Chlamydia trachomatis infection

in the female reproductive tract – a major concern for reproductive health

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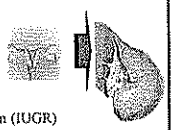
Importance

Chlamydia trachomatis

- Most common bacterial STI — Worldwide
- *C. trachomatis* is the **leading causes of**
  - Pelvic inflammatory disease
  - Ectopic pregnancy and
  - Tubal infertility

- **Serious diseases and consequences:**
  - Endometritis, salpingitis
  - PID
  - Sterility
  - Ectopic pregnancy
  - Premature rupture of membranes (P ROM)
  - Preterm birth, Intrauterine growth restriction (IUGR)
  - Low birthweight
  - Reactive arthritis
  - Reiter's syndrome



Silent infection > 80% asymptomatic

- **Diagnosis ??!!!**

- **Enormous cost** — only in 1990 in US total cost was 2.6 billion dollars.
- **Increased transmission of HIV**

Risk factors for infection

- Age less than 25 years
- Younger age at first intercourse
- Multiple sexual partners
- Recent new sex partner
- Lack of barrier contraception
- Use of oral contraception
- Cervical ectopy
- Lower socioeconomic status
- Unmarried status
- ther sexually transmitted infection
- Nulliparity
- Black race

Chlamydia trachomatis

Microbiology

- **Small (250-1000 nm)**
- **Kokoid**
- **Nonmotil**
- **Gram - negative**
- **Obligate intracellular bacteria**
- **Preferentially infect squamocolumnar epithelial cells**
- **Small and known genome (RNA and DNA)**
- **Strict human pathogen**

Epidemiology

Chlamydia prevalence

Epidemic particularly among young women

- **2.3% (No. 1 149) University health service US**
  Cook, RL, St. George, K, Lassak, M. et al. Screening for Chlamydia trachomatis infection in college women with a polymerase chain reaction assay. Clin Infect Dis 1999; 28:1002.
- **5.7% pregnant women in Tailand**
  Kilmarx PH, Black CM, Limpakarnjanarat, K. et al. Rapid assessment of sexually transmitted diseases in a sentinel population in Thailand: prevalence of chlamydial infection, gonorrhoea, and syphilis among pregnant women--1996. Sex Transm Infect 1998; 74:189.
- **16% adolescent females US**
  Burstein GR, Waterfield G, Joffe A, et al. Screening for gonorrhea and chlamydia by DNA amplification in adolescents attending middle school health centers. Opportunity for early intervention. Sex Transm Dis 1998; 25:395.
- **28.5% female sex workers in Dakar (Senegal)**
  Sturm-Ramirez K, Brunblay H, Diop K, et al. Molecular epidemiology of genital Chlamydia trachomatis infection in high-risk women in Senegal, West Africa. J Clin Microbiol 2000; 38:138.
- **=> 4,000,000 cases of C. trachomatis infection annually in the US**
  Centers for Disease Control, Division of Sexually Transmitted Diseases. 1997 Annual Report.

Chlamydia trachomatis - age- and sex-specific rates - SAD

More than 70% of all reported cases are between the ages of 15 and 24 years

Chlamydia trachomatis

Transmission - contact infection

Contact with the:

- Sperm
- Eyes
- Blood
- Vaginal (genital) discharge
  - Sexual intercourse
  - Passage through the birth canal




Risky groups:

Different segments of the population have different prevalences of CT

Newboorn bebies of infected mothers
passed from mother to her newborn child during birth, causing conjunctivitis (1/2) or pneumonia (¼)

Sexually active adolescents and young adults (15- 25 years)

Sex workers (~ 30%)

Clinical features

Newboorn
- Nasopharingitis
- Pneumonia
- Inclusion conjuctivitis
- Otitis media

Man
- Epididymitis
- Urethritis
- Reaktivni artritis
- Inclusion conjuctivitis
- Proctitis
- Faringitis
- Reactive arthritis
- Reiter's syndrome
- Trachom
- LGV

Women
- Mucopurulentn cervicitis
- Bartholinitis
- Salpingitis
- Endometritis
- Perihepatitis, Fitz - Hugh-Curtis sindrome
- Urethritis
- Sterility
- Ectopic pregnancy
- Premature rupture of membranes (P ROM)
- Preterm birth
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- Trachom
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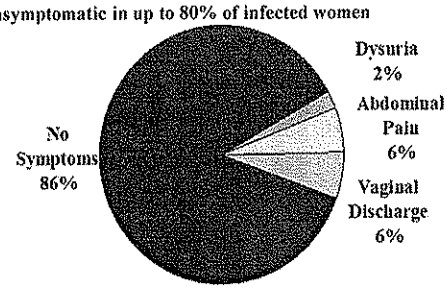
Serovari D-K
Serovari A-C
Serovari L_{1-3}

Symptoms Among Females Diagnosed With Chlamydia

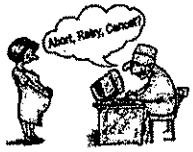
It is asymptomatic in up to 80% of infected women



The incubation period is 1-3 weeks

Perinatal *Chlamydia trachomatis* infections

Infection during pregnancy is associated with
- Abortion
- Preterm contractions
- Premature rupture of membranes
- Preterm delivery
- Low birth weight
- Infection of the fetus
- Postpartum endometritis




Chlamydia trachomatis Neonates

infected mothers


Conjuctivitis >40%

Pneumonia 20%
- Nasopharingitis
- Pneumonia
- Inclusion conjuctivitis
- Otitis media

CT is the most common cause of neonatal eye infections and of (afebrile interstitial) pneumonia (30%) in infants less than 6 months of age

Injected conjunctivae
Mucopurulent discharge from eyes
Bilateral involvement of the eyes

MEN

Asymptomatic in up to 50%

- •Urethritis (non-gonococcal)
- •Epididymitis
- •Prostatitis
- •Infertility
- •Urethral discharge
- •Dysuria
- •Unilateral pain and swelling of the scrotum
- •Fever

- •Proctitis
- •Faringitis
- •Reactive arthritis
- •Reiter's syndrome
- •Inclusion conjuctivitis

***C. trachomatis* - is the most common cause of epididymitis (70%) in men younger than 35**

Mukopurulent cervicitis (MPC)

Presumptive chlamydial infection

MPC can be caused by:

- *C. trachomatis* **30-50%**
- *N. gonorrhoeae*
- *HSV*

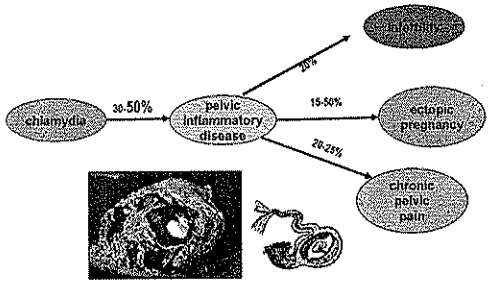
MPC is characterized by a purulent or mucopurulent endocervical exudate visible in the endocervical canal or in an endocervical swab specimen

•increased number of polymorphonuclear leukocytes on endocervical Gram stain

MPC often is asymptomatic, but some women have an abnormal vaginal discharge and vaginal bleeding (e.g., after sexual intercourse).

Complications of *Chlamydia* infections:

Devastating Consequences



Fitz-Hugh and Curtis syndrome, infectious perihepatitis

- •It is associated with right upper quadrant pain
- •FHC syndrome can mimic other abdominal emergencies and often is a diagnosis of exclusion
- •Diagnoses are made with after direct visualization of the liver capsule
- •The classic "violin-string" adhesions of the anterior liver capsule to the anterior abdominal wall or diaphragm are present

CLASIFICATION

Chlamydia trachomatis infection

- ⇨ ACUTE
- ⇨ CHRONIC
- ⇨ PERSISTANT

Clinical significance of persistence has been proved

Risk factors for <u>persistent</u> *Chlamydia trachomatis* infection

- **•Recurrent chlamydial disease**
- **•Duration over two months**
- **•Inefficacy of previously applied antimicrobic therapy**
- **•Use of antibiotics ineffective to chlamydia**
- **•Immune system insufficiency**

Diagnosis

History: history of STDs, dysuria, yellow mucopurulent discharge from the urethra, intermenstrual or postcoital bleeding, lower abdominal pain, fever (in PID)
No symptoms in 80% !!!!!
Physical examination: Mucopurulent cervical or vaginal or rectal discharge, cervical motion tenderness, adnexal tenderness, lower abdominal tenderness, abdominal tenderness

The diagnosis is made on the basis of a positive chlamydia test

Tests that detect antibody responses to chlamydial infection have limited utility in diagnosis of acute chlamydial infection because of the high prevalence of persistent infections

Test methods for *Chlamydia trachomatis*

	SENSITIVITY (%)	SPECIFICITY (%)	TIME - DURATION (H)
Culture	37-97	100	24 -72
Direct Fluorescent Antibody (DFA)	>70	98-99	1-2
Enzyme immunoassay (EIA)	0-100	>99	1 - 2
Nucleic acid hybridization	70 – 90	80 - 90	6
Nucleic Acid Amplification tests (NAA) PCR, LCR	60 – 100	>99	4 - 8

A negative diagnostic tests for *C. trachomatis* does not exclude infection.

Chlamydia trachomatis infection

Treatment

- **All partners need treatment**
- **All partners must abstain from sexual intercourse for 7 days**
- **A test of cure is not recommended after completing treatment with doxycycline or azithromycin**
- **A test of cure is performed for patients with persisting symptoms of those in whom compliance with the regimen is suspected**
- **A test of cure should be done more than three weeks after the end of therapy, because erlier test may detect non-viable organisms**

Recommended Treatment

***Chlamydia trachomatis* - Acute infection**
There are the two recommended regimens

- **Azithromycin** (Sumamed©Zithromax©) 1 g orally in a **single dose** or
- Doxycycline 100 mg orally twice a day for 7 days

Better compliance with single-dose treatment with azithromycin (Sumamed) than with multiple-dose treatment.

Azithromycin should always be available to health-care providers to treat patients for whom compliance is in question.

TREATMENT

Azitromycin (Sumamed®) 1gm PO single dose 100% compliance
§Doxycycline 100 mg PO BID for 7 days
§Ofloxacin 300 mg PO BID /7 days
Eritromicin base 250 mg PO 4x2/14 days
§ contraindicated for pregnant women

Food and Drug Administration (FDA) je Azitromicin odobrio za lijočenje uretritisa i cervicitisa uzrokovanih klamidijom t.

In pregnancy

*Azithromycin (Sumamed®) 1 g PO/single dose
Erythromycin base 500 mg PO QID for 7 days
Amoxicillin 500 mg PO TID for 7 days

*Arch Fam Med 1997 Nov; 6(6):551-5
J Reprod Med 1998 Jun; 43(6):509-14
Obstet Gynecol 1998 Feb; 91(2):165-8

Chlamydia trachomatis

•**Persistent infection:**

Azithromycin (Sumamed®)

(total dose of 3 g)
Single therapy of 1 g PO on the first, seventh and fourteenth day

Gomberg M. Medicus 2003; 12 (2) 179-8.

(total dose of 3 g)

0.5 g PO 1x1/3 days -3 days pause – 0.5 g PO 1x1/ 3 days

Karelovic D.

Screening

Chlamydia trachomatis

C trachomatis screening using the PCR test save money, and is cost-effective even in low-prevalence populations, when the baseline prevalence of C trachomatis infection exceeds 3.9%.

Paavonen J, Paolakkainen M, Paukku M ym. Cost-benefit analysis of first-void urine Chlamydia trachomatis screening programme. Obstet Gynecol 1998;92:292-8

Screening with a DNA amplification assay combined with the single-dose azithromycin treatment of positive patients is the most cost-effective strategy when the prevalence is 6%.

Gene M, Mardh, A. A cost-effectiveness analysis of screening and treatment for Chlamydia trachomatis infection in asymptomatic women. Ann Intern Med 1996; 124:1.

The development of new, noninvasive urine-based and nucleic-acid based technologies will result in substantial expansion of screening activities because of the reduced need to perform clinical exams.

Screening

Chlamydia trachomatis **CDC recommendations**

Annual screening of all sexually active women age 25 years or younger

Annual screening of all sexually active women older than 25 years with risk factors (eg, a new sex partner or more than one sex partner)

Before any intrauterine manipulation

At the first prenatal visit, during the first trimester

Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines 2002. Recommendations and Reports MMWR 2002; 51(RR15):1-27.

Future perspectives

We expect:

- **Urine test** will become the standard of diagnostic testing in the future. **(LCR: sensitivity 90% and specificity 100%)**
- **Novel strategies for control**
- **Early diagnosis**
- **Targeted screening**
- Better diagnostics
- Better evaluation of therapy
- **Development of a vaccine**