A PLAGUE ON U.S.

Course # DL-958

by
Helen M. Sowers, M.A., CLS
Dept. of Biological Science (Retired)
California State University, East Bay

Approved for 1.0 CE
CAMLT is approved by the California Department of Public Health
as a CA CLS Accrediting Agency (#21)

Level of Difficulty: Basic

39656 Mission Blvd. Phone: 510-792-4441
Fremont, CA 94539-3000 FAX: 510-792-3045

Notification of Distance Learning Deadline
DON'T PUT YOUR LICENSE IN JEOPARDY!

This is a reminder that all the continuing education units required to renew your license/certificate must be earned no later than the expiration date printed on your license/certificate. If some of your units are made up of Distance Learning courses, please allow yourself enough time to retake the test in the event you do not pass on the first attempt. CAMLT urges you to earn your CE units early!
DISTANCE LEARNING ANSWER SHEET
Please circle the one best answer for each question.

COURSE NAME: A PLAGUE ON U.S.  COURSE #: DL-958

NAME ________________________ LIC. # ___________________ DATE ____________

SIGNATURE (REQUIRED) __________________________________________________________________

EMAIL __________________________________________________________________________________

ADDRESS ______________________________________________________________________________

STREET      CITY    STATE/ZIP

1.0 CE – FEE: $12.00 (MEMBER) | $22.00 (NON-MEMBER)

PAYMENT METHOD: [ ] CHECK or [ ] CREDIT CARD # ____________________________ TYPE – VISA or MC

EXP. DATE ________ | SECURITY CODE: ___  -  ___  - ___

1. a  b  c  d
2. a  b  c  d
3. a  b  c  d
4. a  b  c  d
5. a  b  c  d
6. a  b  c  d
7. a  b  c  d
8. a  b  c  d
9. a  b  c  d
10. a  b  c  d

DISTANCE LEARNING EVALUATION FORM
According to state regulations, this form must be completed and returned in order to receive CE hours. Your comments help us to provide you with better continuing education materials in the distance learning format. Please circle the number that agrees with your assessment with, with 5 meaning you strongly agree and 1 meaning you strongly disagree.

1. Overall, I was satisfied with the quality of this Distance Learning course.
   5  4  3  2  1
2. The objectives of this Distance Learning course were met.
   5  4  3  2  1
3. The difficulty of this Distance Learning course was consistent with the number of CE hours.
   5  4  3  2  1
4. I will use what I learned from this Distance Learning course.
   5  4  3  2  1
5. The time to complete this Distance Learning course was: __________ hours
6. Please comment on this Distance Learning course on the back of this sheet. What did you like or dislike?
OBJECTIVES
At the end of this course the participant will be able to:
1. outline the history of plague including the introduction to the U.S.
2. discuss the epidemiology of plague
3. list the symptoms of the three forms of plague in humans
4. describe the identification of *Yersinia pestis* in the laboratory
5. discuss the host species and geographical distribution of plague in the U.S.
6. outline the procedure for reporting a suspected case of plague
7. list the characteristics of bioterrorist-released plague

CASE STUDY (1): A middle aged couple was vacationing in New York City from their ranch in New Mexico. After several days of enjoying the luxury of their hotel and seeing the sights, they both began feeling ill. Their symptoms were similar, fever, fatigue, myalgia and one-sided inguinal swelling. Two days later, on Nov. 5, they went to an emergency room (ER) in a New York City hospital after consulting with their physician in New Mexico and the doctor at the hotel.

On admission the 55 year-old man appeared sicker with chills, diaphoresis (sweating), and lower extremity cyanosis. He had tender left inguinal adenopathy with overlying edema. His temperature was 104° F., blood pressure - 78/50, WBC count - 24,000/µL (normal: 4,300 - 10,800/µL), Platelet count - 72,000/µL (normal: 130,000 - 400,000/µL). A blood culture was taken and after 24 hours a gram stain showed bipolar gram negative rods.

The 47 year-old wife had tender right inguinal and femoral adenopathy with overlying erythema and induration. Her temperature was 102.2° F, blood pressure - 120/72, WBC count - 9,500/µL, platelet count - 189,000/µL. Aspiration of the inguinal lymph nodes did not yield any material.

CASE STUDY QUESTIONS:
1. What is the most probable organism recovered from the blood culture?
2. Where did the couple most likely become infected?
3. What is the usual route of infection for this disease?
4. The causative organism is on the list of possible bioterrorist agents. Why wasn't this episode considered to be a bioterrorist incident?

CASE DISCUSSION:
Subculture of the husband's blood culture grew organisms identified as *Yersinia pestis*. This was confirmed on Nov. 6 by positive direct fluorescent antibody to *Y. pestis* F1 antigen and
polymerase chain reaction (PCR) performed on the initial blood culture by the NYC Public Health Laboratory. His diagnosis was acute septicemic plague.

Although no organisms were recovered from the wife, she was given a presumptive diagnosis of bubonic plague because of her clinical signs and symptoms and her husband's *Y. pestis* positive blood culture.

Both were given multiple antibiotics. The wife recovered without complications. The husband developed acute renal failure, acute respiratory distress syndrome and disseminated intravascular coagulation. He required hemodialysis and mechanical ventilation and subsequently underwent bilateral foot amputations because of ischemia. After 6 weeks in the ICU he recovered and was discharged to a rehabilitation facility.

During initial consultation with medical personnel the couple reported that routine surveillance conducted by the New Mexico Department of Health had identified *Y. pestis* in a dead wood rat on their New Mexico property. The hotel physician notified the ER about the arrival of two possible plague patients and the need for respiratory isolation pending the exclusion of pulmonary infection. Various New York State agencies as well as the Centers for Disease Control and Prevention (CDC) were contacted to facilitate diagnostic testing, coordinate public health response and assess the possibility of terrorism. After determining that the two plague cases were probably acquired naturally, the agencies held a press conference to reassure the public that the exposures had occurred in New Mexico, a known plague endemic area, and not in NYC.

One day after the patients were evaluated, New Mexico Department of Health and CDC investigated the couple's New Mexico property. Rodent traps were placed in and around the couple's home and along a nearby hiking trail where wood rat (*Neotoma* species) nests and rodent burrows were abundant. Five flea pools comprising 88 fleas were harvested from 41 trapped rodents. All fleas were cultured for *Y. pestis* and rodents were bled for culture. *Y. pestis* isolates from the husband's blood culture and from flea samples were compared by using pulsed-field gel electrophoresis (PFGE). The PFGE patterns of the isolate from the husband and from seven New Mexico flea pools, two obtained in July and five obtained during the November investigation, were indistinguishable.

Plague warning signs were placed at trailheads near the couple's property. Plague information pamphlets were distributed in the community and close neighbors were contacted directly to inform them of the risk for infection in the area. (2)

**EPIDEMIOLOGY AND HISTORY OF PLAGUE**

Plague, the scourge of the Middle-Ages, is a rodent-associated zoonosis transmitted by the bite of fleas infected with *Y. pestis*. The organism is transmitted from animal to animal and occasionally to humans. For eons it lived in the blood of resistant wild rodents in northern Asia. During the Middle Ages plague began to infect the domestic rats that infested towns and cities. After the rats died, their fleas bit and infected the people. Bubonic plague (the Black Death) swept the continent. Plague traveled by infected rats on ships sailing to various ports and spread to Europe and England. The Black Death caused the death of over half the population.

Plague entered California in 1899 on a ship from Hong Kong. (3) There had been two cases of plague on board, causing the ship to be quarantined at Angel Island in San Francisco Bay. A search of the ship revealed 11 stowaways. The next day two of them were missing. Their bodies were found floating in the Bay and autopsy showed infection with the plague bacillus. When the ship was allowed to dock in San Francisco, rats escaped. Nine months later plague...
cases occurred in S.F.’s Chinatown. Political issues vied with scientific eradication and control efforts. City officials didn’t want it known that plague was present and denied its occurrence. Even the governor refused to believe or to help with anti-plague efforts. Finally, the U.S. Surgeon General got permission from President McKinley to pass anti-plague regulations. Commissions and Boards formed, fought with the governor, and were disbanded, underfunded, and re-formed. Meanwhile additional plague cases occurred. Then, in April 1901, a clean-up campaign scoured Chinatown, halting the epidemic. The last case, in 1904, caused a fatality in a woman in Concord. There were 121 cases in San Francisco and 5 more in the Bay Area with 122 deaths.

Plague remained endemic in the city. After the 1906 earthquake the devastation and refugee camps fostered an increase in the rat population with proximity to people (3). Plague cases again occurred, but this time anti-plague measures, particularly rat control, were started early and halted the epidemic by 1909. With rat poison as well as a 5 cent per rat bounty, over 2 million rats were killed. Cleaning up unsanitary conditions eliminated rat hiding and nesting sites. This epidemic caused 160 cases with 77 deaths.

The elimination of plague cases in the Bay Area did not eliminate the plague bacillus. By this time the organism had become established in deer mice, Peromyscus and other resistant wild rodents. Y. pestis became firmly entrenched in the wild (sylvatic) rodent population in the Coastal Mountains and eventually spread to the Sierra Nevada and beyond. Today plague is maintained in the environment in moderately resistant sylvatic rodents such as deer mice, meadow voles, and certain chipmunks and wood rats throughout the western 17 states (4). Occasionally the organism spreads to more susceptible rodents, such as ground squirrels or certain wood rats. Epizootic outbreaks kill large numbers in squirrel colonies, leaving infected, hungry fleas around the burrows. These sites are dangerous to hunters, campers, and residents living nearby. When these die-offs of ground squirrels occur, public health workers close campgrounds or parks, put up warning signs and apply insecticides to kill the fleas.

Although transmission by infected fleas is the most common method of transmission, predators or scavengers can contract the disease by eating prey and hunters may become infected by handling or skinning infected game animals.

During 1988-2012, a total of 117 human cases of plague were reported from 11 western states. The majority was in Northern Arizona, and Southern Colorado with sporadic cases occurring elsewhere. During the summer of 2015, there were 11 cases of human plague resulting in 3 deaths (1). From 1970-2016, the only case of plague outside the rural West is a lab associated case in Illinois. About 80% of these exposures occurred in environments around houses that provided abundant food and hiding places for plague-susceptible rodents (2). Such conditions were present around the home of the case study couple.

MANIFESTATIONS OF PLAGUE (6)

In addition to the bite of infected fleas, plague can be transmitted by eating infected animals, exposure of infected meat or patient's suppurating lesions through broken skin, or by inhalation of aerosolized plague bacteria. Cats are very susceptible to plague. They are exposed by eating rodents infected with plague. Cats develop pneumonic plague and can pose a risk to their owners and to veterinarians through transmission of infected droplets.

There are three forms of plague in humans, bubonic, septicemic, and pneumonic.

Bubonic Plague: The incubation period for bubonic plague is usually 2-6 days. The symptoms include fever, chills, myalgia, arthralgia, sore throat, and headache. Within 24 hours the patient
notices tenderness and pain in one or more regional lymph nodes proximal to the site of inoculation of *Y. pestis* organisms. A lymphadenitis (bubo) develops. The bubo becomes very painful, swollen and hemorrhagic, finally appearing black, thus leading to the name, Black Death. Early treatment with at least a week of appropriate antibiotics such as streptomycin or aminoglycosides or fluoroquinolones usually results in alleviation of manifestations over 2 to 5 days. Untreated bubonic plague has a fatality rate of more than 50%. A plague vaccine is no longer available in the U.S.

**Septicemic Plague:** Septicemic plague occurs when host defenses are breached and the plague bacillus enters and multiplies in the bloodstream. It is a progressive, overwhelming infection. Gastrointestinal symptoms frequently occur with nausea, vomiting, diarrhea and abdominal pain. Multifocal hepatic and splenic necrosis is common. Diffuse myocarditis and respiratory distress syndrome may occur. DIC, renal shutdown, hypotension with shock are preterminal events. If not treated early with appropriate antibiotics, septicemic plague is frequently fatal.

**Pneumonic Plague:** Primary pneumonic plague occurs from directly inhaling *Y. pestis*. Secondary pneumonic plague develops from a bubonic or septicemic plague infection. The incubation period is 1-3 days for naturally occurring primary; 2-6 days for intentionally (i.e. germ warfare) disseminated pneumonic plague. The initial symptoms occur suddenly with chills, fever, headache, myalgias, weakness, and dizziness. Pulmonary signs, cough, sputum, chest pain, tachypnea, and dyspnea develop on the second day of illness. Transmission of plague to contacts is a grave risk of pneumonic plague. It is the most frequently fatal of the plague forms. If treatment is not instituted within 18 hours after onset of symptoms the fatality rate is close to 100%. Unfortunately, most pneumonic plague cases are not diagnosed and treated within this time. Even the treated cases had a fatality rate of over 40% in the U.S. during the last half of the 20th century. The overall fatality rate for all types of plague in the U.S. since 1950 has been 16%. Most of these deaths were due to delay in seeking or instituting treatment, misdiagnosis, and incorrect treatment.

**LABORATORY IDENTIFICATION OF *YERSINIA PESTIS***

*Yersinia pestis* is a gram-negative, non-motile, fermentative rod. It stains easily with gram stain and appears as single or short-chained pleomorphic gram-negative, fat rods. It may not have a bipolar appearance on gram stain. To show the bipolar characteristic, use Wayson, Giemsa, or Wright's stain. Cultures grow better at 28° than at 35°; grow slowly and must be incubated longer for optimum growth. On blood agar the colony has a fried egg appearance. On clear medium there is a skirt around the young colony. There is a lot of capsular material that forms strings with a loop. Although it ferments glucose and mannitol, it is relatively inert. It is a non-lactose fermenter on MacConkey agar and is oxidase and urease negative. *Yersinia pestis* can be identified by various automated bacteriologic test systems, but some may give erroneous interpretations.

Confirmation is by direct fluorescent antibody testing or antigen capture enzyme-linked immunosorbant assay.

Confirmatory testing of the patient's disease includes culture or a fourfold or greater change in antibody titer between acute and convalescent sera.
DIFFERENTIATION OF NATURALLY OCCURRING PLAGUE FROM BIOTERRORIST RELEASE OF PLAGUE

Naturally occurring plague
- Patient in or from a plague endemic area
- Lymph node swelling indicating infection from a flea bite, i.e., bubonic plague
- Usually individual or few cases

Bioterrorist plague
- May occur in a non-plague endemic area
- Pneumonic plague is most common type
- May involve many cases

REPORTING/APPROPRIATE ACTION (7,8,9)
The following is a generalized response to a possible bioterrorist agent. The CDC and individual states have web sites that give information for procedures and reporting.
1. Any isolate which cannot be ruled out as *Yersinia pestis* must be referred to the Laboratory Response Network (LRN) Reference Laboratory.
2. Sentinel laboratories, such as clinical laboratories, should consult with local public health laboratory director (or designate) prior to or concurrent with testing if *Y. pestis* is suspected by the physician.
3. Immediately notify local public health officer (or designate) in the jurisdiction where the patient resides if *Y. pestis* cannot be ruled out. The local public health officer will notify the state public health department. The state public health laboratory/state public health department will notify local FBI agents as appropriate and the CDC.
4. Immediately notify physician/infection control according to internal policies if *Y. pestis* cannot be ruled out.
5. Preserve original specimens pursuant to a potential criminal investigation and possible transfer to an appropriate Laboratory Response Network (LRN) laboratory. FBI and state public health laboratory/state public health department will coordinate the transfer of isolates/specimens to a higher-level LRN laboratory as appropriate. Start chain-of-custody documentation if appropriate.
6. Obtain guidance from the state public health laboratory as appropriate (e.g., requests from local law enforcement or other local government officials).
7. If *Y. pestis* is ruled out, proceed with efforts to identify using established procedures.

SUMMARY
Plague is a disease caused by the organism, *Yersinia pestis*. There are three types of disease, bubonic, septicemic and pneumonic. It is a zoonosis and usually transmitted by the bite of an infected flea (bubonic) but may be transmitted by eating infected animals, by contact through broken skin with infected animals or patient's suppurating lesions, or by inhalation of aerosolized bacteria, either in infectious body fluids, or intentionally produced.

Plague is endemic in 17 Western sates. It is maintained in resistant sylvatic rodents but can occasionally be spread to susceptible rodents such as ground squirrels.

When plague occurs in humans in the U.S., bioterrorism must be ruled out. Characteristics of bioterrorism spread include pneumonic expression, occurrence in non-endemic areas and multiple cases.
Identification of *Y. pestis* can be done in the laboratory and confirmed by DFA or antigen capture enzyme-linked immunosorbant assay. Possible plague cases must be reported to appropriate Public Health Agencies.

PLAGUE REFERENCES

1. CDC. Human Plague—United States, 2015. MMWR 2015; 64(33); 918-919
2. CDC. Imported Plague--New York City 2002. MMWR 2002;52(31);725-728
8. California Department of Public Health. Health Information, Plague. [www.cdph.ca.gov/HEALTHINFO/DISCOND/Pages/Plague.aspx](http://www.cdph.ca.gov/HEALTHINFO/DISCOND/Pages/Plague.aspx)

REVIEW QUESTIONS
Course #DL-958
Choose the **one** best answer

1. Plague is usually transmitted by
   a. person to person
   b. through the bite of an infected flea
   c. through the air
   d. by the oral route

2. Plague is endemic in wild rodents
   a. in 17 Western States
   b. throughout the U.S.
   c. only in California, Nevada, New Mexico, and Arizona
   d. is not found in the wild in the U.S.
3. Five patients appear in emergency rooms in two Washington, D.C. hospitals. Their symptoms are chills, fever, headache, dizziness, and dyspnea. Plague is suspected. The origin of disease in these infected people is most probably
   a. bites by infected fleas
   b. naturally occurring
   c. terrorist release of aerosolized *Y. pestis*
   d. skinning infected wild rabbits

4. The bipolar characteristic of *Y. pestis* is best shown by all but which of the following stains?
   a. Wayson
   b. Giemsa
   c. Gram
   d. Wright’s

5. Endemic plague is primarily maintained in the wild in
   a. susceptible rodents, i.e., ground squirrels
   b. deer and deer ticks
   c. rabbits and hares
   d. resistant rodents, i.e., deer mice

6. Reporting of a suspected *Y. pestis* is done
   a. directly to the FBI
   b. to the State Public Health laboratory director
   c. to a LRN laboratory
   d. to the Centers for Disease Control and Prevention

7. Plague reached San Francisco by
   a. ship with infected passengers
   b. spread through rodents from Arizona
   c. overland by emigrants to California
   d. gold miners coming through the Panama Canal

8. Plague in a patient can be confirmed by
   a. signs and symptoms
   b. gram-negative rods in a blood culture
   c. isolation of an organism which ferments glucose and mannitol
   d. a four-fold rise in antibody titer between acute and convalescent serum

9. Which of the following is not a symptom of bubonic plague?
   a. fever
   b. myalgia
   c. dyspnea
   d. lymphadenitis
10. Which group of laboratory determined characteristics best typifies *Y. pestis*?
   a. ferment glucose, oxidase negative, motile
   b. abundant capsular material, ferments mannitol, gram-negative coccus
   c. fried egg appearance on blood agar, ferments only glucose, slow growing
   d. bipolar appearance on Wright’s stain, grows slowly, non-motile