Monument of Plague in the Vienna

- **Plague is an acute infectious disease caused**

  by *Yersinia pestis* with severe intoxication, fever, affection of lymphatic system and lungs.

- **It belongs to the group of the extremely dangerous infections (quarantines).**

- **Plague is primarily a disease of rodents and small mammals; human disease results**

  from the bite of an infected flea.

Etiology

Yersinia pestis (Bacillus pestis), **the etiological agent of plague was first described by A. Yersen in 1894 in Hong-Hong, the International committee of systematization of bacteria (1982) referred it to *Yersinia* genus together with bacillus pseudotuberculosis and yersiniosis.**

Etiology

- *Yersinia pestis* is an ovoid, short, gram-negative, nonmotile bacillus, classified with the *Enterobactericeae.*
- The organism grows readily on laboratory media and often exhibits a bipolar, "safety pin" appearance when viewed microscopically - especially if stained with Giemsa or Wayson stain.

Etiology

- **Pleomorphism is marked especially in old cultures, and involution or degeneration forms are particularly noticeable.**
- **These are markedlly enlarged, stain faintly and include globular, pear-shaped, elongated or irregular forms.**

  In fluid culture the bacilli tend to be arranged in chains.
- **The organism is non-motile and non- sporing**

- **The virulence factors and mechanisms of Y. *pestis* are multiple and complex.**

- **Most are plasmid-mediated and several are temperature-dependent. V and W antigens are proteins that are involved in the spread of the organisms through the tissues as well as their resistance to phagocytosis.**

- **The V and W antigens are not synthesized at 20 to 25°C (the temperature of the flea), but are produced within macrophages at 37°C.**
- **Similarly, a chromosomally mediated capsular antigen, fraction 1, that confers antiphagocytic protection to the organism, is only synthesized at 37°C.**

Etiology

- Other temperature-dependent factors are coagulase and fibrinolysin enzymes which may be involved in the dissemination of the bacteria within the body.

- The cell wall contains a lipopolysaccharide with the properties of endotoxin, and a protein murine toxin, lethal for mice, is located in the cell envelope.

Epidemiology

- Epidemics of plague have been the most devastating outbreaks in human history.
- In the 6th century of the present era, a plague epidemic that lasted 50 years killed more than 100 million people, and the "black death" in the l4th century devastated Europe, killing 25% of the population.

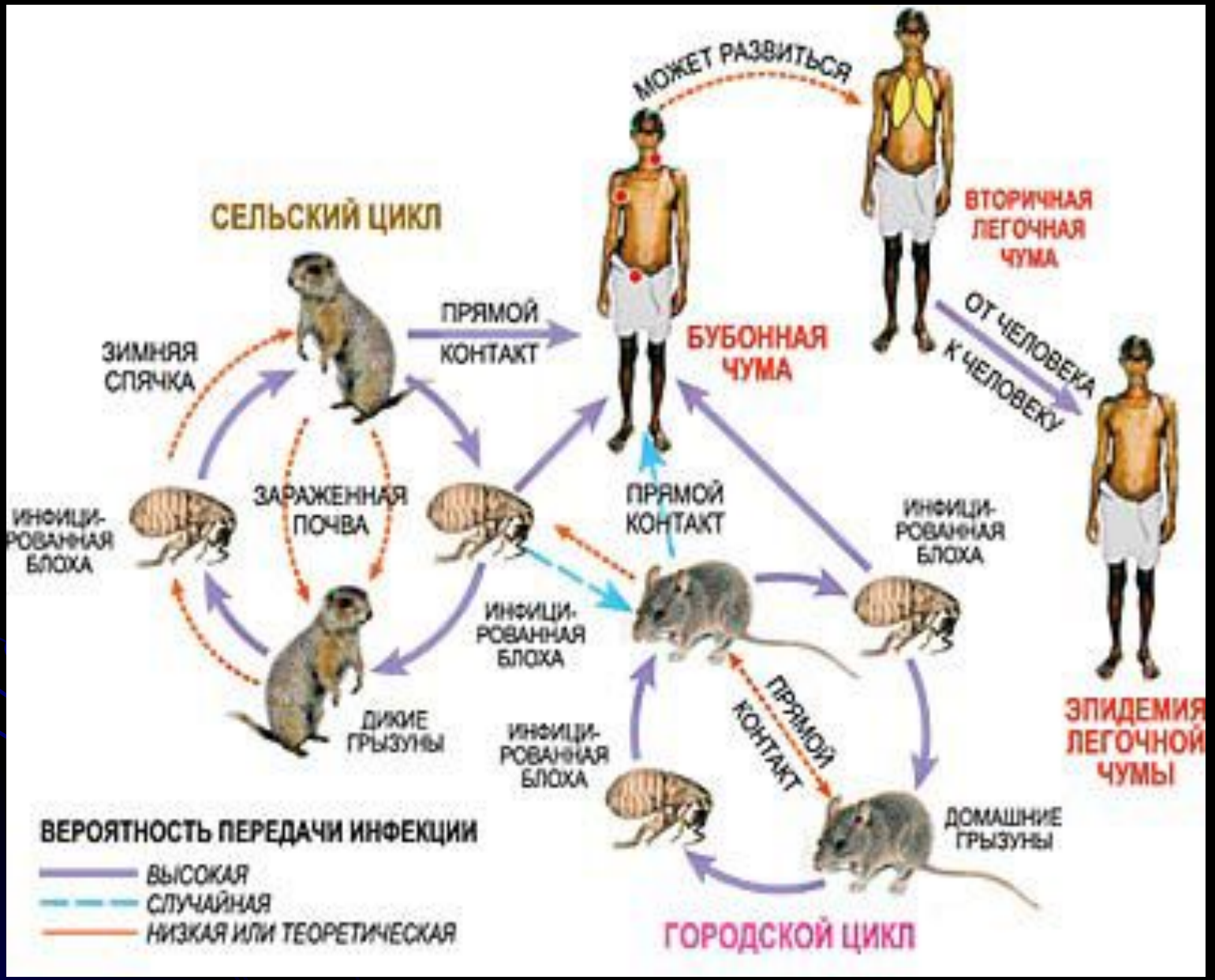
- **Most human cases occur in the developing countries of Asia, Africa, and South America. In the United States most cases are in the south- western states of New Mexico, Arizona, Colorado, Utah, and California, usually during the summer and fall months when people are outdoors and come into contact with rodents and their fleas.**

- **Plague is epizootic in wild rodents (ground squirrels, prairie dogs, mice, wood rats) and is spread by the bite of their fleas. Small mammals such as bobcats may become infected by ingesting infected rodents.**

- **The reservoir of urban plague involving humans is in urban and domestic rats, and is transmitted by the tropical rat flea, *Xenopsylla cheopis.***
- **The infection is transmitted to man when a flea, deserting a dying rat, bites a human.**
- **The bubonic and septicemic forms of plague are not usually transmitted person to person.**
- **Man-to-man transmission by human fleas, *Pulex irritans,* is important in the Andean regions at South America. Persons who develop secondary plague pneumonia (about 5% at cases) shed Y. pestis in their respiratory secretions and can transmit the disease by the airborne aerosol route.**

- **Infection in primary human septicemic plague is usually acquired through the mucous membranes, particularly of the mouth and throat and the conjunctivae.**

Particles of infected sputum which have been accidentally coughed into the eye have produced human septicemic plague.


МОЖЕТ РАЗВИТЬСЯ
ВТОРИЧНАЯ ЛЕГОЧНАЯ ЧУМА
СЕЛЬСКИЙ ЦИКЛ
ПРЯМОЙ КОНТАКТ
БУБОННАЯ ЧУМА
ОТ ЧЕЛОВЕКА К ЧЕЛОВЕКУ
ЗИМНЯЯ СПЯЧКА
ЗАРАЖЕННАЯ ПОЧВА
ПРЯМОЙ КОНТАКТ
ИНФИЦИ-РОВАННАЯ БЛОХА
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ВЫСОКАЯ
СЛУЧАЙНАЯ
НИЗКАЯ ИЛИ ТЕОРЕТИЧЕСКАЯ
ГОРОДСКОЙ ЦИКЛ

Infection are transmitted:

1. bite of flea (transmissible)

2. contact (humans, usually children, may occasionally contract the disease by being bitten by fleas while handling dead rodents, or when pet dogs or cats carry rodent fleas into the household.)

3. aerial-droplet route

4. fecal-oral route

Pathogenesis

1.**When flea ingests blood meal from bacteremic animal infected with *Y. pestis*, the coagulase of the organism causes the blood to clot in the foregut, leading to blockage of the flea's swallowing. *Yersinia pestis* multiplies in the clotted blood.**

2.During attempts to ingest a blood meal, a blocked flea may regurgitate thousands of organisms into a patient's skin.

3.The inoculated bacteria migrate by cutaneous lymphatics to the regional lymph nodes. The flea-borne bacilli possess a small amount of envelope antigen (fraction 1) and are readily phagocytized by the host's polymorphonuclear leukocytes and mononuclear phagocytes

4. ***Yersinia pestis*** **resists destruction within mononuclear phagocytes and may multiply intracellularly with elaboration of envelope antigen.**

If lysis of the mononuclear cell occurs, the bacilli released are relatively resistant to further phagocytosis. The involved lymph nodes show polymorphonuclear leukocytes, destruction of normal architecture, hemorrhagic necrosis, and dense concentrations of extracellular plague bacilli.

5. Transient bacteremia is common in bubonic plague, and in the absence of specific therapy, purulent, necrotic, and hemorrhagic lesions may develop in many organs. Hypotension, oliguria, altered mental status, and subclinical disseminated intravascular coagulation (DIC) may be noted and are attributable to endotoxinemia.

6. The plague bacillus produces a powerful endotoxin which often causes a dilatation of the arteries, lowering of the blood pressure, and alterations in the functional activity of the heart, as well as degenerative changes in the heart muscle.

7. It acts particularly upon the endothelial cells of the blood vessels and lymphatics, the inflammatory reaction frequently causing circulatory obstruction.

8. One of the most characteristic features of the pathology of plague is the tendency to produce general dilatation and engorgement of the vessels, with cutaneous, subserous, submucous. parenchymatous, and interstitial hemorrhages.

Classification of plague:

Forms

1. plague of cellulo-cutaneus
2. plague of *bubonic*
3. plague of pneumonic
4. plague of septicemia

courses

1. asymptomatic
2. mild or abortive
3. moderate
4. severe

Clinical manifestations

Incubation period

The incubation period of human plague varies usually from 2 to 10 days, but is generally from 3 to 6 days. In primary pneumonic plague it may not be over 2 or 3 days.

- ***Cellulo - cutaneous plague*** *- it is characterized*

1. Intoxication

2. Stages of development of local reaction

spot → papule→ vesicula→ pustule (often with hemorrhagic content) → ulcer→ dark crust

- Cellulo-cutaneous form of plague can develop with of bubonic plague
- Pustule is by hyperemia with a cyanotic tint surrounded and filled with blood-purulent content.
- Pustule transformation into an ulcer quickly and is covered by a black crust.
- An ulcer cicatrize later
- Sometimes may appears painful carbuncle with the edema adjacent tissues.

- **Plague carbuncles** occur most commonly on the buttocks or back, sometimes on the flanks or abdomen, the shoulders or posterior surface of the legs and arms. They generally make their appearance in the later stages of the disease and usually originate about ecchymotic patches. Subsequently a vesicle is formed, which soon ruptures and reveals a well circumscribed patch which may measure 1 centimeter or more in diameter. The base of the lesion is usually moist and either brownish red or bluish in color, while the margins are indurated and infiltrated. The necrosis in some instances becomes deeper, and large indolent ulcers are formed. Sometimes there is considerable edema about the ulcers, and plague bacilli may be found in the edematous fluid which exudes. Microscopical examination of the contents of these lesions frequently shows large numbers of plague bacilli.

- ***Symptoms and course of bubonic plague.*** **In bubonic plague premonitory symptoms are not usually observed, though occasionally there may be 1 or 2 days of malaise and headache. The onset, except in mild cases, is usually abrupt, with (ever commonly accompanied by a moderate rigor or repeated shivering.**

- **1.Syndrome of intoxication**
- **2. Appearance of bubo**

1. Syndrome of intoxication:

- **The temperature rises rapidly to 39.4 °*C* or 40 °C, sometimes even reaching 41.7 °C. The pulse becomes rapid and the respirations increased. There is headache. The patient may become maniacal. The skin is hot and dry, the face bloated, the eyes injected, and the hearing dulled. The tongue is usually swollen and coated with a creamy fur, or later with a brown or black layer. The symptoms usually complained of within the first 24 hours are very severe headache and backache. Burning in the throat or stomach, and nausea and vomiting may occur.**

- **The decline in temperature may be sudden or gradual. Cases that do well usually show a gradual fall of temperature, and after 14 days the temperature may be subnormal.**

2. Appearance of bubo

- **Buboes, inflammatory enlargements of the lymph glands are sometimes the first sign to attract attention by their pain.**

- **They more often make their appearance from the second to the fifth day after the onset of the fever. The temperature frequently shows a decline when they appear.**

- **The affected gland is often hard and painful to the touch. The average size of the bubo is from a walnut to an egg.**

- **Buboes appear in 75 % of the cases. In the cases in which buboes are present, they occur in the inguinal glands in approximately 65-70 %, in the axillary - 15-20 %, and the cervical - 5-10 %. Carbuncles appear in about 2 %, in which there are reddened indurated patches of skin, which subsequently necrose.**

- **The spleen is frequently moderately enlarged, but often cannot be palpated.**

- **Secondary bronchial pneumonia also due to the plague bacillus may result metastatically and emboli and abscesses may be formed in the lungs.**

- ***Symptoms and course of pneumonic plague*.**

The onset of the disease is usually somewhat abrupt; prodromal symptoms are rare. The disease usually begins with chilly sensations, but a distinct rigor is unusual. Epistaxis is also rare.

- **There is headache, loss of appetite, an increase in the pulse rate, and fever. Within from twenty-four to thirty-six hour after the onset, the temperature usually has reached 39.4 °C or 40 °C, and the pulse 110 to 130 or more beats per minute.**

- **Cough and dyspnoe appear within twenty-four hours after the onset of the first symptoms. The cough is usually not painful. The expectoration is at first scanty, but soon becomes more abundant. The sputum at first consists of mucus which shortly becomes blood-tinged. Later the sputum becomes much thinner and of a bright red color; it then contains enormous numbers of plague bacilli in almost pure culture.**

- **The conjunctiva become injected, and the tongue coated with either a white or brownish layer. The expression is usually anxious, and the face frequently assumes a dusky hue. Labial herpes is very uncommon.**

- **The patients sometimes complain of pain in the chest, but usually this is not severe. Apart from the disturbances due to the dyspnoe and their anxiety for their condition, they usually appear to suffer but little and usually do not complain of pain.**

- In the later stages of the disease, the respirations become greatly increased and the dyspnoe usually very marked, the patients frequently gasping tor air for several hours before death. Cyanosis is then common.

- The signs of cardiac involvement are always marked in the advanced cases, the pulse becoming gradually more rapid, feeble, and running; finally it can not be felt.

Symptoms and course of septicemia plague

- **Septicemic plague occur during the course of bubonic plague, always occurs in pneumonic plague, and may occur as a form of primary infection. When primary septicemic plague results, the infection has usually occurred through the mucous membrane of the mouth and throat, death resulting from septicemia before macroscopic lesions are visible in the lymphatic glands or lungs. Nevertheless, at autopsy, at least some of the lymphatics are usually found to be enlarged, congested, and even hemorrhagic, and in a few instances early buboes may develop shortly before death.**

- **In this form, the nervous and cerebral symptoms often develop with great rapidity and intensity, and the course of the disease is very rapid, the bacilli appearing in the blood almost at the onset of severe symptoms. The attack usually begins with trembling and rigors, intense headache, vomiting, and high fever. The countenance usually depicts intense anxiety. Extreme nervous prostration, restlessness, rapid shallow respirations, and delirium are common symptoms. In some cases the cardiac symptoms are the most prominent. The patients soon pass into a comatose condition and die sometimes within 24 hours of the onset of the attack, but sometimes not until the third day.**

- **During the clinical course of the disease, hemorrhages are frequent. The bleeding may take place from the nose, mouth, lungs, stomach, or kidney, and sometimes from the uterus and bladder. These hemorrhages generally occur in severe cases of the disease.**

- **On examining the skin small punctiform hemorrhages from about I to 2 millimeters in diameter are sometimes observed scattered over the skin in greater or less profusion. The petechie may occur on the face, neck, chest, abdomen or extremities. Sometimes larger patches of ecchymosis, in the neighborhood of 1 centimeter in diameter are observed in the skin.**

- **The pulse in bubonic plague varies greatly. More commonly, at the onset of the disease it is full and bounding, 100 to 120 per minute, becoming later still more rapid, 120 to 140 per minute, small, irregular, and often dicrotic.**

- **The temperature curve in plague is often very irregular and not characteristic. In the severe cases, the initial rise is usually rapid and may be anywhere from 39.4 °C to 41.1 °C.**

- **Later the temperature may again rise, and in fatal cases it may reach 41.7 °C before death. A sudden fall of temperature during the height of the disease, with a collapsed condition, sometimes occurs and usually also indicates a fatal issue.**

- **In more favorable cases, after the secondary rise the temperature often falls slowly and gradually, with more marked remissions each morning, until the normal or even subnormal point is reached.**

The course of the fever often lasts in uncomplicated cases from 6 to 12 days.

Suppuration of the buboes, however, may cause great irregularity of temperature, and the occurrence of complications may considerably prolong the period of fever.

As a rule, the higher and more continuous the temperature, the severer the other symptoms.

In the late stages of bubonic plague, particularly in the cases with complications, a moderate secondary anemia, polymorphonuclear leucocytes are increased and the large mononuclear cells usually diminished.

The kidneys are usually markedly affected in plague. Congestion and parenchyniatous degeneration are almost always present.

The urine is usually diminished in quantity, of a high color, sometimes smoky, and of high specific gravity. It usually contains a moderate amount of albumin, but albumin is not always present in the less severe cases. The urea, uric acid, and chlorides are often decreased. Microscopically, epithehal cells, pus cells, and sometimes red blood corpuscles and even plague bacilli may be observed.

Complications

of bubonic plague are secondary pneumonia,

carbuncles, subcutaneous abscesses, pyodermia, gangrene.

Plague meningitis is a rarer complication and typically ocurrs more then 1 week following inadequately treated bubonic plague.

complications of *septicemia plague and pneumonic plague* are septicshock, bleeding, pulmonary-cardiac insufficiency, acute cardiovascular insufficiency

Diagnosis

- **Bacteriological test**
- **The materials for the bacteriological diagnostics are taken from the inflamed lymphatic node or bubo, the blood, sputum, CSF, vesicula, pustule, ulcera**
- **Biological method - to contaminate of laboratory animals**
- **The Serologic method is the reaction of hemagglutination – diagnostic titer 1: 16**
- **For retrospective diagnostics – allergic test (intracutaneous test with pestin)**

Differential diagnosis

- Tularemia, syphilis, lupus erythematosus, sodocu, purulent lymphadenitis, tuberculosis, sepsis, lymphogranulomatosis, anthrax

Treatment

- Patients, which suffer from plague necessarily, hospitalize in appropriate hospitals where they are transported by ambulance.

- **Treatment should be started already on place of revealing of the patient. Early prescription of antibiotics (during the beginning of disease), as a rule, salvages the life. Efficiency of antibioticoterapy in later terms is considerably lowest.**

- **From etiotropic agents the most effective is streptomycinum. At the bubonic form immediately 1 gm of preparation is infused into muscle, and then in hospital is indicated 0.5-1.0 gm 3 times per day during one week. At a pulmonary and septic plague a dose of streptomycinum is enlarged to 5-6 gm.**

- **Antibiotics of tetracyclines (oxytetracycline, chlortetracycline), 0.25-1.0 gm 4-6 times are recommended.**
- **From other antibiotics it is possible to indicate monomicin, morphocyclin, ampicilini.**
- **After clinical indications it will be carried out pathogenic and symptomatic treatments.**

- **After normalization of a body temperature and reception of negative data's of bacteriological researching from nasopharynx, sputum, punctate of bubones, patients are discharged from the hospital after 4-6 week.**

Prophylaxis

- Dispensary observation during 3 months is necessary for convalescense with obligatory bacteriological researching from mucosa of pharynx and sputum.
- It is necessary to protect people from expansion of plague diseases. This work is carried out by workers of sanitation center, ambulatory-polyclinic network and antiplague establishments. Plague is the quarantine disease, so the international medico-sanitary rules (WHO, 1969) are distributed on it.

- **Workers of the general medical network observe health of the population with the purpose of early revealing the patients on plague. Each medical worker should know the basic signs of disease, the rules of personal prophylaxis, be able to carry out initial antiepidemic actions.**
- **At presence of epizootia among rats and diseases of camels vaccination of the population by local services under the control of antiplague establishment will be carried out.**

- As active immunization living' plague vaccine is used (dose for epicutaneous indication for children under 7 years is 1 billion, 7-10 years -2 billion, adults 3 billion of microbes bodies, at a hypodermic immunization 1/10 of epicutaneous doses). Immunity is kept during 6 months, then, if necessary, revaccination is performed in one year.

- **At occurrence of a plague among the population the antiepidemic actions are carried out which are directed on localization and liquidation of epidemic pesthole. They include: revealing of patients and their hospitalization in special hospitals in isolation wards with severe antiepidemic regime; and establishment of territorial quarantine: revealing and isolation of all persons which was in contact with patients,**

- they must be isolated for 6 days and undergo emergency prophylaxis with antibiotics - streptomycinum 0.5 gm 2 times per day in muscle or tetracyclinum - 0.5 gm 3 times a day per os, during 6 days; revealing the patients with fever and their hospitalization in special departaments; final disinfection, and also disinfestations and deratization on territory of settlement and around it. Invaluable things are liable to destruction. The personnel should be work in antiplague costumes. Persons who need to leave zone of quarantine, will undergo medical observation.