Neisseria meningitidis - Introduction

Neisseria meningitidis (meningococcus)

- most frequent agent of meningitis (purulent neuroinfection)
- also agent of fulminant meningococemia
- symptoms of meningitis – meningeal syndrome – triad: 1. constant and severe headache, 2. vomitus or nausea, 3. positive meningeal signs (e.g.neck, back stifness) in children can absent (fever)
- symptoms of septicemia - 4. skin efflorescences – petechiae, rash, hemoragic suffusion, 5. DIC disseminated intravascular coagulopathy 6. septic schock

Neisseria meningitis

Physiology and Structure **Gram-negative diplococci** with fastidious growth requirements. **Oxidase** and **catalase** positive; acid produced from **glucose** and **maltose** oxidatively. **Outer surface antigens** include polysaccharide capsule, pili, and lipooligosaccharides (LOS)

Virulence **Capsule** protects bacteria from antibody-mediated phagocytosis
Specific receptors for meningococcal **pili** allow colonization of nasopharynx. Bacteria can survive intracellular killing in the absence of humoral immunity
Endotoxin mediates most clinical manifestations.

Neisseria meningitis

Epidemiology **Humans are the only natural hosts**. **Person-to-person spread** occurs **via aerosolization of respiratory tract secretions**. Highest incidence of disease is in children younger than 5 years, institutionalized people, and patients with late complement deficiencies. **Meningitis** and **meningococcemia** most commonly caused by serogroups B and C. Also **pneumonia** – agent *N. meningitis*. Disease **occurs worldwide**.

Diagnosis Gram stain of CSF is sensitive and specific but is of limited value for **blood specimens** (too few organisms are generally present, except in overwhelming sepsis). Culture is definitive, but organism is fastidious and dies rapidly when exposed to cold or dry conditions. Tests to detect antigens are insensitive and nonspecific. **DNA amplification** (blood, CSF).

Meningococcal infections

TREATMENT

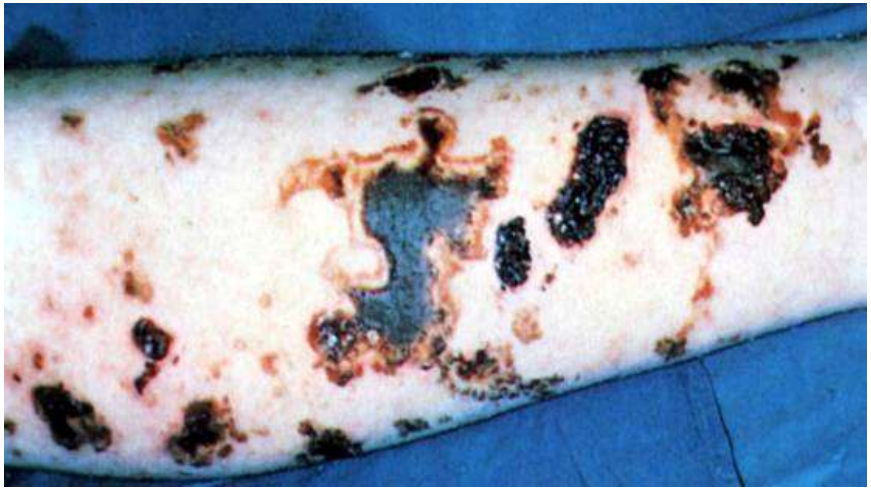
- penicillin, cephalosporins 3rd generation
- supportive multiorgan therapy – ventilation, circulation, renal function

OUTCOME, COMPLICATIONS

- DIC in severe sepsis can result in multiple necroses of peripheral part of extremites, the lost of which can follow (fig.)
- mortality – meningitis up to 2%, sepsis about 30%

PREVENTION, PROPHYLAXIS

- only close contacts (kissing) oral penicillin 7 days
- vaccines serogroup A, C (bivalent) and A,C,Y,W135 (tetravalent), also B



Biological properties

- pilli – allow colonization of nasopharynx
- potent bacterial endotoxin LOS – lipooligosaccharide (lipid A + core polysaccharide) in the cell wall is main virulence facor responsible for symptoms of septicemia

Meningococcal infections

CLINICAL DIAGNOSIS

Initial therapy of meningococcal sepsis and sepsis/meningitis is entirely clinical (acute febrile disease & hemorragic exanthema) because of the urgency.

MICROBIOLOGICAL DIAGNOSIS

- microscopy – Gram staining procedure

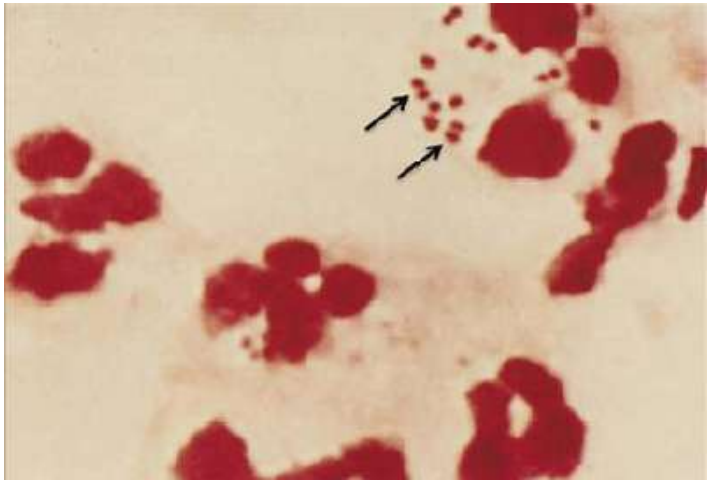


Figure 1. Gram stain of *N. meningitidis as* gram-negative coffee bean-shaped diplococci in CSF with associated PMNs.

Diagnosis - http://www.cdc.gov/meningitis/lab-manual/chpt06-culture-id.html

Purulent (suppurative, bacterial) meningitis

ETIOLOGY

- 5 months – 5 years and in adolescent: most common *N. meningitidis*
- 5 months – 5 years *H. ifluenzae* type B (before vaccination), most common in unvaccinated children

Meningococcal infections

ETIOLOGY

- *Neisseria meningitidis* (meningococcus), gramnegative diplococcus, 13 serogroups most infection caused by A, B, C, Y and W135 serogroups CR prevalent serogroup B (75% cases) and C

EPIDEMIOLOGY

- world-wide (endemic in sub-Saharan Africa)
- primarily a disease of children and young adults
- CR – low incidence (100 cases annually)

CLINICAL SYMPTOMS

- 5 -15% asymtomatic carriers
- **superficial inf.** – pharyngitis, rhinitis, uretritis, conjunctivitis (untreated can result in invesive infection but may-be self limited)
- **invasive inf.** – invasion from mucosa to blood stream, **sepsis and/or meningitis** (obviously sepsis and meningitis)
- **sepsis –** is **peracute infection (hours),** consistent with **multiorgan dysfunction and failure** (severe DIC, petechiae, suffusion, septic shock)

Purulent (suppurative, bacterial) meningitis

DIAGNOSIS

Microbiological examination of cerebrospinal fluid (CSF) is crucial to dg the infection:

- microscopy – Gram or another staining procedure
- culture – enriched and diagnostic culture media (liquid culture media to enhance the growth)
- cultivation free methods – e.g. PCR, agglutination of CSF with most prevalent bacterial agents
- hemoculture

Searching for focal infections or trauma (X ray of nasal cavity, CT of skll or brain…)

Purulent (suppurative, bacterial) meningitis

CAUSATIVE THERAPY

Should be prescribed immediately after CSF is collected

- cephalosporins of 3rd generation (ceftriaxon, cefotaxim) – penetrates in high concentration through hematoencephalic barier (ceftazidim for *P. aeruginosa, K. pneumoniae)*
- betalactam allergy – chloramphenicol
- resistant *P. aeruginosa, K. pneumoniae* – carbapenems (meropenem, imipenem)
- *S. pneumoniae* – vancomycin + 3rd gen.cephalosporins
- *L. monocytogenes* – to cephalosporins (primary resistant) should be added ampicillin

Meningococcal infections

MICROBIOLOGICAL DIAGNOSIS

cultivation free methods – e.g. PCR, agglutination of CSF

agglutination

Latex agglutination procedure for CSF

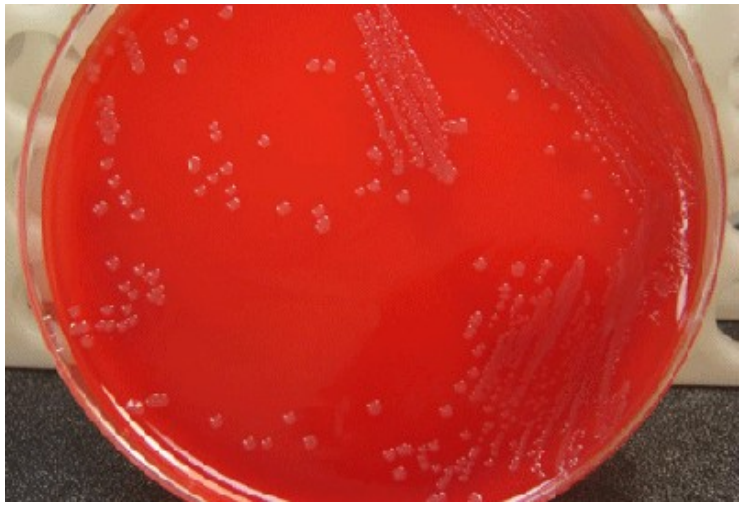
Follow the manufacturer's instructions on the package insert for the specific latex kit being used. General instructions are listed below:

1.Centrifuge the CSF for 10-15 minutes at 1000 x g and collect the supernatant.
    1. The sediment should be used for Gram stain and primary culture.
2.Heat the CSF supernatant to be used for the test at 100°C for 3 minutes.
3.Shake the latex reagents gently until homogenous.
4.Place one drop of each latex reagent on a disposable card provided in the kit or a ringed glass slide.
5.Add 30-50 µl of the supernatant of the CSF to each latex reagent.
6.Rotate by hand for 2-10 minutes. If available, mechanical rotation at 100 rpm is recommended.
    1. Avoid cross-contamination when mixing and dispensing reagents.
7.Examine the agglutination reactions under a bright light without magnification.

Meningococcal infections

MICROBIOLOGICAL DIAGNOSIS

cultivation – enriched and diagnostic culture media (liquid culture media to enhance the growth)



A B C

Neisseria meningitidis cultured on the selective Thayer Martin medium (A) (when commensal flora contaminated the specimen), culture on chocolate agar (B) and blood agar (C). Carbon dioxide enhances growth, but is not required. *N.meningitidis* is oxidase positive. Identification – phenotypical (biochemical, mass spectrometry) or genotypical identification.

Neisseria meningitis

Treatment, Prevention, and Control Breast-feeding infants have passive immunity (first 6 months). Treatment is with **penicillin (drug of choice),** chloramphenicol, ceftriaxone, and cefotaxime. Chemoprophylaxis for contact with persons with the disease is with rifampin, ciprofloxacin, or ceftriaxone.
For immunoprophylaxis, vaccination is an adjunct to chemoprophylaxis; it is used only for serogroups A, C, Y, and W135; no effective vaccine is available for serogroup B.
Polysaccharide vaccines conjugated with protein carriers offer protection for infants younger than 2 years

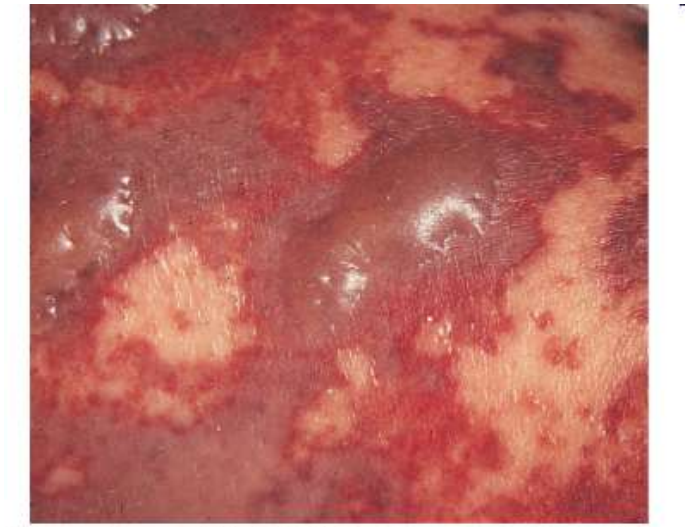


Fig. Skin lesions in a patient with meningococcemia. Note that the petechial lesions have coalesced and formed hemorrhagic bullae

Case Report: Infection with *Neisseria meningitidis*

Abstract

Meningococcal disease caused by *Neisseria meningitidis* is a rapidly progressive and potentially fatal infection. We report a case of acute bacterial meningitis in a young adult presenting with fever, headache, and altered mental status, highlighting the importance of early recognition and prompt treatment.

Introduction

Neisseria meningitidis is a Gram-negative diplococcus that colonizes the nasopharynx and can invade the bloodstream, causing **meningitis** and **meningococcemia**. Despite advances in vaccination, it remains a significant cause of morbidity and mortality worldwide.

Case Presentation

A 21-year-old male presented to the emergency department with:

- High-grade fever (39.5°C)
- Severe headache
- Neck stiffness
- Photophobia
- Vomiting
- Confusion (GCS 13)
- Hypotension
- Petechial rash20

Laboratory findings:

- Leukocytosis (WBC 18,000/µL)
- Elevated CRP and procalcitonin

Lumbar puncture:

- Turbid cerebrospinal fluid (CSF)
- Elevated opening pressure
- CSF analysis:
  - High protein
  - Low glucose
  - Neutrophilic predominance

Microbiology:

- Gram stain: Gram-negative diplococci
- CSF culture: *Neisseria meningitidis*
- PCR: Positive for meningococcal DNA

Outcome

The patient improved after 5 days of targeted antibiotic therapy. Neurological status returned to baseline, and he was discharged after 10 days without complications.

Discussion

Key points:

- Rapid progression can lead to **septic shock and death within hours**
- Classic triad (fever, neck stiffness, altered mental status) is not always present
- Petechial rash is highly suggestive of meningococcemia
- Early antibiotic administration significantly reduces mortality

Risk factors include:

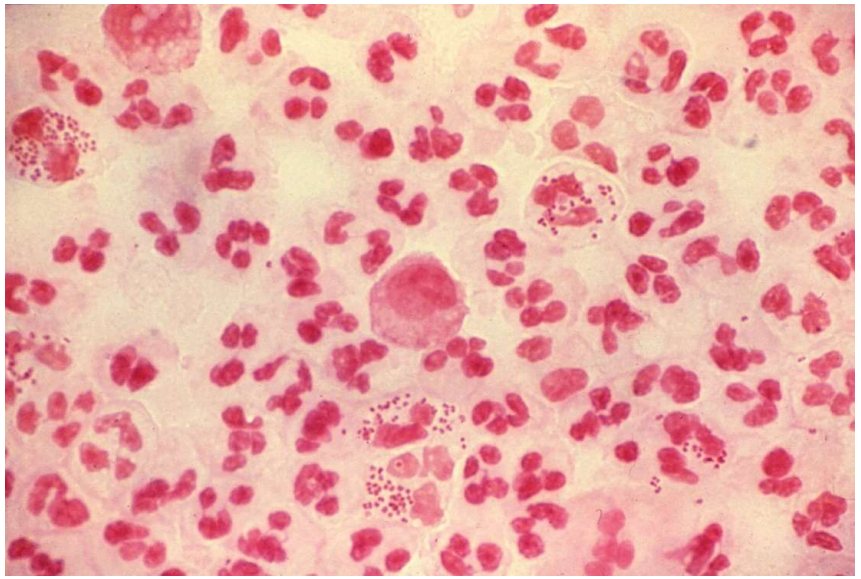
- Close living quarters (e.g., dormitories)
- Complement deficiencies
- Lack of vaccination

Neisseria gonorrhoeae

MICROBIOLOGICAL DIAGNOSIS

cultivation – enriched and diagnostic culture media (liquid culture media to enhance the growth), swab uretra, cervix, urine - PCR

A



B

Neisseria gonorrhoeae cultured on the selective Thayer Martin medium (A) (when commensal flora contaminated the specimen), culture on chocolate agar (B) gonococci in PMNs

Case Report: Infection with *Neisseria gonorrhoeae*

Abstract

A 24-year-old male presented with dysuria and purulent urethral discharge. Laboratory testing confirmed infection with *Neisseria gonorrhoeae*. The patient was treated with ceftriaxone, resulting in complete resolution of symptoms. This case highlights the importance of early diagnosis, antimicrobial resistance awareness, and partner notification in managing gonorrhea.

Introduction

Neisseria gonorrhoeae is a Gram-negative diplococcus responsible for the sexually transmitted infection gonorrhea. It primarily affects mucous membranes of the urogenital tract but may also infect the rectum, pharynx, and conjunctiva. Increasing antimicrobial resistance has made management more challenging globally.

Case Presentation

Patient Information

•Age: 24 years

•Sex: Male

•Medical history: No significant past illness

•Social history: Multiple recent sexual partners, inconsistent condom use

Presenting Complaints

•Burning sensation during urination (dysuria)

•Yellow-green urethral discharge (3-day duration)

Clinical Findings

•Purulent discharge from urethral meatus

•Mild penile tenderness

•No systemic symptoms (fever absent)

Diagnosis

Laboratory Tests

- **Gram stain**: Gram-negative intracellular diplococci
- **PCR**Positive for *Neisseria gonorrhoeae*
- **Culture**: Confirmatory, with antimicrobial susceptibility testing

Differential Diagnosis

- *Chlamydia trachomatis* infection
- Non-gonococcal urethritis
- Urinary tract infection

Treatment

- Single intramuscular dose of ceftriaxone (500 mg)
- Empirical co-treatment for possible chlamydial infection (e.g., doxycycline)

Outcome and Follow-Up

- Symptom resolution within 5 days
- No complications observed
- Patient advised:
    - Abstain from sexual activity for 7 days
    - Notify and treat sexual partners
    - Follow-up testing recommended in 3 months

Discussion

Gonorrhea remains a major public health concern due to:

- High transmission rates
- Frequent asymptomatic cases
- Rising antibiotic resistance

Untreated infections can lead to complications such as:

- Epididymitis in men
- Pelvic inflammatory disease (PID) in women
- Disseminated gonococcal infection (DGI)

Early diagnosis using PCR is highly sensitive and specific.
Current guidelines recommend ceftriaxone as first-line therapy due to resistance to older antibiotics.

Bordetellae

Content

- Physiology and structure
- Structure and pathogenesis
- Diseases
- Epidemiology
- Laboratory diagnosis
- Treatment, prevention and control

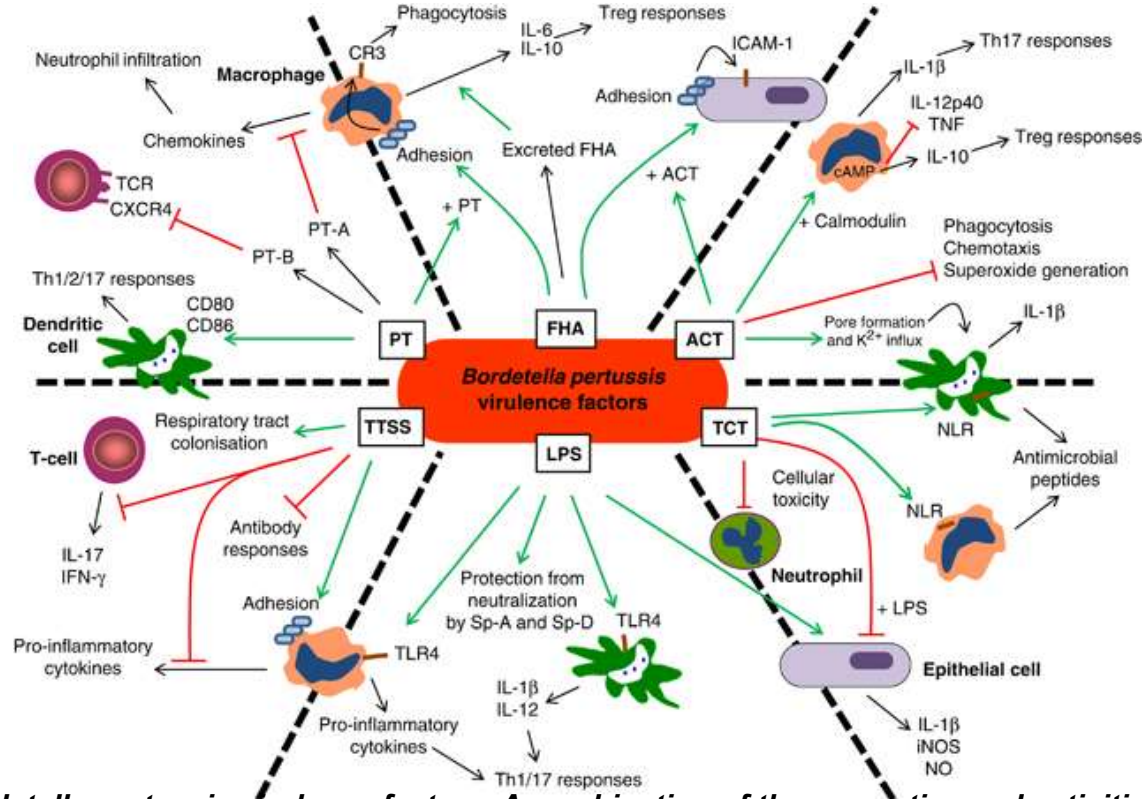
Physiology and structure

- Aerobic
- **Gram-negative extremely small bacteria** (0,2 to 0,5 x 1 μm) – coccobacilli
- **Significant human pathogens**: ***B. pertussis*** (**pertussis** – whooping cough) and ***B. parapertussis*** **(parapertussis)**
- **Fastidious** - highly susceptible to toxic substances in common culture media – **require special culture media** (contain charcoal, starch, albumin) to absorb these toxic substances

Structure and pathogenesis

- *B. pertussis* binds (**FHA – filamentous hemagglutin** and **peractin**) to cilliated epithelium in upper respiratory tract
- Other virulence factors cause **toxin mediated disease**:
- **pertussis toxin** (PT) – bicomponent A-B toxin, ADP –ribosylating activity – increase cAMP and **respiratory secretions** and **mucus production**
- **adenylate cyclase toxin** - bicomponent A-B toxin, **increases cAMP** (as PT does), inhibits leucocyte chemotaxis, phagocytosis and killing)
- **dermonecrotic toxin** – vasoconstriction and ischemic necrosis
- **tracheal toxin** – inhibits cilia movement and regeneration of damaged cells

Diagram of structure related pathogenesis



Immunomodulatory effects of Bordetella pertussis virulence factors. A combination of the properties and activities of filamentous hemagglutinin (FHA), pertussis toxin (PT), tracheal cytotoxin (TCT), adenylate cyclase toxin (ACT), type III secretion system (TTSS), and lipopolysaccharide (LPS) provide B. pertussis with multiple mechanisms to evade detection and elimination by the host immune response. *Selected effects of individual virulence factors are separated by black dashed lines. Green arrows indicate a positive regulatory effect on the target cell or process. Red bars indicate a negative regulatory effect on the target cell or process. Cells crossing the black dashed lines are targeted by the virulence factor on either side of the line; this layout is for presentation purposes only and does not imply that there is any association between these separate effects. ICAM-1, intracellular adhesion molecule 1; IL, interleukin; iNOS, inducible nitric oxide synthase; NLR, nucleotide-binding and oligomerization domain (NOD)-like receptor; NO, nitric oxide; SP, surfactant protein; TCR, T-cell receptor; Th, T helper; TNF, tumor necrosis factor; Treg, regulatory T cells. Mucosal Immunology* advance online publication 20 June 2012. doi:10.1038/mi.2012.54

Diseases

Pertussis – incubation period (1-3 weeks)

- **1. catarrhal phase** - begins with nonspecific symptoms such as mild conjunctivitis, rhinorrhea, malaise, mild fever, and then progresses to induce dry, nonproductive cough
- **2. paroxysmal phase** - begins after 1 to 2 weeks, cilliated epithelia are extrude from the respiratory tract and clearence of mucus is impaired, mucus production is responsible for causing airway restriction and whoping cough (whoop – inspiring against a partially closed glottis), vomiting, daily 40 – 50 paroxysms (spasms of 10-15 uncontrollable coughing), complications - pneumonia
- **3. convalescent phase** – begins after 2 to 4 weeks, paroxysms diminished in number and severity

Papertussis - caused by *B. parapertussis*, milder symptoms

Epidemiology

- **historically - a pediatric disease**
- **today – infants (majority – children < 1 year), adults** and **seniors** could be affected
- **highly contagious** (small infection dose)
- **source of the infection** – usually **patient** in the early catarrhal stage of the disease
- **transmission via dropplets**, the agents survives only briefly outside the human respiratory tract
- **endemic worldwide** (60 milion people affected annually) – fatality rates in developing countries – up 3%

  – incidence in Europe – less than 1 case/100 000 population

Laboratory diagnosis

- **Culture** – pinpoint colonies from nasoparynx (wash, swab) or cough of symptomatic patients into 3 to 6 days (special culture media e.g. Charcoal agar)
- 

B. pertussis minute colonies on charcoal agar supplemented by a selective agent (fig. author)

- **PCR** - high sensitivity (80-100%)
- **Direct fluorescent antibody** (DFA) test – in smear of nasopharyngeal specimens
- **Serology** – significant seroconversion or initially high titer is consistent with a recent infection

Treatment, prevention and control

Treatment – more effective in catharral stage than in paroxysmal where already toxin-mediated disease developed

- **longer treatment:** 14-days treatment course is recommended
- **drug of choice – macrolides** (erythromycin, azithromycin, clarithromycin)
- **alternatives** – co-trimoxazole, fluoroquinolones
- **supportive care** – is in adition to antibiotics paramount for the managment of pertussis especially intubation and mechanical ventilation in infants

Prevention and control

Vaccination – cellular vaccines caused complications and was replaced by **acellular vaccines** (usually contain **inactivated pertussis toxin and one or more other bacterial** components (e.g. FHA, peractin, hemagglutinin)

- **administered** in combination with the **vaccine** for diphteria and tetanus (DTP) to children at ages 2, 4, 6 and 15 to 18 months with the 5th dose between the ages of 4 and 6 years (included in the hexavaccine in the Czech Republic)
- **chemoprophylaxis is used for household contacts**
- **protection of infants at greatest risk** of life-threating *B. perussis* infection – vaccination initiated when the infants is 2 months old

Current issues for adults and adolescents

In recent years, there has also been an **increase in pertussis in adolescents and young adults**. In the 1990s, Canada experienced a resurgence of pertussis, primarily in young adolescents. This was a result of the low effectiveness of the whole-cell pertussis vaccine used between 1985 and 1998 in this country. This resulted in a "marching cohort" effect or the age of peak incidence increasing, each year, by 1 year, revealing the existence of a susceptible cohort. This was addressed with universal immunization programs to vaccinate adolescents with a more effective acellular pertussis vaccine. **Immunity after pertussis immunization also diminishes over time. It is estimated that immunity following acellular pertussis vaccination may begin to decline after 4 to 5 years, suggesting that a booster dose may be appropriate.**

The carrier state

In the past, based on knowledge obtained from **traditional culture methods, there was not considered to be a carrier state for B. pertussis in the nasopharynx.** However, **this may no longer be true**, according to studies done with more sensitive polymerase chain reaction (PCR) methods. **In addition to circulating among adults, there may also be transient nasopharyngeal carriage of *B. pertussis* in immunized children.** A recent report has described a laboratory-confirmed (primarily by PCR) outbreak of pertussis occurring in preschool-aged children. This was not a classic pertussis, as evidenced by a lower number of cases meeting a clinical case definition, a very low hospitalization rate of unimmunized infants, and a low secondary attack rate in households. High vaccine rates may have moderated the outbreak and, with respiratory co-infection in a significant proportion of cases, a positive **PCR result may simply have reflected transient nasopharyngeal carriage of B. pertussis in the absence of evidence of seroconversion.**

Clinical presentations – young children

There is a spectrum of disease caused by B. pertussis infection and its presentation will vary according to the patient's age, degree of immunity, use of antibiotics, and respiratory co-infection.

Young Children. Joseph Lapin wrote a detailed description of typical or classic pertussis in 1943 that remains true to this day. Pertussis is classically divided into three stages: the catarrhal or prodromal stage, the paroxysmal stage, and the convalescent stage. The catarrhal stage begins after a usual incubation period of 7 to 10 days, with a range of 5 to 21 days. In the catarrhal stage, children will present with signs and symptoms of a common upper respiratory tract infection including rhinorrhea, nonpurulent conjunctivitis with excessive lacrimation, occasional cough, and low-grade fever. The catarrhal stage typically lasts 1 to 2 weeks and is followed by the paroxysmal stage. As its name suggests, the paroxysmal stage is characterized by paroxysms or fits of coughing. The child will typically have spasms of uncontrollable coughing, often 10 to 15 coughs in a row in a single expiration, the face may turn red or purple and, at the end of the paroxysm, he or she may have an inspiratory whoop. The whoop is caused by inspiring against a partially closed glottis. With the force of the coughing, they may produce mucus plugs and often have post-tussive vomiting.

Paroxysms occur more frequently at night. The paroxysmal stage lasts 1 to 6 weeks. During the end of the first stage and beginning of the second stage, patients may exhibit signs of systemic disease, such as leukocytosis with lymphocytosis, both risk factors for worse clinical outcome. Hyperinsulinemia may also occur, although it is rarely associated with hypoglycemia. Lastly, as symptoms begin to wane, the patient enters the convalescent stage. The length of the cough distinguishes pertussis from other respiratory tract illnesses. In classic pertussis, it usually lasts 1 to 6 weeks, although it can last longer; pertussis is known as the "cough of 100 days" from the Chinese. Most clinical case definitions require a cough of at least 14 days and at least one of the following symptoms: paroxysmal cough, inspiratory whoop, or post-tussive vomiting. The mean duration of cough in adults with pertussis is 36 to 48 days. For up to 1 year following pertussis infection, it is not uncommon to have recurrences of the paroxysmal cough or inspiratory whoop with other respiratory illnesses.

Some notes to diagnosis pertussis

The **first step** in the diagnosis of pertussis is to have the appropriate index of **suspicion for pertussis disease**. For vaccine trials, WHO defines a case of pertussis as a patient with a paroxysmal cough for 21 days or longer and one or more of the following criteria: **positive culture for B. pertussis, significant increases in IgG and IgA antibody**, PT, or proven contact with a culture-confirmed case. This definition favors specificity of diagnosis rather than sensitivity. According to the CDC and WHO, for pertussis surveillance, a clinical case is defined as a **patient with cough for 14 days or longer** and at least one of the following: **paroxysmal cough, whoop, or post-tussive vomiting**. This is a more sensitive definition but confirmation requires a positive laboratory finding by **culture or PCR assay** or a confirmed **epidemiologic link.**

Case Report: Bordetella pertussis Infection in an Adult Patient

Abstract

Pertussis is a highly contagious respiratory illness classically affecting infants, but increasingly recognized in adults. We report a case of laboratory-confirmed *Bordetella pertussis* infection in a 34-year-old vaccinated adult presenting with prolonged cough. The case highlights diagnostic challenges and the importance of early recognition and treatment.

Introduction

Bordetella pertussis is a Gram-negative coccobacillus responsible for pertussis, or whooping cough. Despite widespread vaccination, outbreaks continue due to waning immunity and asymptomatic transmission. Adult cases are often underdiagnosed because symptoms may be atypical.

Case Presentation

A 34-year-old male presented with a **3-week history of persistent paroxysmal cough**, worse at night and occasionally followed by post-tussive vomiting. He denied fever but reported mild fatigue.

- **Medical history:** Fully vaccinated in childhood
- **Recent exposure:** His child had a recent prolonged cough illness
- **Physical examination:** Normal vital signs, intermittent coughing fits
- **Laboratory findings:**
    - Nasopharyngeal swab positive for *B. pertussis* by PCR
    - Mild lymphocytosis on CBC

No radiographic abnormalities were observed on chest X-ray.

Treatment

The patient treated with azithromycin
Close contacts were advised post-exposure prophylaxis

Outcome and Follow-Up

Symptoms gradually improved over 2 weeks, though mild cough persisted for an additional month. No complications occurred.

Discussion

This case illustrates several important points:

- **Atypical presentation in adults:** Absence of classic “whoop” sound
- **Waning immunity:** Even vaccinated individuals remain susceptible
- **Transmission risk:** Adults often serve as reservoirs for infant infection
- **Diagnostic delay:** Pertussis is often mistaken for bronchitis or viral illness

Early antibiotic treatment reduces transmission but may not significantly shorten symptom duration if started late.

Haemophilus influenzae

- Haemophilus genus - small, pleomorphic, gram-negative rods or coccobacilli present on the mucous membranes of humans

- ***Haemophilus influenzae*** is the species **most commonly associated with disease** (**meningitis** – specimen CSF & blood culture, **epiglottitis** – blood culture, pneumonia – sputum, blood culture, sinusitis, otitis - aspirates)

- facultative anaerobes, fermentative, **require** X (hemin) and V (NAD) **factors for growth** – **satelite growth** or **special media** – e.g. Chocolate agar

- microscopy is a sensitive test for detecting *H. influenzae* in cerebrospinal fluid (CSF), synovial fluid

Haemophilus influenzae

- antigen tests for *H. influenzae* type b are less useful following the introduction of *H. influenzae* type b (HIB) vaccine
- noncapsular *Haemophilus* commonly colonized in humans; encapsulated *Haemophilus* species, particularly *H. influenzae* type b, are uncommon members of normal flora
- disease caused by *H. influenzae* type b was primarily a pediatric problem; eliminated in immunized populations
- most *Haemophilus* infections are caused by the patient's bacterial flora (endogenous infections)

Other Haemophilus spp.

• Other *Haemophilus* species and the syndromes they cause include *H. parainfluenzae* (pneumonia and endocarditis), *H ducreyi* (genital chancre), and *H. aegyptius* (conjunctivitis).

Diagnosis

• microscopy (pleomorphic rods, fig.1), culture (satelite growth, fig.2), phenotypic or genotypic identification

Fig.1

Fig.2. Satelite growth of *H. influenzae* around line of *S. aureus* releasing NAD from lysed RBC ob blood agar

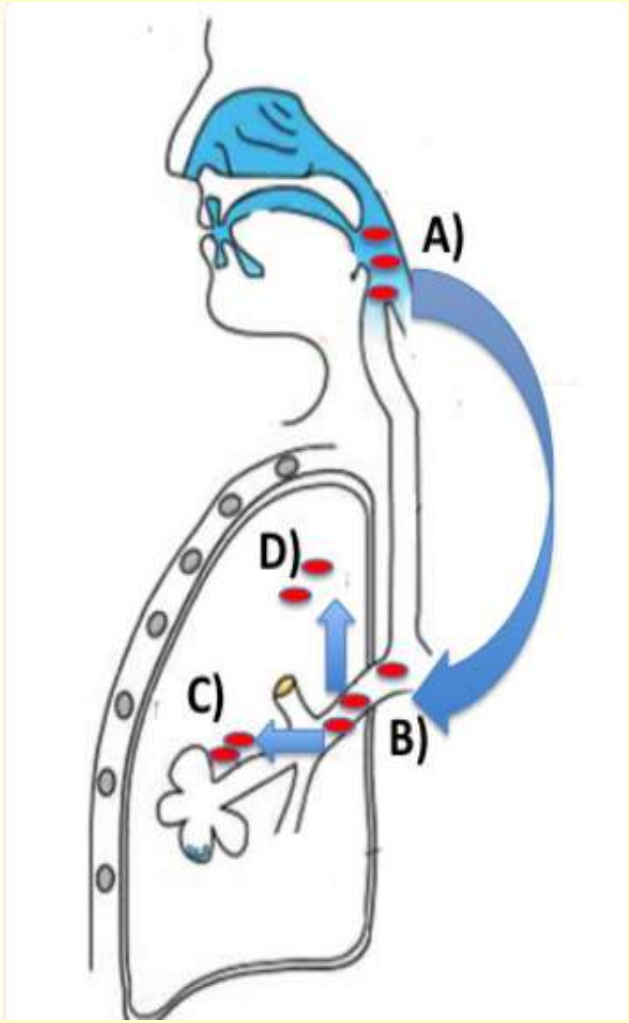
Treatment

A proportion of *H*. *influenzae* isolates **produce β-lactamase** and in this circumstance, **extended spectrum cephalosporins**, **amoxicillin-clavulinic acid**, **trimethoprim-sulfamethoxazole, tetracyclines, quinolones and macrolides** are appropriate. **For hospitalized patients** particularly if **there is associated respiratory failure** the **parenteral route** of administration may be **preferred**.

For patients who have repeated isolation of *H*. *influenzae* despite the use of appropriate antibiotics consideration should be given to the use of longer-term antibiotics or those with good intracellular penetration.

Vaccination

The vaccine to **type b encapsulated *H. influenzae*** induces humoral immunity to the capsule and has been **highly effective in reducing the incidence of disease** from this pathogen. This vaccine is now standard for children in industrialized countries. Vaccination is usually given at 2 months, 6 months and 12–15 months.



The potential spread of nontypeable strains of*H. influenzae*(NTHi) into the lung.A), Most healthy subjects have nasopharyngeal colonization with NTHi. A combination of bacterial pathogenic mechanisms and defects in host defense may allow NTHi to move down into the lower respiratory tract **B**). In the bronchi, NTHi may cause acute exacerbations of airway disease and/or chronic colonization. **C**), The bacterium may invade into bronchial cells such as macrophages or epithelial cells or **D**), may in more advanced lung disease invade into the parenchyma.

Case Report: Pneumonia Due to *Haemophilus influenzae*

Abstract

Haemophilus influenzae is a Gram-negative coccobacillus that commonly colonizes the upper respiratory tract and can cause invasive infections, particularly in vulnerable populations. We report a case of community-acquired pneumonia caused by *H. influenzae* in an adult patient with underlying risk factors, highlighting diagnostic challenges and treatment considerations.

Introduction

Haemophilus influenzae, especially non-typeable strains, is a significant cause of respiratory infections such as bronchitis and pneumonia. While vaccination has reduced infections from type b strains, non-typeable strains remain prevalent in adults, particularly in those with chronic lung disease or immunocompromise.

Case Presentation

A 68-year-old male presented to the emergency department with a 4-day history of productive cough, fever (38.5 °C), dyspnea, and pleuritic chest pain. His medical history included chronic obstructive pulmonary disease (COPD) and a 40-pack-year smoking history.

On examination:

- Respiratory rate: 26/min
- Oxygen saturation: 89% on room air
- Crackles in the right lower lung field

Laboratory findings:

- Elevated white blood cell count (15,000/mm^3)
- C-reactive protein: 120 mg/L

Chest X-ray revealed consolidation in the right lower lobe.

Microbiological diagnosis of community-acquired pneumonia
Purulent sputum Gram stain showed small Gram-negative coccobacilli. Culture grew *Haemophilus influenzae*. The isolate was beta-lactamase positive.
Blood cultures grew also *Haemophilus influenzae*.

Treatment
The patient was initially treated **empirically** with intravenous **ceftriaxone** and **azithromycin.** After culture results **confirmed beta-lactamase–producing *H. influenzae***, therapy was continued with ceftriaxone.
The patient improved clinically within 72 hours and was **transitioned to oral amoxicillin-clavulanate** to complete a **7-day course**

Outcome and Follow-Up
Symptoms resolved completely. A repeat chest X-ray at 4 weeks showed resolution of consolidation.

Discussion

H. influenzae pneumonia is more common in:

•Elderly patients

•Smokers

•Individuals with COPD

Key points:

•Non-typeable strains are now the predominant cause

•Beta-lactamase production is common, influencing antibiotic choice

•Empiric therapy for community-acquired pneumonia should cover this organism in at-risk populations

Vaccination against type b strains (Hib vaccine) has significantly reduced invasive disease but does not protect against non-typeable strains.

Conclusion

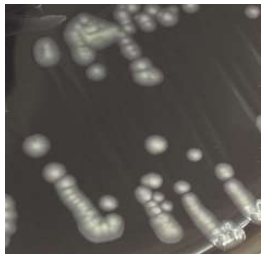
Haemophilus influenzae remains an important cause of pneumonia in adults with comorbidities. Prompt diagnosis and appropriate antibiotic therapy are essential for favorable outcomes.

Legionella pneumophila

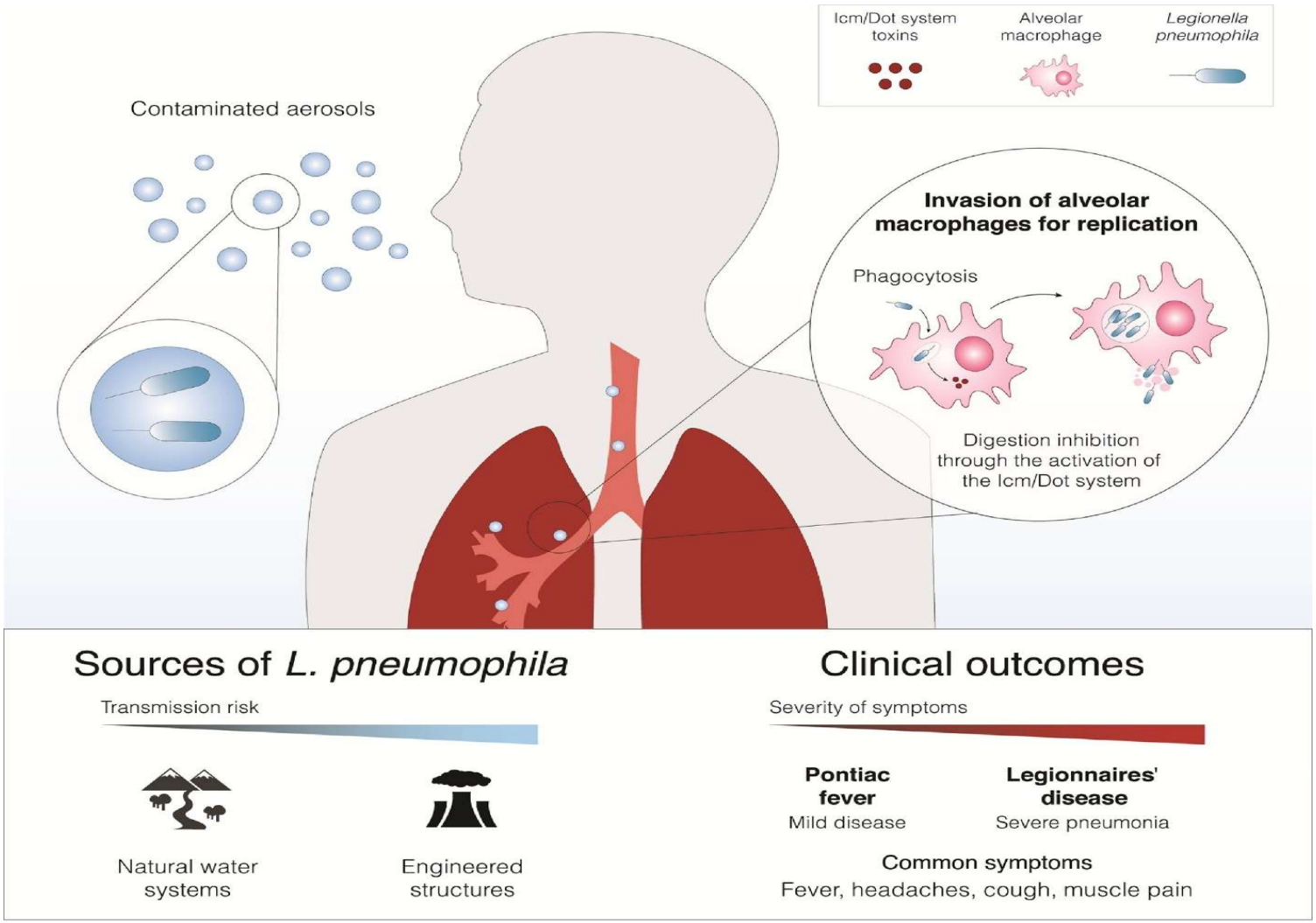
- **Facultative intracellular, Gramnegative rod**
- **Transmission** from inhaled of aerosolized organisms

Pathogenesis

Laboratory diagnosis – sputum culture and/or PCR, urine Ag



Therapy – macrolides, fluorochinolones



Trends in Microbiology

Case Report: *Legionella pneumophila* Pneumonia (Legionellosis)

Abstract

We report a case of severe community-acquired pneumonia caused by *Legionella pneumophila* in a middle-aged patient presenting with fever, respiratory symptoms, and gastrointestinal manifestations. Diagnosis was confirmed by urinary antigen testing. The patient responded well to targeted antibiotic therapy.

Introduction

Legionellosis is an infection caused by *Legionella* species, most commonly *Legionella pneumophila*. It typically presents as either:

- **Legionnaires' disease** (severe pneumonia)
- **Pontiac fever** (mild, flu-like illness)

Transmission occurs via inhalation of contaminated aerosolized water (e.g., cooling towers, showers).

Case Presentation

Patient Information

- Age: 58 years
- Sex: Male
- Medical history: Hypertension, former smoker
- Occupation: Office worker
- Recent history: Stayed in a hotel 7 days prior to symptom onset

Physical Examination and CRP

- Tachypnea (RR 26/min)
- Crackles in right lower lung field
- Oxygen saturation: 90% on room air
- Elevated CRP

Imaging

- Chest X-ray: Right lower lobe consolidation

Clinical Presentation

- Fever: 39.5°C
- Dry cough
- Dyspnea
- Diarrhea and nausea
- Confusion (mild)

Microbiological diagnosis

- Urinary antigen test: **Positive for *Legionella pneumophila***
- Sputum culture: Negative (common limitation)

Differential Diagnosis

- Streptococcus pneumoniae pneumonia
- COVID-19
- Mycoplasma pneumonia

Treatment

- Initial empiric therapy: Ceftriaxone + azithromycin
- Targeted therapy: Azithromycin continued (macrolide)

Alternative options include:

- Levofloxacin (fluoroquinolone)

Outcome and Follow-Up

- Clinical improvement within 72 hours
- Fever resolved by day 4
- Discharged after 7 days
- Full recovery at 2-week

BRUCELLA

* small Gram-negative coccobacilli
* facultative intracellular pathogens
* non-motile, do not form spores (but survive in the environment)

SOURCES OF HUMAN INFECTION:
* *Brucella melitensis* (sheep, goats – most pathogenic to humans)
* *Brucella abortus* (cattle)
* *Brucella suis* (pigs)
* *Brucella canis* (dogs)

Virulence factors

Brucellae are not "classically toxigenic," but their are able to survive within cells:
* intracellular persistence in macrophages
* inhibition of phagosome–lysosome fusion
* lipopolysaccharide (LPS) less toxic than in other G− bacteria → weaker immune response → chronic course
* VirB system (type IV secretion system) enables survival and replication within the cell
* enzymes (catalase, superoxide dismutase) protection against oxidative stress
* ability for long-term persistence → chronic infection

Brucellosis

Transmission

* contact with animals (veterinarians, farmers), unpasteurized milk and cheese, inhalation (laboratories!)

Pathogenesis

* entry through the skin/mucous membranes → phagocytosis → survival in macrophages
* spread to: liver, spleen, bone marrow → granuloma formation
* most pathogenic to humans – ***B. melitensis***

Symptoms

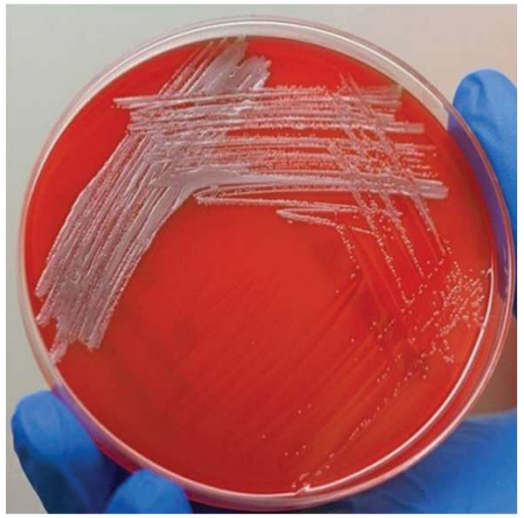
*intermittent fever (typical!)
*sweating (mainly at night)
*fatigue, weakness
*hepatosplenomegaly
*complications: osteomyelitis, spondylitis, endocarditis (most serious)

DIAGNOSTICS

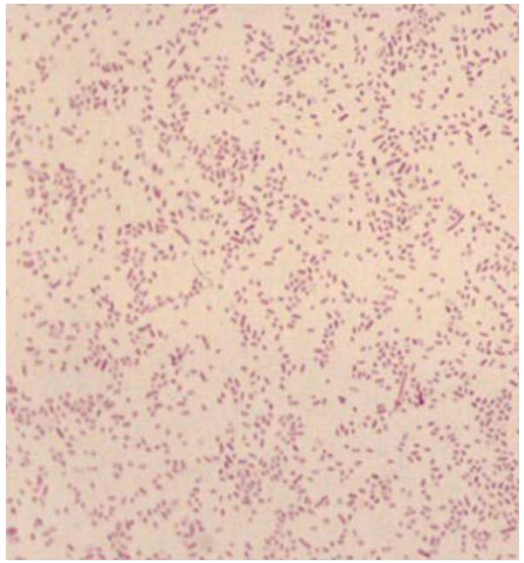
Direct detection
culture - blood, bone marrow
slow growth (risk to laboratory personnel!)

Indirect detection
serology (most important)
Wright's reaction (agglutination)
ELISA

Molecular methods
PCR – blood, affected tissue



Brucella grows on both blood agar and chocolate agar but not on MacConkey agar. **Colonies are pinpoint at 24 hours and are easily visible as white, nonhemolytic colonies at 48 hours.**



Brucella appearing as faintly staining **Gram-negative coccobacilli**

Treatment
Combined and **long-term therapy is required** (due to intracellular localization):
Standard regimen:
doxycycline + rifampin (at least 6 weeks)
Alternative regimen:
doxycycline + streptomycin
In cases of complications:
longer treatment (sometimes several months)

Prevention
milk pasteurization, protective equipment when working with animals
infection control in livestock

Case report – Brucellosis caused by *B. melitensis*

A 42-year-old aged patient presented with prolonged fever, malaise, and joint pain after exposure to unpasteurized dairy products. Blood cultures confirmed infection with *Brucella melitensis*. The patient responded well to combination antibiotic therapy.

Brucella melitensis is a Gram-negative intracellular coccobacillus and the most virulent species causing human brucellosis. It is commonly transmitted through:

- Unpasteurized milk or cheese
- Direct contact with infected animals (goats, sheep)
- Inhalation in occupational settings

Anamnesis - recent travel to a rural area, consumption of unpasteurized goat cheese, no significant past medical history

Symptomatology - intermittent fever (up to 39°C) for 3 weeks, night sweats (notably “drenching”), fatigue and anorexia, arthralgia (especially knees and lower back), hepatosplenomegaly

Laboratory diagnosis

- mild anemia, leukopenia
- elevated CRP
- liver enzymes: mildly elevated
- blood cultures: positive for *Brucella melitensis*
- Serology: high titers of specific antibodies

Diagnosis - treatment

acute brucellosis – doxycyklin + rifampin (6 weeks)

Outcome

•Fever resolved within 1 week

•Full clinical recovery after completion of therapy

•No relapse at 6-month follow-up

Discussion

Brucella melitensis causes more severe disease compared to other *Brucella* species. Key clinical features include:

• Undulating fever

• Night sweats with characteristic odor

• Musculoskeletal involvement

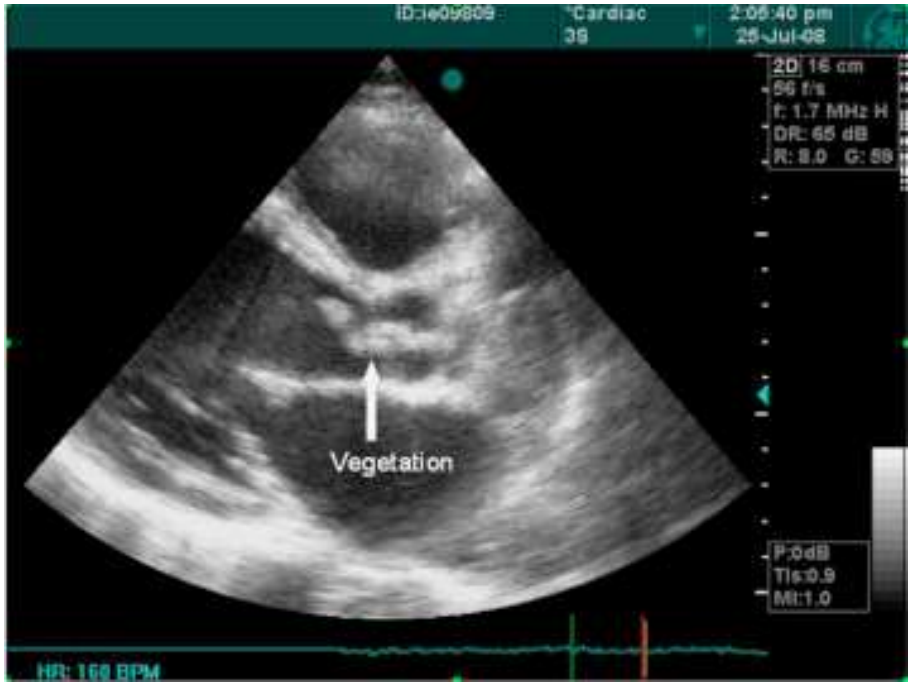
Complications may include:

• Spondylitis

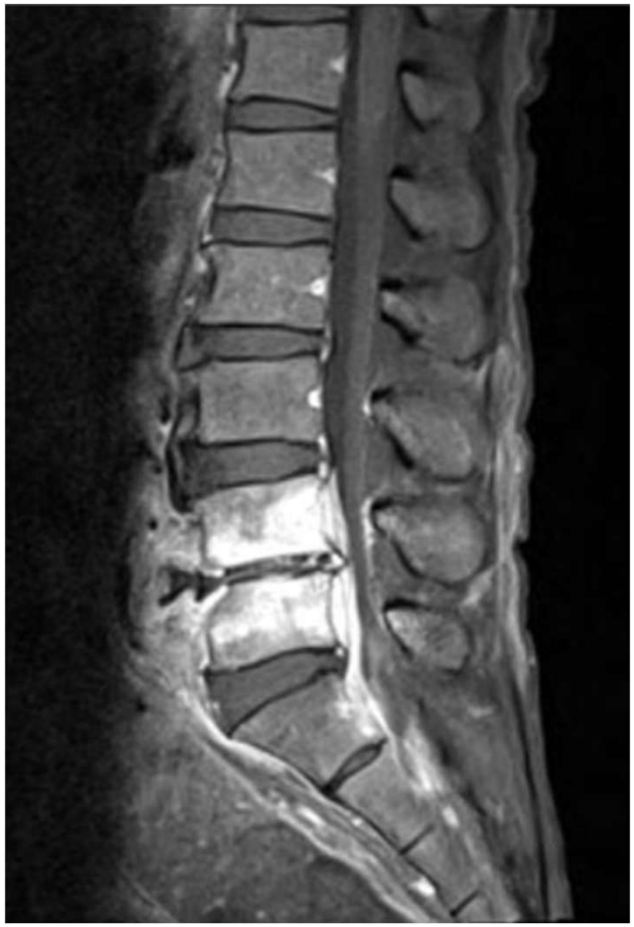
• Endocarditis (most serious)

• Neurobrucellosis

Early diagnosis is often difficult due to nonspecific symptoms, especially in non-endemic regions.



On transthoracic echocardiography, parasternal long axis view showing a large vegetation on aortic valve in a case of brucella infective **endocarditis**.
Ref: https://www.sciencedirect.com/science/article/pii/S0010865013001380



Brucella spondylitis - Lumbosacral spine contrast-enhanced T1-weighted magnetic resonance imaging shows abnormal signal change with enhancement in L4 and L5 body
https://www.e-arm.org/upload/pdf/arm-36-282.pdf

Francisella tularensis is a small, Gram-negative, intracellular coccobacillus that causes a disease called **tularemia**.

Characteristics
***small, Gram-negative coccobacillus**
***strictly aerobic, but difficult to culture** (requires cysteine)
***facultatively intracellular** – survives and multiplies in macrophages
***very low infectious dose** (10–50 bacteria)
subspecies:
F. tularensis* subsp. *tularensis (type A – highly virulent, North America)
F. tularensis* subsp. *holarctica (type B – less virulent, Europe)

Virulence factors
***intracellular survival** (escape from the phagolysosome into the cytoplasm)
***inhibition of macrophage oxidative burst**
***capsular structures** (antiphagocytic effect)
***lipopolysaccharide** (has weak endotoxin activity but evades immune detection), ability to modulate the host immune response

Transmission
***contact with infected animals** (mainly hares and rodents)
***bites from arthropods:** e.g. ticks
***inhalation of aerosols** (e.g., when handling animals)
***contaminated water or food**

Pathogenesis
1. entry into the body (skin, respiratory tract, gastrointestinal tract)
2. phagocytosis by macrophages
3. escape from the phagolysosome → replication in the cytoplasm
4. spread via the lymphatic system
5. formation of granulomas and necrosis (similar to tuberculosis)

Symptomatology (forms)

Depends on the site of entry:
1. Ulceroglandular (most common)
skin ulcer at the site of entry
regional lymphadenopathy
2. Glandular
enlarged lymph nodes without an ulcer
3. Oculoglandular
conjunctivitis + lymph nodes
4. Oropharyngeal
sore throat, tonsillitis
5. Pneumonia
cough, shortness of breath (most severe)
6. Typhoid form
sepsis, fever without a clear focus

Diagnosis
***Serology** (most common – antibodies)
***PCR – tissue, lymph node**
***Culture** (high-risk – requires a BSL-3 laboratory)
***Medical history** (contact with animals, ticks)

Treatment / Therapy (10-21 days)
Aminoglycosides:
streptomycin (treatment of choice)
gentamicin
Alternatives:
doxycycline
ciprofloxacin
Without treatment, the condition can be severe, but mortality rates in Europe are low

Prevention
tick protection
wearing gloves when handling animals
thorough cooking of meat
water testing
laboratory safety
A vaccine exists, but it is not widely available to the public

Case report

Medical history: A 35-year-old man, a hunter, presents with a 5-day history of fever (39 °C), chills, fatigue, and headache. A week ago, he handled a hare he had caught. Two days after exposure, a painful papule appeared on his hand, which developed into an ulcer

Symptomatology

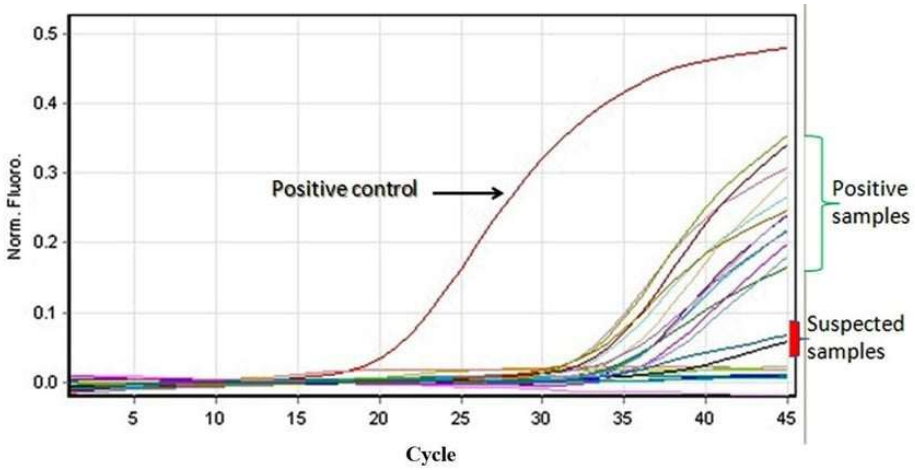
ulceration on the finger with a black base
marked regional lymphadenopathy (axillary lymph nodes)
lymph nodes tender and enlarged
fever

Laboratory findings:

leukocytosis
elevated CRP
(culture – fastidious)
serology: positive antibodies against F. tularensis
PCR from lymph node: positive

Diagnosis – ulceroglandular tularemia

General symptoms improved within 5 days treatment with doxycyclin. After one months regional lyph node shrink but one require drainage and small scare leave.



The positive reaction of real time PCR. The positive and suspected divisions have done based on Ct values of each reaction

Ref: https://www.researchgate.net/figure/The-positive-reaction-of-real-time-PCR-The-positive-and-suspected-divisions-have-done_fig1_331968507