countries who may require them. The research workers from various countries should meet periodically to review the advances made and assess their utility for the control of plague.

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