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Human Plague in New Mexico: Report of Three Autopsied Cases

Plague is an ancient bacterial disease of rodents that occurs in man in sporadic and epidemic forms. The causative organism is the Gram-negative bacterium *Yersinia pestis*, which multiplies in the stomach of fleas (particularly the Oriental rat flea *Xenopsylla cheopis*) [*1,2*]. Microscopic examination of infected fleas reveals large masses of bacteria in their stomachs. The bacterial masses eventually block passage of the victim's blood and when blockage occurs, bacteria are regurgitated into the wound and passed in the feces of the flea. Fortunately, the rat flea prefers the rat as a host but, if the rat dies, the flea seeks a new warm-blooded host. The nearest warm-blooded animal may be man, and when man is infected the symptoms are those of many febrile diseases and include fever, malaise, tachycardia, headache, vomiting, lymphadenopathy, delirium, and shaking chills. The flea bite is rarely seen, and if it is present a papule or vesicle is identified which is usually pustular. Sixty to seventy-five percent of lymphadenopathy occurs in the inguinal areas because the majority of flea bites occur on the legs. Enlarged inguinal nodes were named buboes, but the use of this term has been expanded to include other lymph node groups as well. Plague occurs in three forms: bubonic, septicemic (bacteremic), and pneumonic. Bubonic plague is now the most common form seen in man and fever, malaise, and buboes are the usual symptoms. Proliferation of plague organisms produces enlargement of the lymph node and the organisms may escape into the circulation, causing septicemia (bacteremia). Organisms may be trapped in the lungs, resulting in secondary plague pneumonia. The pneumonic form can result in man-to-man infection by aspiration of infected exhaled droplets from a plague victim and this mode of transmission potentially can produce an epidemic (primary plague pneumonia) [*3*]. The last cases of primary plague pneumonia occurred in California in 1924 [*4*]. Unfortunately, pulmonary findings in plague pneumonia may be lacking until the final day when the victim coughs up copious bloody sputum. In bubonic plague, the disease can be transmitted from man to man by the human flea, *Pulex irritans*. If septicemia occurs, subcutaneous hemorrhages can occur which, if massive, impart a "black" color to the patient and therefore the term "Black Death" evolved.

Plague that occurs in rodents (sylvatic plague) serves as the reservoir of the disease. Sylvatic plague was first observed in California in 1908 and spread eastward into Arizona, New Mexico, Oklahoma, Texas, and Kansas. Between 1925 and 1948 nearly 80% of plague

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cases occurred in California, but since 1949 almost 90% of the cases occurred in New Mexico, Arizona, Utah, and Colorado [*4*]. Sylvatic plague is present throughout New Mexico, but human cases have occurred primarily in the north central portion of the state, with six counties accounting for 80% of New Mexico human cases.

Sylvatic plague was first detected in New Mexico in 1938. Since that time infected animals have been found in 27 of the state's 32 counties. Carnivores such as coyotes can be infected with plague, but these animals rarely serve as sources of human infection. Human cases may result from the skinning or evisceration of plague-infected animals. Domestic dogs and cats often play an important role in the epidemiology of plague. These domestic carnivores, when allowed to run loose, may come into contact with infected wild animals and the infected fleas may be transported to the pet owner's house [*3*]. The residents of the home may thus be exposed to plague. The frequent use of flea powders on domestic carnivores during the plague season should decrease the possibility for this mode of transmission. Approximately 85% of all plague cases occur in the summer (June through September), but out-of-season cases can occur when an infected animal is skinned.

Plague is primarily a disease of the young in New Mexico. The incidence for persons less than 20 years old was four times the rate for persons 20 years and older during 1965 to 1976. In 1949 human plague was first diagnosed in New Mexico in Taos and since 1949 a total of 78 cases have been reported with 12 deaths (Fig. 1).

In New Mexico, the medical investigator has the legal authority to autopsy persons suspected to have died from infectious or contagious disease wherein the diagnosis and extent of disease are undetermined at the time of death. Since the inception of the statewide Office of the Medical Investigator of New Mexico in 1973, three persons dying with plague have been autopsied and those findings will be presented and discussed.

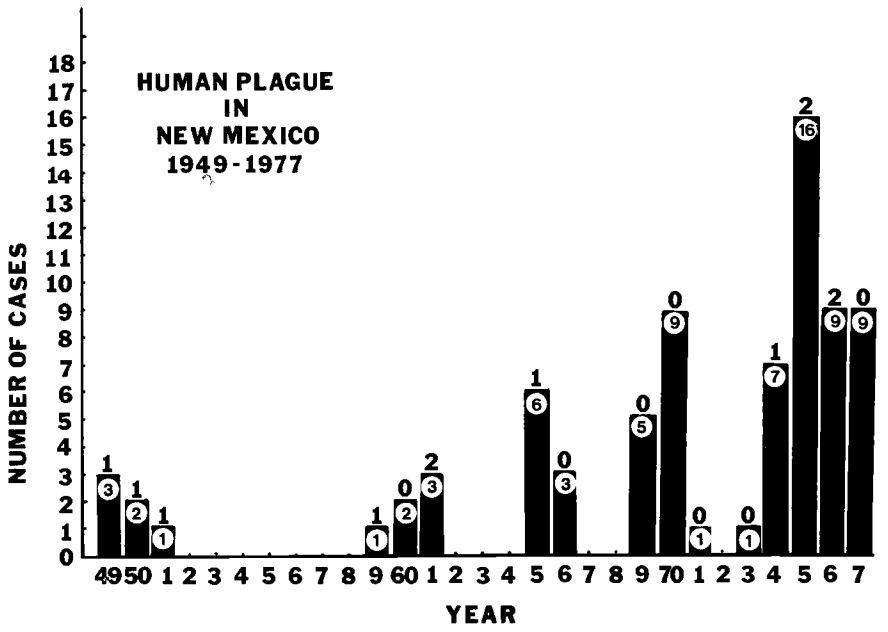

FIG. 1—*Diagram representing human plague cases in New Mexico from 1949 to 1977. The numbers inside the bars represent case numbers for that year and the numbers above the bars represent the number of deaths during that year.*

Case Reports

Case 1

A 13-year-old rural northwestern New Mexico Indian girl complaining of headache and malaise was taken on 27 June 1974 to a clinic where she was noted to have a temperature of 40°C (104°F) (Table 1). Physical examination revealed a tonsillar exudate. The remainder of the physical examination and a chest X-ray were negative. The patient was treated with Bicillin® and told to return to the clinic. The girl returned to the clinic on 28 June 1974 with fever (39°C or 102°F), vomiting, and malaise. The white blood cell count was 52 700 with 48% segmented neutrophilic bands, 5% monocytes, and 33% lymphocytes. Platelets were reported to be adequate. Physical examination revealed no petechiae and absence of nuchal rigidity. Before a thorough physical examination could be completed, the girl died despite resuscitative measures.

On 29 June 1974 an autopsy was performed and massive hemorrhagic lymphadenopathy of the left inguinal femoral iliac nodes and marked congestion of the left adrenal medulla were the major findings. Evidence of insect bites was not identified. Touch preparations of the lymph nodes were positive with fluorescent antibody staining for *Y. pestis* (Fig. 2). Blood cultures were also positive for *Y. pestis*.

Lymph nodes histologically demonstrated massive numbers of Gram-negative rod-shaped organisms and hemorrhagic necrosis with moderate acute inflammatory component, and the perinodal adventitial tissues were edematous. The left adrenal gland demonstrated congestion, mild acute inflammation, masses of bacteria in sinusoids, focal necrosis, and a few fibrin thrombi in sinusoids (Fig. 3). Lung sections revealed fibrin thrombi in a few capillaries. A moderate increase in the numbers of polymorphonuclear leukocytes was present in the splenic red pulp. All other organs, including the kidneys, were histologically unremarkable.

Case 2

A 3-year-old rural northwestern New Mexico Indian girl was taken to a local hospital by her mother on 2 Aug. 1975 (Table 1). She was found to be febrile (40°C or 104°F) and restless with slightly swollen inguinal lymph nodes. The white blood cell count was 15 000 with 60% segmented neutrophils and 26% neutrophilic bands. Platelets were reported to be adequate. Electrolytes were normal. The child was kept in the hospital for several hours during which time she was treated for fever and blood cultures were taken. Later that day the child improved and she was released from the hospital. The following day, the fever was down and the child seemed better to the parents. On 4 Aug. 1975 the child again was febrile and she was taken back to a local hospital where she had marked respiratory difficulty. Mouth-to-mouth resuscitation was attempted but the child died.

An autopsy was performed on 5 Aug. 1975. No insect bites were identified on the skin. The major finding in this case was massive hemorrhagic lymphadenopathy of the inguinal, femoral, external iliac, and mesenteric lymph nodes (Fig. 4). The nodes measured to 1.5 cm in diameter, and all were hemorrhagic but none were suppurative. Lymph node touch preparations demonstrated large numbers of *Y. pestis* organisms with fluorescent antibody staining (Fig. 2). Blood cultures were also positive for *Y. pestis*. Frozen sections were made of the lungs and no evidence of pneumonia was present. Lung cultures were negative, and touch preparations of lymph nodes stained with fluorescent antibody were negative for plague organisms.

Histologically, lymph nodes revealed hemorrhagic necrosis with massive numbers of Gram-negative organisms with mild acute inflammatory infiltrate (Fig. 5). Masses of Gram-negative organisms were present in blood vessels in the perinodal soft tissues (Fig. 6). A few fibrin thrombi were present in the pulmonary capillaries (Fig. 7). A marked increase in the

TABLE 1—*Case data.*

Case	Age	Sex	Race	Presenting Symptoms	Disease Duration, days	Autopsy Findings
1	13	f	American Indian	fever, headache, malaise	1	massive hemorrhagic lymphadenopathy of inguinal iliac and femoral chains; congestion of left adrenal medulla; few fibrin thrombi in lungs and left adrenal; acute splenitis
2	3	f	American Indian	fever, restlessness, mild bilateral inguinal lymphadenopathy	2	massive hemorrhagic lymphadenopathy of inguinal, iliac, femoral, and mesenteric lymph node groups; few fibrin thrombi in lungs; acute splenitis
3	15	m	white	fever, headache, malaise	4	acute pneumonia; moderate hemorrhagic lymphadenopathy of inguinal and paraortic chains; fibrin thrombi in kidneys, adrenals, liver, and lungs; small hepatic abscesses; acute splenitis

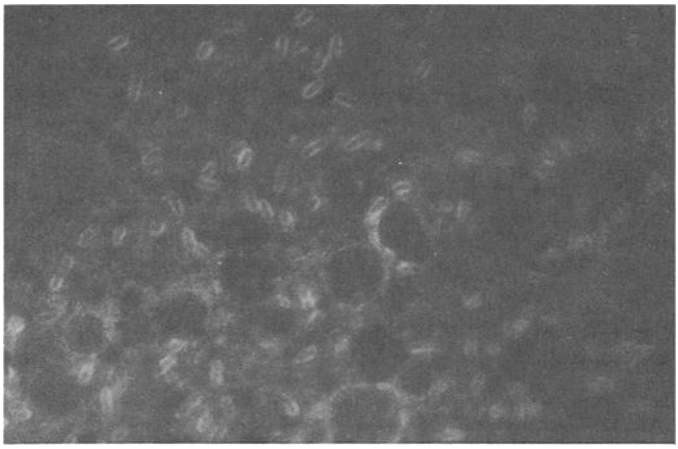

FIG. 2—*Direct immunofluorescent stain for* Y. pestis *on bubo aspirate smear. Organism capsules are outlined by fluorescent staining (magnification, approximately ×620).*

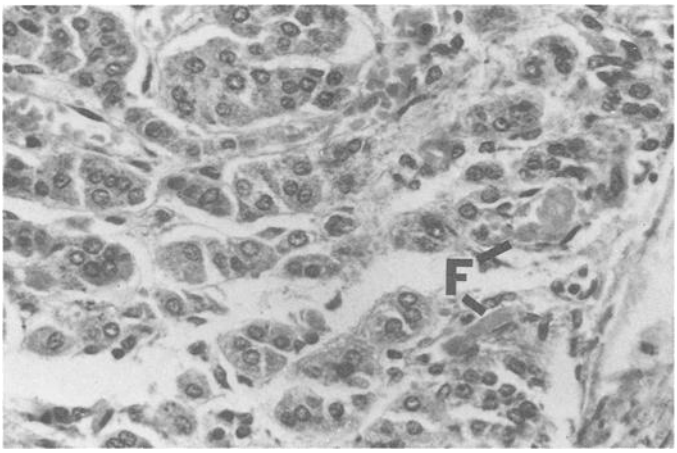

FIG. 3—*Section of adrenal gland with fibrin thrombi in sinusoids* (F) *(magnification, approximately ×225; hematoxylin and eosin stain).*

numbers of polymorphonuclear leukocytes with fibrin strands were present in the splenic red pulp. The lungs, adrenals, and kidneys were congested, but all other organs were unremarkable.

Case 3

A 15-year-old white male went on a family picnic in the Sandia Mountains near Albuquerque, New Mexico, on 14 Aug. 1976 and reportedly came into contact with a chipmunk (Table 1). On 15 Aug. 1976 the youth presented with fever (39°C or 102°F), headache, and malaise to a local emergency room. Physical examination was negative. None of the other family members were ill. He was treated for fever and released.

On 16 Aug. 1976 he returned to a local hospital with fever (40°C or 104°F), occipital

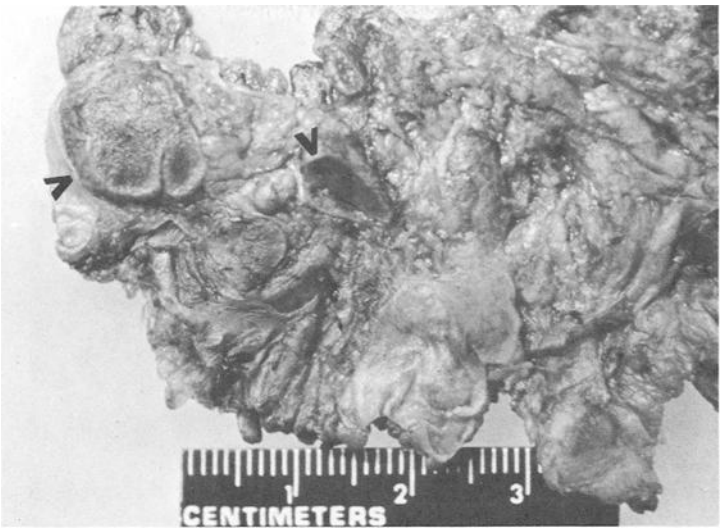

FIG. 4—*Enlarged mesenteric lymph nodes* (arrowheads) *from Case 2.*

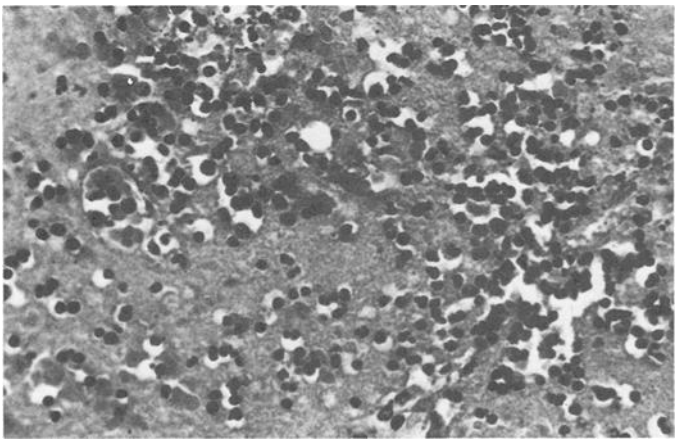

FIG. 5—*Section demonstrating massive numbers of organisms (small granular areas) and hemorrhagic necrosis in lymph node (magnification, approximately ×225; hematoxylin and eosin stain).*

headache, and malaise. The white blood cell count was 7000 with 65% segmented polymorphonuclear leukocytes. A throat culture was taken.

On the following day, 17 Aug. 1976, a tender left inguinal mass appeared and the patient continued to have a temperature ranging from 39 to 40°C (102°F to 104°F) with partial relief with acetaminophen.

The youth was admitted to the hospital for further evaluation on 8 Aug. 1976. The white blood cell count was 7500 with 82% segmented neutrophilic leukocytes. Physical examination revealed four to six tender, enlarged left inguinal lymph nodes. The throat culture was reported positive for β-hemolytic streptococci, and the patient was given oral penicillin. A blood culture was taken.

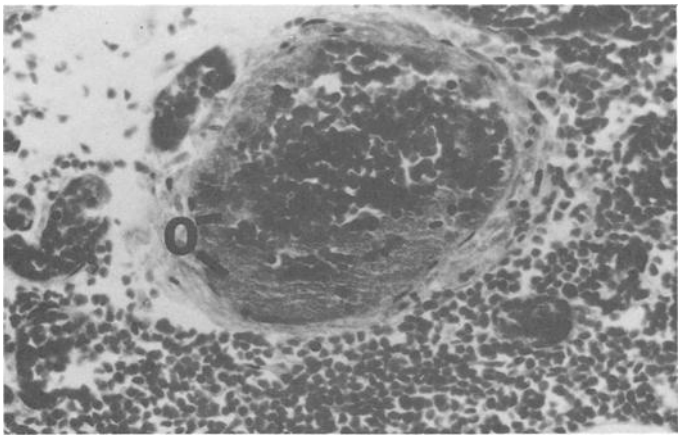

FIG. 6—*Section revealing vein packed with plague organisms* (O) (*magnification, approximately* ×*225; hematoxylin and eosin stain*).

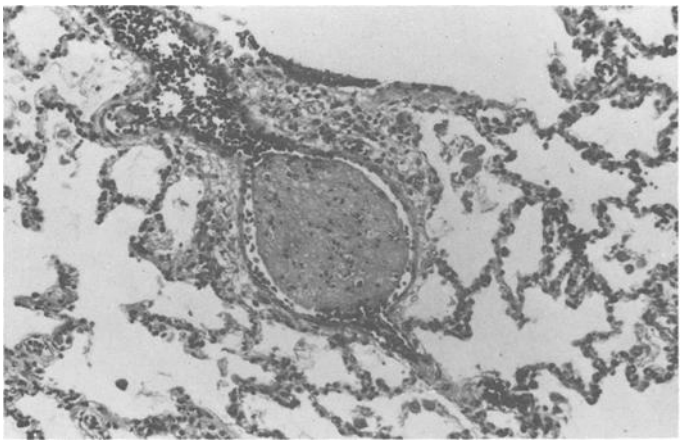

FIG. 7—*Section of lung demonstrating a fibrin thrombus* (*magnification, approximately* ×*320; hematoxylin and eosin stain*).

On 19 Aug. 1976, fever, lassitude, and tender left inguinal nodes were still present. The white blood cell count was 20 200 with 85% segmented neutrophilic leukocytes. A left inguinal node was aspirated and blood cultures were obtained. The aspirate revealed Gram-negative bacilli that demonstrated bipolar staining with Wayson's stain. The patient was given streptomycin with a working diagnosis of plague. Dark stools demonstrated 4+ occult blood. The partial prothrombin time was 45.4 s (31.9 s control), prothrombin time was 12.9 s (11.9 s control), platelets were 100 000/mm^3 and 48 000/mm^3 later, and the fibrinogen level was 843 mg/100 ml. The patient became progressively dyspneic, his blood pressure dropped to 86/54 mm/Hg, and he had one episode of light brown emesis. The patient suffered a cardiorespiratory arrest and died despite resuscitative measures.

An autopsy performed on 20 Aug. 1976 demonstrated pulmonary edema, bilateral pleural effusions, hemorrhagic lymphadenopathy of the inguinal and paraortic chains, epicardial petechiae (Fig. 8), and altered blood diffusely throughout the gastrointestinal tract.

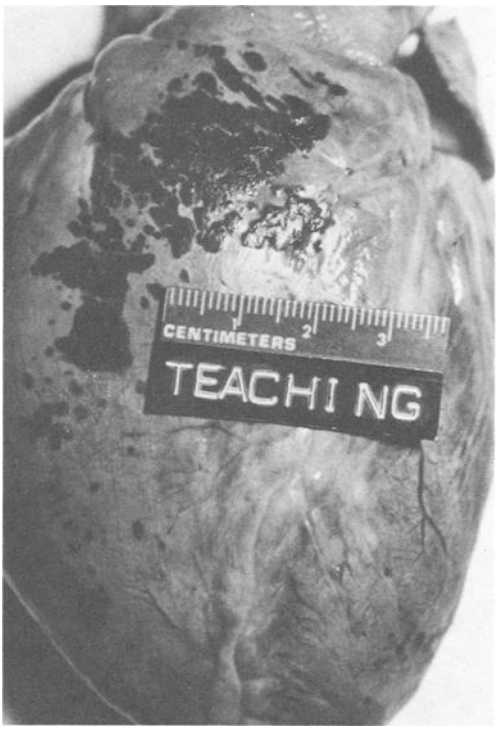

FIG. 8—*Heart from Case 3 demonstrating confluent epicardial petechial hemorrhages.*

Evidence of insect bites was not identified. Touch preparations of the lungs and lymph nodes were positive for *Y. pestis* with fluorescent antibody stains (Fig. 2). Blood cultures were also positive for plague organisms.

Lymph nodes histologically revealed hemorrhagic necrosis and acute inflammation with massive numbers of Gram-negative organisms (Figs. 5 and 9). Sections of the lungs demonstrated acute pneumonia (Fig. 10) with masses of Gram-negative bacteria and a few fibrin thrombi in pulmonary capillaries (Fig. 11). Fibrin thrombi distended many renal capillary loops (Fig. 11). Fibrin thrombi were also noted in the adrenal central vein radicals (Fig. 12) and hepatic vein radicals. Small hepatic abscesses (Fig. 13) with masses of Gram-negative bacteria were present. A moderate increase in polymorphonuclear leukocytes was present in the splenic red pulp. Sections of other organs were unremarkable.

Discussion

Since 1961, human cases of plague in New Mexico have tended to follow a 4- or 5-year cycle, with peaks occurring in 1961, 1965, 1970, and 1975 (Fig. 1). Reasons for this cycle are not yet clear. The number of cases during these peak years has increased, with 3 cases in 1961, 6 cases in 1965, 9 in 1970, and 16 cases in 1975. The 1975 peak represented a 30-year high for case incidence in one year in any state [5].

Of the 1975 New Mexico plague cases, 75% (twelve patients) had clinical buboes. In the four cases without buboes, two patients had secondary plague pneumonia, one had plague meningitis, and one had septicemic plague. The patient with meningitis recovered. One patient with pneumonia recovered and a teenage male with pneumonia died in California. The 1975 septicemic case was described above (Case 2). Initial laboratory studies often reveal

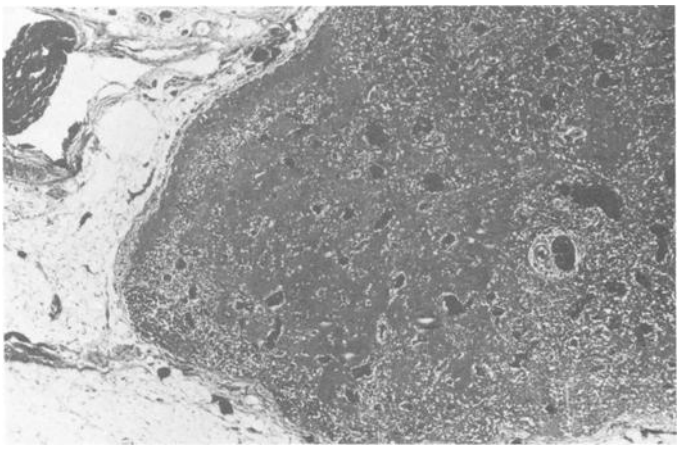

FIG. 9—*Section of a bubo revealing massive numbers of plague organisms (dark gray amorphous areas) and congestion of blood vessels (magnification, approximately ×55; hematoxylin and eosin stain).*

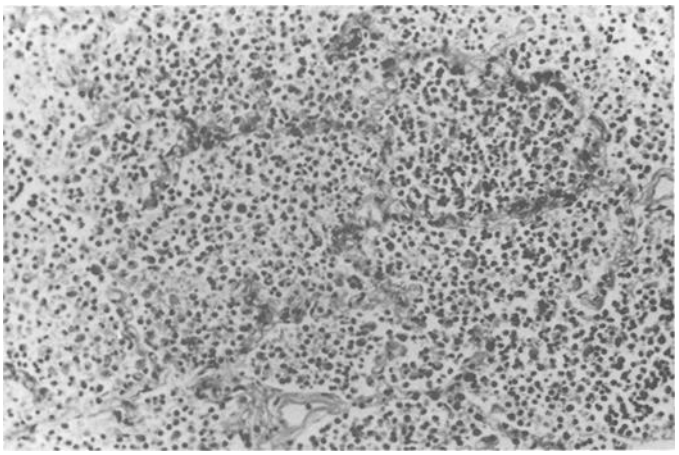

FIG. 10—*Lung section from Case 3 demonstrating acute inflammatory cells in alveoli (magnification, approximately ×110; hematoxylin and eosin stain).*

leukocytosis with a left shift; however, in 1975, only ten New Mexico patients (60%) had white blood cell counts greater than 10 000/mm^3.

The incubation period is two to six days, and if the disease is untreated death occurs in 50 to 90% of plague cases within ten days of the onset of symptoms. Early diagnosis and treatment with tetracycline or streptomycin, or both, are essential. With early treatment, the mortality rate may be reduced to 5 to 10%. Bacteriologic diagnosis may be made by blood cultures, aspiration of buboes followed by stained smears and cultures, cultures and smears of internal organs (especially the spleen), and fluorescent antibody staining of smears (Fig. 2). The fluorescent antibody stain is highly specific for *Y. pestis* but other *Yersinia* species may produce false-positive staining because of similarities of capsular antigens. The bipolar ("safety pin") appearance can best be demonstrated by using Wayson's or Giemsa's stains

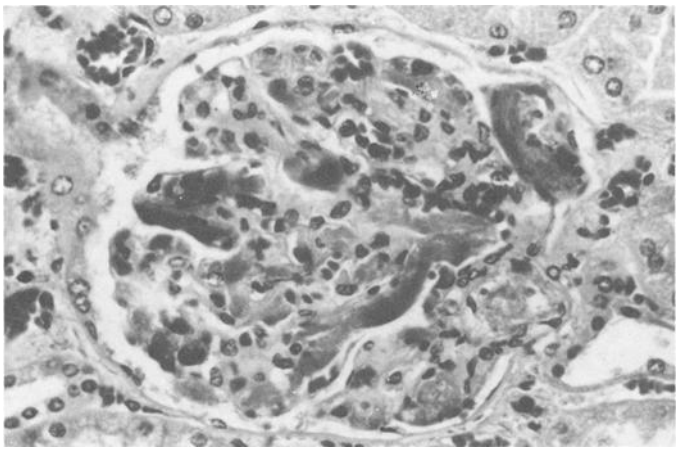

FIG. 11—*Kidney section from Case 3 revealing fibrin thrombi in glomerular capillaries (magnification, approximately ×225; hematoxylin and eosin stain).*

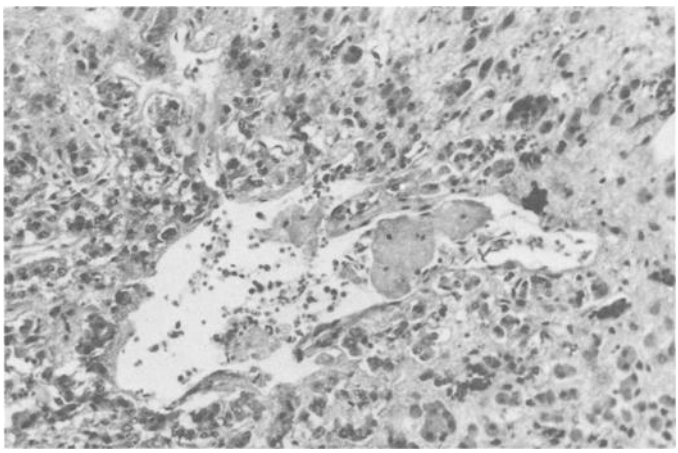

FIG. 12—*Section of adrenal with fibrin thrombus in central vein (magnification, approximately ×110; hematoxylin and eosin stain).*

[*1*]. Occasionally, the diagnosis cannot be confirmed bacteriologically, and if the patient dies autopsy may reveal the diagnosis but strict autopsy precautions must be exercised (Table 2).

The presence of fibrin thrombi (confirmed by phosphotungstic acid-hematoxylin staining) in all three cases is in agreement with the findings of Finegold [*6*], who reported fibrin thrombi in four of seven autopsied plague cases. Those four cases were all children with ages ranging from 4 to 14 years; the three adults in his series did not demonstrate fibrin thrombi. All of the cases in our series were children from 3 to 15 years old (Table 1).

In 1977, Dr. Boyd Stephens, chief medical examiner-coroner, San Francisco, California, autopsied a white male who died of pneumonic plague without buboes identified or the source of infection elucidated. The patient had been admitted with a diagnosis of disseminated intravascular coagulation (DIC) to a hospital two days prior to death. At autopsy only a few pulmonary fibrin thrombi attested to the clinical diagnosis of DIC.

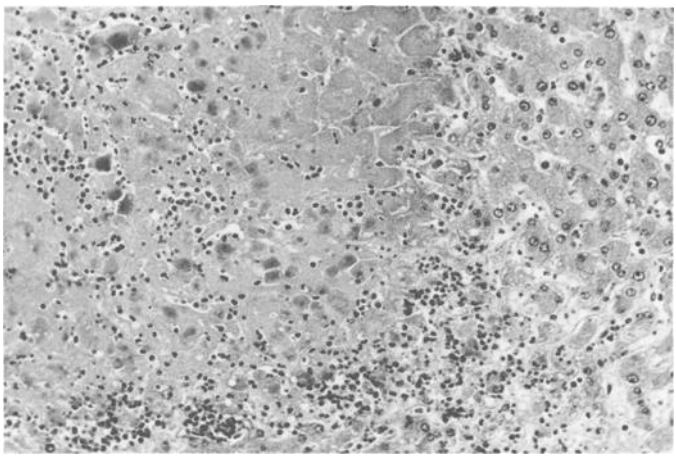

FIG. 13—*Liver section from Case 3 demonstrating abscess formation (magnification, approximately ×110; hematoxylin and eosin stain).*

TABLE 2—*Plague autopsy precautions.*

These procedures should be supervised by a microbiologist.

a. The autopsy room must be completely sealed off.

b. Doors, windows, ventilation ducts, and so forth must be covered and taped to avoid contamination.

c. Water must be off during the autopsy to avoid microbial aerosolization.

d. Instruments to be used should be capable of being autoclaved or disposable.

e. Instruments and equipment not necessary for the autopsy should be removed from the room.

f. A minimum number of persons should be involved in the autopsy, preferably only the pathologist and one assistant. A scrub suit, gown, shoe covers, surgical cap, double surgical mask, and double gloves should be worn by those in contact with the body.

g. During the procedure, extra care must be taken to avoid accidental puncture wounds and aerosolization of tissue particles.

h. The autopsy must be meticulous and thorough, yet rapid enough to avoid prolonged exposure to organisms.

i. Upon completion of the autopsy, the body should be wiped with a standard hospital antibacterial solution and double bagged.

j. The body should not be embalmed (to avoid further human contact) and should be promptly cremated or buried.

k. All instruments and equipment must be autoclaved or treated with approved antibacterial solutions in appropriate concentrations for at least 30 min and then air dried.

l. The walls, floors, doors, and tables must be wiped down with similar antibacterial solutions.

m. All clothing worn must be deposited in decontamination containers. All contaminated materials must be properly handled by microbiology technicians.

n. As a prophylactic measure, tetracycline capsules should be administered (for a period of ten days) to those involved with the autopsy.

Fibrin thrombi do not represent a new discovery in plague pathology. Herzog [*2*] described glomerular fibrin thrombi in 7 of 20 plague cases from a Philippine epidemic in 1904. Observers of the Manchurian (1910 to 1911) [*8*] and Manilan (1912 to 1914) [*9*] plague epidemics also found glomerular fibrin thrombi.

Finegold [*6*] postulated that the similarity of the fibrin thrombi distribution in autopsied human cases to those lesions seen in the generalized Shwartzman reaction in experimentally produced plague in monkeys [*10*] suggested that lipopolysaccharide endotoxins of the plague

organism may play a major pathogenic role in the disease. This thesis was supported by the clinical plague study of Butler [*11*], who found 11 of 35 plague patients to have evidence of DIC based on decreased platelet counts, prolonged partial thromboplastin times, and positive ethanol gelation tests, which detect circulating fibrin monomers.

Case 3 (Table 1) demonstrated clinical as well as morphological [*12,13*] evidence of DIC with decreased platelets, prolonged partial thromboplastin and prothrombin times, and presence of occult blood in the stool. The fibrinogen level was elevated, which could be a result of the overwhelming sepsis. Infection has been postulated as a possible mechanism of increasing fibrinogen production [*10,14*]. Finegold et al [*10*] noted a striking rise in the fibrinogen levels as the infection progressed in plague-infected monkeys. Simon et al [*15*] found fibrinogen turnover to be increased more than three times normal in burn patients.

The pathological findings of the cases presented in this report (especially Case 3) lend support to the premise that DIC can be a major factor in the pathogenicity of plague.

Summary

Plague is a deadly disease of obvious concern to individuals, communities, and public health officials. The rapid recognition of plague victims is of paramount importance in saving the lives of the victims and in the protection of contacts.

Three autopsied plague cases have been presented and the pathological features have been discussed.

Acknowledgments

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