Brucellosis

Swedish – Ethiopian course in Tropical Infections and HIV

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47-year old male

- Referred from local health center to emergency dep
- Fever since two weeks (max 38.5).
- Slight muscular pain right leg and arm.
- Feeling tired.
- Lost 5kg in weight.
- Two months earlier met relatives (from Irak) in Syria

47-year old male, cont

- God general condition, no path. findings
- CRP 48 mg/L, Hb 123 g/L.
  WBC 5.2 x 10(9)/L with normal diff count.

- Blod cultures were taken and the patient went home

Other family members sick

- 3 d later patient calls - still febrile.
- The two other family members to Syria also sick.
  12 year old niece fever since 2 ½ week
  49 year old brother not feeling well.
- All had regularly been eating white cheese

This can only be one disease!

Next day - the family at the OPD

The niece is a little pale but physical exam normal

- Temp 38 and on a few occasions <39.5 since 3w
- After 1w mild dry cough.
- Last 3d pain in left knee and ankle.
- 4 times at local health station 19/6 – 4/7 – viral infection?
- CRP 40 mg/L, ESR 41 mm, liver enzymes normal, creatinine and electrolytes normal

The family at the OPD, cont

The 49 y old brother has had periodic fever and body and joint ache

- The day before 38.6.
- Physical examination normal.
- CRP 34 mg/L, WBC 5.9 x 10 (9)/L, slightly elevated liver enzymes

Growth in blood culture

- When the family is in the waiting room the laboratory calls: growth in both flasks after 66 hours in the index case.

- All immediately start treatment with rifampicin (600 or 900mg x 1) and doxycycline (100mg x 2) for 6w
- Later growth of Brucella melitensis in blood in all three patients

MIC and serology

- MIC (index case)

  rifampicin 1 mg/L (S)

  doxycycline 0.19 mg/L (S)

  ciprofloxacin 1mg/L (I)

  streptomycin 0.75 mg/L (S)

- Serologies taken - both positive

Uneventful outcome!

- Alla became afebrile within 2-4 days
- Healthy again with normalized CRP within 1 ½ - 3 weeks.
- No problems with adverse reactions
- No relapse

Risk for laboratory infection

- A small gram neg coccoid rod that grows very slowly – up to 3w before pos culture
- Very low infective dos
- Risk for spread by aerosol when the flasks are opened
- Referral form to lab. (remiss) must be clearly labelled to inform about risk of Brucella.
- Positive cultures are sent to special security lab (P3) without opening

Diagnosis

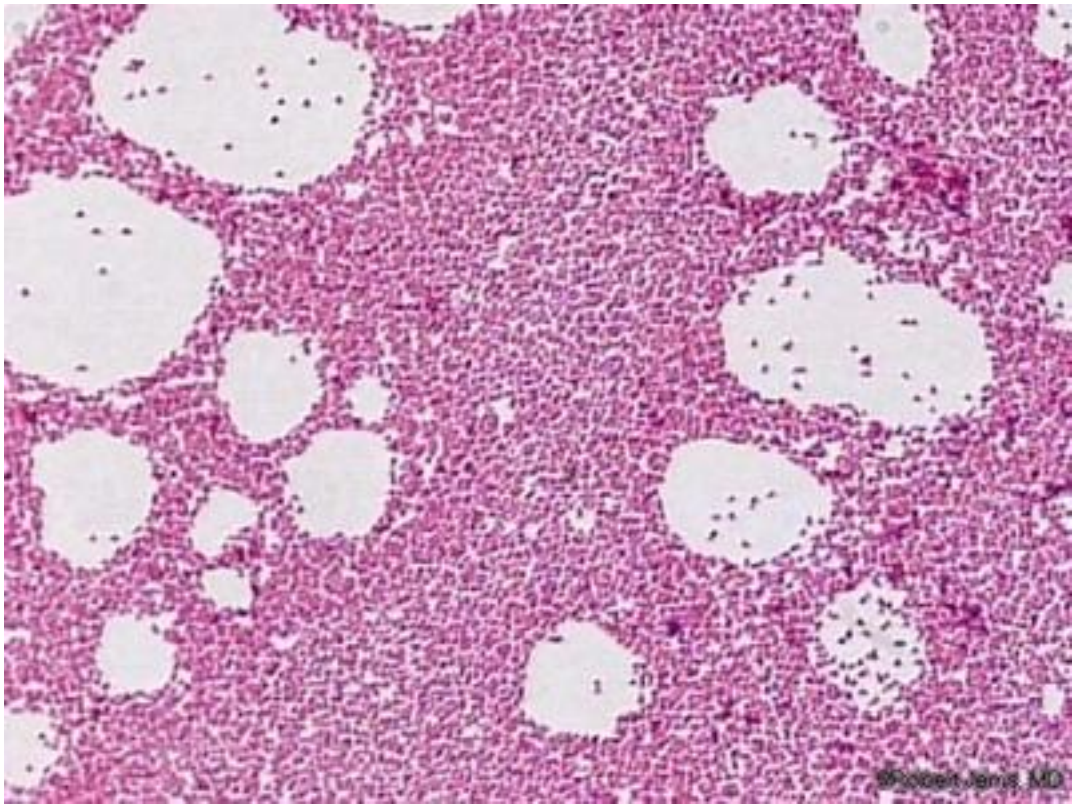
- Diagnosis ususally based on pos cultures from blood or other sterile locations.

- Specific and sensitive serological methods (ELISA) are available.

  IgG and IgM pos efter ca 1-2 w

- Unspecific serological methods commonly used with high risk false positive results.

Many small gram negative bacteria



Beautiful colonies

Pathogenesis

- Infected trough GI tract (orally)
  (airways, conjunctiva, wounds)
- Bakteria grow intracellularly in monocytes
- Both humoral and cell mediated immune response

Pathogenesis cont

- Localized in lymph nodes, spleen, liver and bone marrow (RES)
- Occasional secondar spread to CNS, bone tissue, mycardium, genital organs etc
- Granulomas (necrosis, abscess) in affected organs

Symptomatology

- Incubations period can be very long, usually 2-4w
- An intermittant low grade fever for long periods is characteristic (undulant fever).
- Body aches and joint pains are very common
- Profues sweating, triedness, headache, anorexi and dry cough are common .

Symptomatology, cont

- Fokal complications in some patients:

  Endocarditis (ca 1%), meningitis, spondylodiscitis, arhritis, orchitis (5-10%)

- The majority of patients recover spontaneously even without treatment.

- Very low mortality except for endocarditis.

Laboratory examinations

No typical laboratory finding:

- WBC normal or slightly depressed
- Sometimes low platelets and anaemia
- Frequently slightly elevated liver enzymes
- Slightly elevated ESR and CRP

Treatment

Antibiotic requirements

* Susceptible strain (in vitro susceptible)
* Intracellular penetration and activity
* Bactericidal effect
* Synergistic effect if combined
* Given orally (long treatment duration)
* Well tolerated (and afordable)

Treatment uncomplicated infect.

* Monotherapy less effective
* Treatment duration ≥6 weeks (shorter less effective)

Rifampicin (900mg/d) + doxycyklin (200mg/d)

alt

Doxy+ aminoglycoside (*gentamycin/streptomycin 2-3w)

less overall failure (8%VS19%) and relapse (4%VS14%)

but more resource demanding (*gentamycin 5mg/kg/d)

Rifampicin + ciprofloxacin less effective (but NS)

Meta-analysis. Skalsky K et al BMJ research, 2008

Treatment cont

Complicated Brucellosis

- Add an aminoglycoside to doxy and rifamp (gentamycin/streptomycin for 2-3w)

CNS infektion

- Rifampicin + trimethoprim /sulfamethoxazole

- Treatment duration ≥3-6 months

History

Hippokrates described a similar clinical picture

Common in English Navy, Malta 19th century

Isolated from spleen 1887

Different names

Malta fever

Mediterranean fever

Febris undulans

Genus Brucella

Total 6 species

4 species pathogenic to man

- B. melitensis, B. abortus, B. suis och B. canis
- B. melitensis dominates.
- B. melitensis most common in Mediterranean region and Middle East

Routes of infection

* Consumption of infected animals / products
* Contact with infected animals / products

  Special professions: veterinarians, slaughter house workers etc
* Laboratory infection

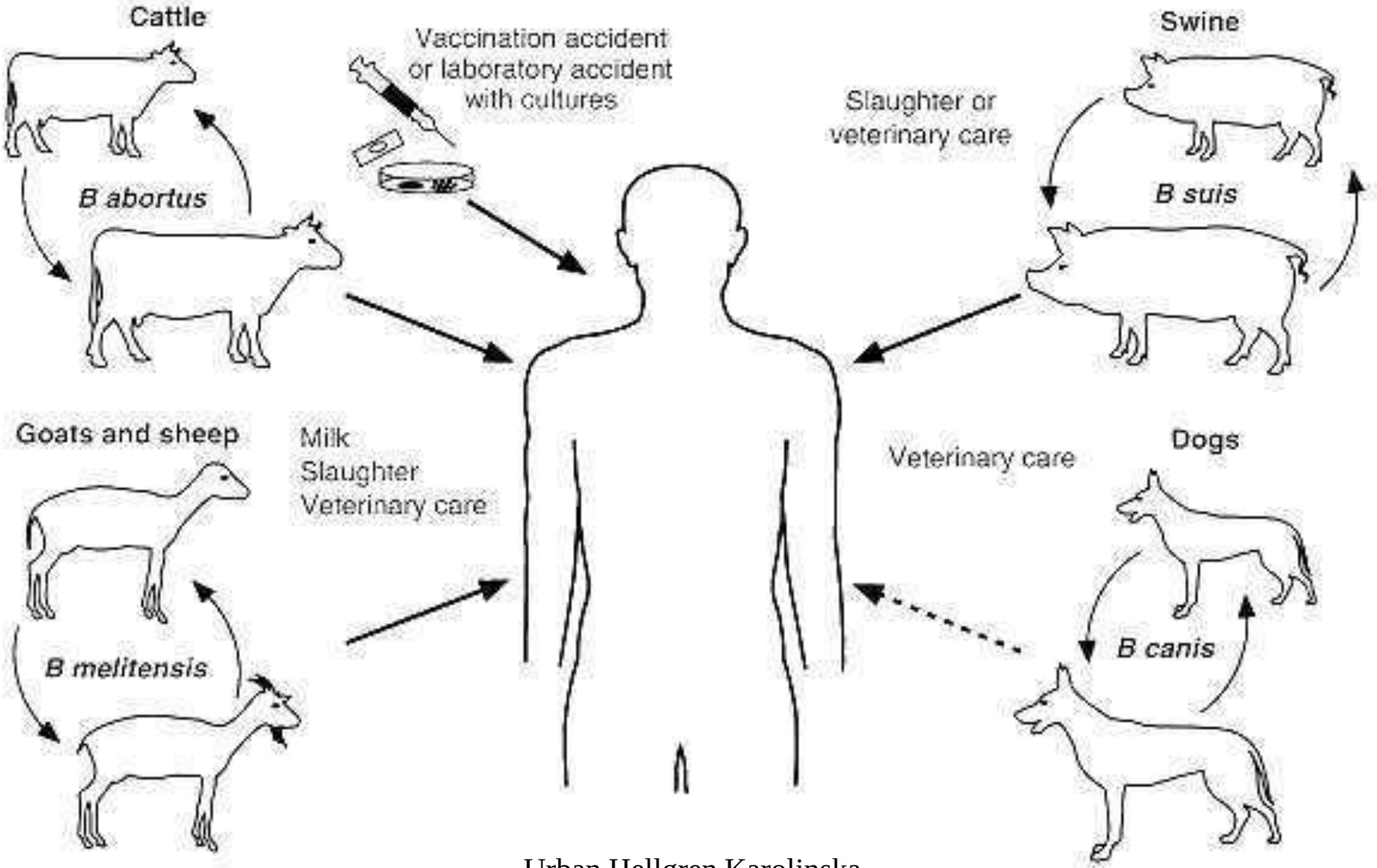
  ”One of the most common infection risks faced by microbiologists”

Sources of infection

- B. melitensis usually transmitted through consumption of unpasteurized milk or milk products..
- One common source is fresh white cheese or goat`s cheese
- Brucella actively eradicated in Sweden 1944 - 56

Unpasteurized milk

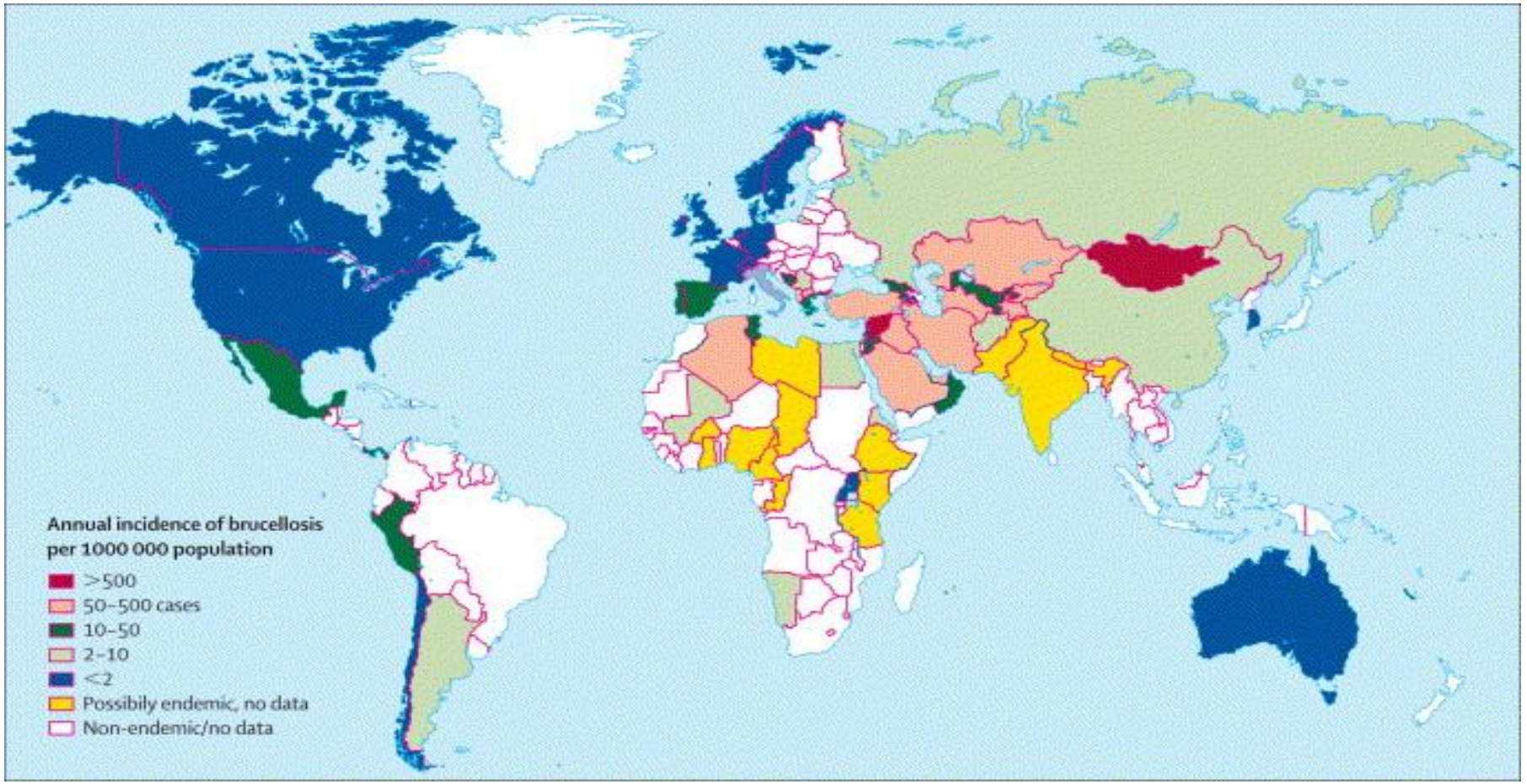
There are many ways to get Brucellosis



The animals also get sick

A common disease in the Middle East

- Brucella is a cosmopolitan disease
- Quite common in the Middle East, in some republics of the former Sovjet Union and in Mongolia
- Syria has probably the highest yearly incidens with 1603 human cases / million (WHO 2004)



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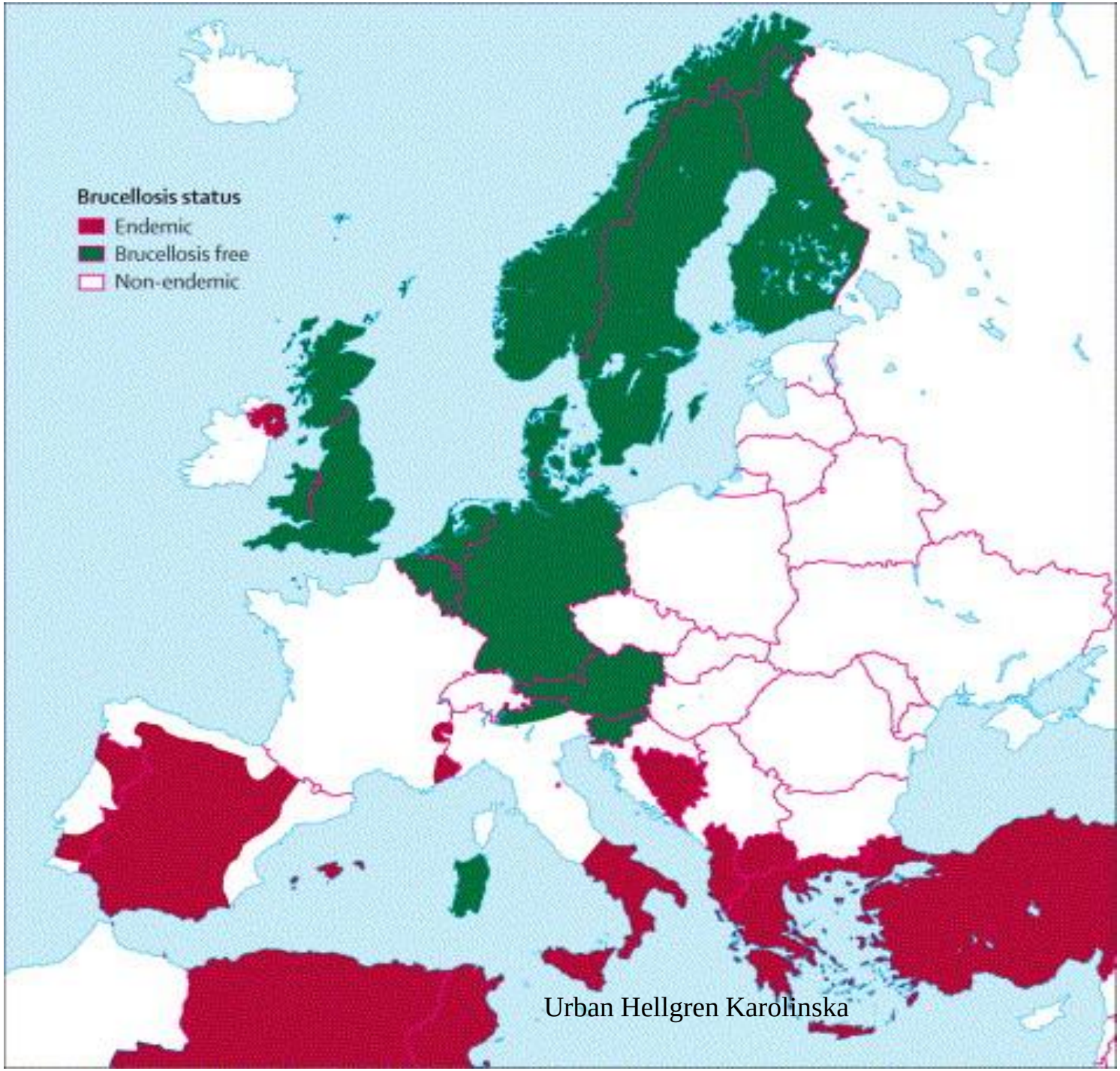

Brucellosis In Europe

Brucellosis in Sweden

No animal cases since 1957

A notifiable disease since July 1st 2004

Totalt 61 cases 2004 – 2011 (8/year)

23 cases (july 2004 – okt 2007)
infected in Irak (8) och Syria (3)

Summary

* Brucellosis is common in the Middle East
* Transmission usually through intake of unpasteurized milk or milk products.
* Diagnosis based on blood cultures but they must be labelled to avoid exposure of laboratory personel

Consider Brucellosis in patients with long standing fever after visits to endemic areas