Systemic Bacterial Infections

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Leptospirosis (Weil's disease)

- Leptospirosis is a worldwide zoonosis caused by the spirochaete Leptospira interrogans which is a motile, obligately aerobic spirochaete.
- Leptospira stain poorly but can be visualized on dark- field or phase contrast microscopy.
- There are over 200 serotypes. The main types affecting humans are:
  - L. i. icterohaemorrhagiae (rodents)
  - L. i. canicola (dogs and pigs)
  - L. i. hardjo (cattle)
  - L. i. pomona (pigs and cattle).

Epidemiology

- Leptospirosis appears to be ubiquitous in wild mammals such as rats, dogs, cats, pigs, and cattle, among others, and also in many domestic animals.
- The organisms persist indefinitely in the convoluted tubules of the animal's kidney and are shed into the urine in massive numbers, but infection is asymptomatic in the animal host (most frequently rodents).
- The incubation period is between 2 days and 4 weeks (average 1-2 weeks) and the illness begins abruptly with fever and other symptoms.

Transmission

- Leptospirosis is a water-borne disease mainly transmitted by rodents.
- Leptospires enter a human host through a skin abrasion or intact mucous membranes and also by ingestion of contaminated water.
- The organism can survive for many days in warm fresh water and for up to 24 h in sea water.
- Leptospirosis is an occupational disease of farmers, vets, sewer workers and others who are in potential contact with animals' urine. Flooding-associated outbreaks were also reported.

Clinical features

- First phase (septicemic or bacteremic):

  Positive culture from blood, CSF, and most tissues.

  Lasts from several days up to a week.

  Flu- like illness with fever, chills, headache, and myalgia.

  Improvement for few days ensues during which the patient may become afebrile.

- Second phase (immune or leptospiruric phase):

  Antibodies detected, and organism isolated from urine.

  Features are due to immunological responses to infection and may last up to a month.

- Symptoms can involve multiple different organ systems but 4 main syndromes are recognized.
- *Bacteraemic leptospirosis:*

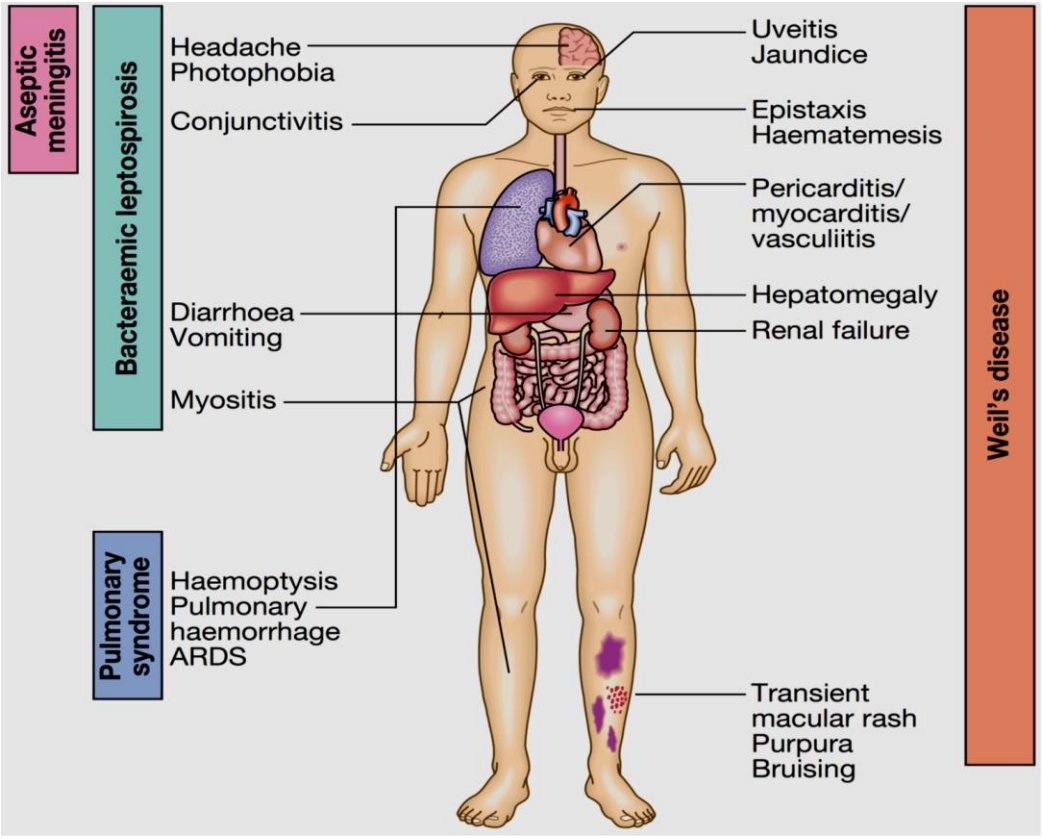
- Febrile illness with weakness, myalgia, headache and photophobia, and sometimes diarrhea/vomiting. Conjunctival congestion is the only notable physical sign.
  The illness comes to an end after about 1 week, or else merges into one of the other forms of infection.

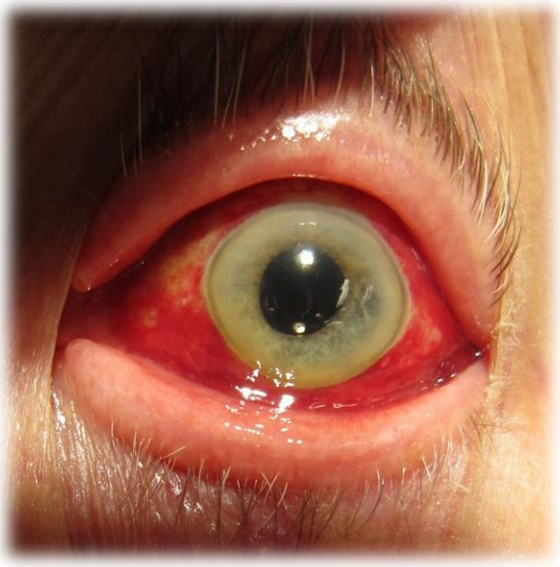
- *Aseptic meningitis:*
  - Difficult to distinguish from viral meningitis. Conjunctival congestion can be a useful sign. Laboratory clues: neutrophil leucocytosis, abnormal LFTs, albuminuria and urine casts.

- *Icteric leptospirosis (Weil's disease):*
  - Occur in < 10% of symptomatic infections. Life-threatening illness, characterized by fever, bleeding, jaundice and renal impairment. Conjunctival hyperemia is a frequent feature. Purpura with large areas of bruising, epistaxis, hematemesis and melena, bleeding into the pleural, pericardial or subarachnoid spaces. Thrombocytopenia (50% of cases). Jaundice is deep and the liver is enlarged. Renal failure, primarily caused by impaired renal perfusion and acute tubular necrosis (oliguria or anuria, albuminuria, hematuria and urinary casts).

- *Pulmonary syndrome:*
  - This is characterized by hemoptysis, patchy lung infiltrates on chest X-ray, and respiratory failure. Total

bilateral lung consolidation and ARDS with multi-organ failure may develop, with a high mortality (over 50%).





Subconjunctival hemorrhage is present in >90% of patients with leptospirosis.

Diagnosis

- Dark field microscopy:
    - Examination of blood, CSF, or urine may demonstrate *Leptospira*, but there is a high false-positive rate (misinterpretation of fibrils, RBCs fragments). It is not recommended.
- Culture:
    - Organisms isolated from blood and CSF in the first week, and from the urine during the second phase of illness. Culture is difficult, insensitive, requires special media and may take several weeks.
- Molecular techniques:
    - Quantitative PCR assays for leptospiral DNA. Sensitive, distinguish different species, allow early diagnosis, and organisms can be detected after starting antibiotic therapy. They are expensive.
- Serology (the mainstay for diagnosis):
    - Antibody tests are diagnostic if seroconversion or a 4 folds increase in titer is demonstrated (end of 1st week onward).
      Microscopic agglutination test (MAT) is the test of choice.
      IgM ELISA, immunofluorescent techniques, and rapid immunochromatographic tests are also available.
- Other tests:
    - CBC: neutrophil leukocytosis, thrombocytopenia

- LFTs: raised ALT, AST, and bilirubin, prolonged PT
- Increased creatine kinase (muscle enzyme)
- CSF: lymphocytosis, raised protein, normal glucose
- Urinalysis: proteinuria, hematuria, cellular casts.

Management and Prevention

- General supportive care:
  - IV fluids and blood transfusion for bleeding and careful attention to renal function, as renal failure is the usual cause of death. Renal failure is potentially reversible with adequate iv fluid support and dialysis.
- Antibiotic therapy:
  - Mild disease: oral doxycycline 100 mg bid for 1 week.
  - Severe disease: IV penicillin G or ceftriaxone for 5-7 days.
- Prophylactic doxycycline 200 mg weekly has been shown to be effective in preventing the disease in military personnel.

Plague

- Plague is caused by *Yersinia pestis*, a small Gram-negative coccobacillus that is spread between rodents by their fleas.
- The main reservoirs are wild rodents, which transmit infection to domestic rats.
- The usual vector is the rat flea. These fleas bite humans when there is a sudden decline in the rat population.
- Hunters and trappers can contract plague from handling rodents.
- In the late stages of human plague, *Y. pestis* may be expectorated and spread between humans by droplets, causing ‘pneumonic plague’.

Clinical features of Plague

	Bubonic	Pneumonic	Septicemic
Transmission	Rat flea bites	Aerosols from rat fleas Person- to- person spread in crowded, unhygienic conditions during epidemics. Complication of bubonic or septicemic plague	Primary infection Complication of bubonic or Pneumonic plague
Diagnostic specimen	Fluid aspirated from buboes	Sputum	Blood culture/ blood film
Clinical symptoms	Fever, painful buboes, (inguinal adenopathy)	Cough, dyspnea, hemoptysis, ARDS ± buboes	Fever, vomiting, diarrhea, DIC, hypotension. no buboes
Incubation period	2-8 days	1-4 days	2-8 days
Mortality if untreated	~60%	~100%	~100%

Diagnosis

- Culture:
  - blood, sputum and bubo (lymph node) aspirates.
- Smears stain:
  - Gram, Giemsa.
- Serology (rapid and reliable):
  - Immunofluorescence test for *Y. pestis.*
  - Serum anti-F1 antibodies (seroconversion or a single high titer).
- DNA detection by PCR is under evaluation.

Treatment

- If the diagnosis is suspected on clinical and epidemiological grounds, treatment must be started as soon as, or even before, samples have been collected for laboratory diagnosis.
- Streptomycin (1 g bid) or gentamicin (1 mg/kg tid) is of choice.
- Tetracycline (500 mg qid) and chloramphenicol (12.5 mg/kg qid) are alternatives.
- Fluoroquinolones (ciprofloxacin and levofloxacin) may be as effective, but there is less clinical experience.
- Supportive care for acute circulatory failure, DIC and respiratory failure may be needed.

Listeriosis

- *Listeria monocytogenes* is an environmental Gram-positive bacillus which can contaminate food.
- Outbreaks have been associated with raw vegetables, soft cheeses, undercooked chicken, fish, meat.
- Listeria demonstrates 'cold enrichment', outgrowing other contaminating bacteria during refrigeration.

Clinical features

- Self-limiting foodborne outbreaks of gastroenteritis in immunocompetent individuals.

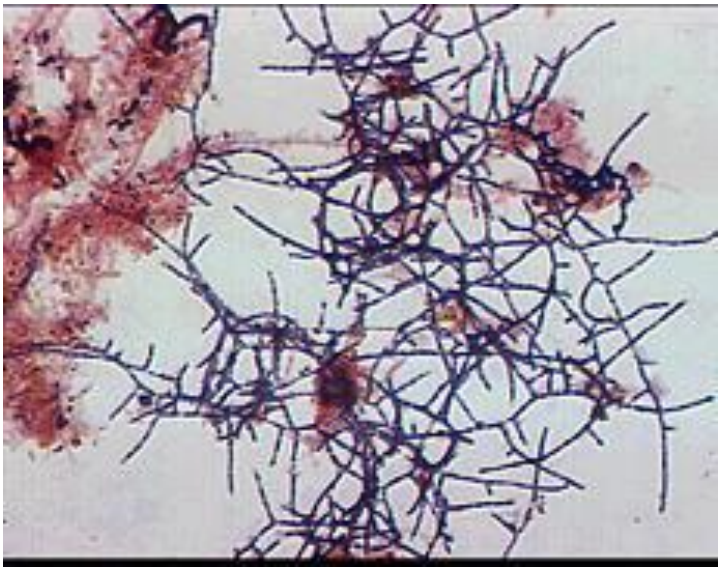
- Invasive systemic febrile illness may occur especially in pregnancy, neonates, the elderly and the immunocompromised.
- In pregnancy, complications may include chorioamnionitis, fetal deaths, abortions and neonatal infection.
- Meningitis, similar to other bacterial meningitis but with normal CSF glucose, may occur; CSF shows increased neutrophils but occasionally only mononuclear cells are increased.

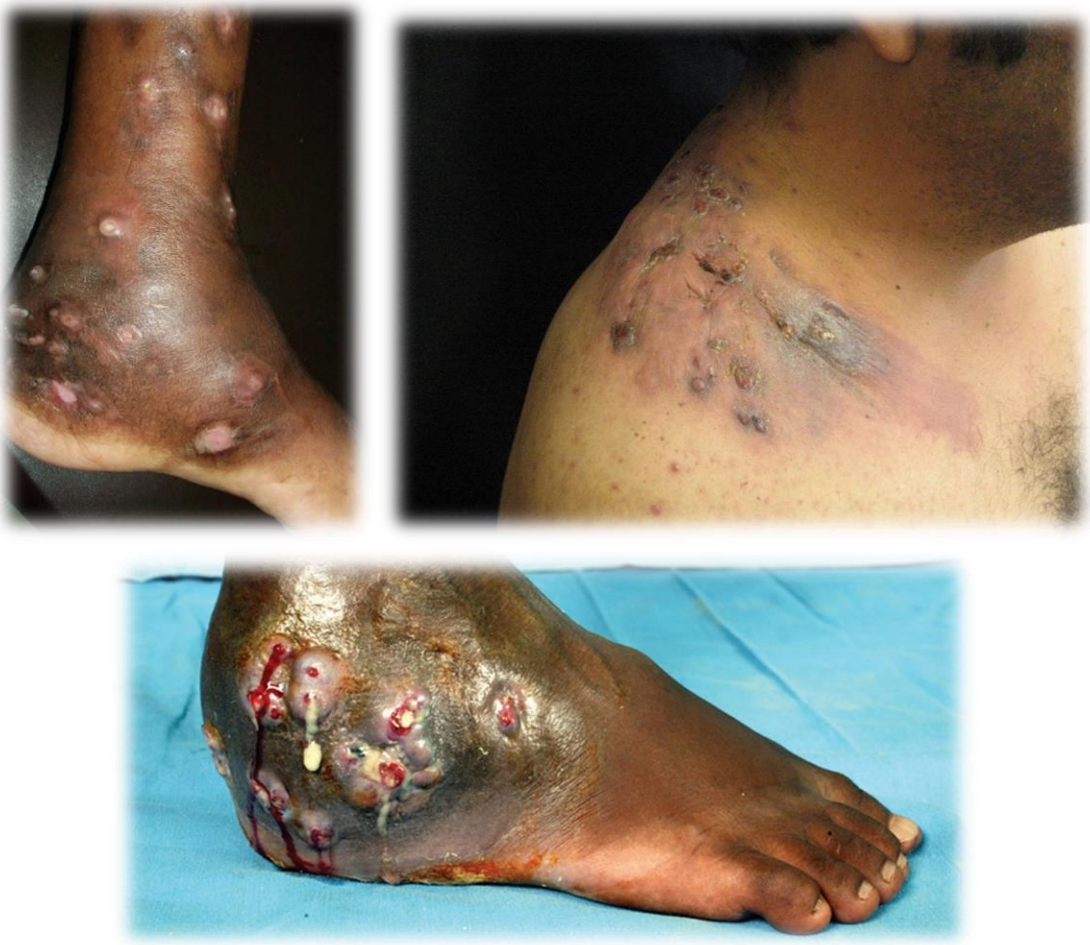
Diagnosis and Management

- Diagnosis:
    - Blood and CSF culture.
- Treatment:
    - Combination of an IV aminopenicillin (amoxicillin or ampicillin) plus an aminoglycoside, is of choice.
    - Trimethoprim/sulfamethoxazole combination can be used in those with penicillin allergy.
    - Cephalosporins (e.g. ceftriaxone or cefotaxime) are not effective, as the organism is inherently resistant, an important consideration when empirically treating meningitis.

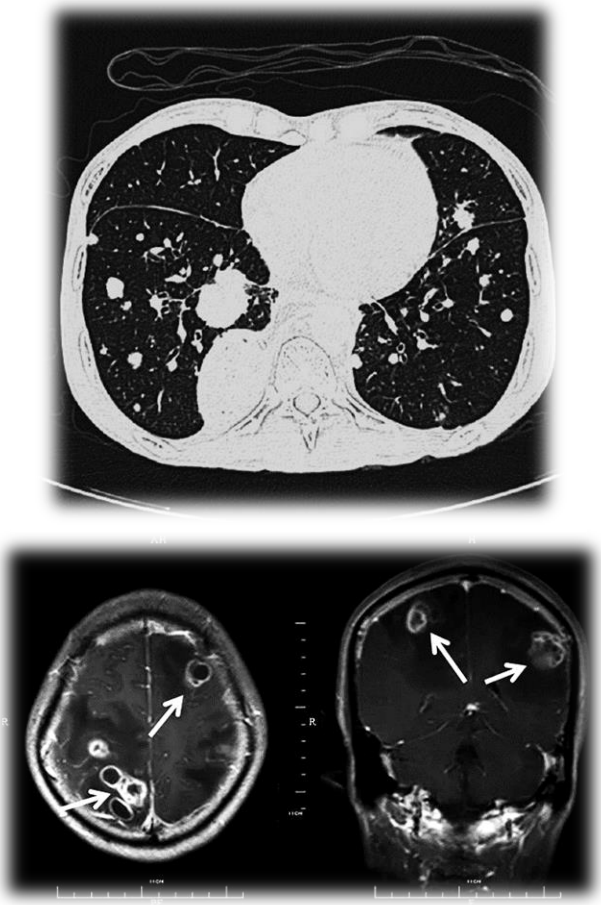
Nocardiosis

- *Nocardia* species are environmental saprophytes that occasionally cause chronic granulomatous infections in humans and animals.
- *Nocardia* is an aerobic Gram-positive, weakly acid-fast filamentous bacterium, which can be found in the soil.
- Infection arises by direct inoculation through the skin or by inhalation.
- Mycetomas from *Nocardia* species, affect immunocompetent hosts in tropical countries.
- Immunocompromise, alcoholism, and certain lung diseases predispose patients to pulmonary and disseminated nocardiosis.





Mycetoma (*Nocardia brasilensis*)



Disseminated Nocardiosis with pulmonary and brain abscesses

Treatment

- Guided by culture and sensitivity testing.
- Systemic infection requires combinations of antibiotics such as ceftriaxone, meropenem, amikacin and co-trimoxazole, often for 6–12 months or longer.
- Abscesses are drained surgically when feasible.
- Localized cutaneous infection is usually treated with a single agent, e.g. co-trimoxazole, for 1–3 months.

Actinomyces israelii

- *Actinomyces israelii* can cause deep suppurative infection in the head and neck, and also suppurating disease in the pelvis associated with intrauterine contraceptive devices (IUCDs).
- Treatment is usually with penicillin or doxycycline.