
PLAGUE

Plague

(lat. Pestis - contagion; tur. Çuma - pimple, abscess) - an acute zoonotic natural focal infectious disease of the group of quarantine infections, proceeding with an extremely severe general condition, fever, damage to lymph nodes, lungs and other internal organs, often with the development of sepsis.

The disease is characterized by high mortality and extremely high infectivity.

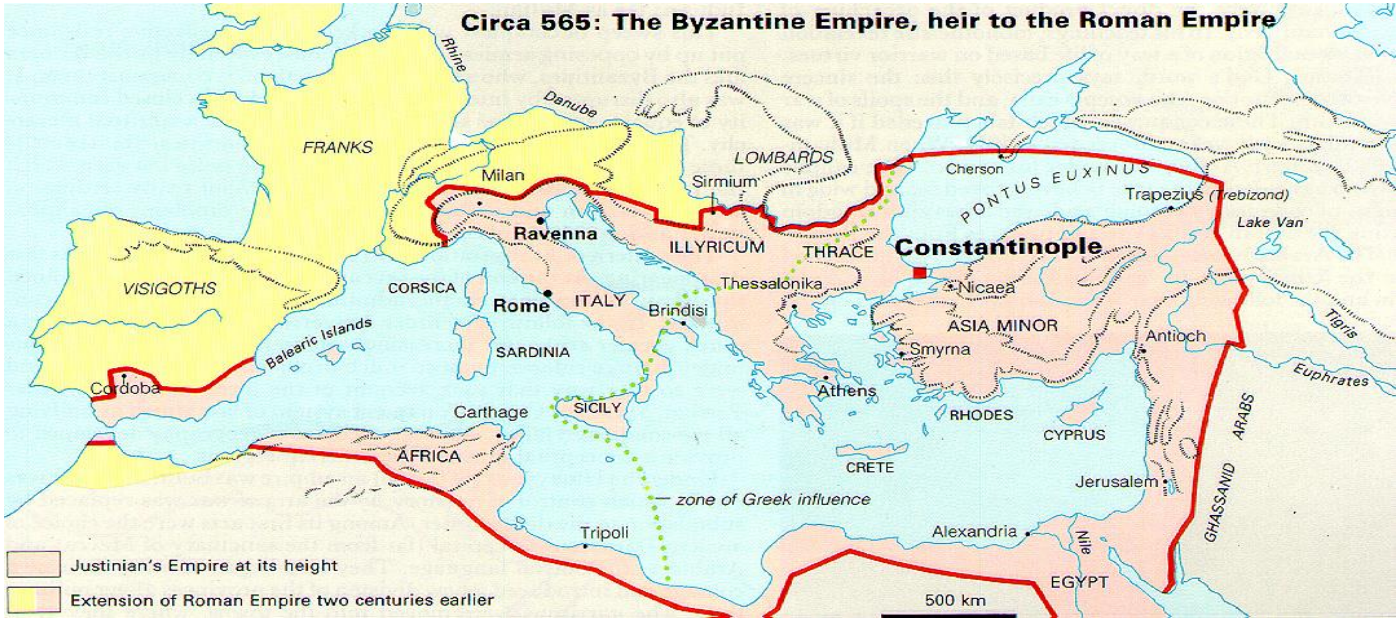
As human civilizations flourished, so did infectious disease.
Large numbers of people living in close proximity to each other and to animals, often with poor sanitation and nutrition, provided fertile breeding grounds for disease.
And new overseas trading routes spread the novel infections far and wide, creating the first global pandemics.

Three of the deadliest pandemics in recorded history were caused by a single bacterium, *Yersinia pestis*, a fatal infection otherwise known as the plague.

1. Plague of Justinian—No One Left to Die

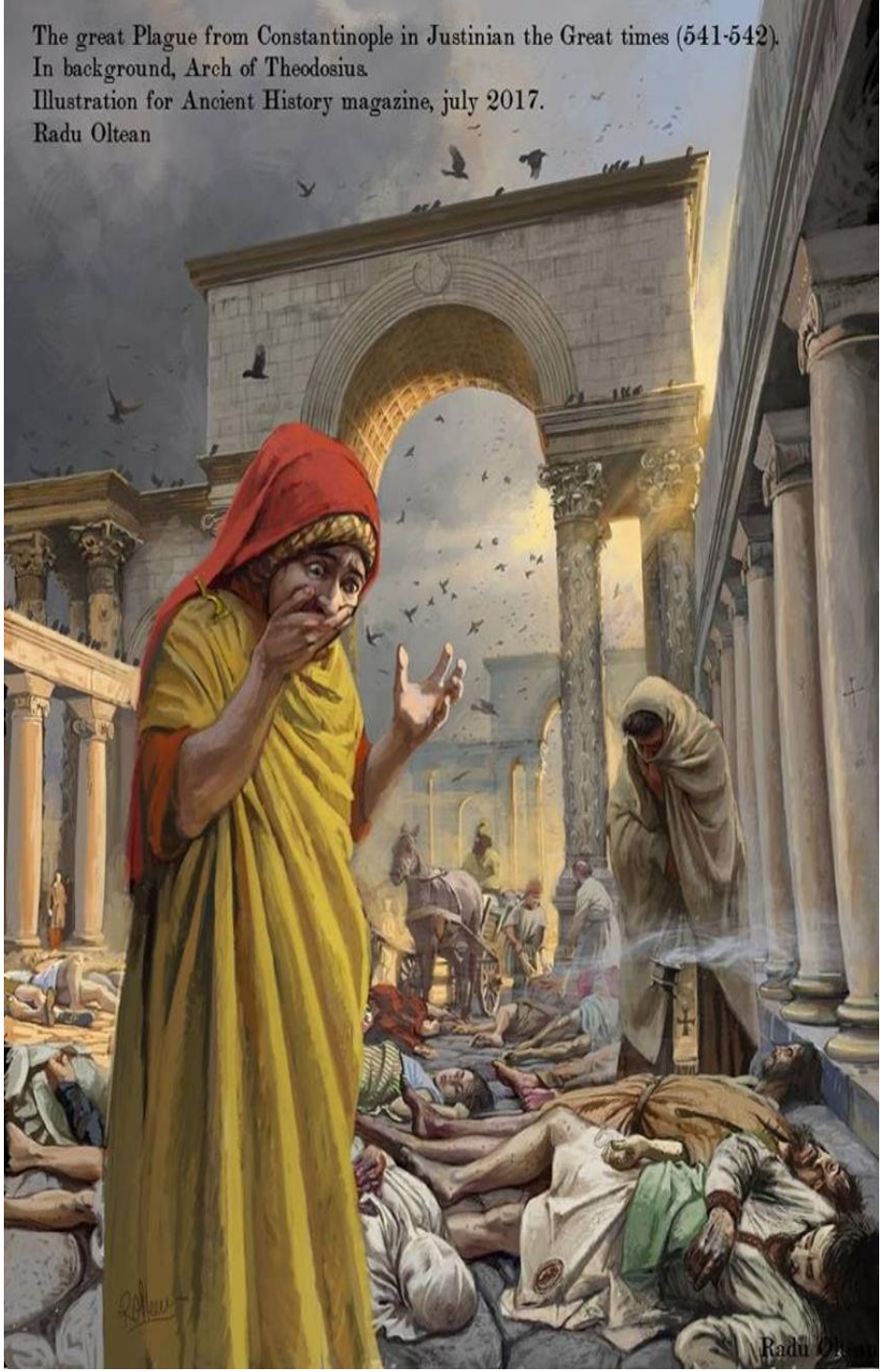
The Plague of Justinian arrived in Constantinople, the capital of the Byzantine Empire, in 541 CE. It was carried over the Mediterranean Sea from Egypt, a recently conquered land paying tribute to Emperor Justinian in grain. Plague-ridden fleas hitched a ride on the black rats that snacked on the grain.

The plague decimated Constantinople and spread like wildfire across Europe, Asia, North Africa and Arabia killing an estimated 30 to 50 million people, perhaps half of the world's population.



“People had no real understanding of how to fight it other than trying to avoid sick people,” says Thomas Mockaitis, a history professor at DePaul University.

“As to how the plague ended, the best guess is that the majority of people in a pandemic somehow survive, and those who survive have immunity.”



2. Black Death—The Invention of Quarantine

The plague never really went away, and when it returned 800 years later, it killed with reckless abandon. The Black Death, which hit Europe in 1347, claimed an astonishing 200 million lives in just four years.

As for how to stop the disease, people still had no scientific understanding of contagion, says Mockaitis, but they knew that it had something to do with proximity. That's why forward-thinking officials in Venetian-controlled port city of Ragusa decided to keep newly arrived sailors in isolation until they could prove they weren't sick.

At first, sailors were held on their ships for 30 days, which became known in Venetian law as a *trentino*.

As time went on, the Venetians increased the forced isolation to 40 days or a *quarantino*, the origin of the word quarantine and the start of its practice in the Western world.

"That definitely had an effect," says Mockaitis.

3. The Great Plague of London—Sealing Up the Sick

London never really caught a break after the Black Death. The plague resurfaced roughly every 20 years from 1348 to 1665—40 outbreaks in 300 years. And with each new plague epidemic, 20 percent of the men, women and children living in the British capital were killed.

By the early 1500s, England imposed the first laws to separate and isolate the sick. Homes stricken by plague were marked with a bale of hay strung to a pole outside. If you had infected family members, you had to carry a white pole when you went out in public. Cats and dogs were believed to carry the disease, so there was a wholesale massacre of hundreds of thousands of animals.

The Great Plague of 1665 was the last and one of the worst of the centuries-long outbreaks, killing 100,000 Londoners in just seven months.
All public entertainment was banned and victims were forcibly shut into their homes to prevent the spread of the disease. Red crosses were painted on their doors along with a plea for forgiveness:
"Lord have mercy upon us."

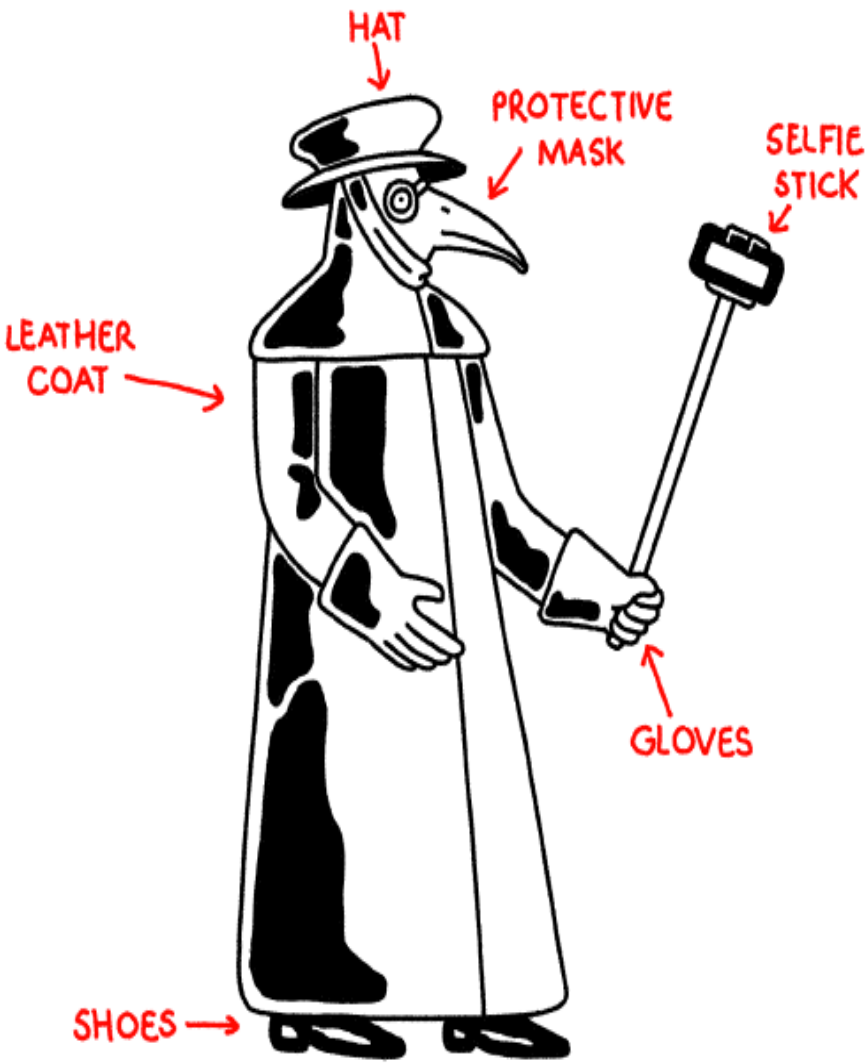
As cruel as it was to shut up the sick in their homes and bury the dead in mass graves, it may have been the only way to bring the last great plague outbreak to an end.

Plague doctor

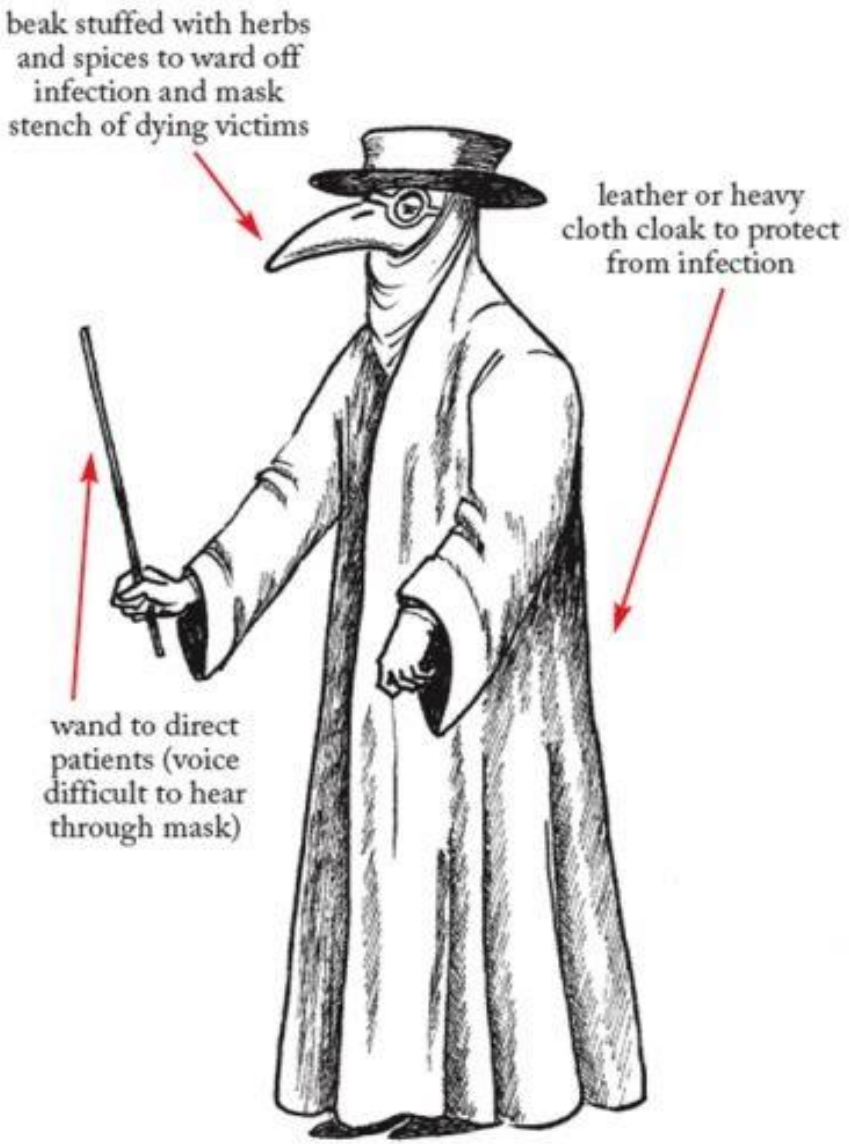
A plague doctor was a medical physician who treated victims of the bubonic plague. In times of epidemics, these physicians were specifically hired by towns where the plague had taken hold.

Some plague doctors wore a special costume.
The garments were invented by Charles de L'Orme in 1630, and were first used in Naples, but later spread to be used throughout Europe. The protective suit consisted of a light, waxed fabric overcoat, a mask with glass eye openings and a beak shaped nose, typically stuffed with herbs, straw, and spices. Plague doctors would also commonly carry a cane to examine and direct patients without the need to make direct contact with them.

PLAGUE FASHION



DOCTOR IN PLAGUE GEAR



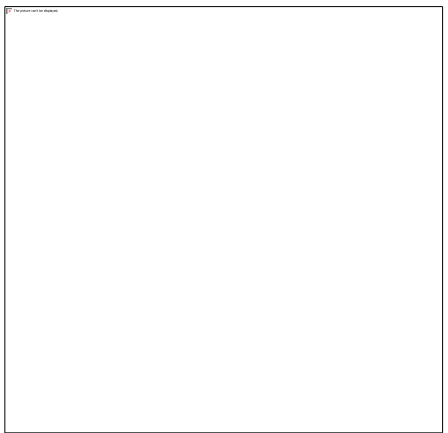
Consult your physician at the first sign of symptoms.

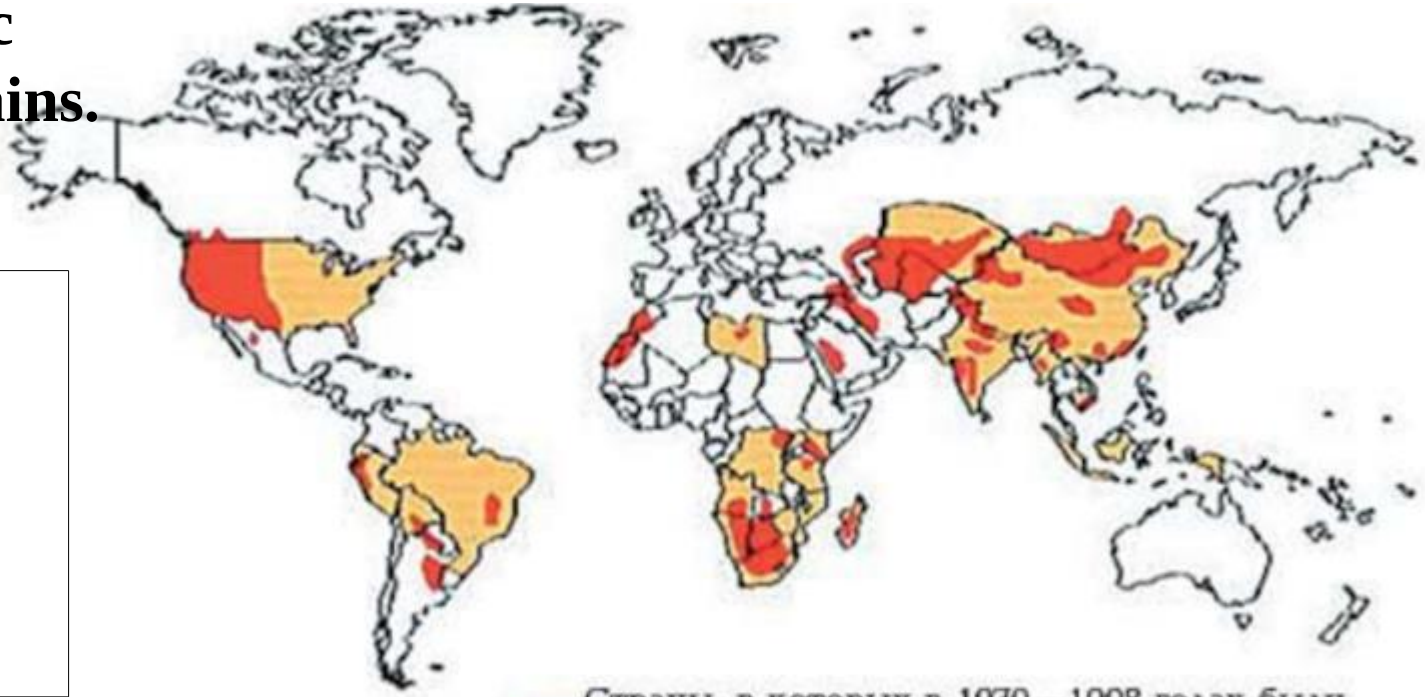
Plague doctors would also commonly carry a cane to examine and direct patients without the need to make direct contact with them.
The scented materials included juniper berry, ambergris, roses (Rosa), mint (*Mentha spicata* L.) leaves, camphor, cloves, laudanum, myrrh, and storax.

Due to the primitive understanding of disease at the time, it was believed this suit would sufficiently protect the doctor from miasma while tending to patients.

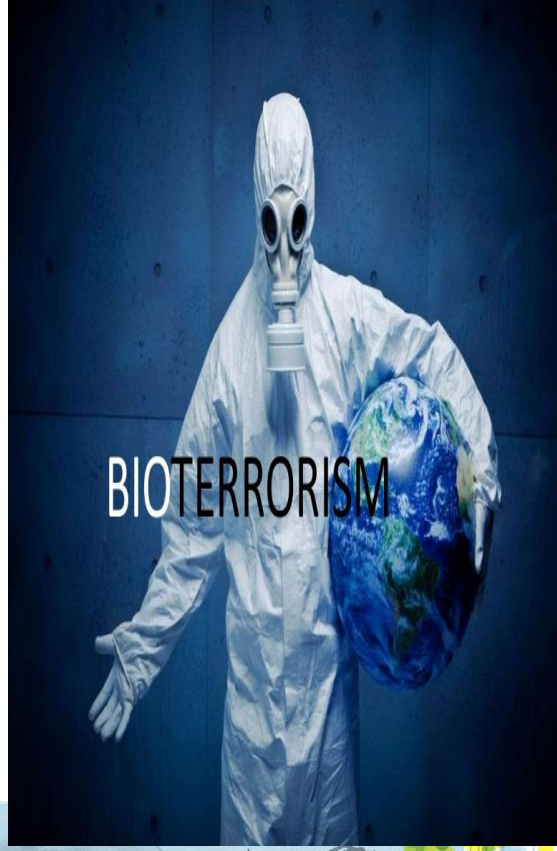
Plague is infamous for killing millions of people in Europe during the Middle Ages.

Today, modern antibiotics are effective in treating plague. Without prompt treatment, the disease can cause serious illness or death. The World Health Organization reports 1,000–3,000 cases per year. During the recent years cases of the disease have been reported annually from the Madagascar, Congo, Tanzania, China, Vietnam, Peru and the USA. Although most cases are now sporadic, occurring singly or in small clusters, the potential for outbreaks and epidemic spread remains.





Because of its virulence and transmissibility, *Y. pestis* is considered an important potential agent of biological terrorism that requires special countermeasures to protect the public's health.



Etiology

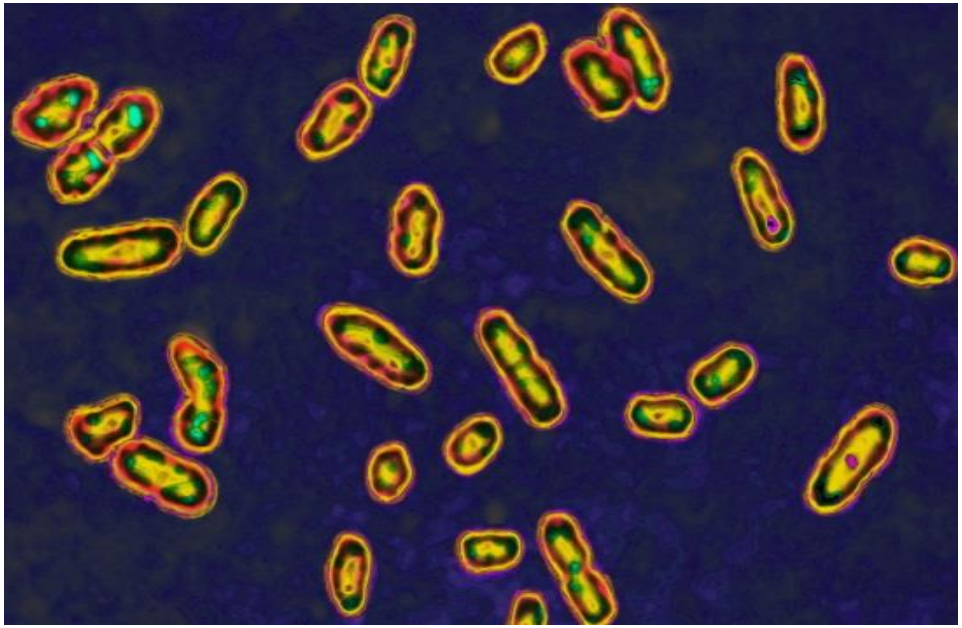
The causative agent is the bacterium *Yersinia pestis* (lat.Yersinia pestis), discovered in June 1894 by the French Alexander Yersen and the Japanese Kitasato Sibasaburo.

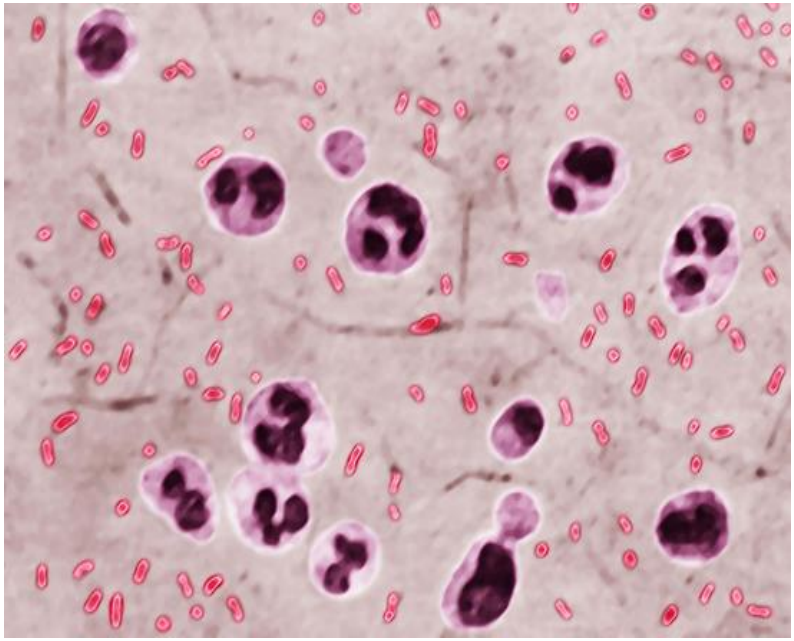
Yersinia pestis

Yersinia pestis

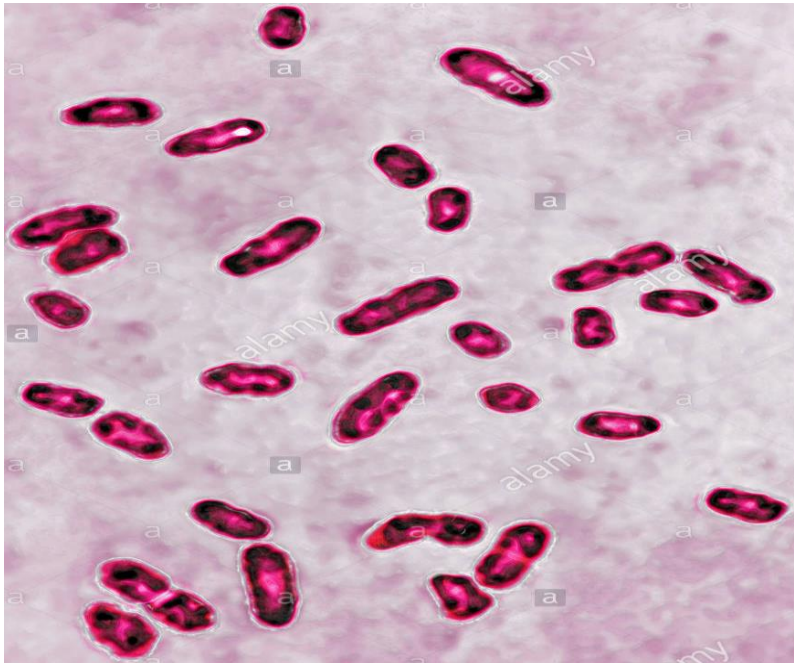
is a gram-negative, aerobic, bipolar-staining bacillus that belongs to the family *Enterobacteriaceae.*

Y.pestis is resistant to low temperatures, it is well preserved in sputum, but at a temperature of +55 ° C it dies within 10-15 minutes, and when boiled - almost instantly.





Yersinia pestis. Here it's seen under optical microscopy X 1000.



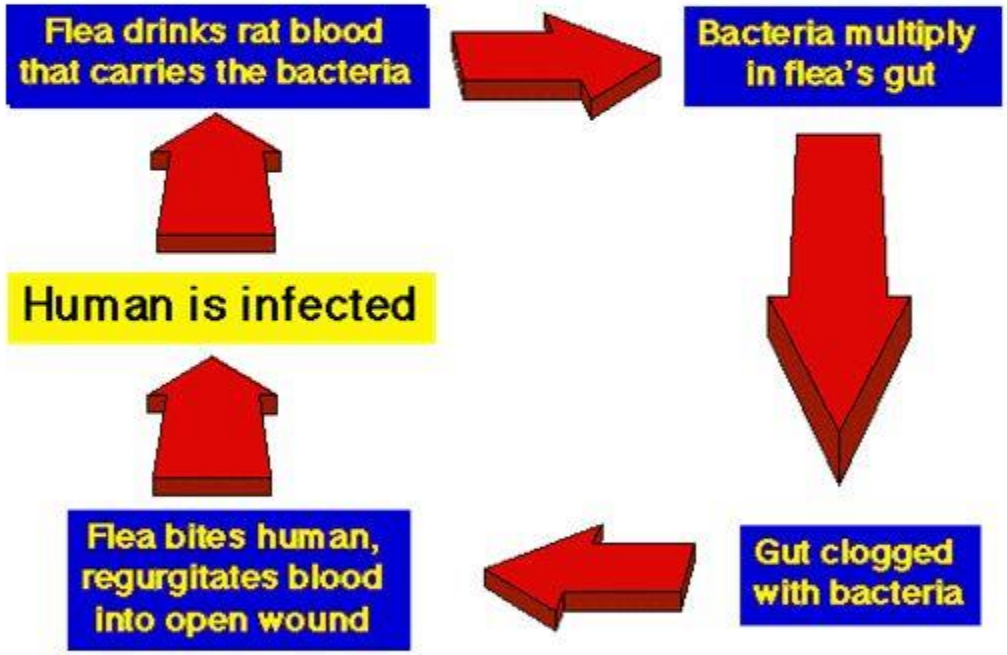
Epidemiology.

Transmission of *Y. pestis* to an uninfected individual is possible by any of the following means.

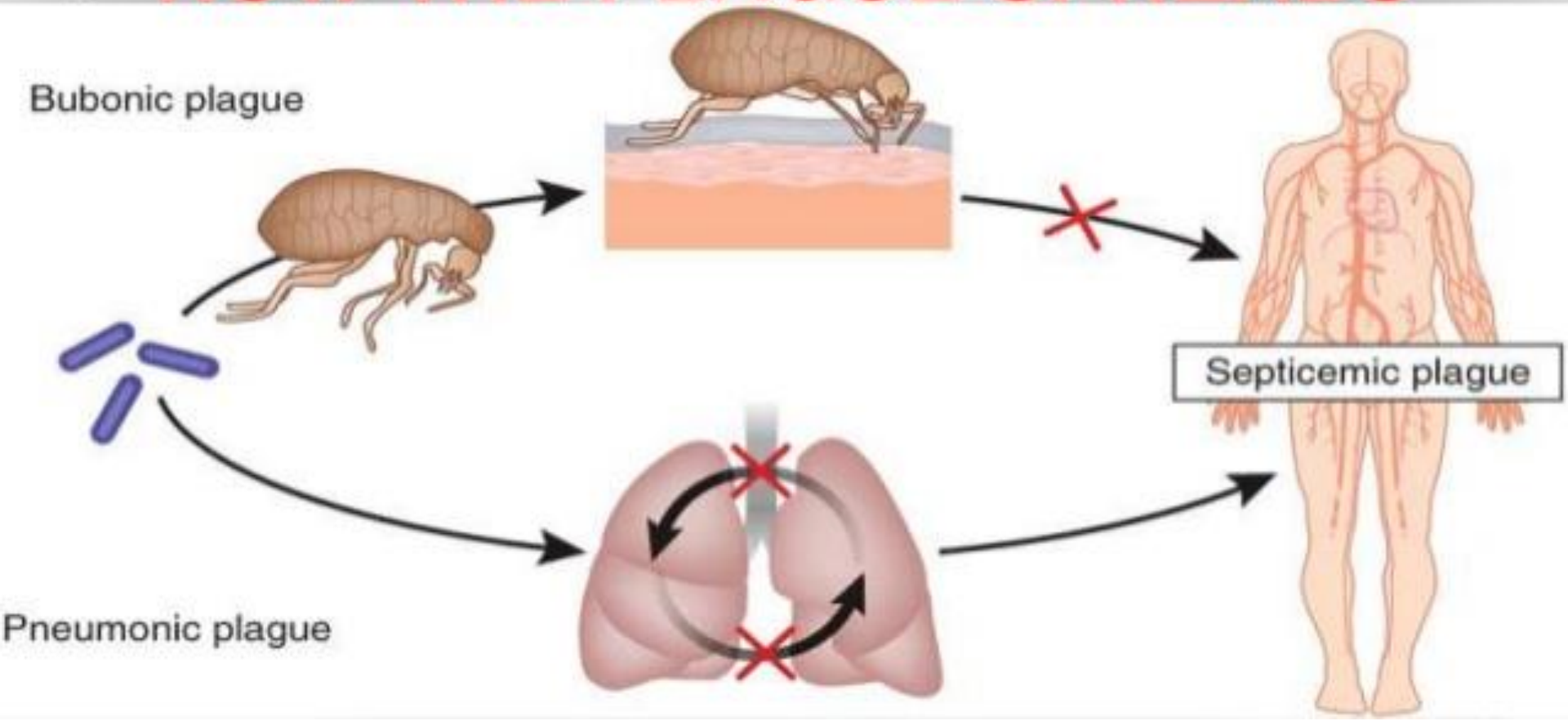
- **droplet contact – coughing or sneezing on another person**
- **direct physical contact – touching an infected person, including sexual contact**
- **indirect contact – usually by touching soil contamination or a contaminated surface**
- **airborne transmission – if the microorganism can remain in the air for long periods**
- **fecal-oral transmission – usually from contaminated food or water sources**
- **vector borne transmission – carried by insects or other animals.**

Plague life cycle

- Reservoir
  - Rats
  - Mice
  - Voles
- Vector: Flea
- Hosts
  - Amplify
    - Prairie dogs
    - Rabbits
    - Deer
    - Dogs/Cats
- Cycle
  - Flea bite
  - Exposure to infected animals



HOW THE PLAGUE SPREADS



Gates of infection - damaged skin (with a flea bite, usually Xenopsylla cheopis), mucous membranes of the respiratory tract, digestive tract, conjunctiva.

It is mainly a disease in the fleas (*Xenopsylla cheopis*) that infested the rats, making the rats themselves the first victims of the plague. Rodent-borne infection in a human occurs when a person is bitten by a flea that has been infected by biting a rodent that itself has been infected by the bite of a flea carrying the disease. The bacteria multiply inside the flea, sticking together to form a plug that blocks its stomach and causes it to starve. The flea then bites a host and continues to feed, even though it cannot quell its hunger, and consequently the flea vomits blood tainted with the bacteria back into the bite wound. The bubonic plague bacterium then infects a new person and the flea eventually dies from starvation. Serious outbreaks of plague are usually started by other disease outbreaks in rodents, or a rise in the rodent population.

PATHOGENESIS.

The inoculated bacteria are firstly captured by tissue macrophages, and then undergo intracellular multiplication within them followed by lysis of macrophages, bacterial release, and dissemination through lymphatic system and bloodstream. Via lymphatic system bacteria spread to regional lymph nodes with inflammation and necrosis with creation of buboes. Hematogenous spread leads to sepsis and multiorgan disease.

Classification and clinical features.

Incubation period is generally between **2–8** days.

The principal clinical forms of plague are

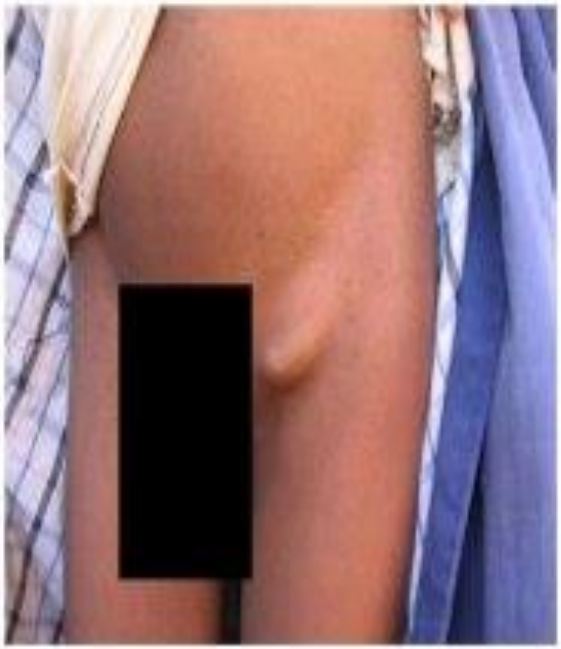
1) bubonic

2) septicemic

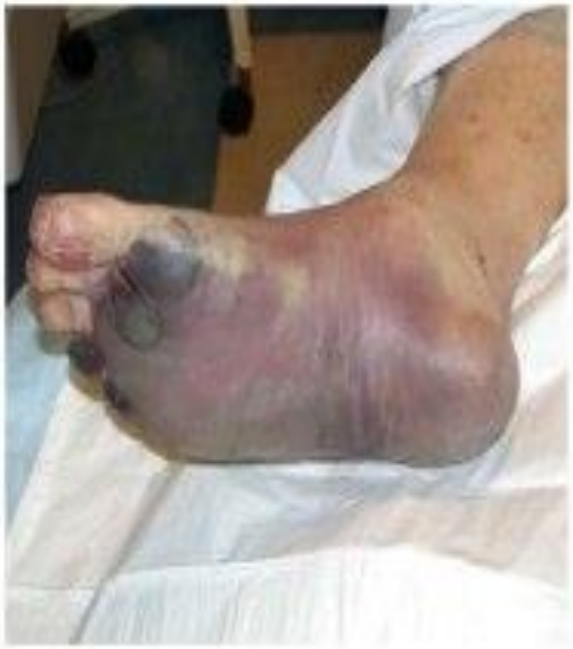
3) pneumonic.

Bubonic plague is almost always caused by the bite of an infected flea but occasionally results from direct contact with infectious materials. Septicemic and pneumonic plague can be either primary or secondary to metastatic spread.

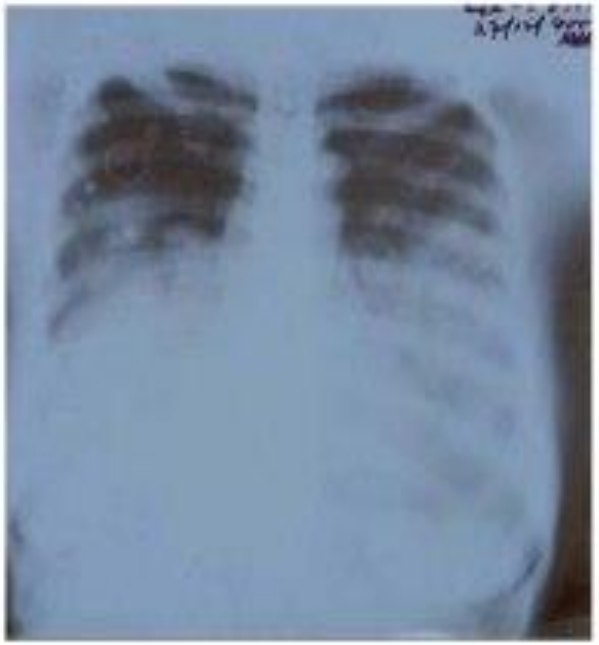
Unusual forms include *plague meningitis, endophthalmitis, lymphadenitis* at multiple sites, and primary plague *pharyngitis.*



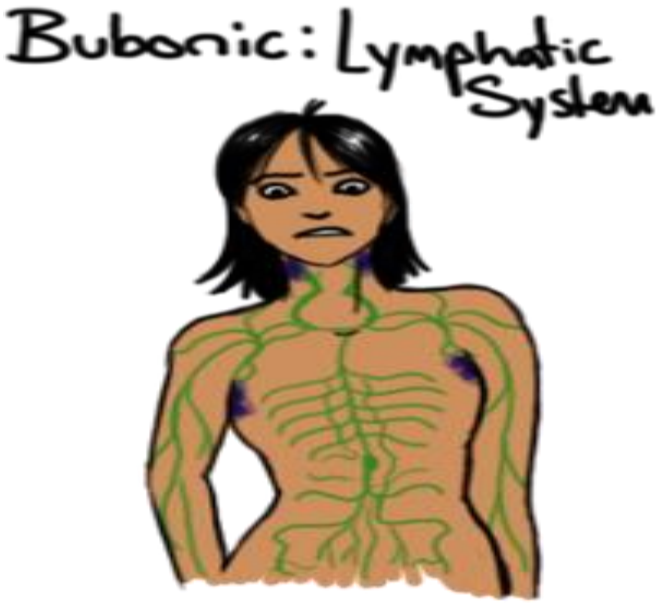
Bubonic plague

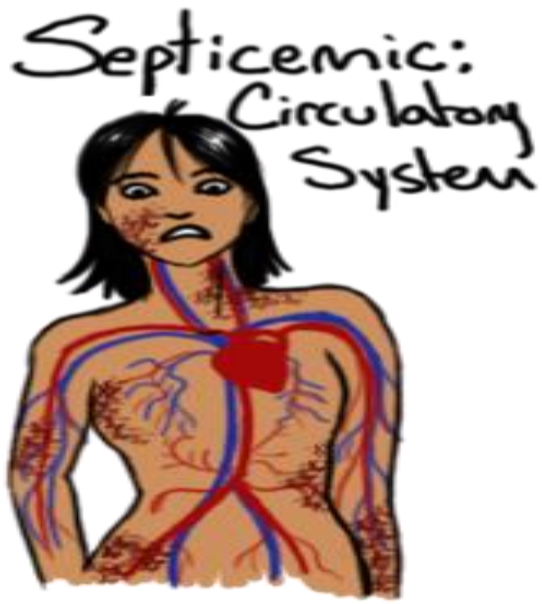


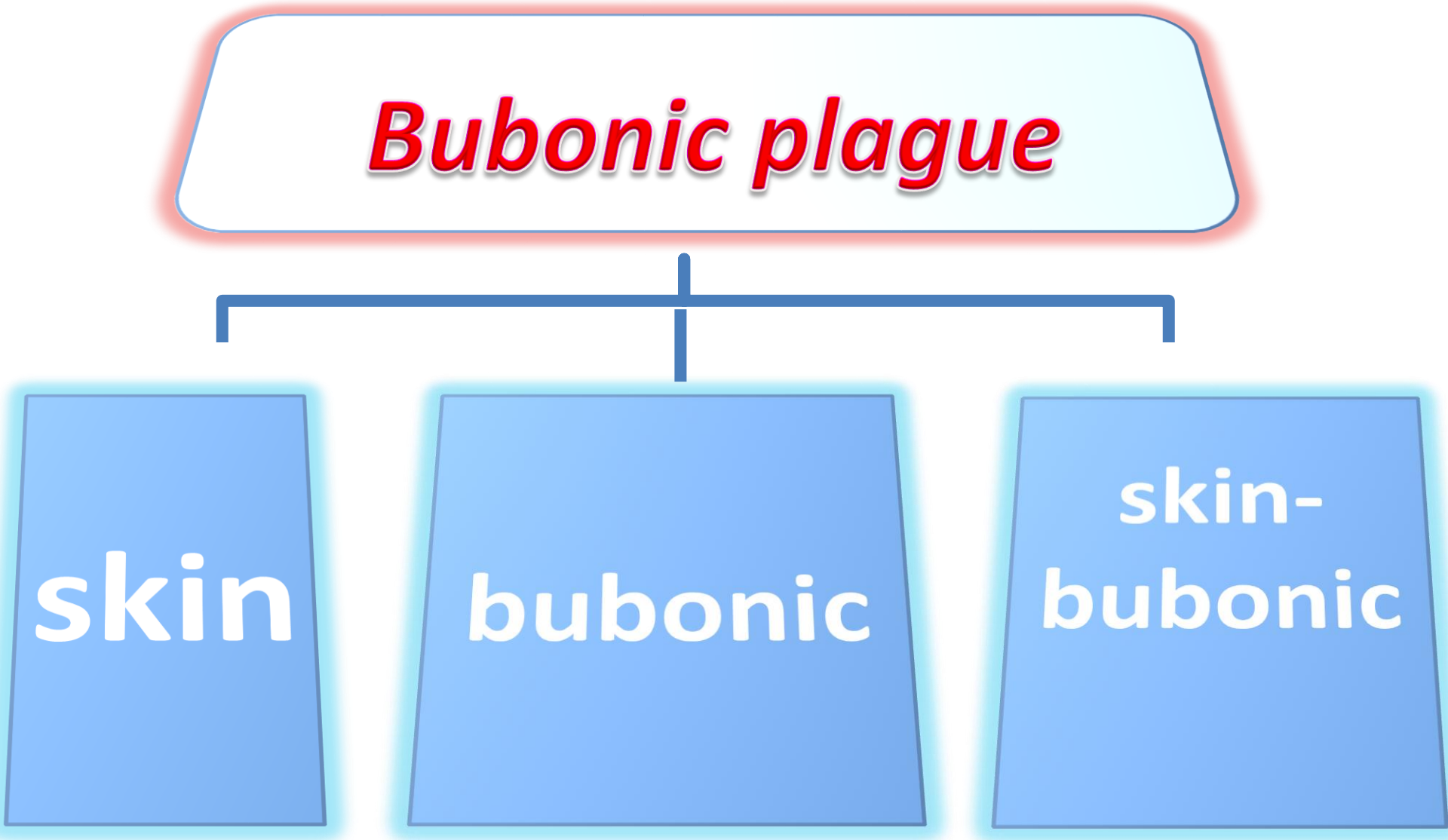
Septicemic plague



Pneumonic plague






Bubonic plague
skin
bubonic
skin-bubonic

Bubonic plague.

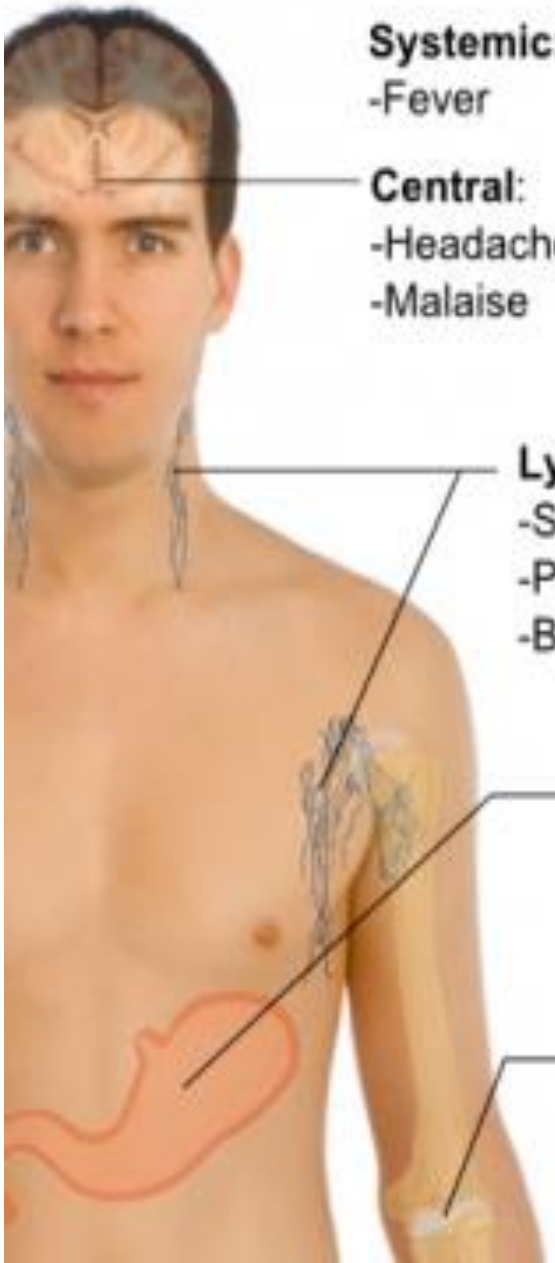
Patients experience

- **chills;**
- **fever, with temperatures that rise within hours to 38–40°C;**
- **myalgias;**
- **arthralgias;**
- **headache;**
- **and a feeling of weakness.**

Soon—usually within 24 h—the patient notices tenderness and pain in one or more regional lymph nodes proximal to the site of inoculation of yersinia. Because fleas most often bite the legs, femoral and inguinal nodes are most commonly involved; axillary and cervical nodes are next most commonly affected.

Symptoms of

Bubonic plague



Systemic:
-Fever

Central:
-Headache
-Malaise

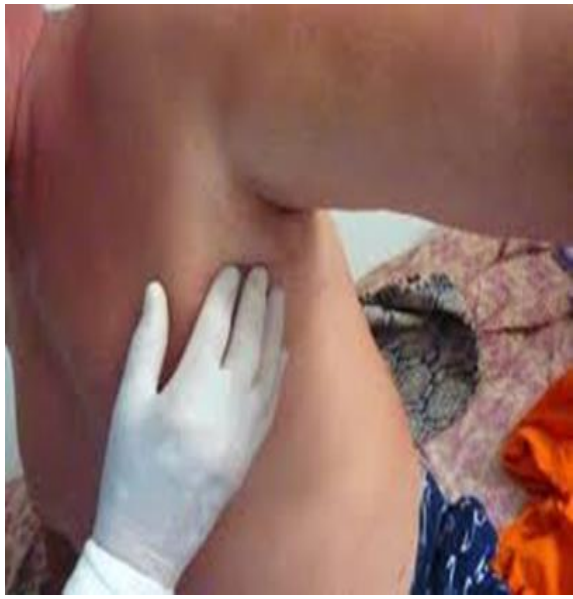
Lymph nodes:
-Swelling (buboes)
-Pus exudation
-Bleeding

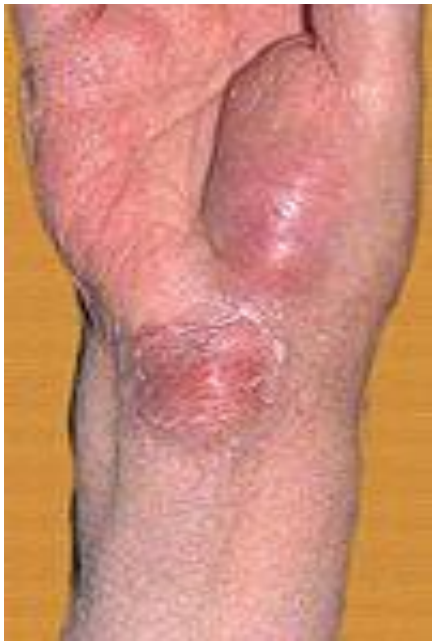
Gastric:
-Nausea
-Vomiting

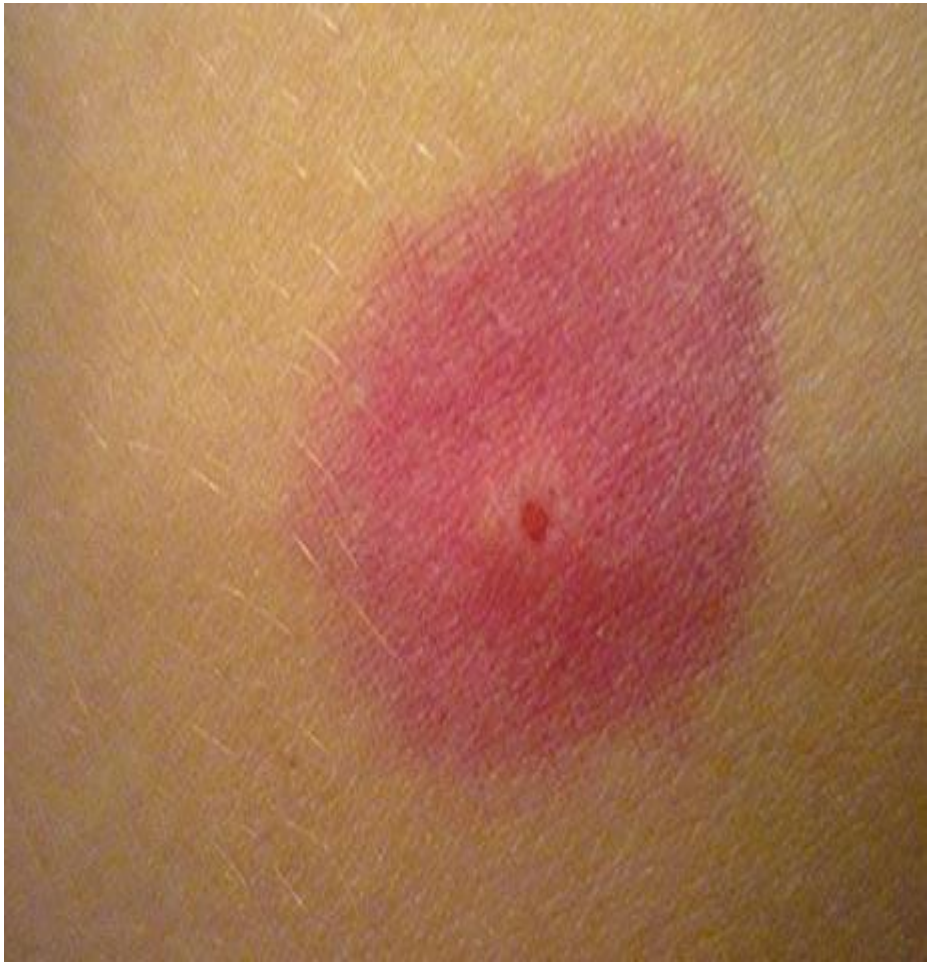
Joints:
-Pain
-Ache

Within hours, the enlarging bubo (up to 10 cm in diameter) becomes progressively painful and tender, sometimes exquisitely so. The patient usually guards against palpation and limits movement, pressure, and stretch around the affected bubo.

The surrounding tissue often becomes edematous, sometimes markedly so, and the overlying skin may be erythematous, warm, and tense. On careful examination skin lesions (most common, papules, vesicles, or pustules) are found distal to the affected lymph nodes in as many as one fourth of patients with bubonic plague, presumably representing sites of the infective flea bites.

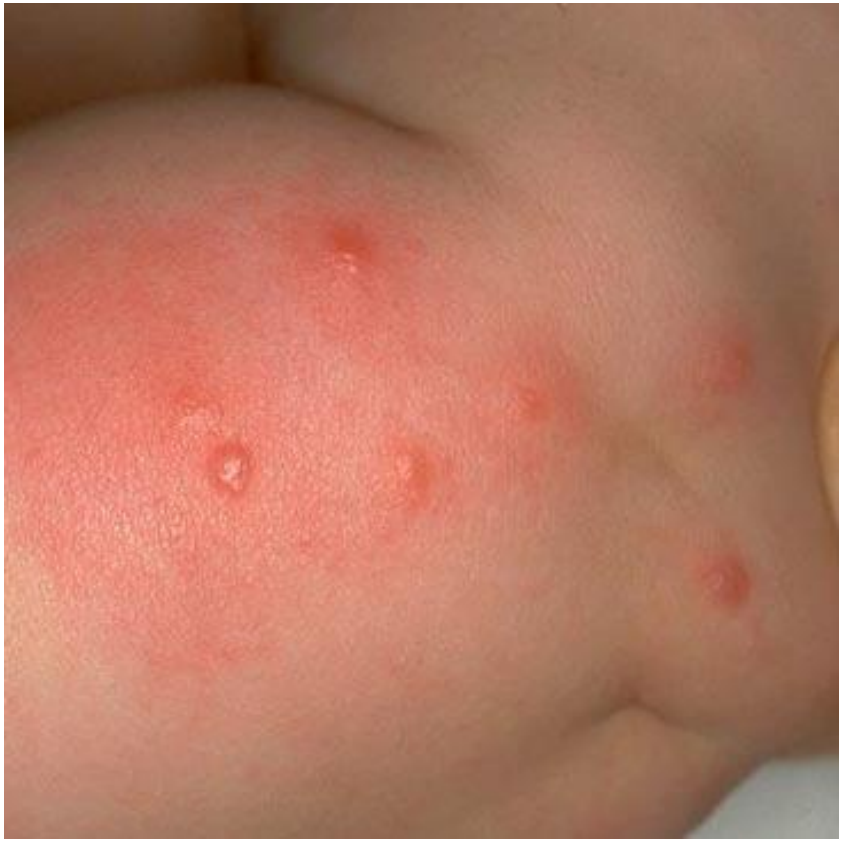


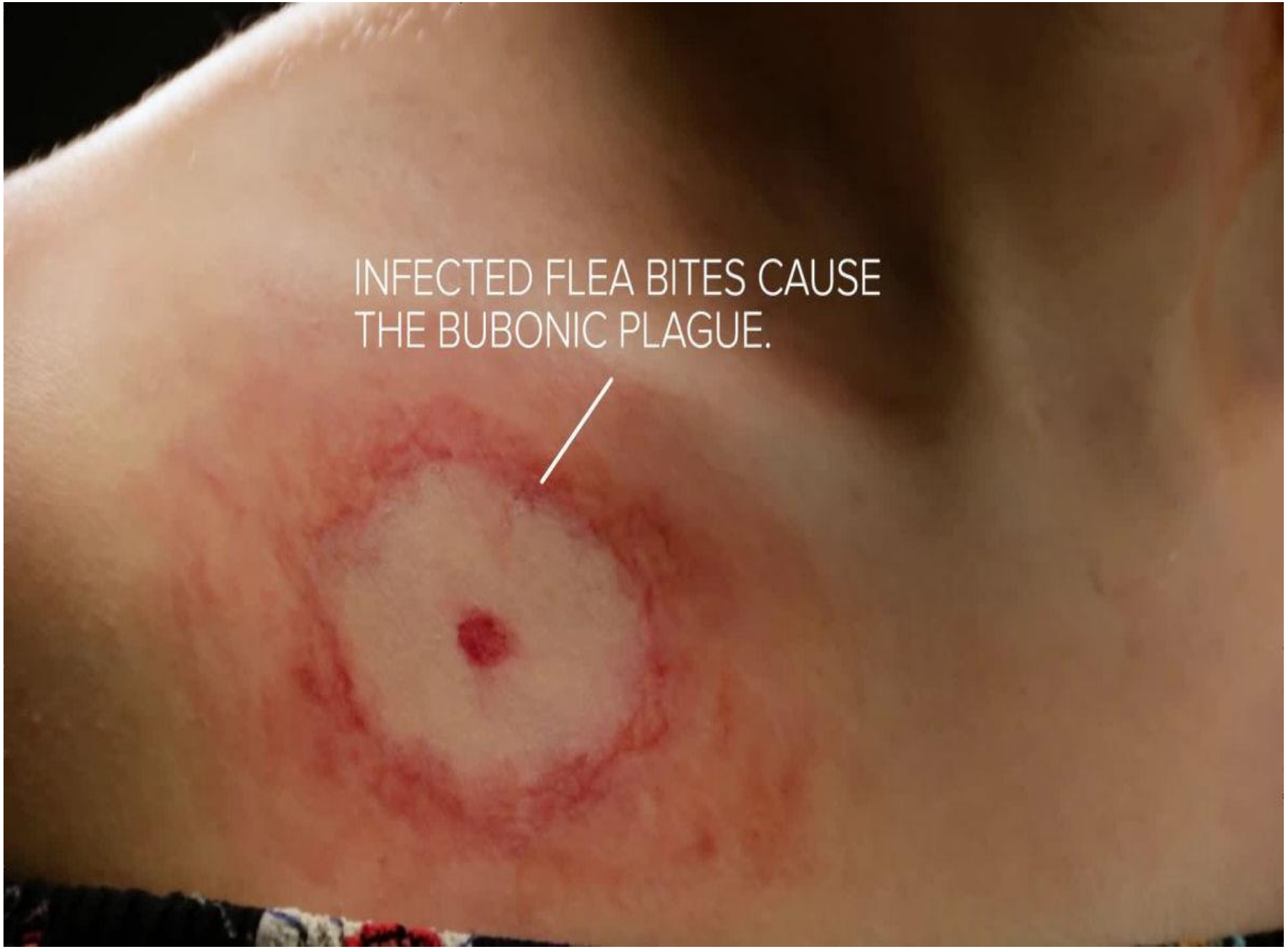


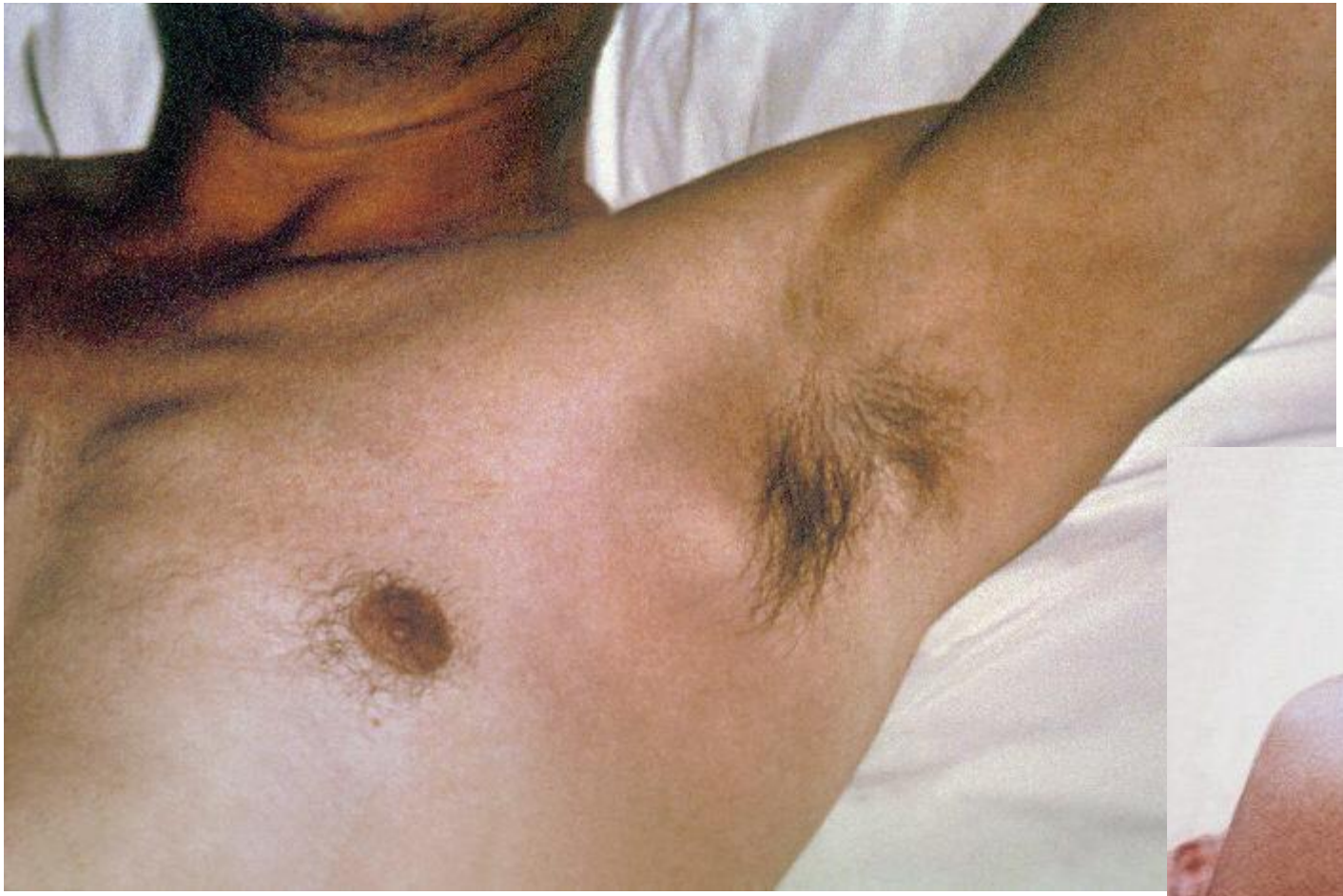


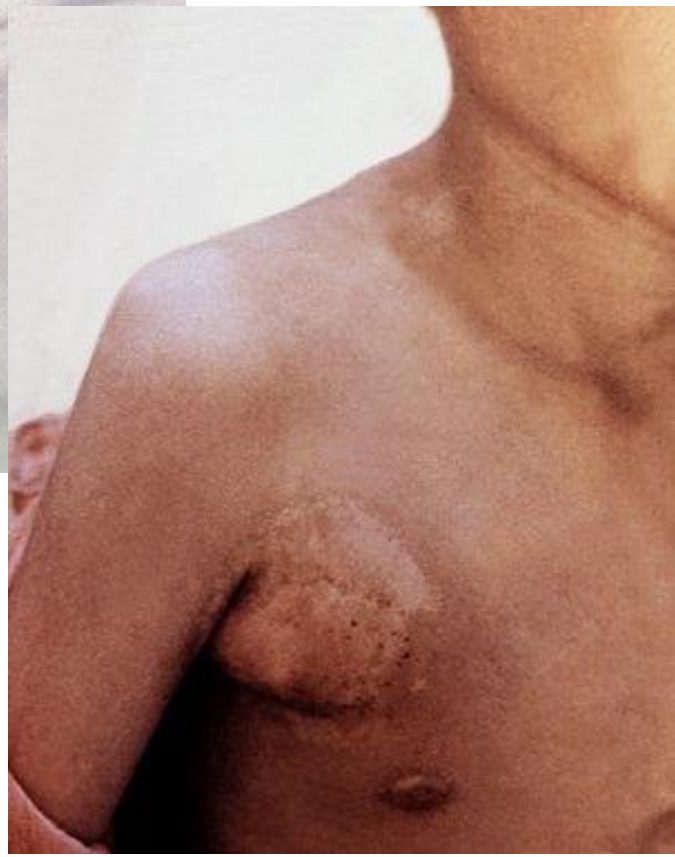
In the photo, the sight of a flea bite is pulyotic irritation.

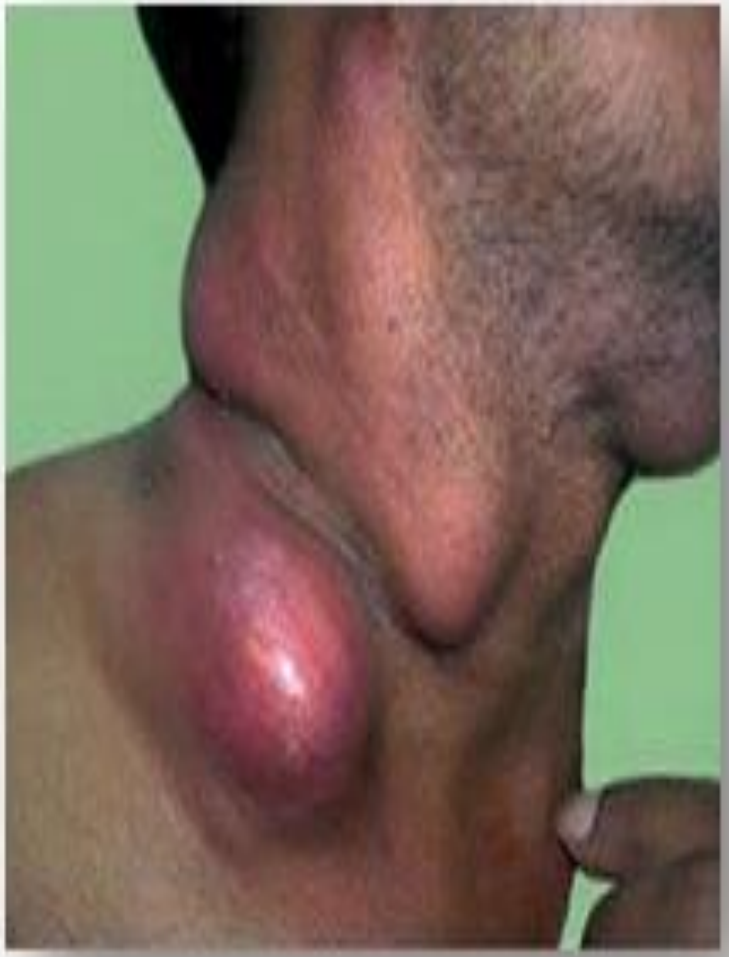
The photo shows a characteristic series of flea bites.

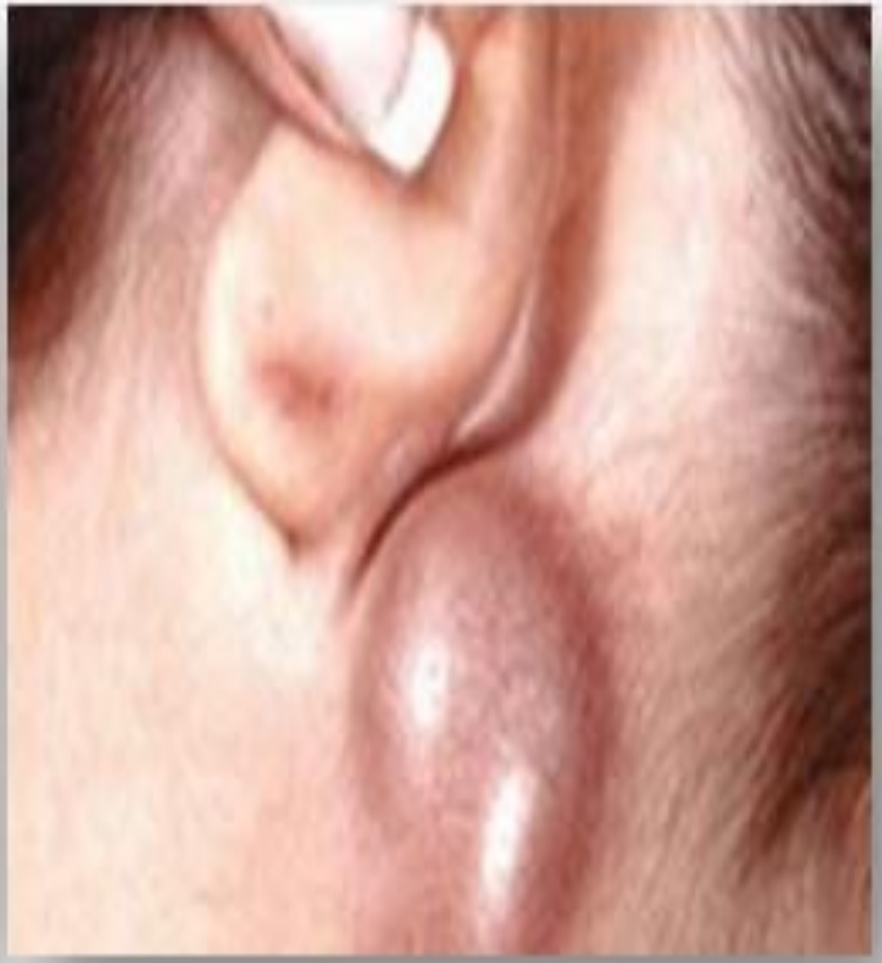


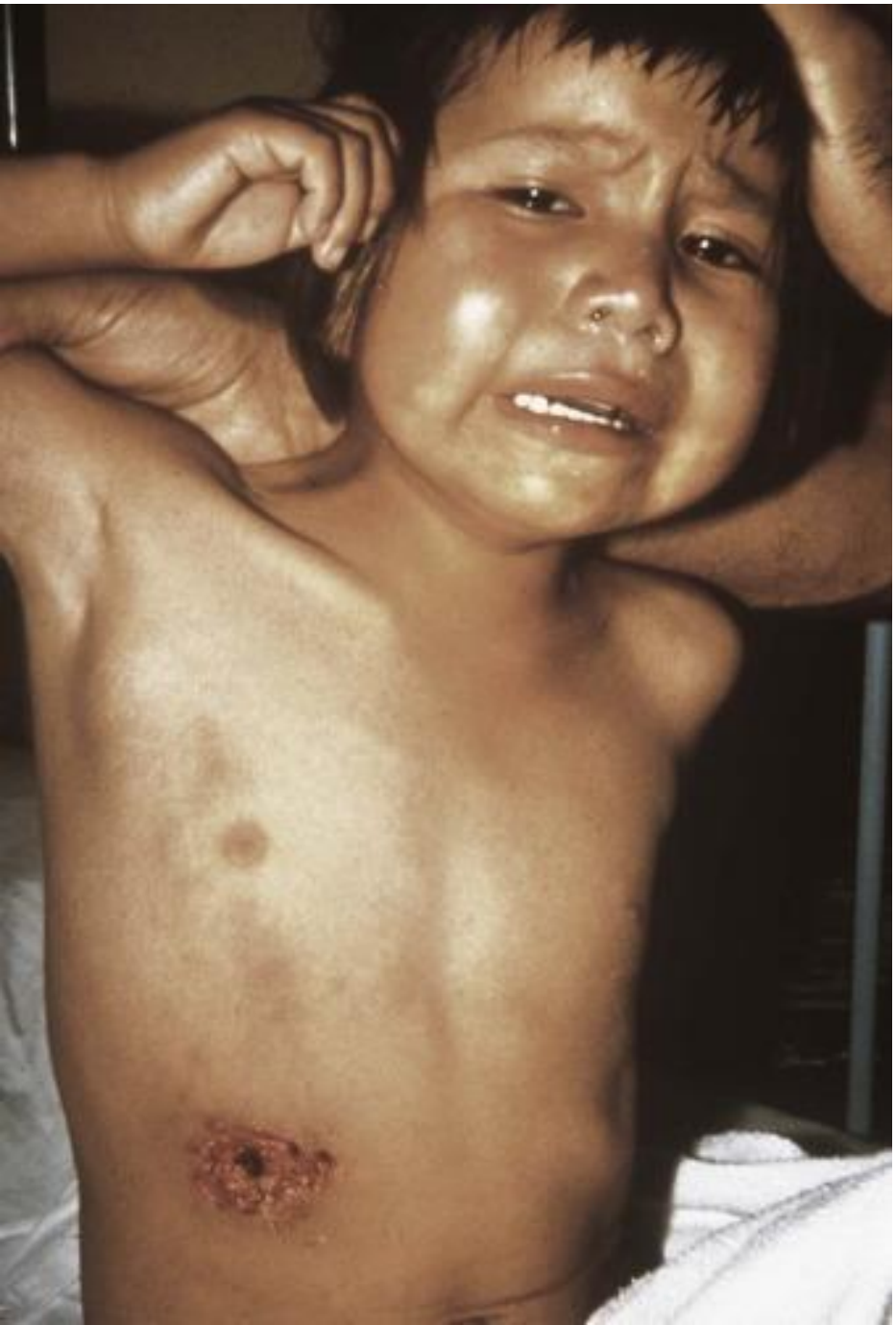

INFECTED FLEA BITES CAUSE
THE BUBONIC PLAGUE.

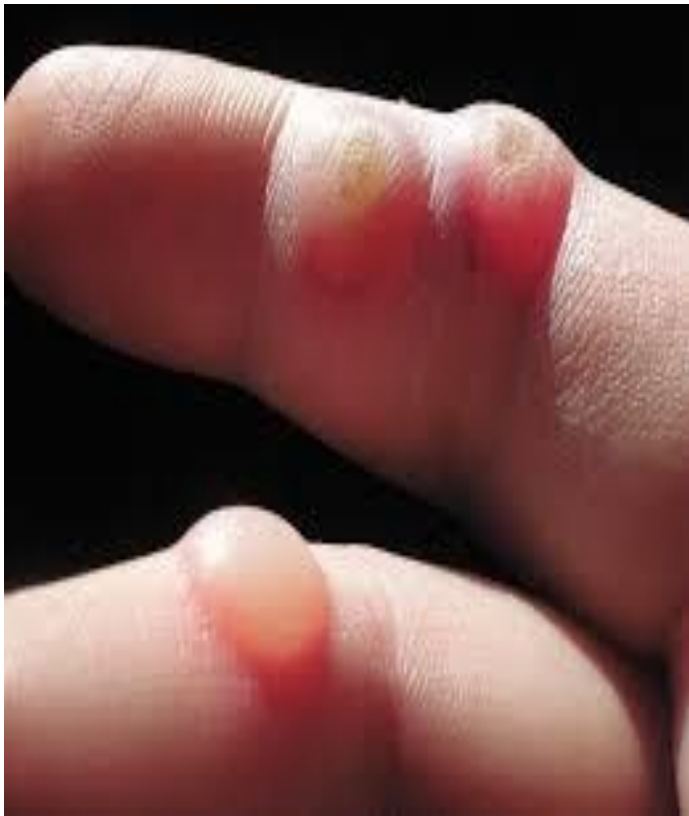




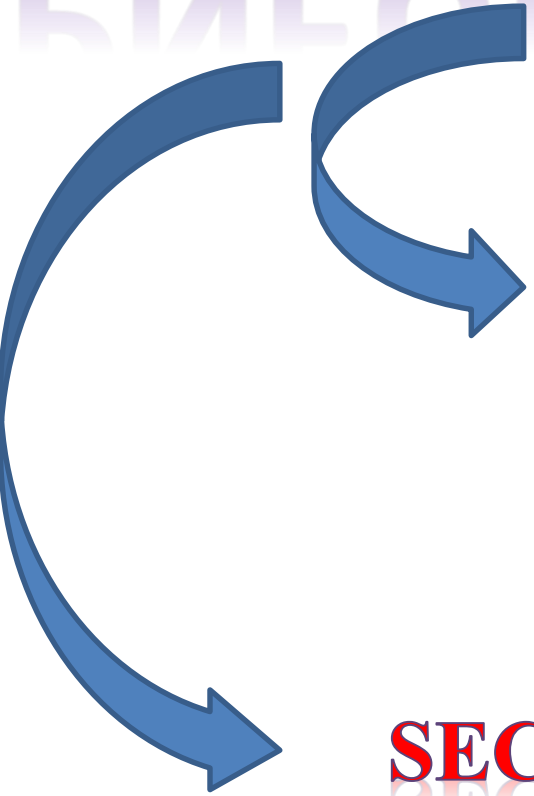








PNEUMONIC PLAGUE

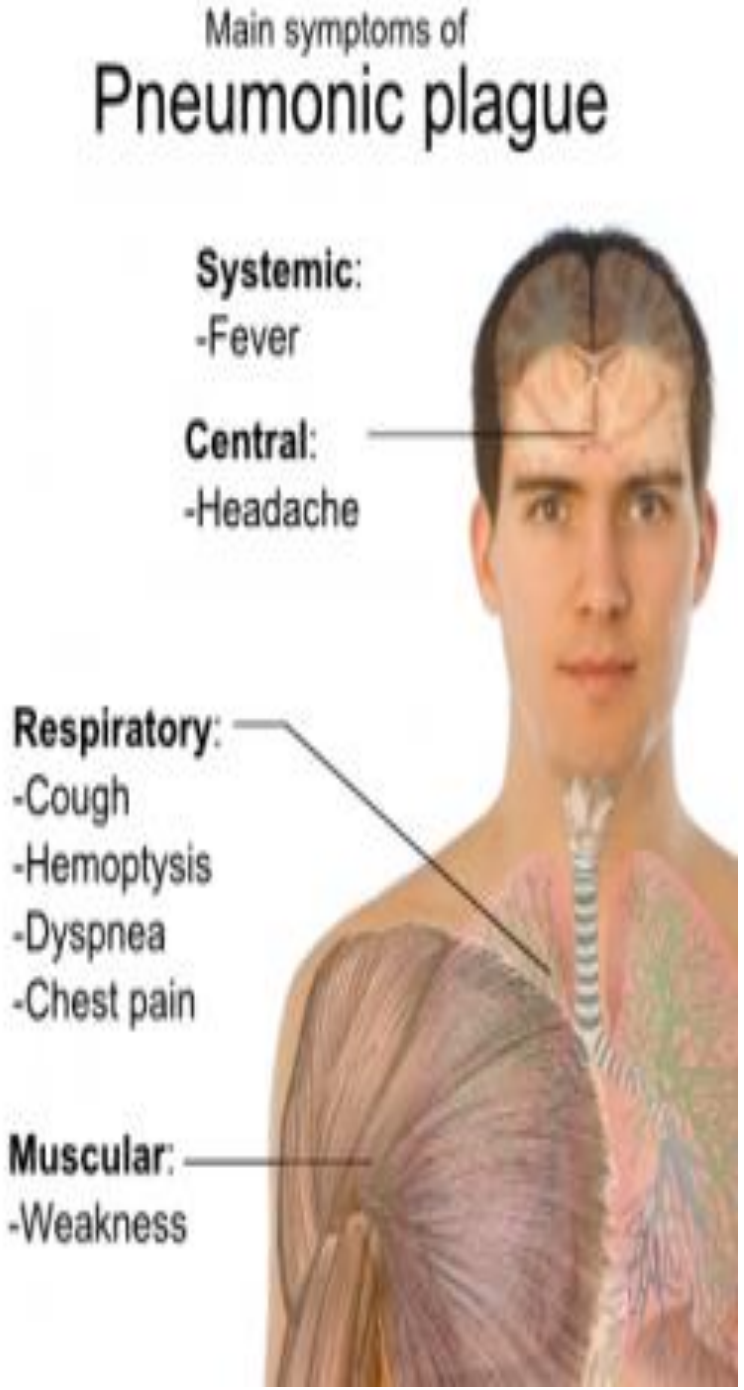


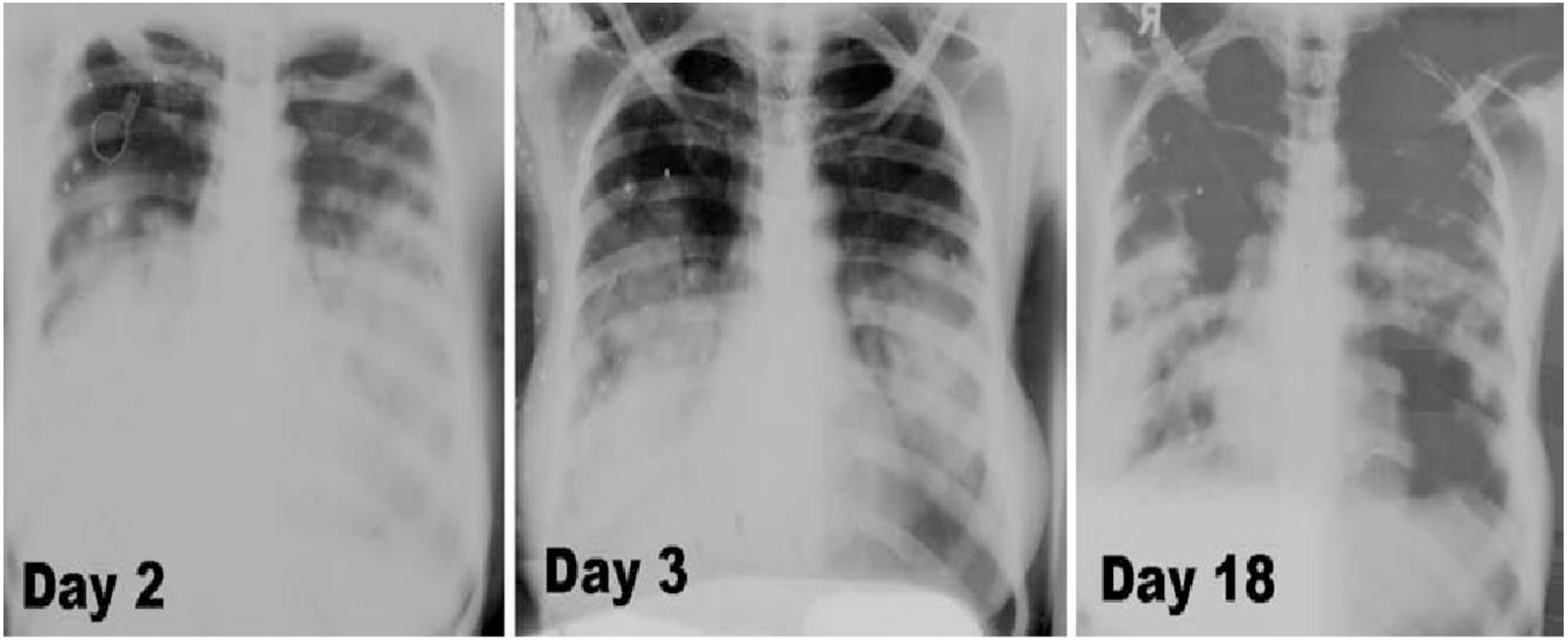
PRIMARY PLAGUE PNEUMONIA

SECONDARY PLAGUE PNEUMONIA

Pneumonic plague.

Primary inhalation pneumonia is a rare but serious threat to unprotected persons in direct and close respiratory contact with the symptomatic patient. Secondary plague pneumonia is complications of bubonic plague. Both primary and secondary pneumonic plague are a malignant pneumonia with rapid advance and is often complicated by sepsis and its consequences. Patients with plague pneumonia experience rapidly advancing tachypnea, dyspnea, hypoxia, chest pain, cough, hemoptysis, and general signs of endotoxemia. The sputum is often purulent but may be watery, frothy, and copious, and may be blood-tinged or grossly hemorrhagic, and it usually contains large numbers of plague bacilli. Radiographs show patchy bronchopneumonia, cavities, or confluent consolidation, and the radiologic findings may be more impressive than indicated by physical examination.





Serial frontal chest radiographs from surviving caregiver B2 with primary pneumonic plague obtained on illness days 2, 3, and 18, showing bilateral lower lung zone predominant airspace disease associated with right>left pleural effusions.

Septicemic plague

- Primary septicemic plague
- Secondary septicemic plague

Septicemic plague

Primary septicemic plague develops in the absence of a detectable bubo or plague pneumonia. The diagnosis often is not suspected until preliminary blood culture results are reported to be positive by the laboratory.

Secondary septicemic plague occurs as a complication of the bubonic or pneumonic plague.

By the time of examination, patients are typically prostrate and lethargic but may exhibit restlessness or agitation. Temperatures are usually elevated in the range of 38.5° C to 40° C. Occasionally, patients are delirious with high fever. Pulse rates are increased to 110 to 140 beats per minute. Blood pressure is characteristically low, owing to vasodilation.

Petechiae, ecchymoses, bleeding from puncture wounds and orifices, and gangrene of acral parts are manifestations of disseminated intravascular coagulation.

Adult respiratory distress syndrome (ARDS) can occur at any stage of septicemic plague.

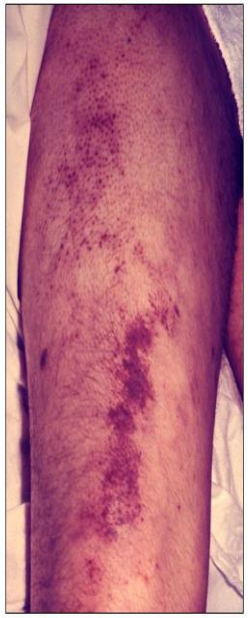
The liver and spleen are often palpable and tender.

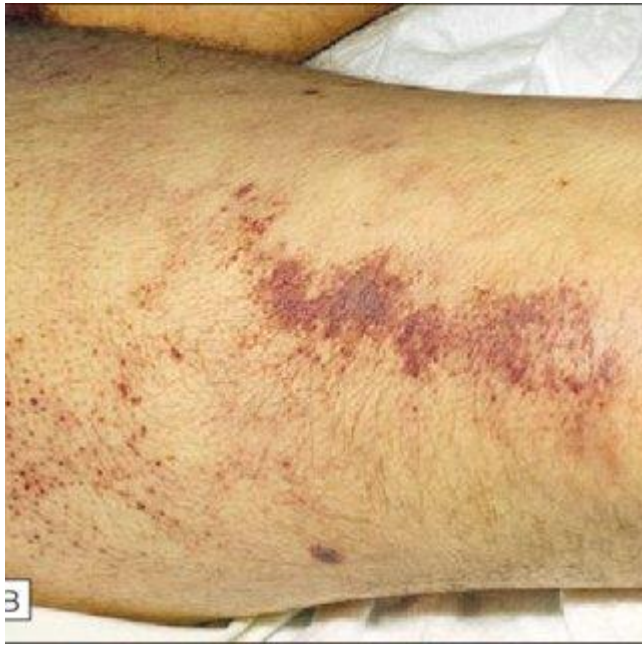
Septic patients often present with gastrointestinal symptoms of nausea, vomiting, diarrhea, and abdominal pain, which may confound the correct diagnosis.

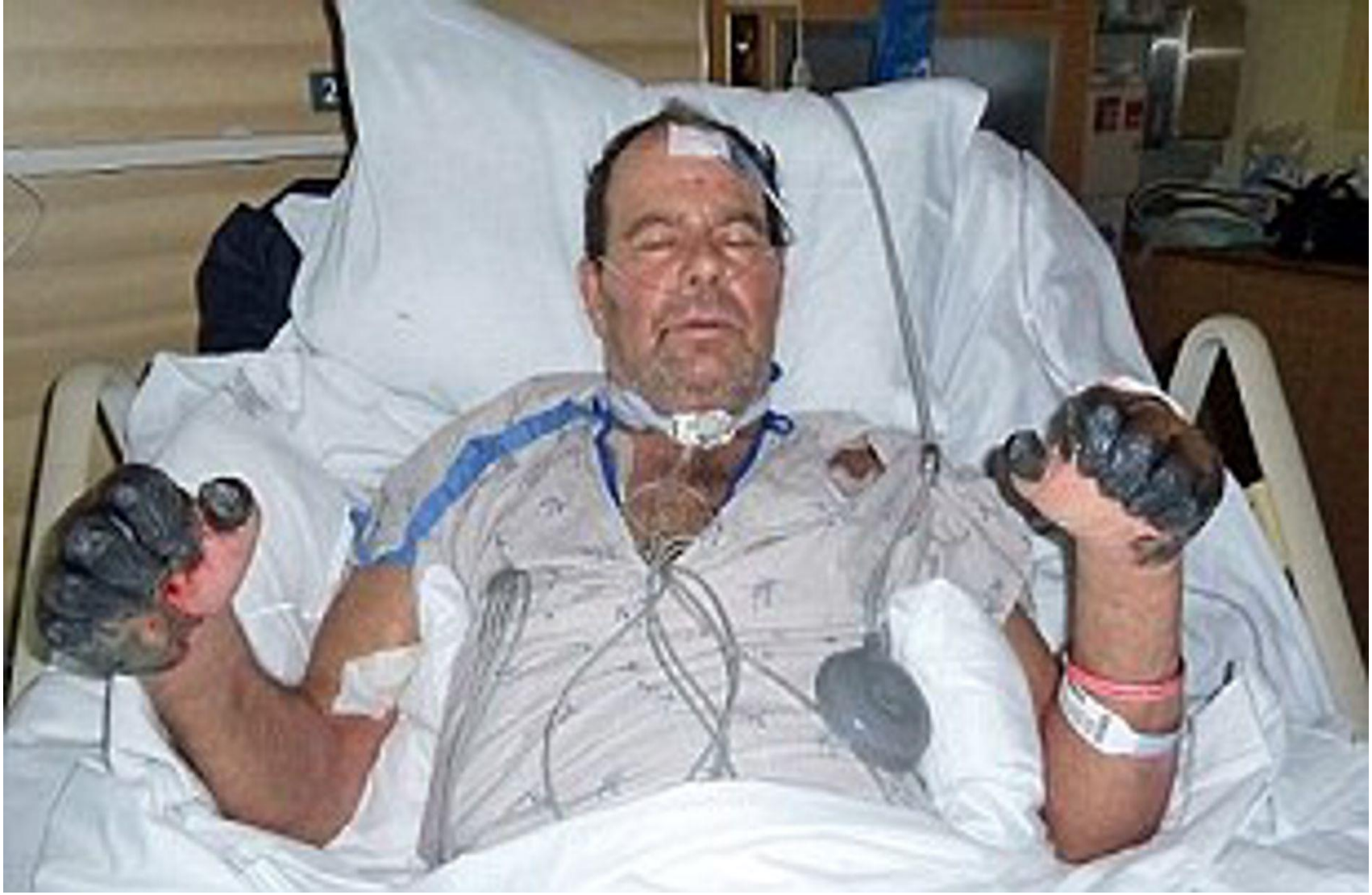
Refractory hypotension, renal shutdown, obtundation, and other signs of shock are preterminal events.

Plague: Petechiae

(Spots Caused by Broken Blood Vessels)

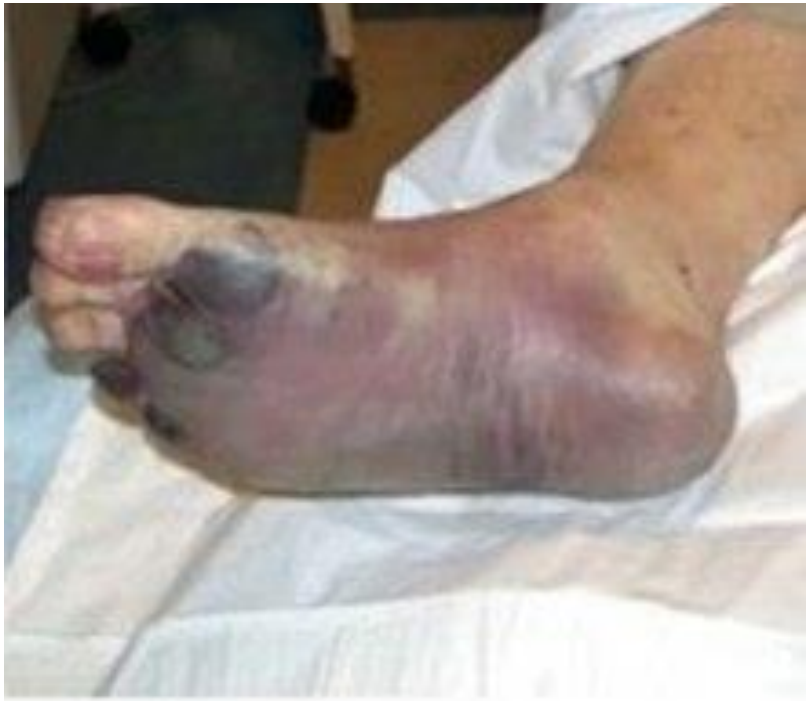


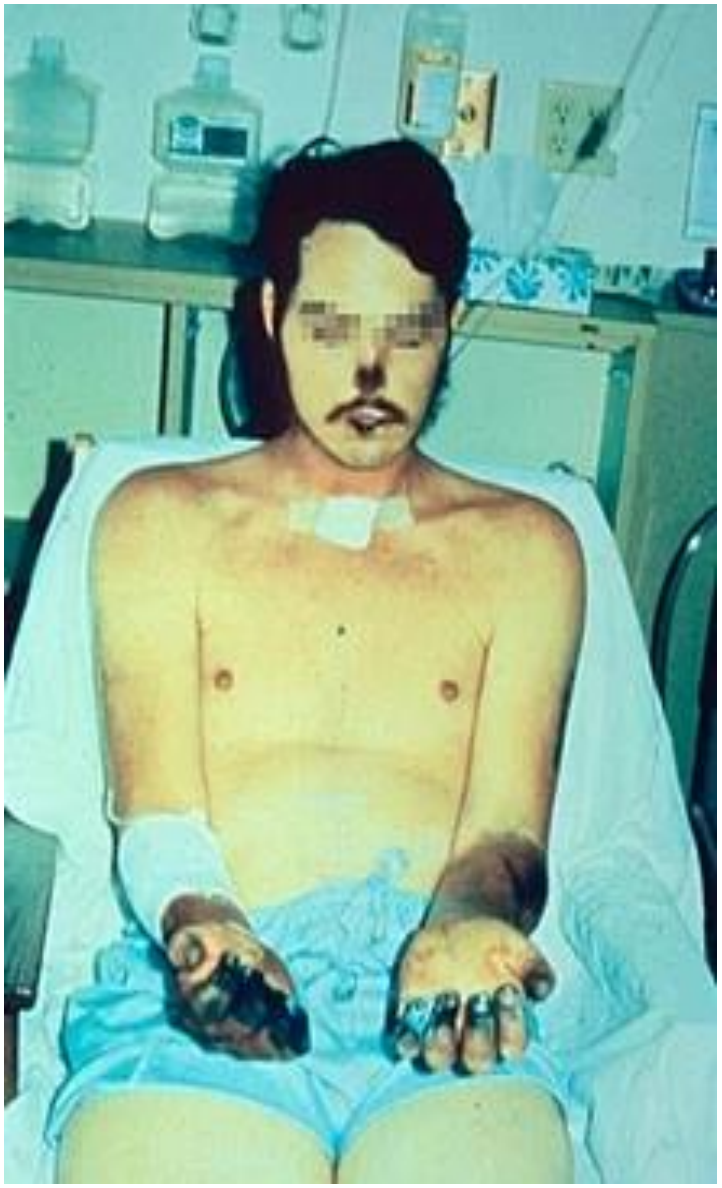




59-year-old Paul Gaylord (resident of Portland, Oregon, USA). The plague bacteria got into his body from a stray cat. As a result of the developed secondary septic form of the disease, his fingers and toes were amputated.


07/11/2012





Septicemic plague resulting in necrosis

Other syndromes

Plague meningitis is a rare complication. It may occur as a delayed manifestation of inadequately treated bubonic plague or as a manifestation of acute early disease.

Plague meningitis is characterized by fever, headache, sensorial changes, meningismus, and cerebrospinal fluid pleocytosis with a predominance of polymorphonuclear leukocytes. Bacteria are frequently demonstrable with a Gram or Wayson stain of spinal fluid sediment, and endotoxin has been demonstrated in spinal fluid with the limulus test.

Plague can produce pharyngitis resembling acute tonsillitis. The anterior cervical lymph nodes are usually inflamed, and *Y. pestis* may be recovered from a throat culture or by aspiration of a cervical bubo. This is a rare clinical form of plague that follows the inhalation or ingestion of plague bacilli.

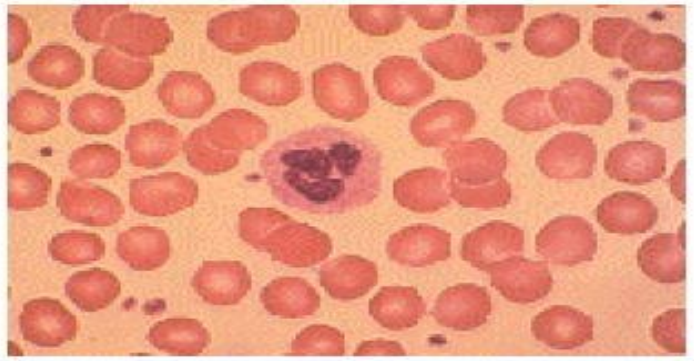
Asymptomatic pharyngeal colonization with *Y. pestis* has been reported in close contacts of pneumonic plague cases.

Diagnosis and differential diagnosis

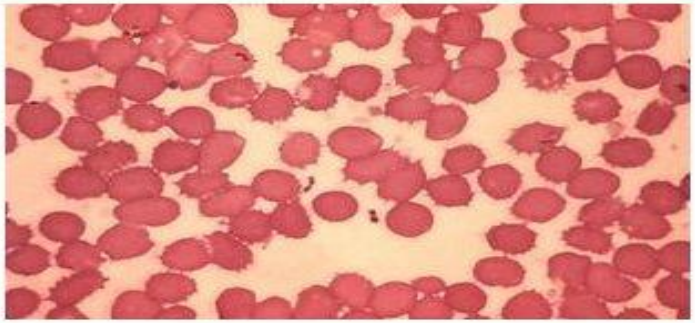
Plague should be included in the differential diagnosis of an acute febrile illness in a patient who was recently in a plague-endemic area and at risk of exposure to infected animals or their fleas. Appropriate diagnostic specimens include blood cultures and other materials as indicated, such as bubo aspirates, sputum, tracheobronchial washes, swabs of skin lesions or pharyngeal mucosa, and cerebrospinal fluid.

A variety of appropriate culture media (including brain-heart infusion broth, sheep blood agar, chocolate agar, and MacConkey agar) should be inoculated with a portion of each specimen.

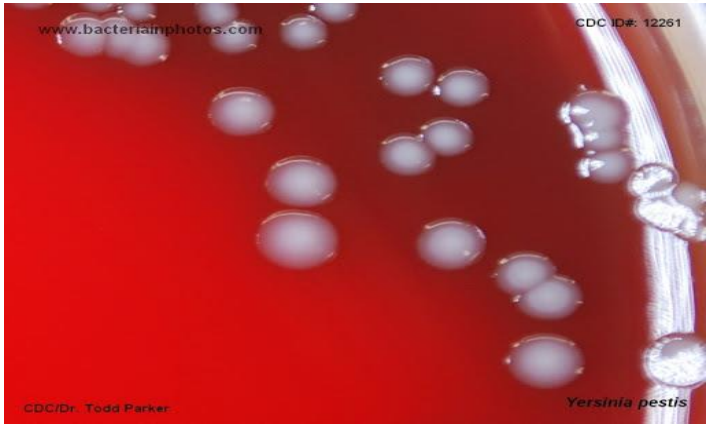
For each specimen, at least one smear should be examined immediately with Wayson or Giemsa stain and at least one with Gram's stain.



Normal red blood cells



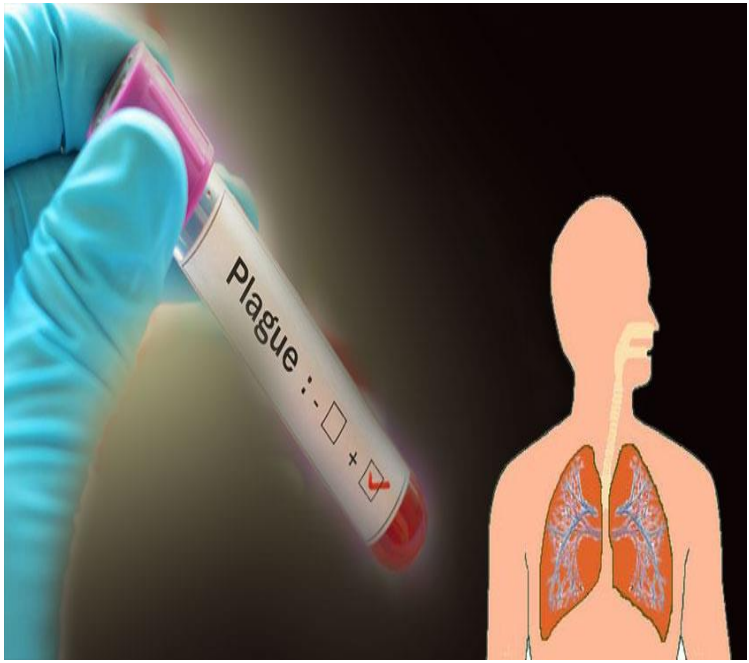
Yersinia pestis infected red blood cells



In patients with negative cultures, plague can be confirmed by serologic tests: passive hemagglutination test (4-fold increase between acute and convalescent antibody titers), ELISA based serologic tests (IgG and IgM antibodies to F1 antigen).

Rapid antigen test based on F1 antigen detection using monoclonal antibodies also seems promising for rapid presumptive diagnosis at the bedside, even when performed under primitive field conditions.

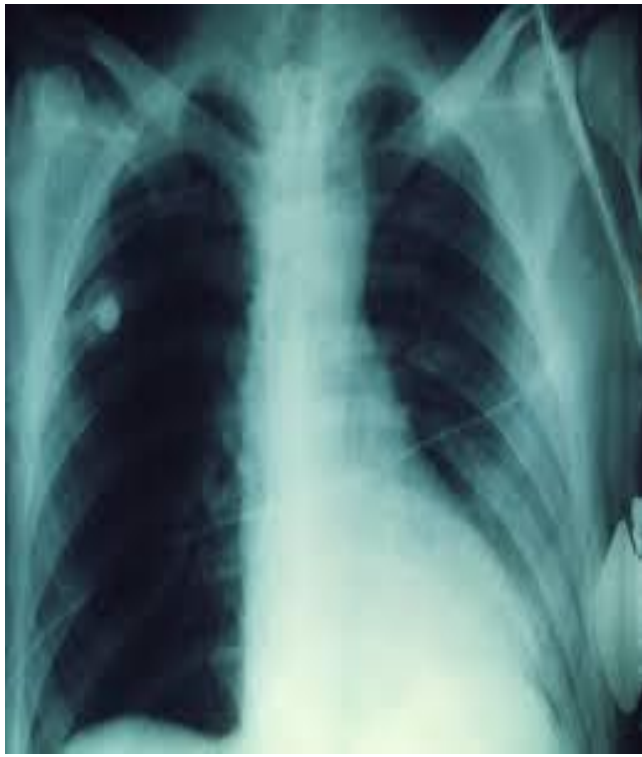
Polymerase chain reaction has been studied in respiratory specimens, but is not routinely available as a diagnostic tool.



Chest radiographs should be obtained to rule out plague-associated damage (patchy or lobar pneumonia that progresses to cavitation, pleural effusions, mediastinal or hilar lymphadenopathy, or acute respiratory distress syndrome).

Patients with plague typically have white blood cell counts of 10,000–25,000/ L, with a left shift.

Modest thrombocytopenia is usually present, and fibrin-fibrinogen split products are often detected, even in patients without frank disseminated intravascular coagulation.



Differential diagnosis includes:

- streptococcal or staphylococcal lymphadenitis,
- other bacterial skin abscesses,
- cat scratch disease, incarcerated inguinal hernia,
- chancroid and lymphogranuloma venereum,
- streptococcal skin infection,
- anthrax,
- tularemia,
- hantavirus pulmonary syndrome.

Treatment.

Without treatment, plague is fatal in more than 50% of bubonic cases and in nearly all cases of septicemic or pneumonic plague.

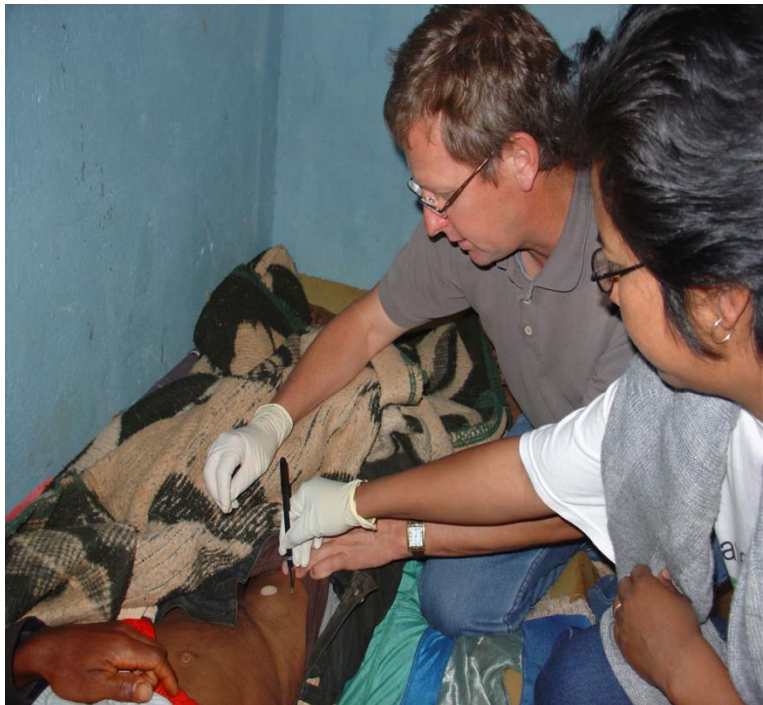
Effective antibiotic therapy should be given immediately after obtaining diagnostic specimens. Streptomycin (30mg/kg/day bid IM for 7 days or at least 3 days after remission of fever and other symptoms) has been considered the drug of choice since its introduction in the 1940s.

Where streptomycin is not available for immediate use, an acceptable alternatives are gentamicin (2.5 mg/kg bid IM), tetracycline (0.5-1 g qid orally), doxycycline (0.1 g bid IV), chloramphenicol (0.5 g qid IV), ciprofloxacin (0.4 g bid IV).

Patients initially given IV antibiotics may be switched to oral regimens upon clinical improvement. Such improvement is usually evident 2–3 days after the start of treatment, even though fever may continue for several days.

The patient's hemodynamic status should be monitored closely and shock managed according to general principles used to combat endotoxic shock.

Buboes usually recede during the first week of antibiotic treatment, but it may be several weeks before they completely resolve; occasionally, they enlarge or become fluctuant, requiring incision and drainage. The aspirate is usually sterile, but persistence of viable *Y. pestis* in buboes after apparent clinical cure has been reported. This persistence has not been associated with relapse of systemic plague.



Prevention.

Personal protective measures include:
the avoidance of areas with known epizootic plague (in which warning signs may be posted) and of sick or dead animals;
the use of repellents, insecticides, and protective clothing when at risk of exposure to rodents' fleas;
and the wearing of gloves when handling animal carcasses.
Short-term antibiotic prophylaxis is recommended for persons known to have had close contact with a patient with suspected or confirmed pneumonic plague.
Tetracycline (2 g/d orally divided in 2-4 doses for 7 days), doxycycline (100-200 mg orally bid for 7 days) or trimethoprim/sulfamethoxazole (160/800 mg bid for 7 days) are the most suitable antimicrobial agents for post-exposure prophylaxis.

Vaccination is indicated for high risk individuals (laboratory workers, ecologists, field workers in high risk areas).

Primary vaccine series: 3 doses given at 0, 1-3 and 5-6 month intervals.

Booster doses: up to 3 doses at 6 month intervals depending on antibody response and continuing risk of exposure.

Additional boosters at 1-2 year intervals for continued risk may be given.


GIANT microbes
The Plague
Black Death
(Yersinia pestis)