Leptospirosis

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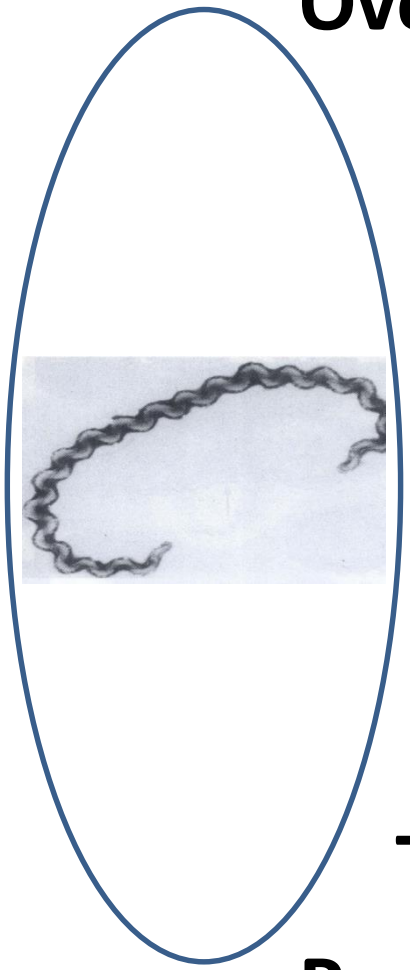
Outline



Overview

Etiology

Epidemiolgy

Pathogenesis

Clinical manifestations

Laboratory test

Diagnosis

Treatment

Prophylaxis

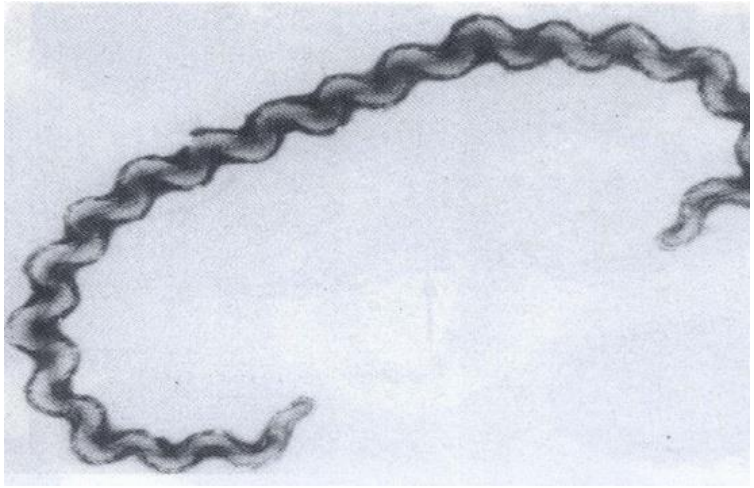
Overview

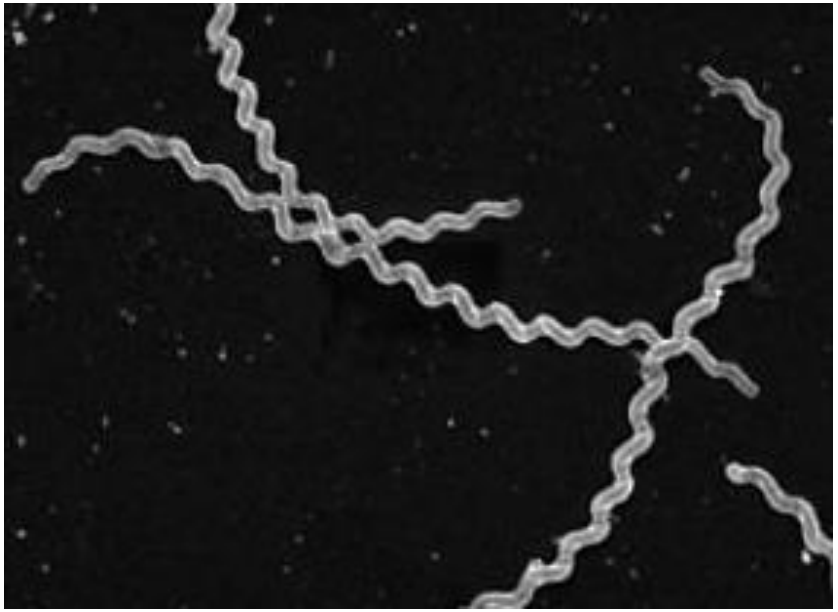
- An acute febrile infectious diseases
- Caused by leptospira from mice、pig、dog et al
- Range from none to mild such as headaches, muscle pains, and fevers; to severe with bleeding from the lungs or meningitis with high mortality

Etiology

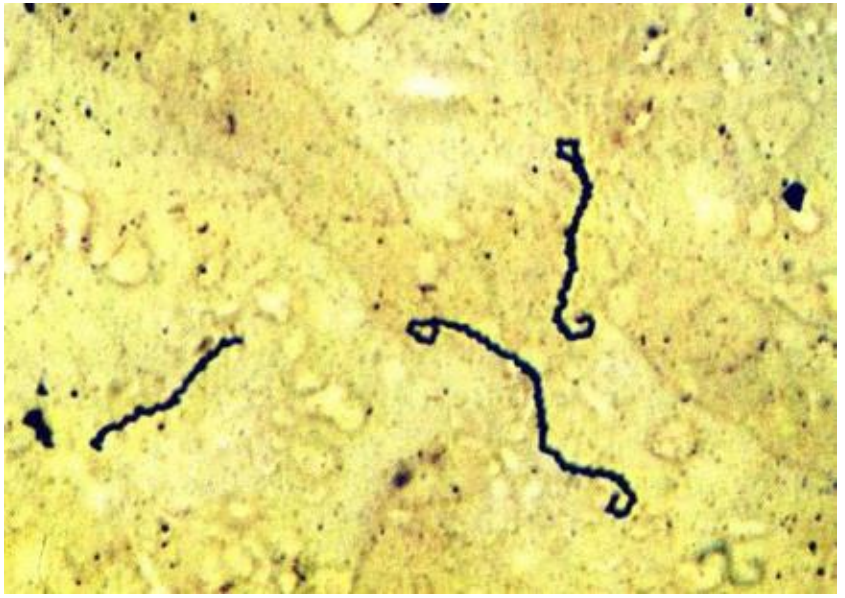
Leptospira

- Coiled spirochete, bent or hooked
- Active motility by rotating and bending
- Visualized by phase contrast or dark field microscopy
- Obligate aerobes, cultured in media enriched with rabbit serum or bovine serum albumin and protein free media

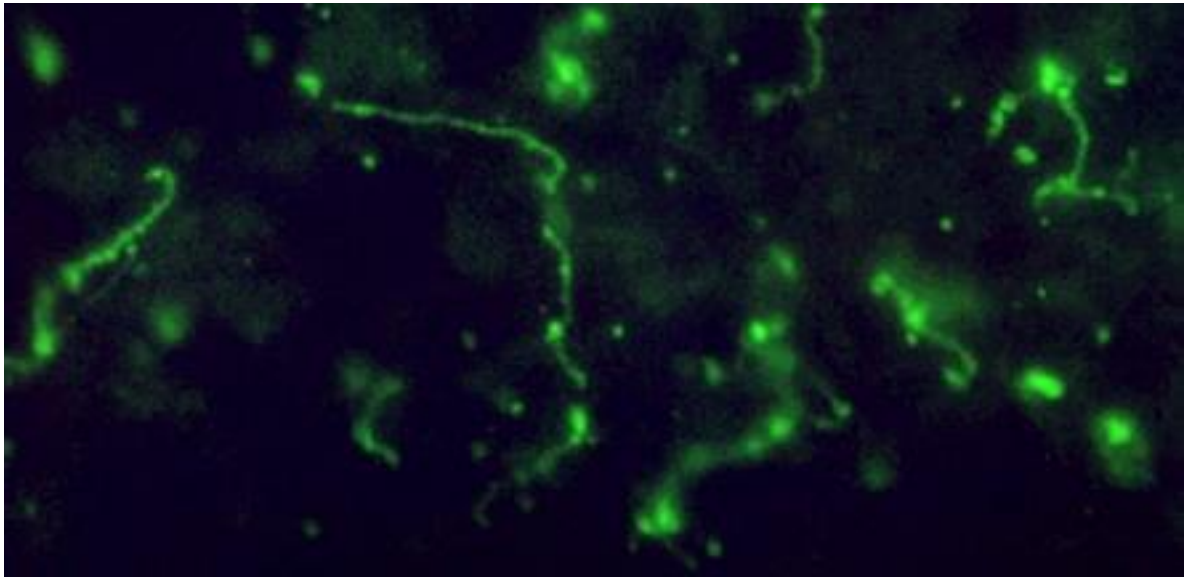




India-ink negative stain



Silver stain



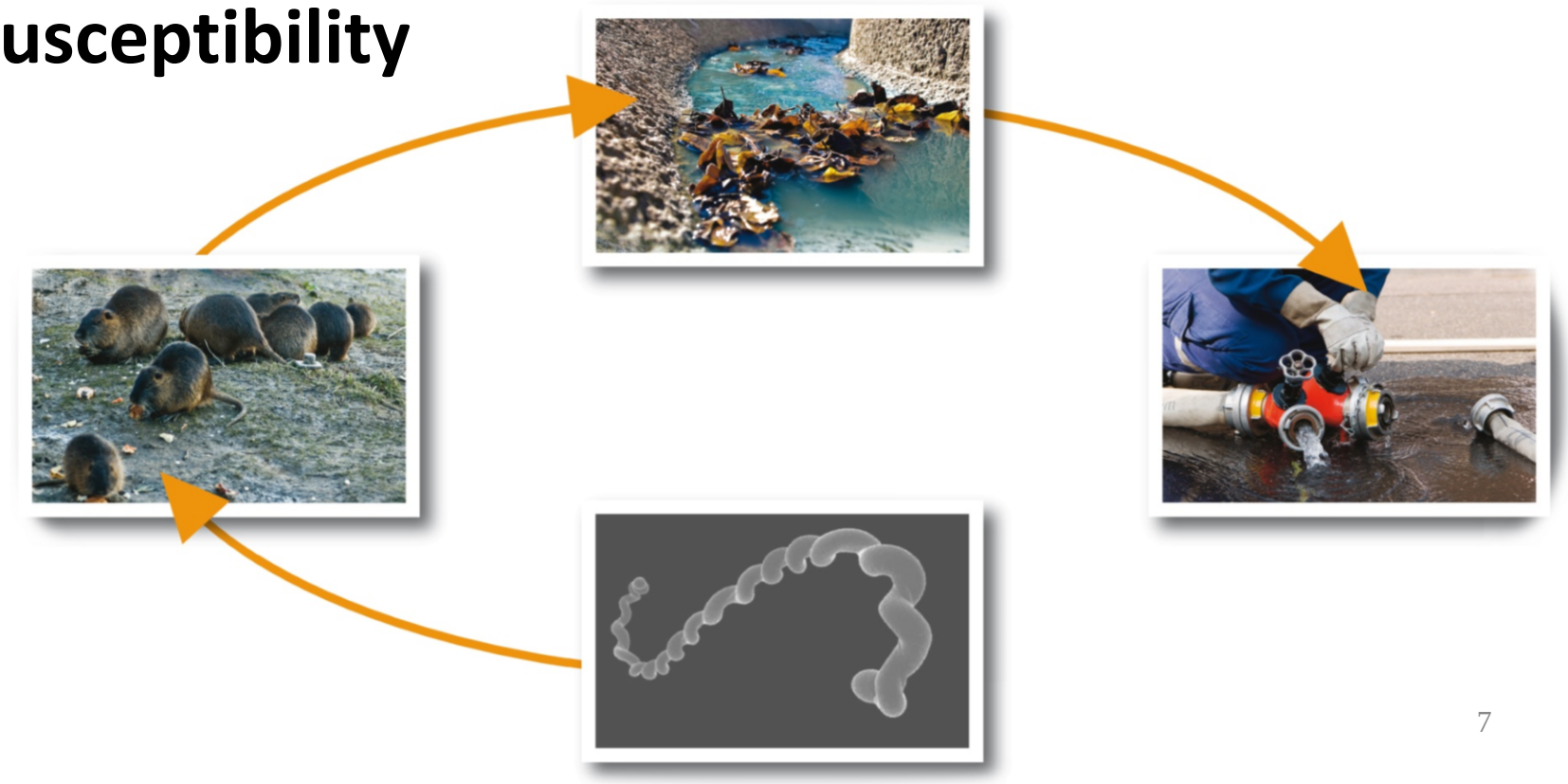
fluorescent stain

Etiology

- Complex antigenic structure
- Somatic antigen — genus specific
- Surface antigen — serovar specific
- Over 20 serogroups and 200 serovars
- Common serogroups: icterohemorrhagie, pomona, canicola and hebdomadis

Epidemiology

- Source of infection
- Route of transmission
- Susceptibility



Source of infection

zoonosis

The disease is not known to spread between humans

Routes of transmission

- **Usually direct or indirect contact with the urine of an infected animal**
- **Contaminated water, infected tissue or fluid**
- **Through cuts, mucous membranes and abraded skin**

This may happen by swallowing contaminated food or water

Susceptibility

- **The immunity against leptospira are type specific**

  No cross immunity between different serovars

- **Universal**

  People are universal susceptible to leptospires.

Occupations at risk : farmers, sailors on rivers, slaughter, sewer maintenance workers, et al.

Water-sport enthusiasts

Rodent carriers

Leptospira in urine

Risk factors:

Contact with animals

Butchering

Hunting

Farming

Free-living leptospira

Leptospira spp.

Contaminated mud, soil

Human infection

Human infection

Leptospira in urine

Mammalian reservoirs

Risk factors:

Water sport

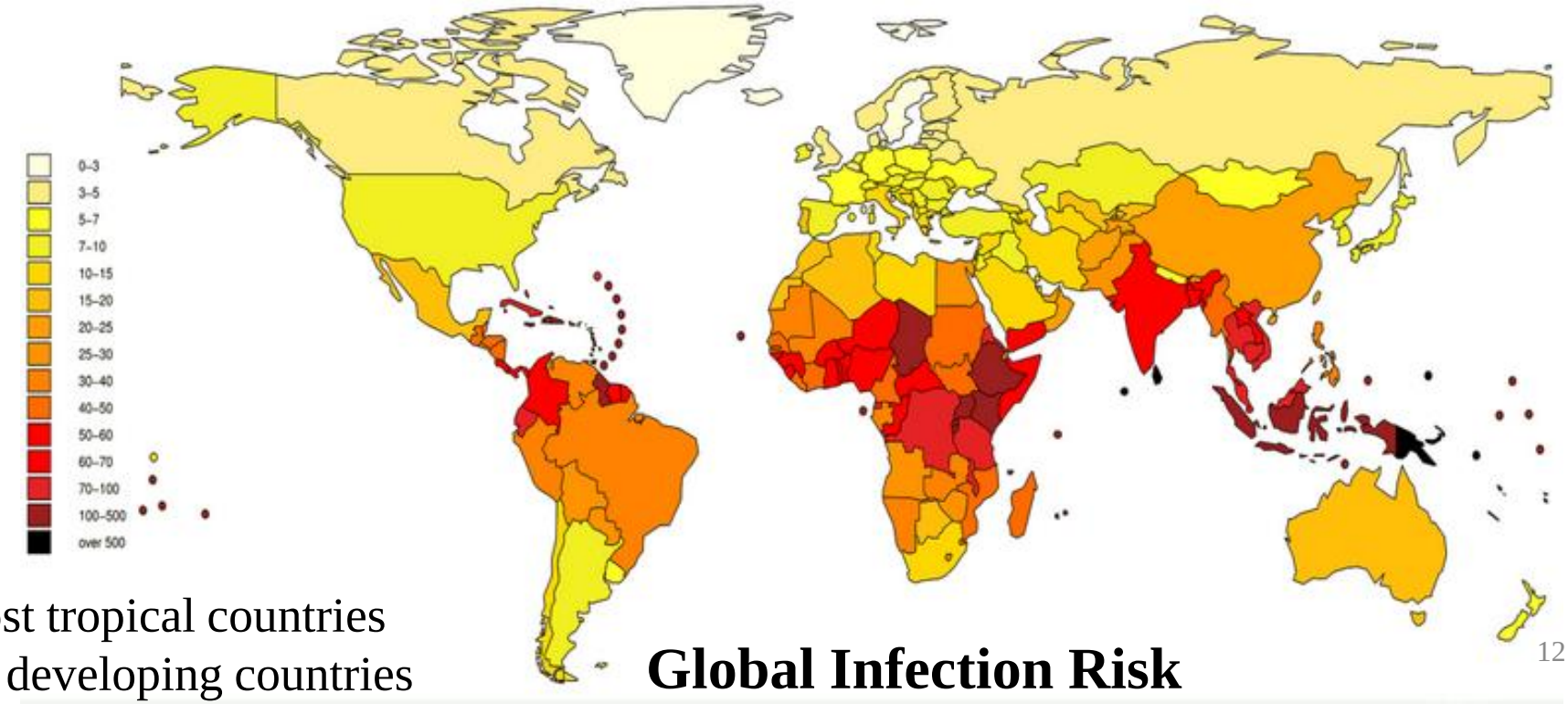
Fishing

Bathing

Swimming

Epidemiology

- **Geographic distribution: worldwide, higher in warm climate countries than temperate regions**
- **Seasonal: peak incidence in summer and fall in temperate regions**
  - ✓7 -10 million people are infected by leptospirosis annually
  - ✓1 million cases of severe leptospirosis occur annually, with 58,900 deaths.

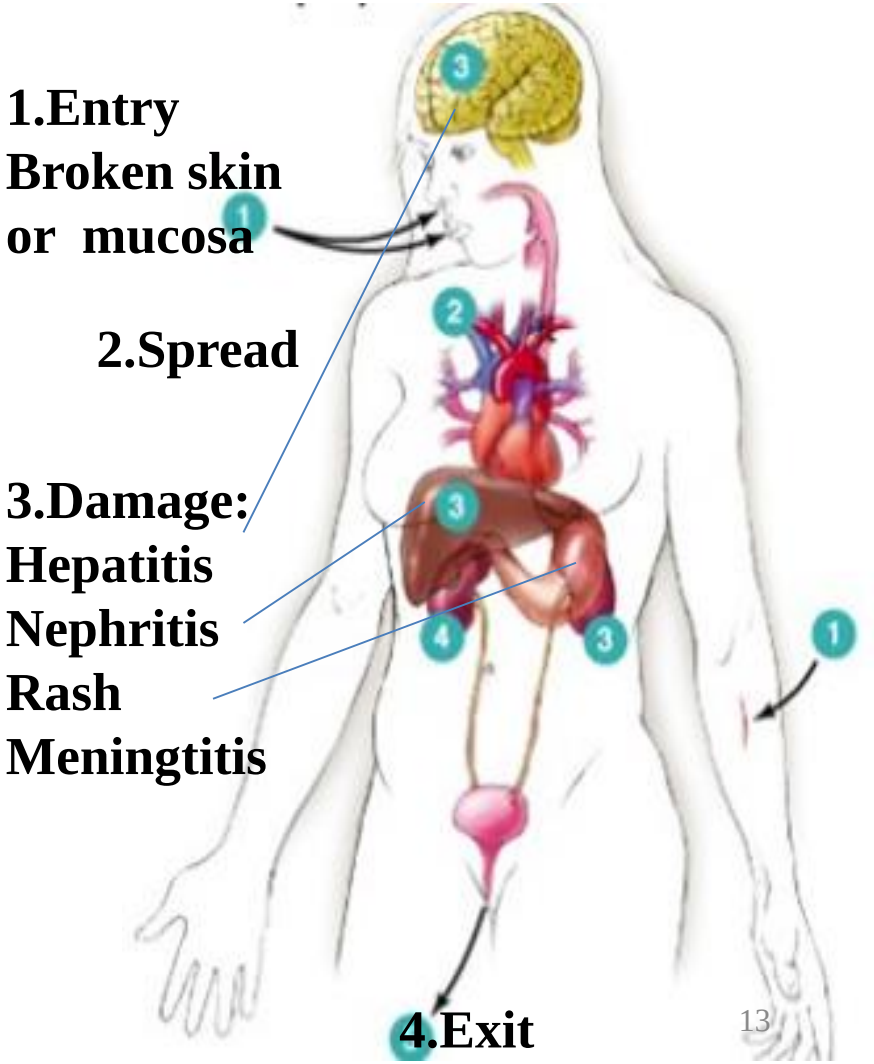


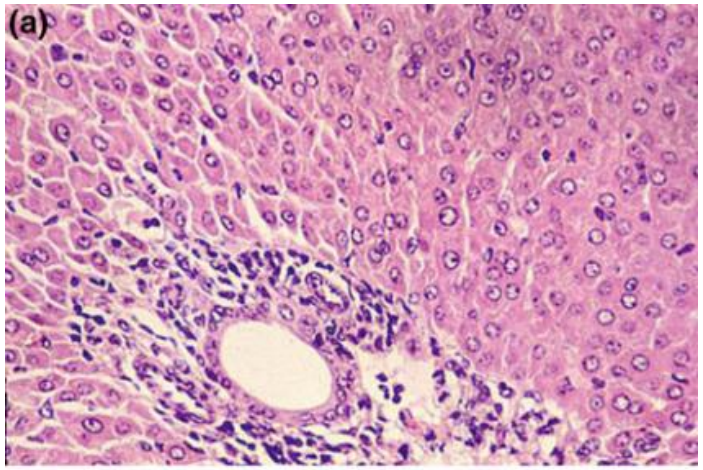
Most tropical countries are developing countries

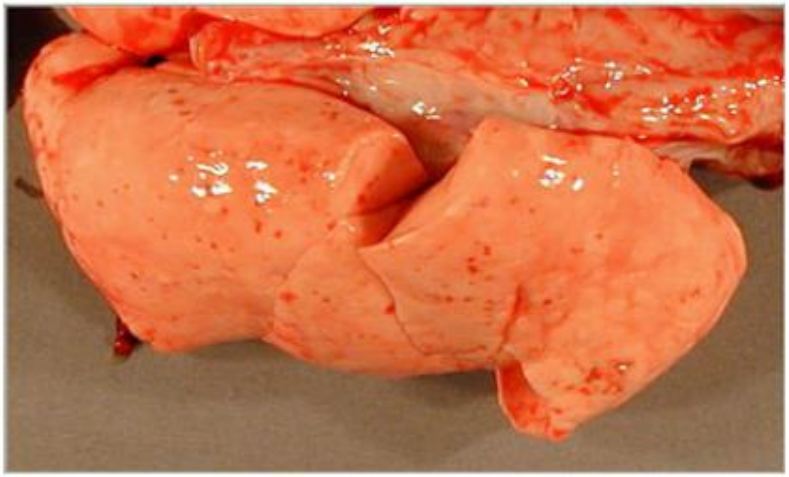
Global Infection Risk

Pathogenesis

- Enter via small abrasions or breaches of surface skin
- Enter into the bloodstream or lymphatic system and propagate
- Glycoprotein toxin lead to development of vasculitis, endothelial damage and inflammatory infiltrates of organs
- Evident in kidney, liver and lung: hyperemia,edma,necrosis and bleeding



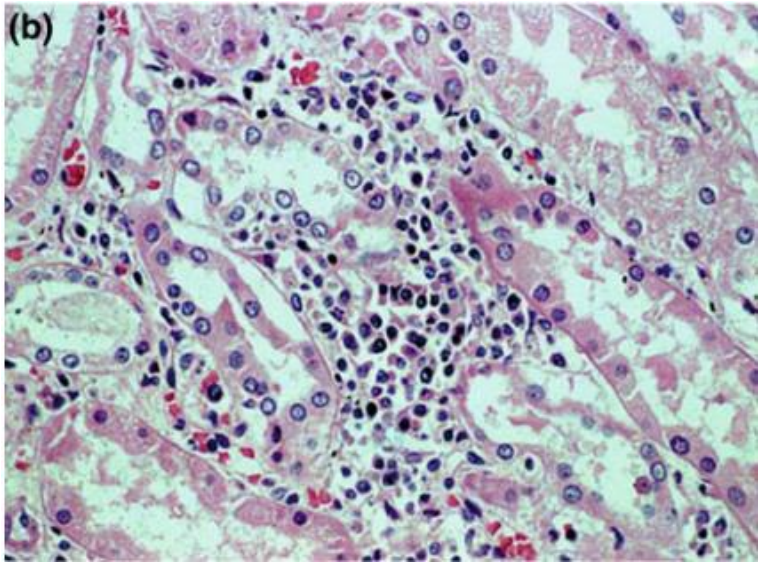




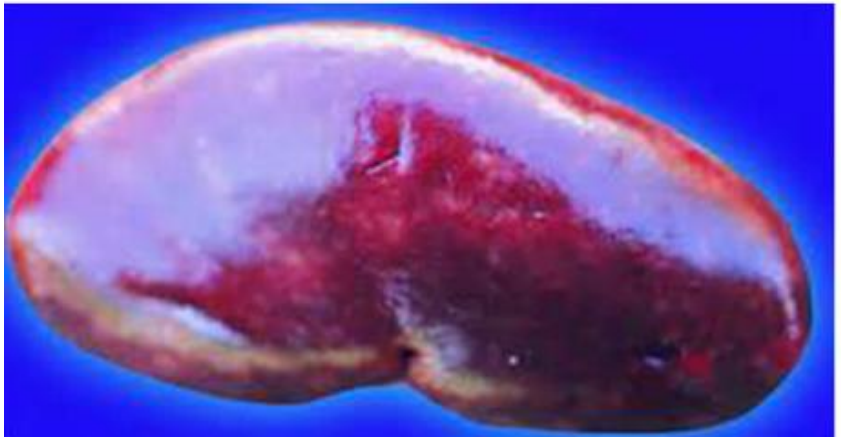
lack of the normal adhesion between hepatocytes

hepatocellular damage and disruption of hepatocyte intercellular junctions

hyperemia, hepatocellular necrosis , jaundice



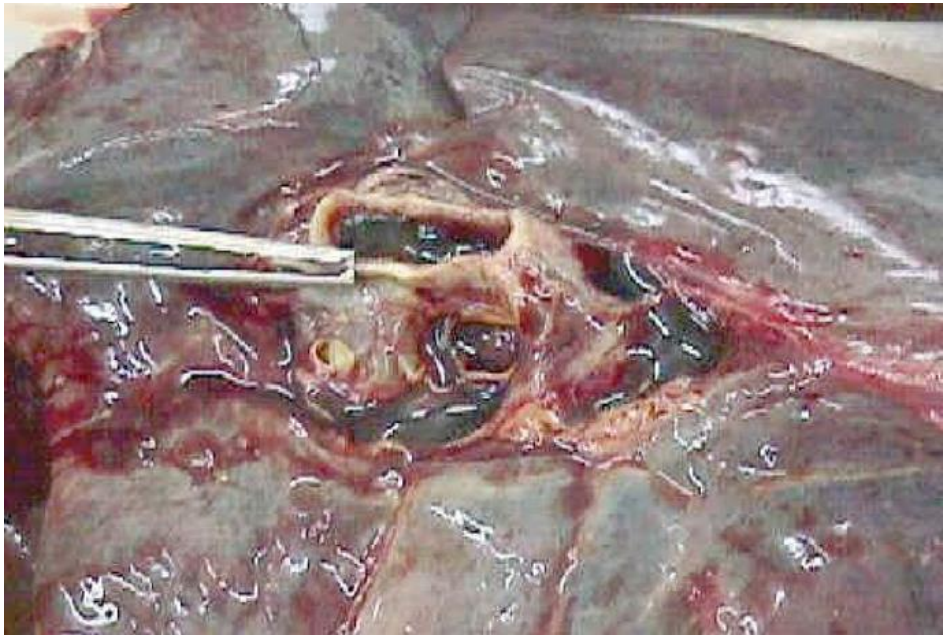
acute tubular necrosis and interstitial nephritis



Renal tubular degeneration and necrosis,
Renal interstitial edema，bleeding

renomegaly

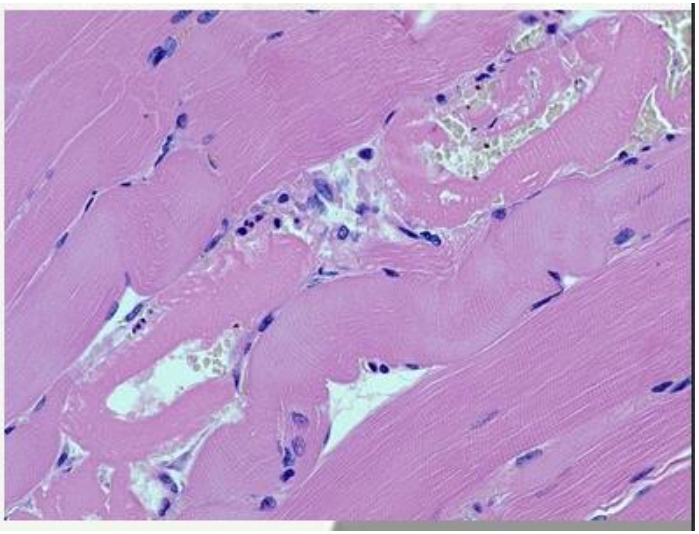
proteinuria, tube cast, hematuria



intra-alveolar haemorrhage

hemoptysis

basal and mid zone opacity



Muscle damage, swelling, hyperemia

Meningitis
Meningo encephalitis

Clinical Manifestations

- **Clinical manifestation vary greatly in different patients**
- **One serotype can lead to many kinds of clinical manifestations**
- **One clinical type can be caused by different serotypes**
- The commonest syndrome is anicteric leptospirosis which is a self limited disease and occurs in 85% to 90% of the cases.
- Icteric leptospirosis is a more serious, potentially fatal syndrome and occurs in 5% to 10% of the cases.

Clinical Manifestations

Leptospira

↓ Incubation period (always 7-12d, from 2 to 20 days)

Blood **vasculitis, endothelial damage**

↓

Initial phase (blood poisoning) → **Mid phase (Organ damage)** → **Late phase (Relapse, Late complications)**

- Fever
- Chills
- Headache
- Myalgia
- Nausea and vomitting

Clinical patterns

- Liver
- Kidneys
- Lungs
- Meningitis
- Meningo encephalitis
- Haemorrhage

- Aseptic meningitis
- Chronic fatigue
- Uveitis Iridocyclitis

Initial phase
(blood poisoning , 1-3rd day)

- An acute febrile illness
- Non-specific symptoms caused by leptospiremia and its toxins
- Such as : chills, headache, myalgia, anorexia, nausea and vomiting
- Sometimes persistent high fever

Initial phase

So-called “three symptoms and three signs”

Fever and chill
Myalgia and back pain
Malaise

Conjunctival suffusion
Calf muscle tenderness
Lymphadenopathy

pericorneal hyperemia

Mid phase
(Organ damage, 3-10th day)

Clinical patterns

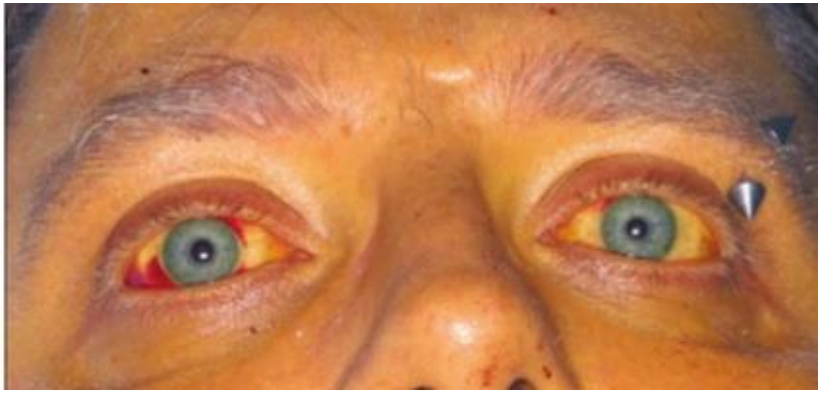
- With prominent clinical presentation
- Typical patients can be classfied into the following clinical types:
- 1.Ordinary leptospiremia
- 2.Pulmonary hemorrhage
- 3.Weil`s syndrome
- 4.Renal function failure
- 5.Meningoencephalitis

1.Ordinary leptospiremia

- **Septic toxic form, with symptoms similar to influenza or typhoid fever**
- **Characterized by abrupt onset of fever, headache, severe muscle ache, malaise, conjunctival suffusion, tenderness of calf muscle, lymphadenopathy**
- **Fever: high (usually over 39 ° C), continued or remittent fever accompanied by chill, malaise, headache**
- **Myalgia: remarkable, muscles of the calf ache**

1.Ordinary leptospiremia

- **Conjunctival suffusion: not conjunctivitis, but pericorneal hyperemia**



- **Lymphadenopathy: easpecially inguinal lymph nodes, painful, not purulent**
- **Last 5 to 10 days, after that temperature go down**

2.Pulmonary hemorrhage

- **Mild pulmonary hemorrhage:**
  - **Cough, blood-stained sputum, moist rales**
  - **Spotty shadow**
- **Hypoxemia, short breath, precordial fullness, chest pain, feeling of asphyxia, increasing bloody sputum, moist rales.**

  Extensive spotty or massive fusion shadow
- **In severe cases, changes in the level of consciousness, hemoptysis and respiratory failure**

2.Pulmonary hemorrhage

Factors related with diffuse pulmonary hemorrhage

- **Strong virulence of leptospira**
- **Low immunity of patients to leptospira**
- **Without prompt treatment**
- **Herxheimer reactions**

3.Weil`s syndrome

The more severe form of disease with severe liver and kidney involvement is known as Weil’s syndrome.

4.Renal function failure

- **Renal insufficiency: proteinuria, tube cast, hematuria**

- **Renal failure type: oliguria, uremia, commonly combined with Weil`s disease**

5.Meningoencephalitis

- Severe headache, vomiting, convulsion
- Neck stiffness, coma, positive Kernig`s sign,
- Abnormal CSF, cerebral edema, even brain hernia and respiratory failure

Late phase (Recovery)

(2nd week – 6th month)

➢ **Late fever**

- Usually moderate, around 38 ° C
- Last 1 to 3 days
- Without leptospiremia

➢ **Reactive meningitis**

- Meningeal symptoms, asceptic meningitis
- Leptospires not detected in CSF
- Good prognosis

➢ **Ocular sequelae**

- Iridocyclitis, uveitis

Late phase

Obliterating cerebral arteritis

- Appears 2-5 months after initial illness caused by L.pomona
- Subclinical leptospira infection correlated with delayed allergy
- Abnormal CSF, basal multiple arteritis

Laboratory Findings

Non-specific laboratory test

- **Leukocyte counts,**
- **abnormal urine finding (proteinuria, tube cast, microscopic RBC and WBC)**
- **ALT, AST , TBIL**

Laboratory Findings

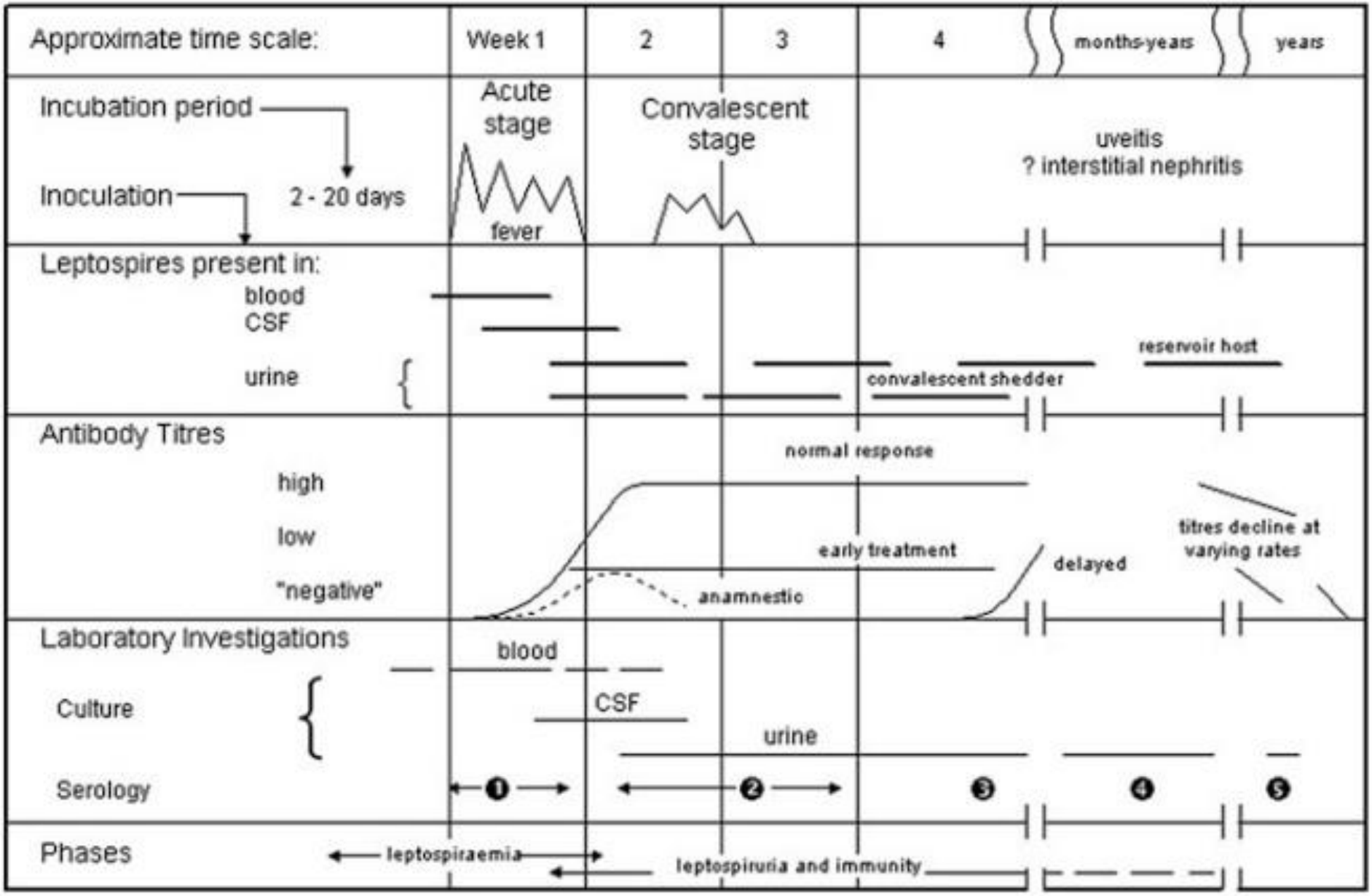
Specific tests:

- Specimens from blood, CSF, body fluid, urine
- Sediment observed by dark field microscopy
- Culture: complicated , expensive, long incubation, low sensitivity and rarely used
- **Antibody detection:**

  microscopic agglutination test (MAT) or ELISA

- Polymerase chain reaction (PCR) for DNA test

Nature of leptospirosis and relevant investigations at different stages of disease.



Clin Microbiol Rev 2001,14 (2):296 – 326.

Diagnosis

- Epidemiological data: endemic area and epidemiological season, exposure history
- Clinical characteristics
- Laboratory findings

Differential diagnosis

- Leptospiremia: influenza, typhoid and septicemia
- Pulmonary hemorrhage: pneumonia
- Icterohemorrhage: acute and severe viral hepatitis, epidemic hemorrhagic fever
- Renal failure: epidemic hemorrhagic fever,
- Meningoencephalitis: viral encephalitis, tubercular meningitis

Prognosis

- Good in most cases
- Higher mortality rate in patients with pulmonary hemorrhage, renal failure, serious icterohemorrhage, meningoencephalitis, age over 36 years

Treatment

- Early diagnosis and efffective treatment are important
- Antibiotic treatment will shorten the duration of fever and reduce the incidence of complications
- Antibiotic treatment: penicillin G, doxycycline, cephalosporins
- Penicillin G: first choice, 0.4 million units, IV, q6h, for 5 to 7days
- Herxheimer reaction

Treatment

Herxheimer reaction

- 0.5-4 Hours after initiation of PG therapy
- Rigors, high fever, hypotension or shock
- Lasting about ½~2 hours
- Caused by the lysis of massive leptospira and the release of toxin after PG therapy

Treatment

- Supportive and symptomatic treatment
- Careful clinical observation, bed rest, Corticosteroid for high fever, brain edema, and pulmonary hemorrhage

Prevention

➢ Relatively difficult

Widespread in so many animals and places all over the world

➢ Comprehensive measure

•Effective rat control and avoidance of urine contaminated water sources are essential preventive measures.
•Human vaccines are available only in a few countries, such as Japan and China.
•Animal vaccines only cover a few strains of the bacteria. Dog vaccines are effective for at least one year.

➢ Chemoprophylaxis

Doxycycline can prevent leptospirosis if given before and during exposure

High risk people should know of the disease and how to avoid it.

Rodent carriers

Leptospira in urine

Risk factors:

Contact with animals

Butchering

Hunting

Farming

Free-living leptospira

Leptospira spp.

Contaminated mud, soil

Human infection

Human infection

Risk factors:

Water sport

Fishing

Bathing

Swimming

Leptospira in urine

Mammalian reservoirs

Take Home Message

- Main source of infection: rats and field mice and pigs
- Infected through contact with animals and their discharges
- Characterized by fever, headache, myalgias
- Severe leptospirosis with jaundice, pulmonary hemorrhage, renal failure, meningeal signs
- Effective with treatment of penicillin G

THANKS