Genomic Epidemiology and Outbreak Investigation of Brucellosis in a One Health Context

Epidemiological background of *Brucella* spp., diversity, overview of brucellosis

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Intended Learning Objectives

Specific objectives of this session:

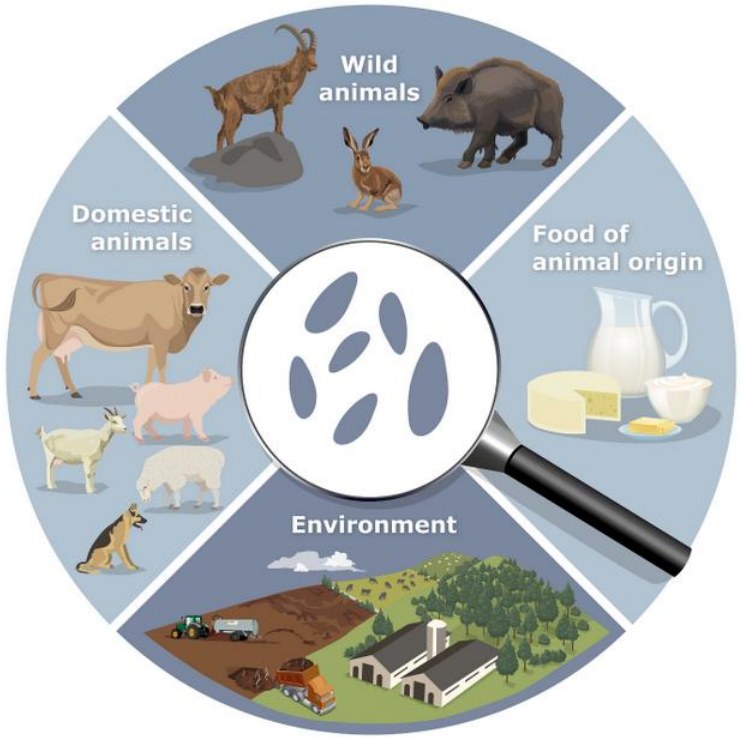
ILO 1. Understand the biological diversity within the *Brucella* genus and its significance within the One Health context.

ILO 10: Understand the value of the One Health approach for real-world applications.

Outline

This session consists of the following elements

- Learn about *Brucella*
  - Epidemiology
  - Endemicity
  - Host relation
  - Pathogenicity



[3] EFSA: Brucella story map. 2025

Epidemiological Background of *Brucella* spp.

- Brucellosis is a globally widespread zoonotic disease caused by Gram-negative bacteria of the genus *Brucella*.
  - It remains endemic in many low- and middle-income countries
- It affects livestock, wildlife, and humans, with major public health and economic consequences
- Transmission most commonly occurs through
  - Occupational exposure (farmers, shepherds, veterinarians, slaughters)
  - Contact with infected animals (small ruminants, cattle, pigs, and dogs)
  - Consumption of contaminated, unpasteurized animal products (milk and dairy)

Endemic presence of *Brucella*

Brucella shows a substantial health burden with persistent endemicity and regional variation

Particularly in:

- North Africa, Middle East, Central Asia and parts of China

Brucellosis is often underdiagnosed and underreported

- Symptoms are nonspecific
- Laboratory capacity is limited in many endemic regions
- Molecular confirmation is rarely available

This leads to an underestimation of true disease burden.

Human seroprevalence can reach 6–7% in some regions, and animal infection varies widely by species, geography, and production systems

Brucella species

There are +10 *Brucella* species described

Four species causes the majority of human clinical cases

- *B. abortus*, primarily infects cattle
- *B. melitensis*, infects sheep and goats
- *B. suis*, infects mainly swine
- *B. canis,* infects mainly dogs
- + additional species from marine mammals and environmental niches

Despite high overall genomic similarity, *Brucella* species show host preference and ecological specialization with *B. melitensis* being the most pathogenic in humans

Brucella in animals

Brucella infections in animals (species dependent)

- Animals can carry *Brucella* asymptomatically

- *Brucella* typically causes:
  - reproductive disorders,
    - Incl. abortions, infertility, mastitis, orchitis
  - Arthritis (joint pain)
  - Lesions

- Infections can be acute (1-3 weeks) or chronic (6-24 months)

Prevention of *Brucella* infections

Vaccination is a prospective approach for controlling the spread of brucellosis, particularly in livestock.[6]

- Traditionally, inactivated, live-attenuated vaccines were developed
  - Widely used vaccines, such as *B. abortus* S19 and *B. melitensis* Rev1, complicating the differentiation between vaccinated and infected animals
- Genomic advances has led to DNA vaccines with more complete immunization and less drawbacks
- There is no human vaccination available
  - Controlling animal brucellosis is the most efficient approach to preventing human infection
- Some EU countries are officially free of Brucella in cattle etc.

Brucella in humans

Human brucellosis is less recognized and understood than animal infections

The disease is typically characterized by

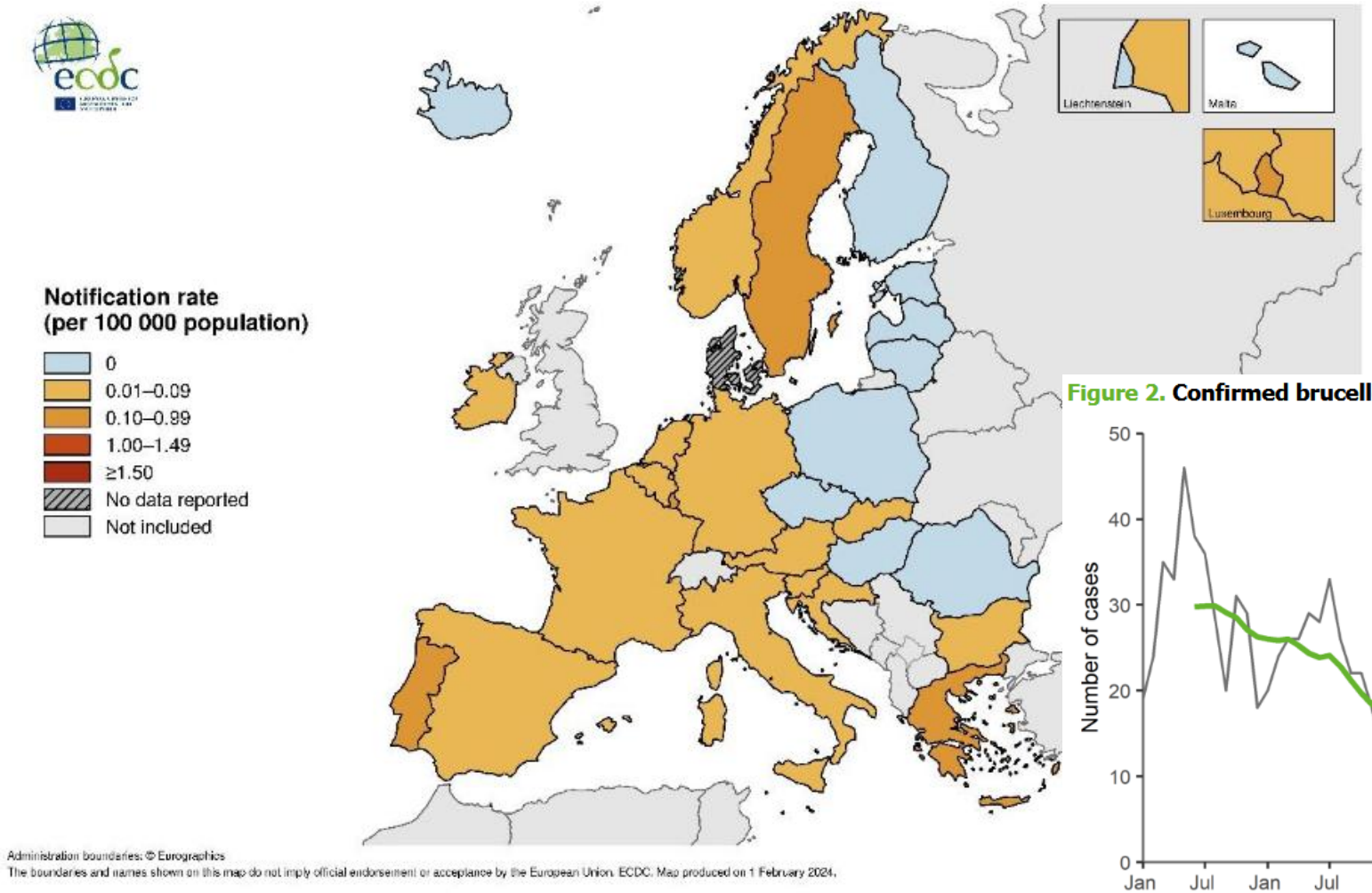
- Nonspecific influenza-like illness
  - undulating fever, sweats, headache, fatigue, malaise

- Incubation: 5- 60 days; occasionally several months
- <2% case fatality rate for untreated cases
- May have long recovery period

- *Brucella* lacks classical virulence factors (e.g. exotoxins, cytolysins and exoenzymes)
- Pathogenesis is attributed to unique factors, such as lipopolysaccharide (LPS), type IV secretion system (T4SS) and the BvrR/BvrS system.

Human brucellosis cases

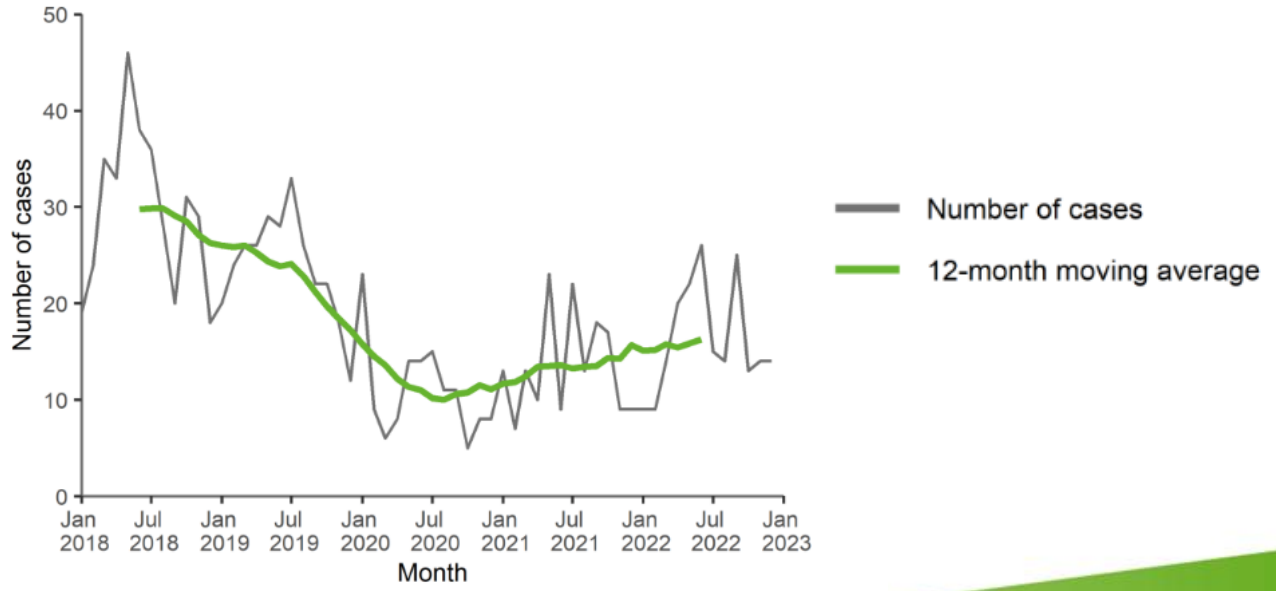
Figure 1. Number of confirmed brucellosis cases per 100 000 population by country, EU/EEA, 2022



The number of brucellosis cases at the EU/EEA level dropped from 2018 to 2020 and slightly increased in 2021– 2022

In 2022, the lowest number of cases was reported in January and February and the cases peaked in June and September

Figure 2. Confirmed brucellosis cases by month, EU/EEA, 2018–2022



Source: Country reports.

https://www.ecdc.europa.eu/sites/default/files/documents/BRUC_AER_2022_Report.pdf

Brucella outbreaks

- There is a high overall genomic similarity between the species
- Genomic studies reveal population structure shaped by geography, host species, and long-term endemic circulation
- Genome-wide SNP and cgMLST analyses have become critical tools for distinguishing outbreak-related clusters, with **≤7 SNPs** often used as a threshold for epidemiological linkage
- Multiple studies show that *B. melitensis* lineages may persist for decades with limited genetic change, complicating outbreak detection and requiring high-resolution genomic tools

Brucellosis outbreaks

Recent examples of outbreaks:

- In Tunisia (1988–2022), *B. melitensis* showed remarkable genetic stability, clustering into a single lineage (biovar 3, ST11)
- In East China (2011–2024), more than 500 isolates fell into two major clades with multiple novel cgMLST genotypes, revealing sustained circulation and microevolution
- In Shaanxi, China (2024), outbreaks were driven by multiple co-circulating *B. melitensis* lineages, highlighting regional complexity and multi-source transmission

Brucella in the lab

Challenging to work with and identify in the lab

- Fastidious and slow-growing
  - blood cultures might need incubation for weeks or up to a month for detection
- Airborne transmission of *Brucella* bacteria is a risk

Brucella bacteria can be rough or smooth (appearance of colonies on agar)

- Smooth strains including *B. melitensis, B. abortus* or *B. suis* are typically more pathogenic than rough strains such as *B. canis*

Current diagnostic tests are often inaccurate

- A pan-*Brucella* species PCR test is only accredited for smooth strains of Brucella
- Serological methods can be used

In summary

- Brucellosis causes reproductive losses in animals, chronic illness in humans, and substantial economic costs
- *Brucella* spp. are globally distributed zoonotic pathogens with substantial human and animal health impacts
- Effective control requires integrated One Health strategies—animal vaccination, improved diagnostics, food safety, and coordinated surveillance
- *B. melitensis* is the most virulent and epidemiologically important species for human disease
- Genomic studies reveal both remarkable stability and lineage diversity, depending on the region
- Multiple regions show persistent endemic circulation with periodic outbreaks driven by several co-existing lineages
- High-resolution molecular tools (WGS, SNP analysis, cgMLST) are now essential for outbreak detection and tracing

References

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Acknowledgements

The creation of this training material was commissioned by ECDC to Institut Pasteur with the direct involvement of Jette Kjeldgaard, DTU Food