Leptospirosis

Summary

- Bacterial zoonosis
- Most common in humid tropics
- Animal reservoirs, small rodents
- Humans infected from animal urine
- Usually mild, self-limiting, sometimes serious multi-organ failure (liver, kidneys)

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The organism

- Genus Leptospira

  Fine spiral bacteria of 0.1 x 6-20 µm

  Aerobic, difficult to grow (26-30C)

  Aquatic. survive in water weeks - months

  Species L. Biflexa

  L. Parva

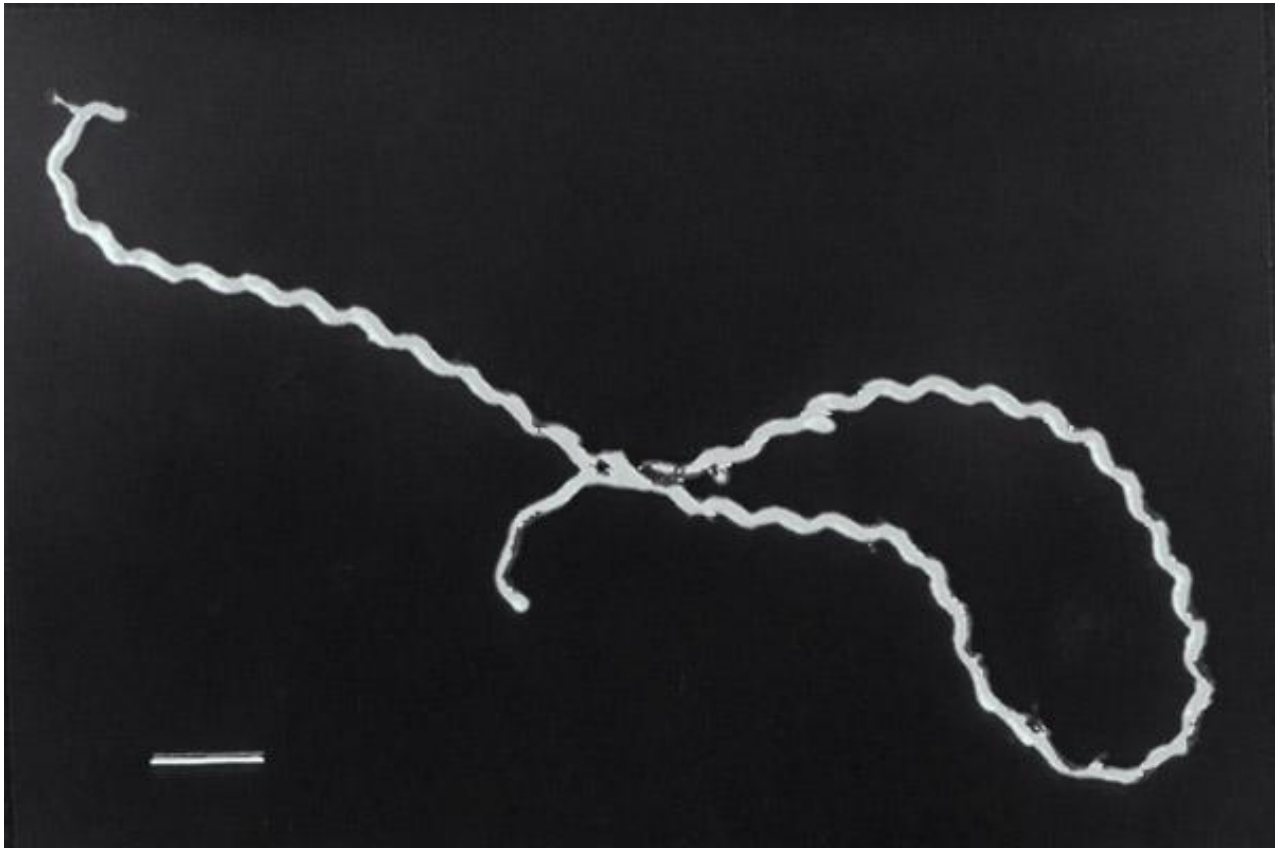
  L. Interrogans (pathogenic)

  >200 serovariants;

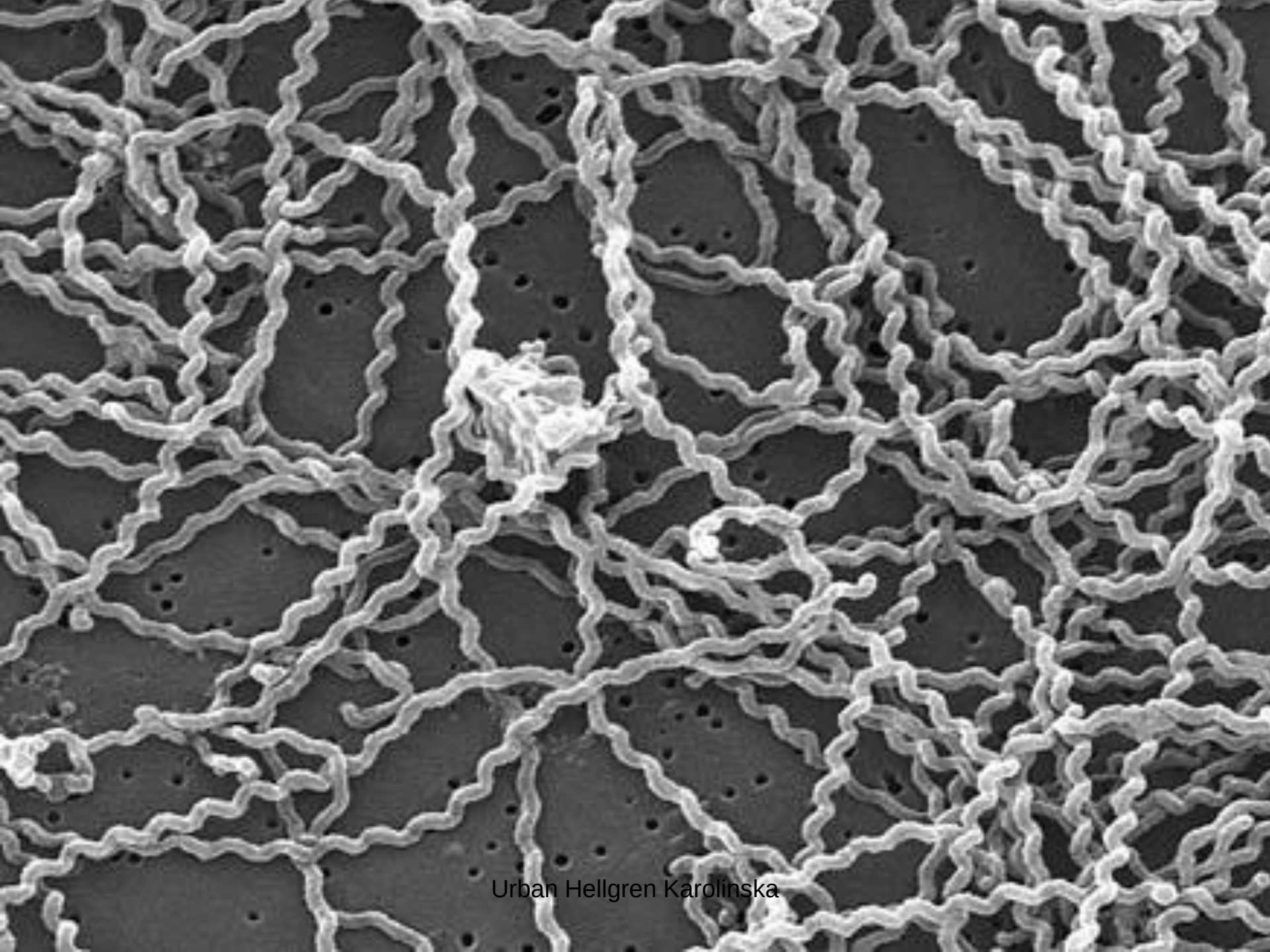
  diff geographic distrib.

  diff major maintenance host

- *Leptospira interrogans* in blood cultured in Korthof's medium.



- Scanning electron micrograph of *Leptospira interrogans*. Regular spiral structure of 0.5 µm periodicity is characteristic of cultured *Leptospira interrogans*.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Leptospirosis

- Worldwide zonotic infection
- The rat is the main maintenance host, but affects virtually every small mammal and also pigs, dogs, horses, camels, cows

  Often asymptomatic

  Continued replication in the renal tubles for months/years after primary infection

  Chronic carriers (maintenace host)

- *Mastomys natalensis*, a rat that carries diseases including plague, Lassa fever, leptospirosis and toxoplasmosis

Human transmission

Exposure to urine contaminated water, food or soil

* Skin contact (broken)
* Mucosal surface eyes, nasal
* (Swallowing)

Person –person spread very rare

Epidemiology

- Weils disease, Swineheard disease, swamp or mud fever (fältfeber)
- Most common in temperate or tropical climates
- Occupational hazard if work outdoors or with animal: farmers (paddy fields), sewer workers, veterinarians, military personal etc
- Recreational hazard: rafting, caves, swiming
- Urban children in slum areas


WARNING !
LEPTOSPIROSIS
HEALTH HAZARD
FRESH WATER STREAMS AND MUD
POSSIBLY POLLUTED WITH BACTERIA
SWIM OR HIKE AT YOUR OWN RISK
FOR MORE INFORMATION CALL
HAWAII DEPARTMENT OF HEALTH

Epidemiology cont

- Incidence (underreported)

  Temperate climat: 0.1 – 1 / 100000/year

  Humid tropics: ≥ 10 / 100000/year

  Outbreaks ≥ 100 / 100000/year

  Often following heavy flooding, post cyclone

  Occasional cases reported in tourists

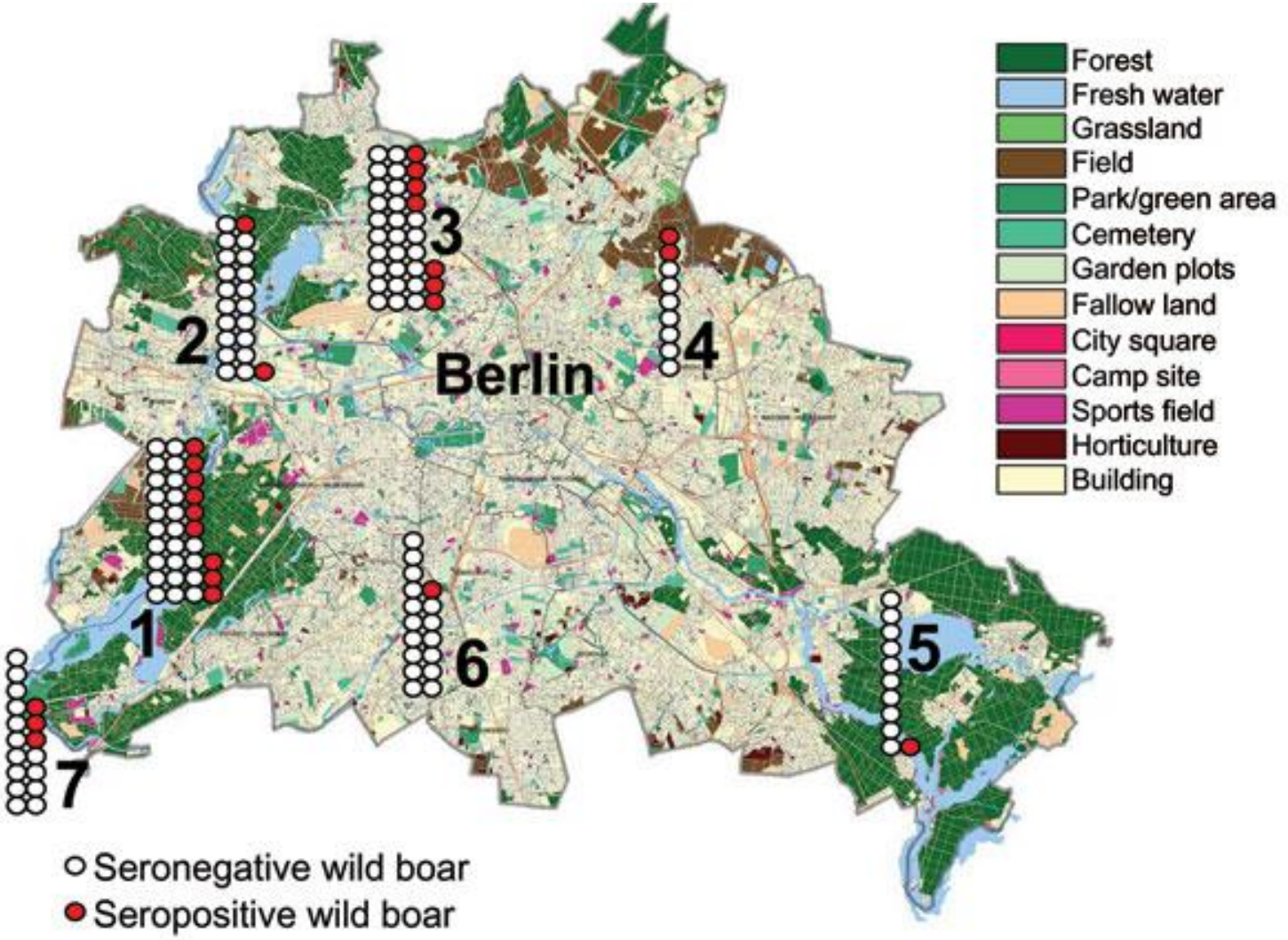
  Sweden 1-6/year, usually SE-Asia (1 Gotland)

Leptospirosis in Denmark

- 1970-96, n=118 lab confirmed
- Icterohaemorrhagie 72%
- Occupational exposure 63%
  - Fish farmers / fishery 25%
  - Farmer / agriculture 18%
  - Travel abroad 8%
- Males 90%, ¾ June - November

Holk et al, SJID, 2000

Figure 1



Berlin wild boars 2005-06 (n=141)
18% seropos against pathogenic leptospires

Pathogenesis

- Bacteria disseminates to various tissues
- Systemic vasculitis with endothelial injury

  Leptospires found in large and medium sized blood vessels and capillaries

  Major affected organs

  Kidneys: nephrits and tubular necrosis

  Lungs: intra alveolar bleeding

  Liver: cholestasis, hepatocyte degenerat.

Pathogenesis cont

Mechanism for vasculitis?

- Direct toxic effect of the bacteria?
- Immune complex mediated?

- Production of IgM in the 2nd and 3rd week (IgG later)

- Leptosopires excreted in the urine in humans until a few days after recovery

Clinical presentation

- Incubation period 1w–4w, median 11d
- Often asymptomatic
- **90 % mild and self-limiting,** last 3-7d

  flue like disease fever, headache, myalgia, sore throat, abd. pain, nausea vomitting

  In Australia:15% renal involvment, 15% respiratory symptoms (4% hemorrages)

Clinical presentation cont

Severe disease 10% (Weil s syndrome)

- 1st septic phase flue like, sometimes skin rash: maculopaular or purpuric
- Leptospires cultured from blood and CSF
- Defeverscence after 5-7days
- Remission lasting around two days

OBS! Not always biphasic course

Clinical presentation cont

<u>Second inflammatory phase</u>

Cased by the immune response

Symptoms reoccur

- Meningeal (aseptic picture)
- Renal (oliguria – failure)
- Hepatic (ikterus)
- Pulmonary (bleeding, diffuse pneumonitis)
- Myocarditis

Clinical presentation cont

Second inflammatory phase cont

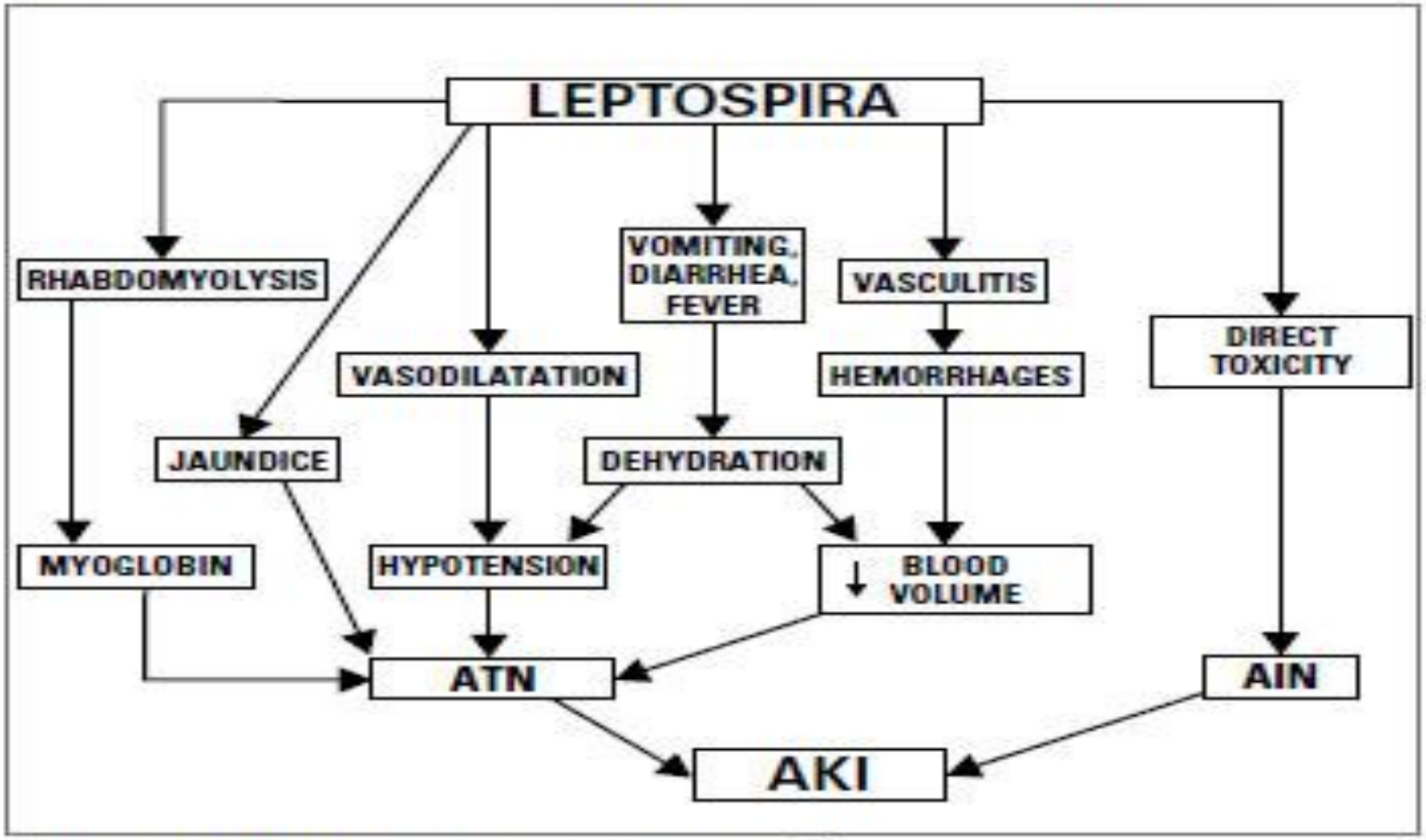
- Skin (purpura, echymosis, bleeding)
- Eye (retinal bleeding, infl changes)

Laboratory parameters

Leukocytosis, low platelets, signs of renal and hepatic involvment

Mortality 10-15% (arrythmias, pulm bleeding, multi - organ failure)

Figure 1. Physiopathology of AKI in leptospirosis.



Adapted from Abdulkader & Silva.[56]

De Francesco Daher et al 2010

ATN = acute tubular necrosis
AIN = acute interstitial nephritis
AKI = acute kidney injury

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Diagnosis

- (Dark-field microscopy)

- (Blood and CSF culture)
  Special media, takes several weeks

- Serology
  IgM after 5-6 days, acute sera (specific)
  or paired sera
  Confirmatory Micro agglutination test (Denmark)

- PCR on urine or blood (if available)

Management

”Early antibiotics may shorten duration of renal failure and hospital stay but evidence not convincing” (Cochrane)

Mild disease no treatment

More severe illness
Iv penicillin or cefotaxime (any betalactame) or Doxycycline (200mg x1 x VII)

Supportive care: Renal, pulmonary, cardiac etc

Control and prevention

Reduce incidence by

- Rodent control, animal vaccination
- Interrupt transmission, clothing, water contact etc
- Chemoprophylaxis in some situations

  Doxycline 200mg weekly (95% effective)

Human vaccine: availible but serovar specific and need for yearly booster + side effects

Animal vaccine: Domestic livestock

Case 26 years male

- Previously healthy
- Studies in Australia since 2 years
- Returns to Sweden via Thailand
- Spent 3w in T, one in the southern jungles

- Since 2 days feeling unwell, chills, sore throat, headache. No cough

Case 26 years male cont

- **Admitted late evening July 25th, 2006**
- 38.3 C, no exanthema, no neck stiffness, chest clear Bp 100/60
- Chest X-ray: disseminated diffuse nodular bilateral infiltrates
- Lab: CRP 302, kreatinin 184, platelets 133, WBCs + diff normal, liver enzymes normal
- Given cefotaxim iv, pneumonia?
- Deteriorates, Low Bp 80/60 despite iv fluids. Needs more oxygen

Case 26 years male cont

- To ICU the same night. More fluids, NA infusion, CPAP Antibiotics changed to gentamycin, meropenem and levofloxacin
- CT chest: Suspected ARDS
- Back to ward after 3 days. Leaves the hospital 3 days later with levofloxacin for another 5 days

- All standard tests for different etiologies negative Leptospira IgM (ELISA) pos, (confirmation pos)

Is Leptospirosis more common than we have thought?

Swedish multicenter study 2005-2008

Travellers with fever from malarious areas

- 202/526 unknown fever
- 5/202 serologically confirmed leptospirosis

  Indonesia (2), Tobago (1) India and South Africa (1), Thailand (1 = 26y male above)
- 3/5 cases leptospirosis not suspected