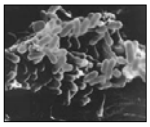
Slide 1	Typhus *Gaol Fever, Epidemic Typhus Tabradillo, War Fever, Jail Fever*	Other common names associated with typhus are Brill-Zinsser disease, classical typhus, European typhus, tabardillo, war fever, jail fever, European, classic, or louse-borne typhus. This is a different disease than typhoid fever, which is caused by *Salmonella typhi*.
Slide 2	**Overview** • Organism • History • Epidemiology • Transmission • Disease in Humans • Prevention and Control Center for Food Security and Public Health Iowa State University - 2004	In today's presentation we will cover information regarding the organism that causes typhus and its epidemiology. We will also talk about the history of the disease, how it is transmitted, species that it affects, clinical and necropsy signs observed. Finally, we will address prevention and control measures and typhus as a biological weapon.
Slide 3	The Organism	
Slide 4	**The Organism** • *Rickettsia prowazekii* – Obligate intracellular bacteria – Pleiomorphic rods – Susceptible to moist heat and dry heat  Center for Food Security and Public Health Iowa State University - 2004	Like other *Rickettsia* species, *R. prowazeki* is an obligate intracellular bacteria in both its mammalian and arthropod host, the human body louse. It forms pleiomorphic rods and *R prowazekii* is susceptible to moist heat (121 ^{o}C for at least 15 minutes) and dry heat (160-170 ^{o}C for at least one hour). The organism can remain viable in louse fecal material for several weeks, but is destroyed by proper disinfections. Photo of *Ricketsia prowazekii*, http://www.nature.com/genomics/papers/r_prowazekii.html
Slide 5	History	

Slide 6

History

- 1489: Arrival in Europe
  - Soldiers returning from Cyprus
- 1557-59: Outbreak in England
  - Killed 10% of the population
  - Poor sanitation
- 1880
  - Typhoid bacillus identified

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Typhus arrived in Europe in 1489 with soldiers who had been fighting in Cyprus. An outbreak in 1557-59 killed about 10% of the English population. Typhus mainly killed poor people living in places where sanitary conditions were very bad. It was also a common disease in prisons and for this reason typhus was also known as gaol fever (gaol is an Old English word for jail). The typhoid bacillus was first identified in 1880.

Slide 7

History

- 17th-19th century
  - Epidemics in Europe as a result of war, disaster, or in prisoners
- 1909: Transmission by lice
- 1917-1925: Russia
  - Estimated 25 million cases
- End of WWII
  - DDT used for control
  - Vaccine developed

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Epidemics of typhus occurred throughout Europe from the 17th to the 19th centuries. Widespread epidemics occurred during the Napoleonic Wars and the Irish Potato famine of 1846 to 1849. Charles Jules Henri Nicolle a Frenchman received the Nobel Prize for his work on typhus in 1928. He demonstrated that the transmission of typhus was by the human body louse. During World War I the disease caused three million deaths in Russia and more in Poland and Romania. Later epidemics were avoided due to the discovery of DDT. A vaccine was also developed in World War II, and today epidemics mainly occur in Eastern Europe, the Middle East and parts of Africa where living conditions and hygiene are poor. Image: A U.S. soldier is demonstrating DDT-hand spraying equipment while applying the insecticide. The use of DDT increased enormously on a worldwide basis after WWII, because of its effectiveness against the mosquito that spreads malaria and lice that carry typhus. The World Health Organization claims that the use of DDT saved 25 million lives. Decline in the use of DDT began the 1970's and was attributed to a number of factors including increased insect resistance, development of more effective alternative pesticides, growing public and use concern over adverse environmental side effects and increased government restriction. The lower photo shows a typhus ward after the liberation of the prison camps in WWII. fcit.coedu.usf.edu/holocaust/ PICS31/16951.jpg

Slide 8

Epidemiology

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Slide 9

Epidemiology

- United States
  - 30 cases since 1975
- Africa
  - 1997: Burundi 1997
    - 20,000 cases from Jan. to March
- Most common in people living under unhygienic conditions
  - Refugee camps

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Thirty cases of typhus have been documented in the United States since 1975. Most outbreaks of typhus however, occur in Africa; mainly Burundi, Ethiopia and Rwanda. In Ethiopia, the number of cases reported annually has ranged between 7,000 and 17,000. Most of these cases have not been confirmed in a laboratory. In the 1970s, major epidemics in Burundi and Rwanda were documented by serology and isolation. In 1975, 9,000 cases were reported in Burundi. In 1996, Burundi reported 3,500 cases. The number for 1997 was reported at 20,000 from January to March. The disease most commonly occurs in people who are living under poor hygienic conditions, such as refugee camps. Photo of refugees in Rwanda and Burundi who have fallen victim to typhus. http://news.bbc.co.uk/1/hi/sci/tech/212548.stm

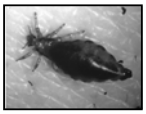
Slide 10

Transmission

Slide 11

Transmission

- Human body louse
  - *Pediculus humanus corporis*
  - Infective for 2-3 days
  - Infection acquired by feeding on infected person
  - Excrete *R. prowazeki* in feces at time of feeding
  - Lice die within 2 weeks



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There are several species of human louse, it is only the body louse that is responsible for transmitting typhus. The louse may take a new blood meal as often as every 5 hours. After ingestion, rickettsiae multiply in the gut epithelial cells of the louse. During the multiplication process the gut cells rupture. The organisms are excreted in the feces of the louse within 2-6 days or earlier if crushed. The louse generally spends its entire life cycle on the same host. If overcrowding occurs the louse may relocate to a new host. Lice remain infective for 2-3 days and acquire the organism from taking a meal from an infective person. People remain infective during the febrile phase of illness and possibly for 2 to 3 days after the temperature returns to normal. The louse dies within 2 weeks after infection, the ricketsiae may remain viable in the dead louse for weeks and may remain infective in the feces for 2-3 days longer. Photo of human body louse, http://www.icrlab.com/BodyLouse.html

Slide 12

Transmission

- Louse feces rubbed into bite or superficial abrasions
- Inhalation of feces
- Sylvatic typhus
  - Flying squirrel
  - 30 human cases in eastern and central U.S.

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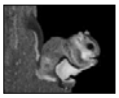
Human infection occurs when *R. prowazekii* are rubbed into the bite wound or a superficial abrasion. Inhalation of *R. Prowazekii* from the infective lice feces may also occur. In 1975, in the United States, a new sylvatic (wild animal) host was found for typhus. The flying squirrel, *Glaucomys volans*, in the eastern United States have been found to act as a host to *R. prowazekii*, in addition to humans. Approximately 30 documented cases of typhus have been reported in the central and eastern United states and these infections are thought to have occurred from transmission of the flying squirrel. Most human infection occurs in people over the age of 20. Photo of human body louse, http://cornellcollege.edu/biology/insects/damonkat/L.HTM

Slide 13

Transmission

- Humans or flying squirrel required for life cycle
  - Organism dies with louse
  - Not transferred transovarially
  - Host responsible for maintaining infection
- No person-to-person transmission



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Humans or the flying squirrel are required for the life cycle of *R. prowazekii*, otherwise the organism dies with the louse. The bacteria that cause typhus are not passed transovarially. Person-to-person transmission is not known to occur. Photo of flying squirrel photo courtesy of P. Myers, http://animaldiversity.ummz.umich.edu/accounts/glaucomys/g._volans$media.html#photos

Slide 14

Disease in Humans

Slide 15

Clinical Symptoms

- Incubation: 7-14 days
- High fever, chills, headache, cough, severe myalgia
  - May lead to coma
- Macular eruption
  - 5-6 days after onset
  - Initially on upper trunk, spreads to entire body
    - Except face, palms and soles of feet

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The incubation period for typhus is generally 12 days. It is often characterized by the sudden appearance of headaches, chills, prostration, high fever, coughing and severe muscular pain. On the fifth to sixth day, a macular eruption (dark spot on the skin) appears initially on the upper trunk, it spreads to the entire body except, the face, palms and soles of the feet. The disease progresses with a high fever that continues for approximately two weeks. Additional symptoms may include severe headaches, bronchial disturbances, and mental confusion. Typhus is from the Greek word "typhos" meaning stupor which may explain the connection with mental confusion .

Slide 16

Diagnosis

- Initial diagnosis
  - Clinical signs and history
  - Laboratory tests not diagnostic
- Confirmatory diagnosis
  - Culture
  - Serology
  - Biopsy
  - PCR

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No laboratory test is diagnostic in the early phases of infection with typhus. Diagnosis is usually suspected based on the symptoms and a history consistent with typhus infection. Confirmatory diagnosis can be made by culture, serology, biopsy and polymerase chain reaction; however, at least 1 week might pass before patients mount a demonstrable immune response that can be measured serologically. Cultures are only available in specialized laboratories, biopsy of either an eschar or the generalized skin rash can lead to a definitive diagnosis based on the appropriate histopathological changes or the presence of the organism using fluorescent antibody conjugates. Indirect IFA and ELISA tests can be used to confirm a diagnosis of typhus, but they do not identify the various rickettsial species. Polymerase chain reaction amplification of rickettsial DNA of serum or skin biopsy specimens can be used for diagnosing typhus. Complement fixation is a serological test that can be used to demonstrate which specific rickettsial organism is causing disease by detection of specific antibodies.

Slide 17

Brill-Zinsser Disease

- Occurs years after primary attack
  - Person previously affected or lived in endemic area
  - Viable retained organisms reactivated
  - Milder symptoms
    - Febrile phase 7-10 days
  - Rash often absent
  - Low mortality rate

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Brill-Zinsser disease is a recurrent form of epidemic typhus, occurring years after an initial attack. Affected patients either had acquired epidemic typhus earlier or lived in an endemic area. When a persons immune systems is weak, viable organisms retained in the body are activated, causing recurrent typhus. The mechanism by which the organism remains viable in the host is not understood. Lice that feed on patients with Brill-Zinsser disease may acquire infection and transmit the agent. The disease is sporadic, occurring at any season and in the absence of infected lice. Symptoms of the illness are almost always mild and resemble epidemic typhus with similar circulatory disturbances and include hepatic, renal, and CNS changes. The febrile period lasts about 7 to 10 days. The rash is often absent and mortality is very rare.

Slide 18

Treatment

- Chloramphenicol
- Tetracycline
  - Doxycycline 200mg
- Response within 48 hrs. usually
- Vaccine
  - Developed after WWII
  - Not commercially available

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Chloramphenicol is empirically used for infections due to its broad spectrum effects. Many physicians prefer to use tetracyclines for treatment of typhus because it is inexpensive and has fewer side effects than chloramphenical. Patients generally respond within 48 hours of treatment. Though both an inactive and live vaccine for typhus have been developed they are not commercially available.

Slide 19

Prognosis

- Case fatality rate
  - 1-20% with antibiotic treatment
  - Up to 100% without treatment
  - Increases with age
- One attack usually confers long lasting immunity

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The case fatality rate for typhus is 1-20% with antibiotic treatment and up to 100% without treatment. Mortality is highest in the elderly. One attack of disease generally confers life long immunity, however disease may reappear as Brill-Zinsser disease.

Slide 20

Prevention and Control

Slide 21

Prevention and Control

- Treat clothing and bedding
  - 160 degrees for one hour
- Chemical control
  - Permethrin (0.5%) temephos (2%), popoxur (1%) and carbaryl (5%)
- Biosafety level 3
  - Handling infectious materials, lice, carcasses
- Proper hygiene

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Prevention and control measures for typhus include measures for treating clothing and bedding to kill the bacteria and the infective lice. Expose clothing to 160 degrees one hour. Chemical control measures are also affective. Use Permethrin (0.5%), Temephos (2%), Popoxur (1%) and Carbaryl (5%). These chemicals can either be dusted on to areas or the clothing and bedding can be treated. Lice and flying squirrels infected with typhus should also be handled using biosafety level 3 requirements. Proper hygiene should also be followed to prevent the spread of body lice.

Slide 22

Typhus as Biological Weapon

- Readily available
- Stable in lice feces for weeks
- Aerosolized
- World Health Organization
  - 50kg of aerosolized typhus
  - City of 5 million would result in
    - 300,000 people exposed in 30 minutes
    - 125,000 people sick
    - 8,000 deaths

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In 1969, the World Health Organization (WHO) estimated that if 50kg of virulent epidemic typhus particles were aerosolized over a city with 5 million people, 300,000 would be exposed downwind from the release, in approximately 30 minutes. The result could be 125,000 illnesses and 8,000 deaths.

Slide 23

Acknowledgments

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Acknowledgments

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