Plan:

1 - **Epidemiology**

2 - **Clinical manifestation**
- Trachoma
- Urogenital infection
- Reiters
- LGV

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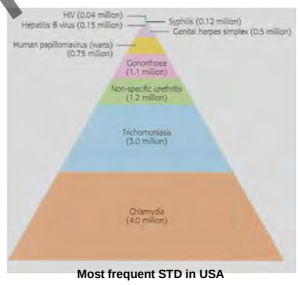
A public health concern

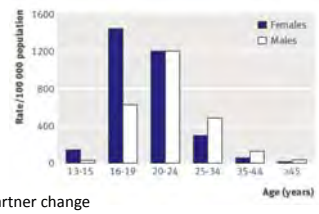
✓ Most common bacterial sexually transmitted disease



Most frequent STD in USA

Epidemiology

- Young people
- Risk factors:
  - multiple partner
  - High frequency of partner change
  - Unprotected sex
  - Single



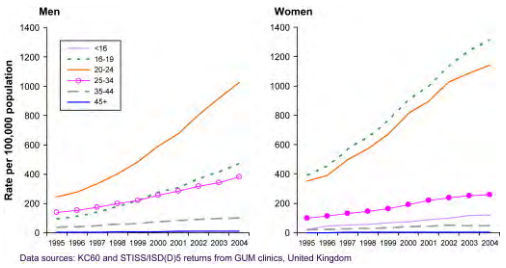
Kalwij S – BMJ - 2010

Epidemiology

Risk factor	Comments
Gender	3.5-fold higher prevalence in women than in men
Ethnicity	Ethnicity appears to be independent of Chlamydia infection
	African-American patients disproportionately affected
Age	Under 25 years
Sexual experience	Multiple sex partners
	New sex partners
	A new infected sex partner in the last 90 days
Sex education	No or rare use of condoms
	Use of oral contraceptives
STDs	Prior STDs

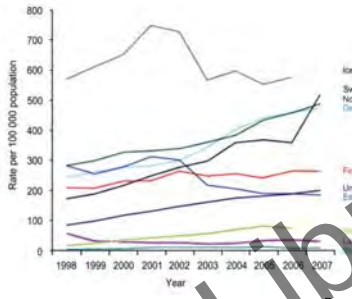
Mylonas - 2012

Increase incidence



Data sources: KC60 and STISS/ISD(D)5 returns from GUM clinics, United Kingdom

Increase incidence



Paavonen J – Ann Med - 2012

Increase incidence

- Increase in number of cases
- Expanded awareness
- Increase in testing
- Increase in reporting

In Switzerland

BMC Infectious Diseases

Open Access

Low prevalence of *Chlamydia trachomatis* infection in asymptomatic young Swiss men

David Baud[1,2], Katia Jaton[1], Claire Bertelli[1], Jean-Pierre Kulling[2] and Gilbert Greub*[1]

- 1.2% of young swiss male
- 3% of gynecological check-up

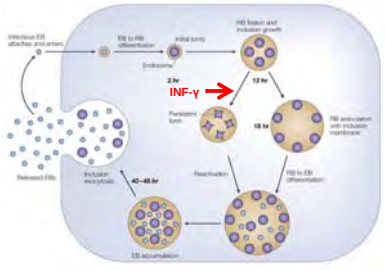
Baud et al BMC Infect Dis 2008

In Switzerland

Characteristics	C. trachomatis negative	(%)	C. trachomatis positive	(%)	p-value*	Odds Ratio	95% CI	Prevalence of C. t.
Total	511	98.8	6	1.2				1.2
Age (year ± SD)	20.6 ± 1.4		20.7 ± 2.7					
≤ 20	274	54	5	83.3	0.23	ref		1.8
> 20	235	46	1	16.7		0.23	0.03 – 2.02	0.4
Nationality at birth								
Switzerland	433	84.7	2	33.3	0.003	ref		0.5
Europe	41	8	1	16.7		5.3	0.47 – 59.5	2.4
Other	37	7.2	3	50		17.6	2.84 – 108	7.5
Place of residence								
> 10'000 inhabitants	134	26.2	4	66.7	0.046	ref		2.9
< 10'000 inhabitants	377	73.8	2	33.3		0.17	0.03 – 0.98	0.5
Main occupation								
Work	265	51.9	4	66.7	0.74	ref		1.5
Studies	231	45.2	2	33.3		0.53	0.1 – 2.69	0.9
Declined to respond	15	2.9	0	0		-	-	0
Monthly income								
< 1000 Frs.	301	58.9	1	16.7	0.064	ref		0.3
1000 – 2000 Frs.	69	13.5	1	16.7		4.4	0.3 – 70.6	1.4
> 2000 Frs.	112	21.9	4	66.7		10.8	1.2 – 97.2	3.5
Declined to respond	29	5.7	0	0		-	-	0
Number of lifetime sexual partner								
0	67	13.1	0	0	0.26	-	-	0
1	125	24.5	0	0		-	-	0
≥ 2	306	59.9	6	100		-	-	1.9
Declined to respond	13	2.5	0	0		-	-	0

Baud et al BMC Infect Dis 2008

Acute vs chronic infections



Brunham & Rey-Ladino, Nature Reviews Immunology, 2005

Plan:

1 - Epidemiology

2 - **Clinical manifestation**
- Trachoma
- Urogenital infection
- Reiters
- LGV

3 - Impact on fertility

4 - Diagnosis
- Direct diagnosis
- Serology

5 - Treatment

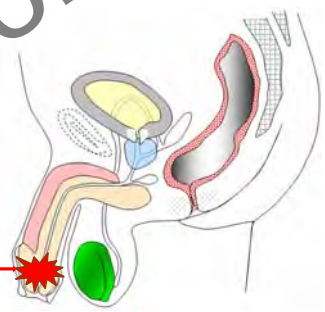
Chlamydia trachomatis serovars

Serovar	Clinical manifestation	Complication
A–C	Keratoconjunctivitis	Scarring trachoma, blindness
D–K	Males: urethritis, proctitis	Epididymitis
	Females: cervicitis, urethritis, proctitis	Endometritis, salpingitis, pelvic pain, ectopic pregnancy, perihepatitis (Fitz-Hugh–Curtis syndrome), infertility
	Males and females: conjunctivitis	Reiter's syndrome, reactive arthritis
L1–L3	Lymphogranuloma venereum: inguinal syndrome, proctitis	Fibrosis, rectal stricture

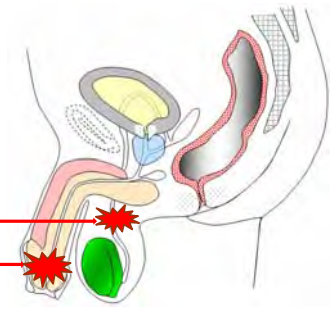
Keratoconjonctivitis / Trachoma

⇒ Blindness
⇒ 6 million people/year

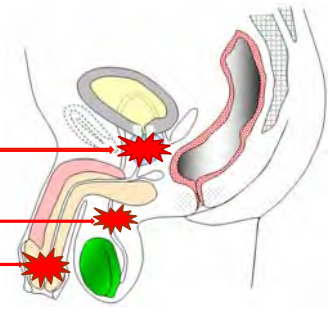
Urogenital infection in Men



Urogenital infection in Men



Urogenital infection in Men



Symptoms in men

- 90% asymptomatic
- Clear or cloudy urethral discharge
- Dysuria
- Burning or itching around the urethral opening
- Pain and swelling around the testicles


Lymphogranuloma Venereum: LGV

1st stage:
Genital ulcer

2nd stage:
Lymphadenitis/Lymphangitis

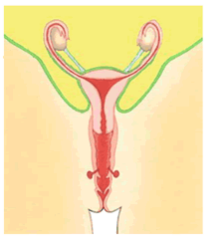


Reiter's syndrome

- Urethritis
- Conjunctivitis
- Arthritis
- Mucocutaneous lesions

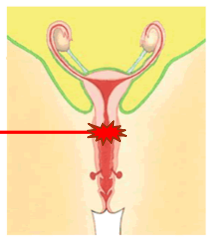



Urogenital infection in women



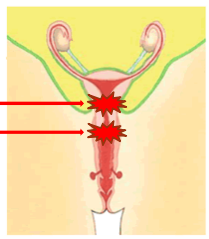
Urogenital infection in women

Cervicitis

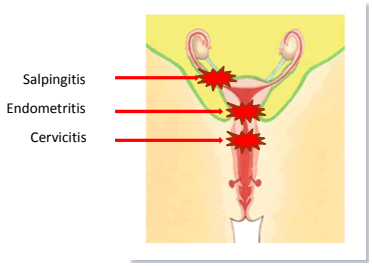



Urogenital infection in women

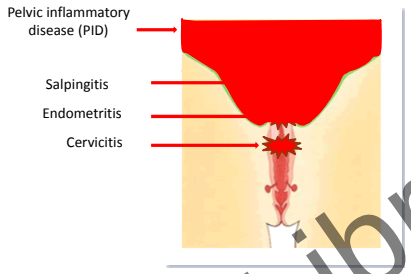
Endometritis
Cervicitis



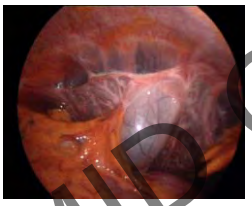
Urogenital infection in women



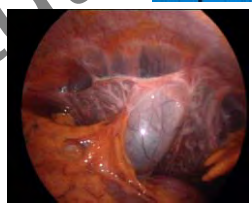
Urogenital infection in women

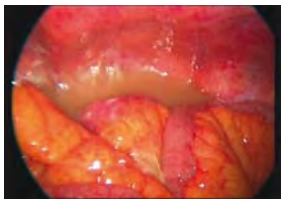


PID

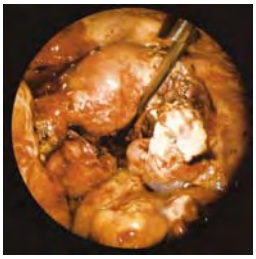


PID





Tubo-ovarian abcess

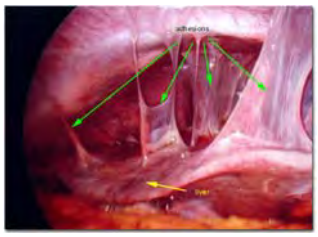


Urogenital symptoms in women

- 80-90% asymptomatic
- Vaginal discharge
- Bleeding between periods
- Painful periods
- Abdominal pain and fever
- Dyspareunia
- Itching or burning in or around the vagina
- Dysuria

Fitz-Hugh-Curtis syndrome

Spread from the pelvis to the liver => **Perihepatitis**



- In 5-15% of salpingitis
- Symptoms in 20%
- Upper abdominal pain

Fitz-Hugh-Curtis syndrome

Spread from the pelvis to the liver => **Perihepatitis**

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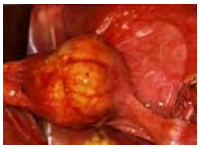
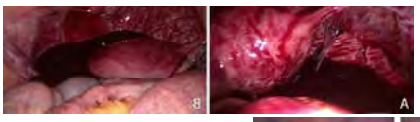
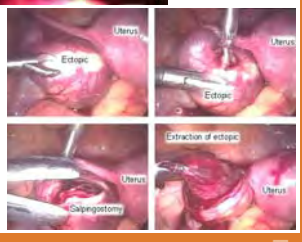
Impact on fertility

- Salpingitis may lead to tubal scarring
- PID lead to adhesive obstruction
- Tubal infertility = 50% of infertility
  - 1 PID: 6x
  - 2 PID: 17x
- Ectopic pregnancy
  - 43% due to Chlamydia



Impact on fertility

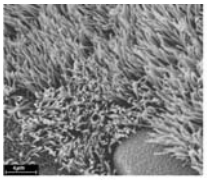


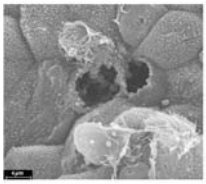


Ectopic pregnancy

Impact on fertility

Stephens AJ – Inf Dis Ob Gyn - 2011





Ectopic pregnancy

Impact on fertility

Anti-*Chlamydia trachomatis* IgG:

- Ectopic pregnancies (n=177): 24.9%
- Uneventful pregnancies (n=166): 6.6%

p<0.0001

Ectopic pregnancy

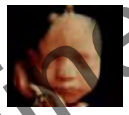
Baud D – in preparation

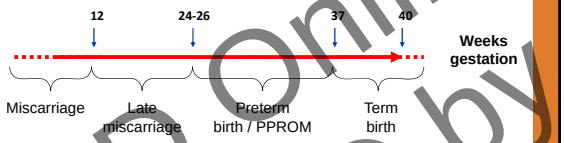
Emerging role of *Chlamydia* and *Chlamydia*-like organisms in adverse pregnancy outcomes

David Baud[a,b], Lesley Regan[b] and Gilbert Greub[a]

Current Opinion in Infectious Diseases 2008, 21:70–76

Pregnancy

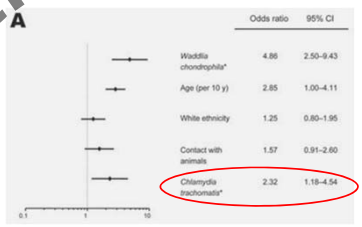




Impact on pregnancy: miscarriage

Table 1. Characteristics of study patients according to miscarriage history*

Chlamydia	Controls (n = 169), no. (%)	Sporadic miscarriages (n = 69), no. (%, p value†)	Recurrent miscarriages (n = 200), no. (%, p value†)
Chlamydia trachomatis (IgG titer >50)	15 (8.9)	9 (13, 0.33)	39 (19.5, 0.004)



Baud D – Emerg Infect Dis - 2007

Impact on pregnancy: miscarriage

Role of *Chlamydia trachomatis* in Miscarriage

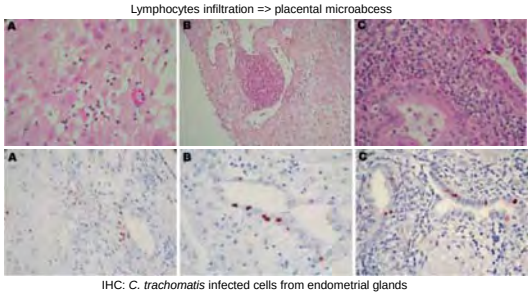
Table 1. Characteristics of 386 women, by miscarriage history, in a study of the role of *Chlamydia trachomatis* in miscarriage, University Hospital of Lausanne, Lausanne, Switzerland, November 2006–June 2009*

Characteristic	Control group, no. (%), n = 261	Miscarriage group, no. (%), n = 125	p value
C. trachomatis serologic results			
IgG+	19 (7.3)	19 (15.2)	0.018
IgA+	10 (3.8)	10 (8.0)	0.091
IgG+ and IgA+	7 (2.7)	9 (7.2)	0.037
IgG+ or IgA+	22 (8.4)	20 (16.0)	0.025
C. trachomatis PCR			
Cervicovaginal swab	2 (0.8)	5 (4.0)	0.026
Placenta	2 (0.8)	5 (4.0)	0.026
≥1 PCR positive	2 (0.8)	6 (4.8)	0.009

Baud D – Emerg Infect Dis - 2011

Impact on pregnancy: miscarriage

Lymphocytes infiltration => placental microabcess



IHC: *C. trachomatis* infected cells from endometrial glands

Baud D – Emerg Infect Dis - 2011

Impact on pregnancy: PTB

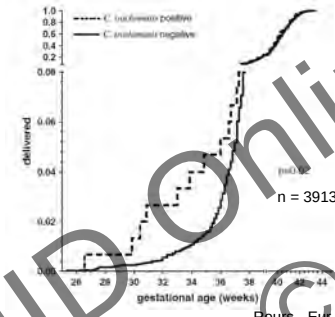
Chorioamniotitis → preterm birth

Impact on pregnancy: PTB

8 million citizens	800 million
80'000 birth / year in Switzerland	8'00'000 birth / year
10% of them are preterm = 8'000 preterm	800'000 preterm
6% due to Chlamydia = 500	50'000
NICU stay = 100'000 $	NICU stay = 100'000 $
50'000'000 $	**5'000'000'000 $**

Baud D – In review 2013

Impact on pregnancy: PTB



n = 3913

Rours - Eur J Epidemiol - 2011

Impact on pregnancy: PTB

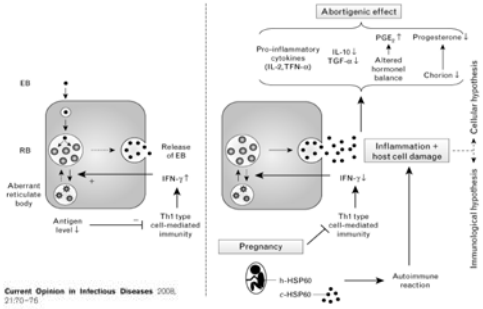
	Risk for preterm delivery	
	< 32 weeks *n* = 22	≤ 35 weeks *n* = 64
	Unadjusted odds ratio	
C. trachomatis infection	5.69 (1.9–17.0)**	3.14 (1.4–7.0)**
	Adjusted odds ratio[a]	
C. trachomatis infection	4.35 (1.3–15.2)*	2.66 (1.1–6.5)*

Analyses are done versus delivery ≥ 37 weeks (*n* = 3,724)
[a] Adjusted for maternal age, ethnicity, education, gravidity and smoking with multiple imputation
Values are odds ratios (95% confidence interval), * *P*-value < 0.05, ** *P*-value < 0.01

Rours - Eur J Epidemiol - 2011

Emerging role of *Chlamydia* and *Chlamydia*-like organisms in adverse pregnancy outcomes

David Baud[a,b], Lesley Regan[b] and Gilbert Greub[a]



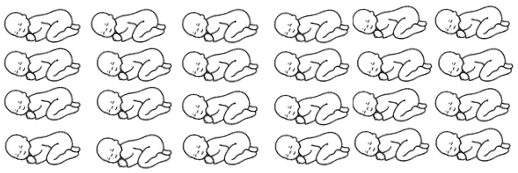
PTB

Misc

Current Opinion in Infectious Diseases 2008, 21:70–76

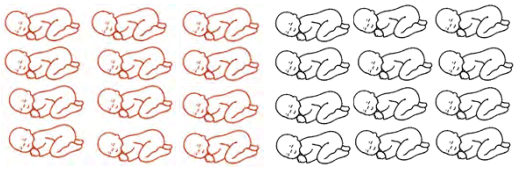
Neonatal infection

Transmission rate: 50 to 70%



Neonatal infection

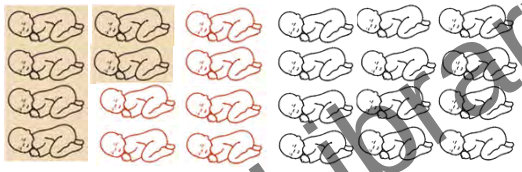
Transmission rate: 50 to 70%



Neonatal infection

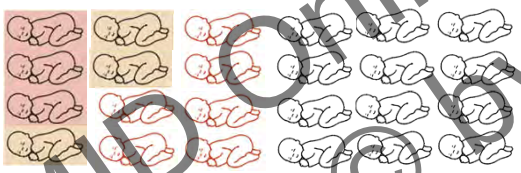
Transmission rate: 50 to 70%

30-50% conjonctivitis (5-10 days PP)



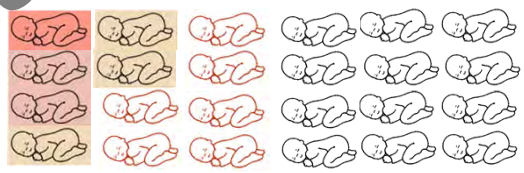
Neonatal infection

- Transmission rate: 50 to 70%
- 30-50% conjonctivitis
- 50% nasopharyngeal infection



Neonatal infection

- Transmission rate: 50 to 70%
- 30-50% conjonctivitis
- 50% nasopharyngeal infection
- 30% chlamydial pneumonia (2-3 weeks PP)



Plan:

1 - **Epidemiology**

2 - **Clinical manifestation**

- Trachoma
- Urogenital infection/Reiters/LGV
- Obstetrical complication
- Neonatal infection

3 - **Impact on fertility / pregnancy**

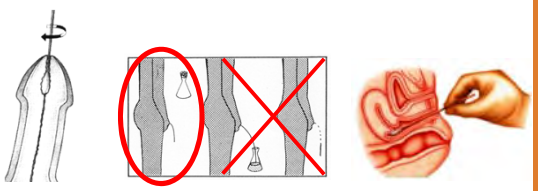
4 - **Diagnosis**

- Specimens?
- Direct diagnosis
- Serology

5 - **Treatment**

Specimens / strategies

Urethral swab | 1st void urine | Vaginal/cervical swab



Specimen

- Site depends on clinical manifestation
- **Invasive specimen:**
  - urethral swab
  - endocervical swab
  - upper genital tract
  - conjunctiva…
- **Self collected specimen:**
  - first void urine, vulvovaginal swab, anal and penil swab

=> screening program

Specimens / strategies

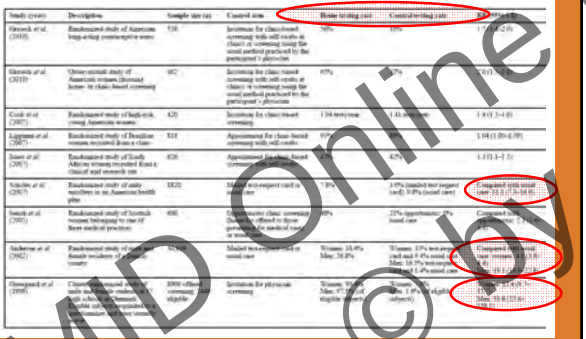
Expert Rev Anti Infect Ther. 2011 February ; 9(2): 183–194. doi:10.1586/eri.10.164.

Home versus clinic-based specimen collection for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*

Anna S Graseck[†], Shirley L Shih[†], and Jeffrey F Peipert[†,‡]

- Clinic
- Home-based
- Partner-based
- Postal tests
- Internet recruitment

Specimens / strategies



Specimens / strategies

3973 women => Self vaginal swab => Cervical swab by clinician

Whole cohort
Endocervical swab
Vulvovaginal swab

Schoeman SA – BMJ - 2012

Specimens / strategies

3973 women => Self vaginal swab => Cervical swab by clinician

	Sensitivity (95% CI)	Specificity (95% CI)	Predictive value	
			Positive	Negative
Whole cohort				
Endocervical swab	88 (85 to 91)	100 (99.9 to 100)	100	98.7
Vulvovaginal swab	97 (95 to 98)	99.9 (99.8 to 100)	99.5	99.7

Schoeman SA – BMJ - 2012

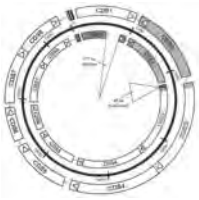
Direct diagnosis - Summary

Method	Turn-around time	Advantages	Limits
Cell culture	72 h	Specificity, strain	Sensitivity 80–85%
Antigen detection			
DFA	45 min	Simple, unit test	Sensitivity 75–80% Subjective reading
EIA	4 h	Automation	Sensitivity 75–80% Low specificity (confirmatory test)
Point of care	30 min	Low cost, unit test	
Molecular methods			
DNA probing	2 h	Easy to perform	Sensitivity 75–80%
Hybrid capture	4 h	Sensitivity 95% Specificity 99%	Only for cervical specimens (FDA)
NAAT (real-time PCR, SDA, TMA, NASBA)	2–4 h	Sensitivity >95% Specificity 99%	Contamination, costly processing of specimen

DFA, direct fluorescent staining with monoclonal antibodies; EIA, enzyme immunoassay; NAAT, nucleic acid amplification test; SDA, strand displacement amplification; TMA, transcription-mediated amplification; NASBA, nucleic acid sequence-based amplification.

Bébéar et al. , CMI, 2009

Chlamydia trachomatis plasmids



Swedish new variant *C. trachomatis* seroptype *E*:

- Identified in 2006
- Deletion covered the region used for NAATs
- 64% of patient in Sweden
- Lesson:
  - dual target
  - on highly conserved region

Indirect diagnosis - Serology

Review Article

Antichlamydial Antibodies, Human Fertility, and Pregnancy Wastage

Infectious Diseases in Obstetrics and Gynecology Volume 2011, Article ID 525182, 9 pages

Amanda J. Stephens, Mitra Anbalagan, and Danny J. Schust

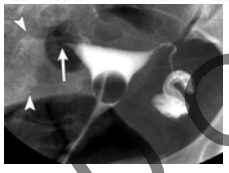
- Previous or persistent infection
- Assess tubal damage
- Reduce chance of achieving pregnancy
- Reduced motility of spermatozoa
- Increased number of dead spermatozoa

Indirect diagnosis - Serology

Review Article

Antichlamydial Antibodies, Human Fertility, and Pregnancy Wastage

Amanda J. Stephens, Mitra Anbalagan, and Danny J. Schust



***C. trachomatis* serology = similar Sens/Spec than HSG**

Indirect diagnosis - Serology

Comparison of five commercial serological tests for the detection of anti-*Chlamydia trachomatis* antibodies

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	LR+	LR-
IF	93.3	95.6	65.8	98.3	18.9	0.17
cHSP60-Medac	93.3	87.4	43.1	99.2	7.4	0.08
MOMP-Medac	93.3	96.9	75.7	99.3	30.5	0.07
MOMP-RB	96.7	99.5	96.7	99.7	284	0.03
InnoDiag	100	89.8	49.2	100	9.5	0

MOMP-Elisa R-Biopharm

Plan:

1 - **Epidemiology**

2 - **Clinical manifestation**
- Trachoma
- Urogenital infection/Reiters/LGV
- Obstetrical complication
- Neonatal infection

3 - **Impact on fertility / pregnancy**

4 - **Diagnosis**
- Direct diagnosis
- Serology

5 - **Treatment**

Treatment

Expert Opinion

Treatment of chlamydial infections

Expert Opin. Pharmacother. (2012)

Antimicrobial	MIC range (µg/ml) *C. trachomatis*	*C. pneumoniae*
Doxycycline	0.031 - 0.25	0.015 - 0.5
Tigecycline	0.03 - 0.125	0.125 - 0.25
Erythromycin	0.016 - 2	0.015 - 0.25
Azithromycin	0.6 - 2	0.05 - 0.25
Clarithromycin	0.015 - 0.125	0.004 - 0.125
Solithromycin (CEM - 101)	0.125 - 0.5	0.25 - 1
Clindamycin	2 - 16	-
Ciprofloxacin	0.5 - 2	1-4
Levofloxacin	0.12 - 0.5	0.25 - 1
Moxifloxacin	0.5 - 1	0.125 - 1
Rifampin	0.005 - 0.25	0.0075 - 0.03
Trimethoprim	≥ 128	≥ 128
Sulfamethoxazole	0.5 - 4	≥ 500
Gentamicin	500	500
Vancomycin	1000	1000

Treatment

Expert Opinion — Treatment of chlamydial infections

- **Recommended regimens**
  - Azithromicin: single dose of 1gr (97%)
  - Doxycycline: 2x100mg/d for 7 days (98%)
    - DNA persist 21 days => Test of cure 1 month after TTT
    - ONLY if concerns about compliance, persistance symptoms, reinfection
- **Pregnant Women**
  - Azithromicin: single dose of 1gr (Test of cure +++ @ 3 Mo)
  - Amoxicillin: 3x500mg/d for 7 days (CDC)
- **PID**
  - Doxycycline 14d + Ceftriaxone (Gono/enterobact/strept) + Metronidazole (Bacteroides)

Thank you !

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