

Yersinia pestis:
antibiotic choices
and attenuated strains and disease

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Primary Clinical presentation – naturally acquired

- Bubonic 78-84%
- Septicemic 10-25%
- Primary pneumonic 2-5%

- Meningitis involvement (1.5 – 6%) – most commonly associated with improper and/or inadequate primary antibiotic treatment for plague.

Perry and Featherstone 1997. Clin Microbiol Rev 10:35

Butler T 1989. Trans Roy Soc Trop Med Hyg 83:458

Prentice and Rahalison 2007. Lancet 369:1196

Plague in US (1970-1979) - 105 cases

- Meningitis, as evidenced by Yp in CSF, was reported in 6(6%) of these cases 9-14 days after onset
- All 6 patients (3 bubonic, 3 septicemic) received antibiotic therapy (penicillin, streptomycin, tetracycline) before meningitis developed
- 4 of 6 were successfully treated with chloramphenicol, 1 treated with iv ampicillin, 1 died prior to Yp diagnosis

Becker TM et al., West J Med 1987 147:554

Plague in New Mexico (1985 – 1999) - 75 cases

1 developed meningitis 6 days after clinical presentation and initiation of tetracycline treatment. Patient successfully treated with chloramphenicol and gentamicin

Boulanger LL, et al 2004 CID 38:663

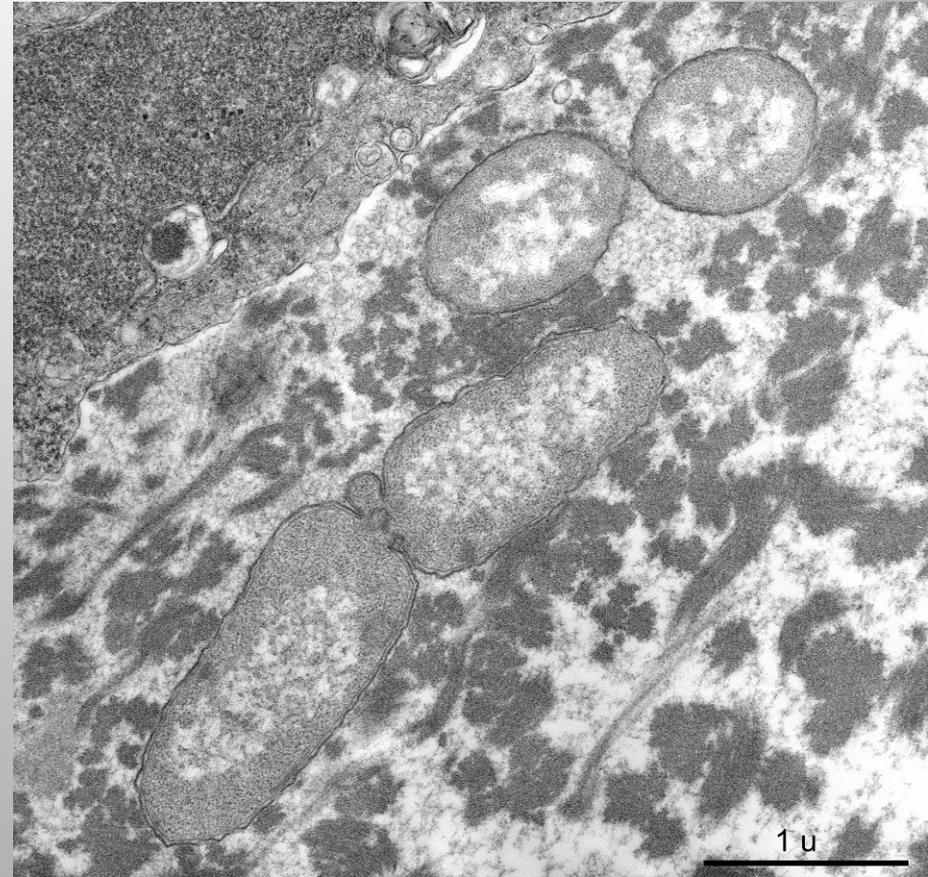
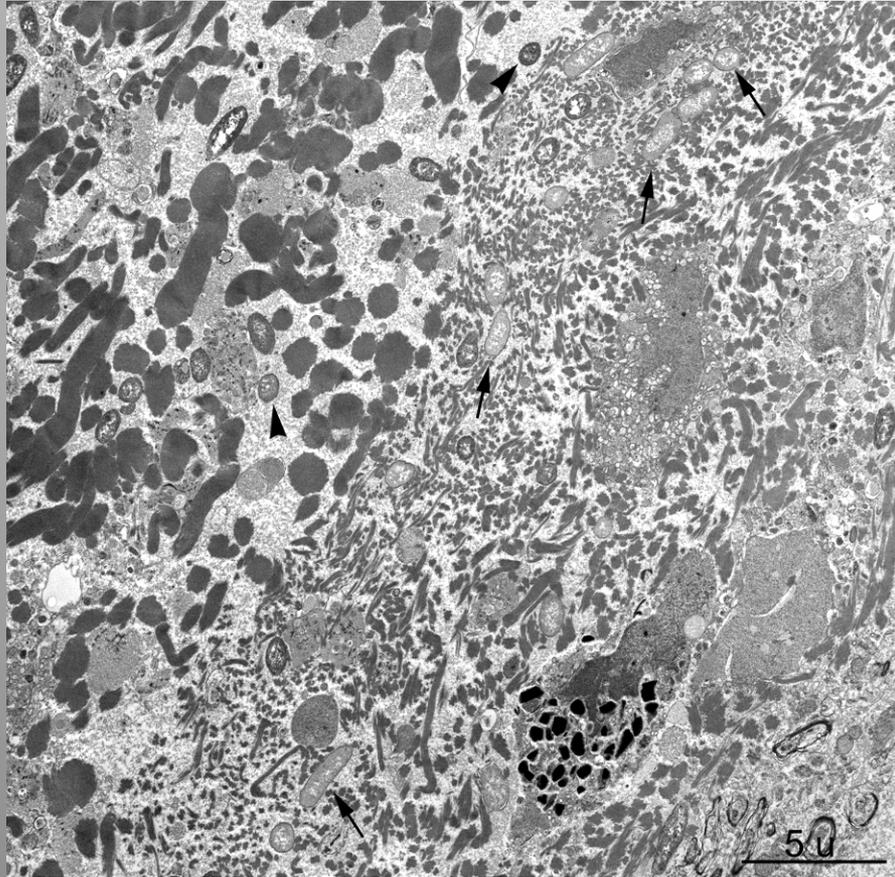
Plague in US (1960-2006) - 446 cases

18 (4%) with meningitis reported

CDC, unpublished

AZ, 2008 - Fatal Plague Case

widespread tissue/organ dissemination of Yp



Yp in meninges

Attenuated *Y. pestis* strains

Disease agents in animals or humans?

- Lcr⁻ complete loss of virulence by intranasal, i.v., and s.c. routes in mice

Lathem WW et al. 2005. PNAS 102:17786

Une and Brubaker 1984 .I&I 43:895

pgm⁻ virulence is animal/species and inoculation route dependent

- mice

- s.c. highly attenuated ($LD_{50} >10^7$)
- i.v. Virulent ($LD_{50} = 1-10$)

- **NHP** (species variation)

- Virulent in African green monkeys, langurs, grivets (aerosol $LD_{50} = 10^4-10^5^*$, s.c. $LD_{50} = 10^5 -10^7$)
- Attenuated in rhesus

Welkos S et al. 2002 Vaccine 20:2206; Meyer KF et al. 1974 JID 129:S85; Une and Bruubaker 1984. I&I 43:895;

Perry and Fetherston 1997. Clin Microbiol Rev 10:35