Chlamydia is caused by gramnegative bacteria from the Chlamydiaceae family. The mainly sexually and perinatally transmitted pathogens cause disease in the eye, genital and pulmonal area. Untreated chlamydial infections may have serious consequences. Learn all about pathogenesis, symptoms, diagnosis and treatment of infections with chlamydia in this article. As a result, we guarantee optimal preparation for clinical examinations and practical medical work.

**Definition and Overview of Chlamydia**

Chlamydia — gram negative bacteria

The family of Chlamydiaceae contains 3 human pathogens:
Chlamydia are immobile, **gram negative bacteria**. The cell wall does not contain a peptidoglycan layer, but lipopolysaccharides. Common to all chlamydia is their complex reproduction cycle. Due to a defect in their own energy metabolism, chlamydia is dependent on that of its host.

*Chlamydiae* have the ability to establish long-term associations with host cells. When an infected host cell is starved for various nutrients such as amino acids (for example, tryptophan), iron, or vitamins, this has a negative consequence for *Chlamydiae* since the organism is dependent on the host cell for these nutrients. Long-term cohort studies indicate that approximately 50% of those infected clear within a year, 80% within two years, and 90% within three years.

The starved chlamydiae enter a persistent growth state wherein they stop cell division and become morphologically aberrant by increasing in size. Persistent organisms remain viable as they are capable of returning to a normal growth state once conditions in the host cell improve.
<table>
<thead>
<tr>
<th>Host</th>
<th>Human</th>
<th>Birds (especially parrots, pigeons and budgies)</th>
<th>Human</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diseases</td>
<td>Serotypes A-C: Trachoma (chronic recurrent disorder of the conjunctivae and cornea of the eye)</td>
<td>Ornithosis/Psittacosis</td>
<td>Respiratory infections</td>
</tr>
<tr>
<td></td>
<td>Serotypes D-K: sexually transmitted urogenital infections and infections of the conjunctiva, perinatal infections</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Serotypes L1, L2, L3: Lymphogranuloma venereum</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Epidemiology of Chlamydia**

Globally, as of 2013, sexually transmitted chlamydia affects approximately 141 million people (3.1% of the population). It is more common in women (3.8%) than men (2.5%). In 2013 it resulted in about 1,100 deaths down from 1,500 in 1990.

In the United States about 1.4 million cases were reported in 2014. The CDC estimates that if one includes unreported cases there are about 2.8 million each year. It affects around 2% of young people. Infections are most common among those between the ages of 15 and 25 and are more common in women than men. In 2013 infections resulted in about 1,100 deaths. Chlamydial infection is the most common bacterial sexually transmitted infection in the UK.

Chlamydia causes more than 250,000 cases of epididymitis in the U.S. each year. Chlamydia causes 250,000 to 500,000 cases of PID every year in the United States. Women infected with chlamydia are up to five times more likely to become infected with HIV, if exposed.

**Epidemiology of Chlamydophila trachomatis**

- 30 – 50 % of all sterility is caused by chlamydia
- 90 % of all sterility caused by tube closure are caused by infections with Chlamydophila trachomatis
- every fourth woman infected with chlamydia is affected by subsequent sterility

**Chlamydophila trachomatis** is one of the most common pathogens of sexually
transmitted diseases worldwide. According to WHO (2001), 89 million new infections with genital chlamydia occur worldwide per year. In Germany, the incidence is annually at 300,000 new infections. Particularly affected are persons with frequently changing sexual partners and children of infected mothers.

“In epidemiological studies using molecular biology methods, up to 13 % of the sexually active adolescent women were identified as infected in Germany. This infection rate varies regionally and decreases with increasing age and entry into a stable partnership relationship” (source: Robert Koch Institute)

In pregnant women, 2-3 % are populated with C. trachomatis. The infant is at risk of 50 % at birth.

The incidence of lymphogranuloma venereum has decreased worldwide, but this sexually transmitted infection is still endemic in Asia, Africa, South America and parts of the Caribbean. In Germany it is an absolute rarity with an occurrence of 1/1 million inhabitants.

Trachoma occurs almost exclusively in tropical countries under poor hygienic conditions. After cataract, trachoma is the second most common cause of blindness in the world.

Age group: Young adults (15-22 years)

Epidemiology of Chlamydophila psittaci

The disease is very rare in Germany: in 2007: 72 diseases, in 2008: 86 diseases. Risk groups are:

- Bird owners
- Animal keepers and vets
- Employees in pet shops, poultry farms or slaughterhouses

The transmission takes place by direct contact or by inhalation of dust particles or feces. A human-to-human transmission has not yet been demonstrated.

Epidemiology of Chlamydophila pneumoniae

“C. Pneumoniae is a very common worldwide cause of respiratory infections of humans. According to seroepidemiological investigations, the prevalence begins at the preschool age and is above 50% for men and over 70 % for men in the 6th decade. There is little known about the distribution of C. pneumoniae infections in Germany. “

A high prevalence of seropositivity is to be expected: Everyone has probably contact with C. pneumoniae once in a lifetime. 5 -15 % of all outpatient acquired pneumonia are caused by C. pneumoniae.

Age group: 60-80 years

Etiology and pathogenesis of Chlamydia

Etiology and pathogenesis of Chlamydophila trachomatis

<table>
<thead>
<tr>
<th>Serotypes A-C:</th>
<th>Infectious eye secret, contaminated hands, towels (smear infection), flies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serotypes D-K:</td>
<td>Sexually transmitted, perinatal</td>
</tr>
</tbody>
</table>
Serotypes L1-L3: Sexually transmitted, causes Lymphogranuloma venereum perinatal

The incubation period is approximately 1-3 weeks.

**Etiology and pathogenesis of Chlamydia psittaci**

Psittaci is the only zoonotic human pathogen from the Chlamydiaceae family. The excitation sources are mainly birds (chickens, ducks, pigeons, exotic birds).

The transfer takes place by direct contact or by inhalation of dust particles or faeces containing pathogens.

The pathogens are partly infectious even after drying out for up to 4 weeks. The incubation period of the ornithosis is about **1-4 weeks**.

**Etiology and pathogenesis of Chlamydia pneumoniae**

Pneumoniae is transmitted from person to person in an aerogenic pathway and by salivary contact.

The incubation time is estimated to be about **1-4 weeks**.

Pneumoniae may remain persistent for a long time in the upper respiratory tract. (It is likely that the infected person will infect others over a long period of time).

**Clinical findings of Chlamydia**

**Symptoms of Chlamydia trachomatis infection**

**Urogenital chlamydia infection**

*Note:* 80% of urogenital chlamydial infections in women are symptomatic!

The pathogens can persist for years undetected in the body and possibly even become chronic.

**Clinical manifestation of Chlamydia trachomatis in men and women**

<table>
<thead>
<tr>
<th>women</th>
<th>men</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Urethritis</td>
<td>• Urethritis: feeling of pressure and pain and burning during urination</td>
</tr>
<tr>
<td>• Conjunktivitis</td>
<td>• Conjunktivitis</td>
</tr>
<tr>
<td>• Reactive arthritis</td>
<td>• Reactive Arthritis</td>
</tr>
<tr>
<td>• Bartholinitis</td>
<td>• Prostatitis</td>
</tr>
<tr>
<td>• Cervicitis</td>
<td>• Epididymitis</td>
</tr>
<tr>
<td>• Endometritis</td>
<td>• Proctitis</td>
</tr>
<tr>
<td>• Salpingitis</td>
<td>• Peritonitis</td>
</tr>
<tr>
<td>• Adnexitis</td>
<td>• Perihepatitis, -splenitis</td>
</tr>
</tbody>
</table>

*Note:* If the ascending infections persist, this can lead to adhesions in the tubes. Tube adhesions is the most common cause of sterility in women, extrauterine pregnancy and chronic pelvic symptoms.
Lymphogranuloma venereum

Image: "Lymphogranuloma venereum: is caused by the invasive serotypes L1, L2, or L3 of Chlamydia trachomatis. This young adult experienced the acute onset of tender, enlarged lymph nodes in both groins." by Herbert L. Fred, MD and Hendrik A. van Dijk. Licence: CC BY 2.0

<table>
<thead>
<tr>
<th>Primary stage</th>
<th>Herpetiform papules, ulcer, rapid scalp-free healing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secondary stage</td>
<td>inguinal, painful lymphadenopathy (Bubo)</td>
</tr>
<tr>
<td>Tertiary stage</td>
<td>Fibrotic transformation of the lymph nodes, inflammation with ulceration, obliteration of the lymphatics, edema of the genital / extremity (elephantiasis), fever, arthralgia, splenomegaly, erythema nodosum</td>
</tr>
</tbody>
</table>

Newborn chlamydiosis

The newborn chlamydiosis appears as conjunctivitis (60 %) or pneumonia (40 %).

Typical symptoms of **inclusion body conjunctivitis** are:

- purulent, mucopurulent, hemorrhagic inflammation of the conjunctiva
- eyelid edema
- follicular infiltration of the inner lid side
- first on one, then on both sides
- mostly inconsequential healing

Typical symptoms of **neonatal pneumonia** are:

- Tachypnea
- Increased respiratory effort
- Snorkeling breathing sounds
- Refusal of food
- In severe cases cyanosis
The follicular keratoconjunctivitis is caused by an initial infection in the child’s age. Repeated infections and, among others, bacterial superinfections lead to the formation of granulomas. The result of the granulomas are scarred shrinkages of the conjunctiva of the eyelids and an entropion. In the course of time, the cornea changes and becomes turbid.

**Symptoms and Clinical Findings of Chlamyaphila psittaci infection**

The typical symptoms of **ornithosis** include:

- Fever, chills, headaches
Photophobia
- **atypical and interstitial pneumonia**
- dry, persistent, non-productive cough
- Myalgia
- extrapulmonary manifestations: hepatosplenomegaly (70% of patients), myocarditis, encephalitis, and exanthema

**Symptoms of Chlamydophila pneumoniae infection**

Frequently, the course of C. pneumoniae infections is asymptomatic.

- acute and chronic infections of the upper respiratory tract (pharyngitis, sinusitis, bronchitis)
- Outpatient pneumonia
- All symptoms of infection with C. psittaci can also occur in C. pneumoniae

**Complications of Chlamydia**

**Possible complications of chlamydia infection**

<table>
<thead>
<tr>
<th>C. trachomatis</th>
<th>C. psittaci</th>
<th>C. pneumoniae</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disorders of the arthrotic circle: joint inflammation (knee, ankle joint, …)</td>
<td>Myocarditis, pericarditis, endocarditis, thrombophlebitis, CNS involvement</td>
<td>Carditis, meningoradiculitis, erythema nodosum, reactive arthritis</td>
</tr>
</tbody>
</table>

**Diagnostics of Chlamydia**

**Smear for the determination of the chlamydial pathogens**

The detection of the pathogen is carried out by taking smear of:

- Trachoma: Conjunctiva smear
- Eye infection: Conjunctiva smear
- Urogenital infections: cervical or vaginal smear, possibly urethral smear
- Lymphogranuloma venereum: Lymph node aspirate, ulcer smear

The **direct detection** of chlamydial antigens is carried out by means of **fluorescence-labeled antibodies** or **ELISA**. An alternative is the **PCR** with high specificity and sensitivity.
The pathogen is detected indirectly by serum antibody determinations. It must be specifically investigated for the appropriate species, i.e. Chlamydophila trachomatis, C. pneumoniae or C. psittaci. The diagnosis of genital chlamydial infections evolved rapidly from the 1990s through 2006. Nucleic acid amplification tests (NAAT), such as polymerase chain reaction (PCR), transcription mediated amplification (TMA), and the DNA strand displacement amplification (SDA) now are the mainstays.

Differential Diagnosis of Chlamydia

<table>
<thead>
<tr>
<th>C. trachomatis</th>
<th>C. psittaci</th>
<th>C. pneumoniae</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Gonococcal urethritis</td>
<td>Pathogens that trigger atypical pneumonia:</td>
<td>As in C. psittaci</td>
</tr>
<tr>
<td>• Trichomonad mycoplasma urethritis – Inflammation of the urethra by mycoplasmas, bacteria type without cell wall</td>
<td>• Legionellosis</td>
<td></td>
</tr>
<tr>
<td>• Urethritis caused by several different bacteria or viruses (for example, herpes simplex virus)</td>
<td>• Influenza</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Typhoid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Spotted fever</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Sepsis</td>
<td></td>
</tr>
</tbody>
</table>

Therapy of Chlamydia

Antibiotic against chlamydia

Drug of choice in chlamydia is antibiotic.

<table>
<thead>
<tr>
<th>C. trachomatis</th>
<th>C. pneumoniae, C. psittaci</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetracyclines (Doxycyclin)</td>
<td>Tetracyclines (Doxycyclin)</td>
</tr>
<tr>
<td>• Macrolides (erythromycin, clarithromycin)</td>
<td>Makrolides (erythromycin, azithromycin)</td>
</tr>
<tr>
<td>• Quinolones (e.g. levofloxacin, moxifloxacin)</td>
<td></td>
</tr>
<tr>
<td>• Azithromycin (in uncomplicated genital infections single dose)</td>
<td></td>
</tr>
<tr>
<td>Duration of treatment: at least 14 days.</td>
<td>Duration of treatment: 10-21 days.</td>
</tr>
</tbody>
</table>

Note: Especially important in the treatment of Chlamyphila trachomatis is the co-treatment of the partner (always!) in order to avoid a constant re-infection (so-called “ping-pong effect”).
Prevention of Chlamydia

Prevention measures for Chlamydophila trachomatis

- Following the principles of preventing sexually transmitted infections
- Since January 1, 2008, sexually active women under 25 years of age is offered a chlamydia screening (reimbursement by the health insurance takes place under certain conditions).
- In Germany screening for chlamydia in pregnant women since 1995 has been part of maternity insurance for statutory health insurance.
- Trachoma: SAFE-Strategy in Global Programme for the Elimination of Trachoma. WHO: Surgery + Antibiotics + Facial cleanliness + Environmental improvement

Prevention measures for Chlamydophila psittaci

- Compulsory reporting: Compliance with the veterinary rules of disease control
- Early onset of diagnosis and therapy in case of suspicion

Notification requirement

Which chlamydia infection is notifiable?

- **trachomatis**: In Germany there is no disease or pathogen specific reporting obligation according to Infection Protection Act IfSG. The disease, once diagnosed, must be reported to the CDC in the US.
- **psittaci**: The Infection Protection Act§ 7 stipulates that the pathogen detection of Cp. Psittaci is notifiable, if there is evidence of an acute infection.
- **pneumoniae**: In Germany there is no disease or pathogen specific reporting obligation according to Infection Protection Act IfSG.

Review Questions

The correct answers can be found below the references.

1. **At what age the chlamydia screening is covered by the statutory health insurance in certain cases?**
   
   A. from 16
   B. from 18
   C. from 25
   D. from 30
   E. from 35

2. A young woman has a new boyfriend recently. Since she has been suffering from itching and pain in the vulva for a week, she is looking for her practiced gynecologist. The physician observes swollen lymph nodes and flat ulcers in vulvar area. Upon asking, the patient states that she has not used any protection in sexual intercourse. What infection is the most likely?

   A. Chlamydia infection
   B. HPV infection
C. Herpes simplex virus infection  
D. HIV infection  
E. Measles infection

3. Which statement about chlamydia is true?

A. Chlamydia psittaci is notifiable  
B. Chlamydia pneumoniae is notifiable  
C. Chlamydia trachomatis is notifiable  
D. Chlamydia psittaci is not notifiable  
E. All Chlamydia groups are not notifiable

References

Genzwürker et al. (2014): AllEX – Alles fürs Examen, Thieme Verlag.  
Institut für Medizinische Diagnostik Universität Greifswald  
Gesetz zur Verhütung und Bekämpfung von Infektionskrankheiten beim Menschen via gesetze-im-internet.de  
International Trachoma Initiative via trachoma.org

Correct answers: 1C, 2C, 3A

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