



### Plan:

- 1 - Epidemiology
- 2 - Clinical manifestation
  - > Trachoma
  - > Urogenital infection
  - > Reiter's
  - > LGV
- 3 - Impact on fertility / pregnancy
- 4 - Diagnosis
  - > Direct diagnosis
  - > Serology
- 5 - Treatment

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### A public health concern

✓ Most common bacterial sexually transmitted disease

Most frequent STD in USA

### Epidemiology

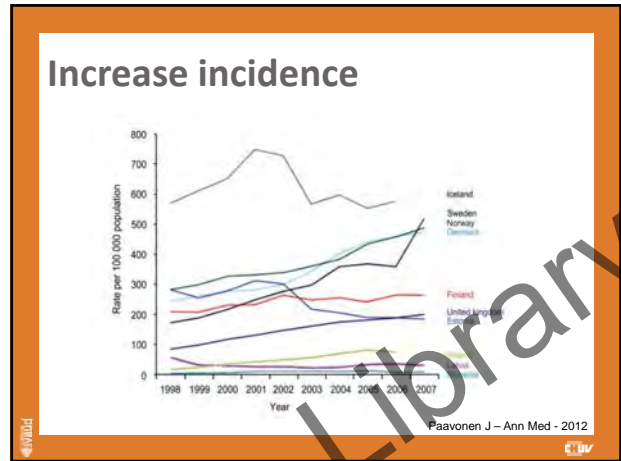
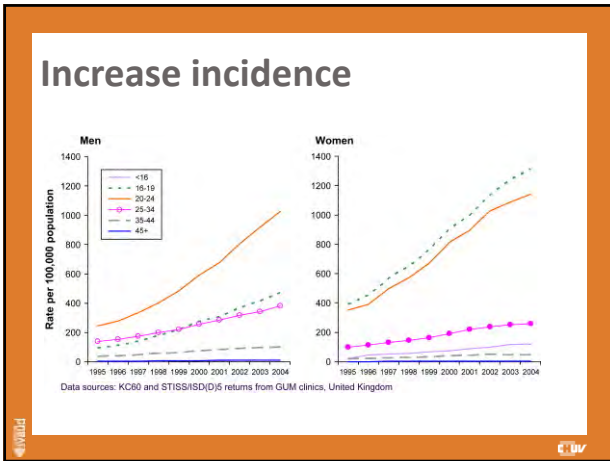
- Young people
- Risk factors:
  - multiple partner
  - High frequency of partner change
  - Unprotected sex
  - Single

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
Sex education	A new infected sex partner in the last 90 days No or rare use of condoms
STDs	Use of oral contraceptives Prior STDs

Mylonas - 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<sup>1</sup>, Katta Jaton<sup>1</sup>, Clairy Bonelli<sup>1</sup>, Jean-Pierre Kurling<sup>1</sup> and Gilbert Gaudin<sup>1</sup>

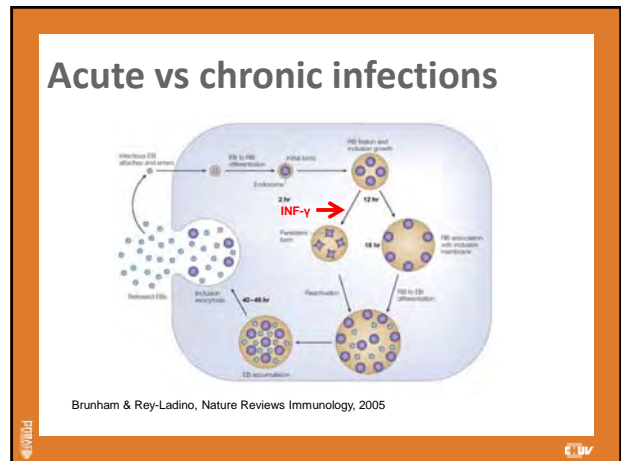
- 1.2% of young swiss male
- 3% of gynecological check-up

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.
<b>Total</b>	511	168	4			1.2
<b>Age (year ± SD)</b>						
≤ 25	276	54	5	83.3	0.23	1.9
> 25	235	114	1	16.7	0.03 - 3.02	4.9
<b>Nationality at birth</b>						
Switzerland	433	84.7	2	33.3	0.003	0.5
Europe	41	8	1	16.7	3.3	2.4
Other	37	7.2	3	50	17.6	2.84 - 108
<b>Place of residence</b>						
> 10'000 inhabitants	134	26.2	4	66.7	0.046	ref
≤ 10'000 inhabitants	377	72.8	2	33.3	0.17	0.03 - 0.96
<b>Main occupation</b>						
Work	245	51.9	4	66.7	0.74	ref
Student	231	45.2	2	33.3	0.33	0.1 - 2.89
<b>Declined to respond</b>	15	2.8	0	0	-	0
<b>Monthly income</b>						
≤ 1000 Frs.	301	58.9	1	16.7	0.064	ref
1000 - 2000 Frs.	49	13.5	1	16.7	4.4	0.3 - 70.6
> 2000 Frs.	112	21.9	4	66.7	10.8	1.2 - 97.2
<b>Declined to respond</b>	29	5.7	0	0	-	0
<b>Number of lifetime sexual partner</b>						
0	47	13.1	0	0	0.36	-
1	123	24.5	-	-	-	0
≥ 2	306	59.9	-	-	-	1.9
<b>Declined to respond</b>	13	2.5	-	-	-	0

Baud et al BMC Infect Dis 2008



**Plan:**

- 1 - Epidemiology
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**Chlamydia trachomatis serovars**

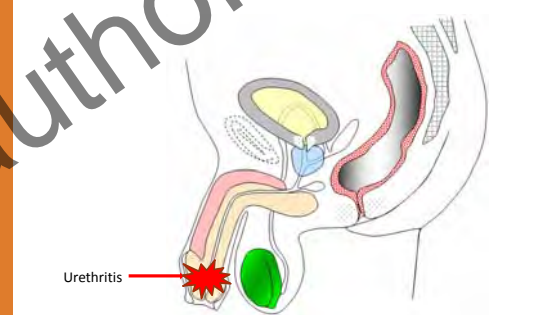
Serovar	Clinical manifestation	Complication
A-C	Keratoconjunctivitis	Scarring trachoma, blindness
D-K	Males: urethritis, proctitis	Epididymitis
	Females: cervicitis, urethritis, proctitis	Endometritis, salpingitis, pelvic pain, ectopic pregnancy, perihepatitis (Fitz-Hugh-Curtis syndrome), infertility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

**Keratoconjunctivitis / Trachoma**



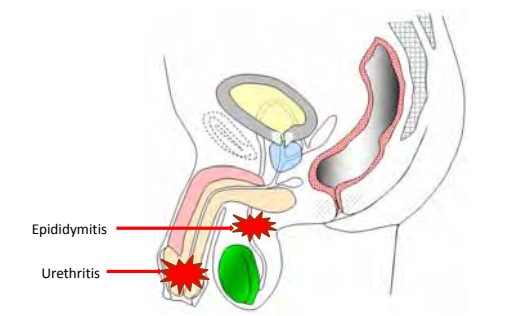
⇒ Blindness  
⇒ 6 million people/year

**Urogenital infection in Men**



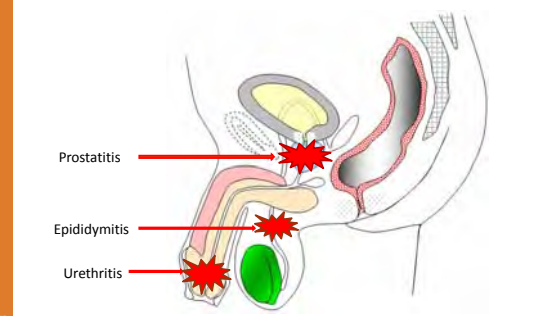
Urethritis

**Urogenital infection in Men**



Epididymitis  
Urethritis


**Urogenital infection in Men**



Prostatitis  
Epididymitis  
Urethritis

### Symptoms in men

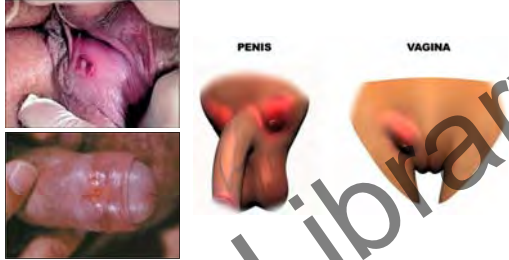
- 90% asymptomatic
- Clear or cloudy urethral discharge
- Dysuria
- Burning or itching around the urethral opening
- Pain and swelling around the testicles



### Lymphogranuloma Venereum: LGV

**1<sup>st</sup> stage:** Genital ulcer

**2<sup>nd</sup> stage:** Lymphadenitis/Lymphangitis

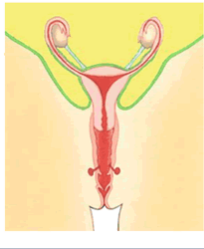


### Reiter's syndrome

- Urethritis
- Conjunctivitis
- Arthritis
- Mucocutaneous lesions

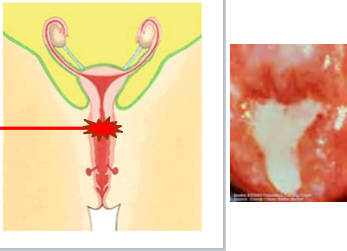


### Urogenital infection in women



### Urogenital infection in women

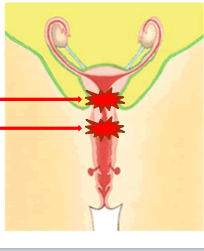
Cervicitis

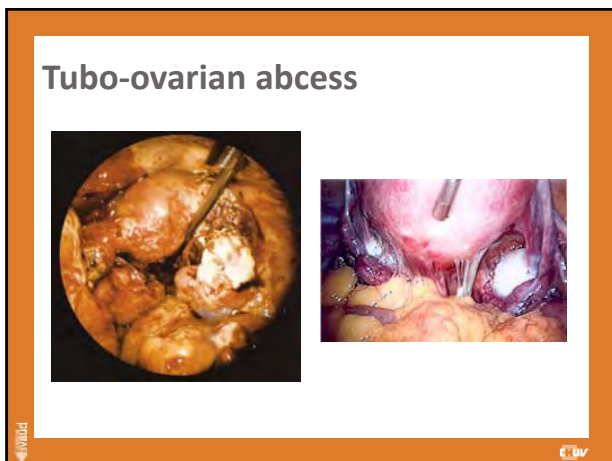
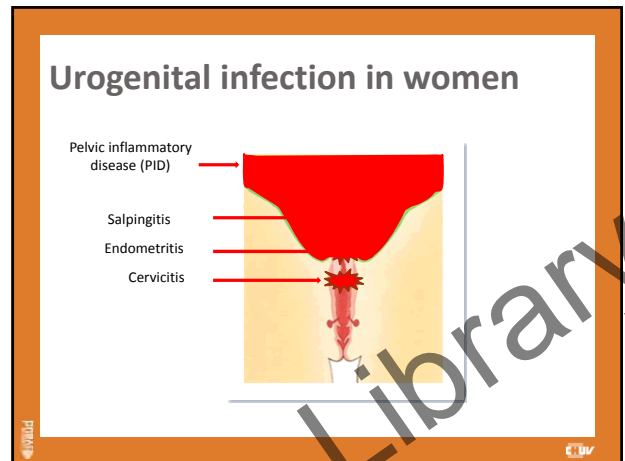
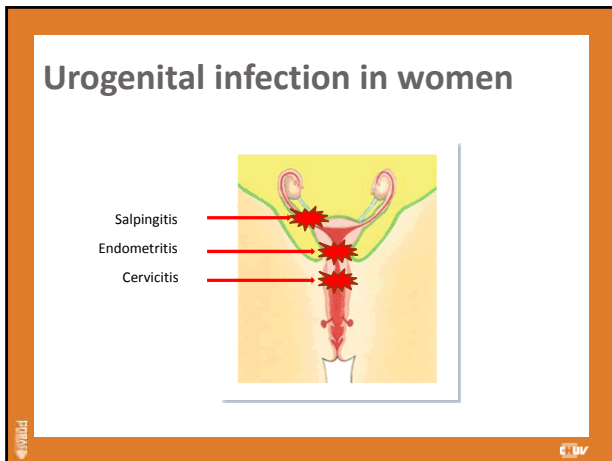


### Urogenital infection in women

Endometritis

Cervicitis

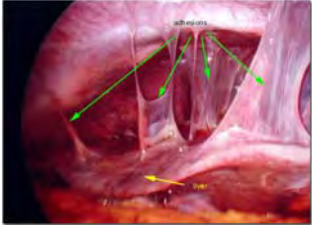




- ### Urogenital symptoms in women
- 80-90% asymptomatic
  - Vaginal discharge
  - Bleeding between periods
  - Painful periods
  - Abdominal pain and fever
  - Dyspareunia
  - Itching or burning in or around the vagina
  - Dysuria

### 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**



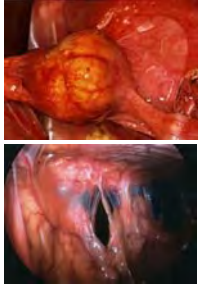
- In 5-15% of salpingitis
- Symptoms in 20%
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### Plan:

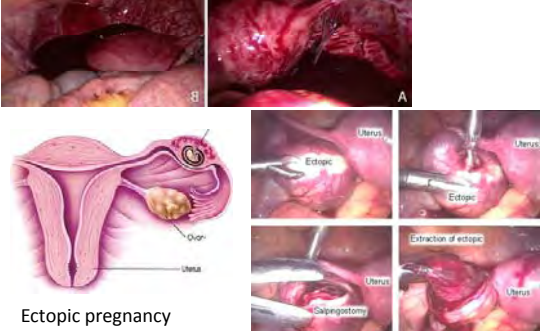
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### Impact on fertility

- 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<sup>1,2,3</sup>, Lesley Regan<sup>4</sup> and Gilbert Graub<sup>5</sup>

1. Choudhry P, Regan L, et al. Association between genital mycoplasma infections and pregnancy losses: a nested case-control study. *Sex Transm Infect* 2002; 76: 131-134

2. Baud D, Regan L. Chlamydia from genital tract infections and spontaneous abortion. *Acta Obstet Gynecol Scand* 1998; 77: 1-13

3. Baud D, Regan L. Effect of treatment of Chlamydia trachomatis on pregnancy outcomes in the women's primary care: a nested case-control study. *Sex Transm Infect* 2005; 81: 120-123

4. Hill P, Tait A, Dalrymple S, et al. First trimester pregnancy loss and active Chlamydia trachomatis infection: a nested case-control study. *Sex Transm Infect* 2002; 76: 370-373

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14. Regan L, Choudhry P, Hill P, et al. Chlamydia trachomatis infection in women with recurrent spontaneous abortion. *Sex Transm Infect* 2002; 76: 131-134

15. Hill P, Regan L, Choudhry P, et al. The frequency and risk of Chlamydia trachomatis infection in women with recurrent spontaneous abortion. *Sex Transm Infect* 2002; 76: 131-134

16. Hill P, Regan L, Choudhry P, et al. Chlamydia trachomatis infection in women with recurrent spontaneous abortion. *Sex Transm Infect* 2002; 76: 131-134

17. Hill P, Regan L, Choudhry P, et al. Chlamydia trachomatis infection in women with recurrent spontaneous abortion. *Sex Transm Infect* 2002; 76: 131-134

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20. Hill P, Regan L, Choudhry P, et al. Chlamydia trachomatis infection in women with recurrent spontaneous abortion. *Sex Transm Infect* 2002; 76: 131-134

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47. Hill P, Regan L, Choudhry P, et al. Chlamydia trachomatis infection in women with recurrent spontaneous abortion. *Sex Transm Infect* 2002; 76: 131-134

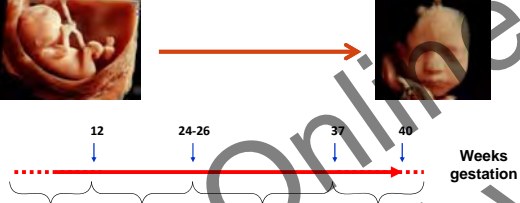
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Current Opinion in Infectious Diseases 2008, 21:70-76

### Pregnancy



12 weeks: Miscarriage

24-26 weeks: Late miscarriage

37 weeks: Preterm birth / PPRM

40 weeks: Term birth

Weeks gestation

### Impact on pregnancy: miscarriage

Table 1. Characteristics of study patients according to miscarriage history

Characteristic	Control (n = 109)	Sporadic miscarriages (n = 69) (% p value)	Recurrent miscarriages (n = 200) (% p value)
Chlamydia trachomatis (IgG) n=50	15 (8.9)	9 (13.0, 0.33)	39 (19.5, 0.004)

Odds ratio 95% CI

Waddie chondroplasia*	4.86	2.50-9.43
Age (per 10 y)	2.85	1.00-4.11
White ethnicity	1.25	0.80-1.95
Contact with animals	1.57	0.91-2.80
Chlamydia trachomatis*	2.32	1.18-4.54

Baud D – Emerg Infect Dis - 2007

### Impact on pregnancy: miscarriage

#### Role of *Chlamydia trachomatis* in Miscarriage

David Baud, Genevieve Doy, Soline Jaton, Marjolaine Chavreau, Isabelle Blum, Nadine Baud, Yvan Vuyl, Fabrice Mouton, Andrew Freytag, and Gilbert Graub

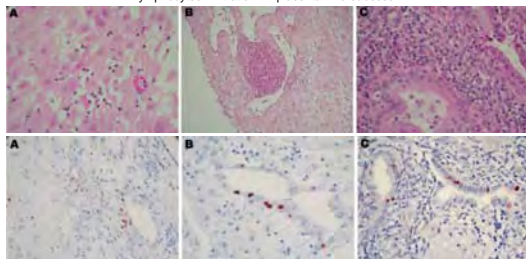
Table 1. Characteristics of 336 women, by miscarriage history, in a study of the role of *Chlamydia trachomatis* in miscarriage. University Hospital of Lausanne, Lausanne, Switzerland, November 2006–June 2009\*

Characteristic	Control group, no. (%) (n = 261)	Miscarriage group, no. (%) (n = 125)	p value
<i>C. trachomatis</i> 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
<i>C. trachomatis</i> 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 microabscess



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

Baud D – Emerg Infect Dis - 2011

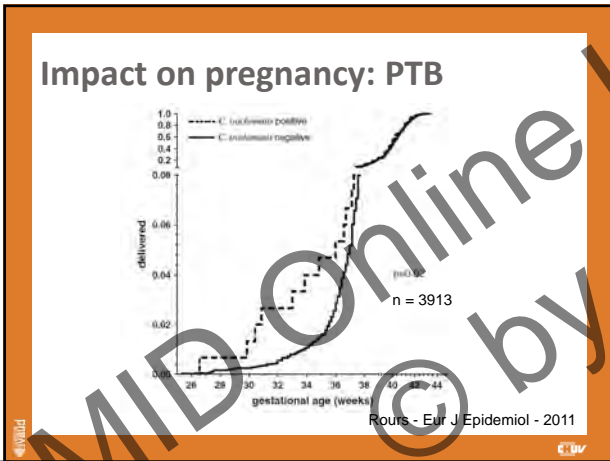
### Impact on pregnancy: PTB

Chorioamnionitis → preterm birth

### Impact on pregnancy: PTB

Switzerland	Europe
8 million citizens	800 million
80'000 birth / year in Switzerland	8'000'000 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 \$
<b>50'000'000 \$</b>	<b>5'000'000'000 \$</b>

Baud D - In review 2013

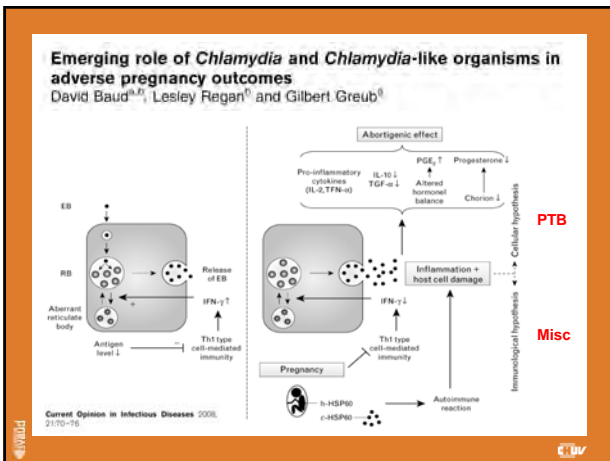


### Impact on pregnancy: PTB

	Risk for preterm delivery	
	< 32 weeks n = 22	≤ 35 weeks n = 64
<i>C. trachomatis</i> infection	Unadjusted odds ratio 5.69 (1.9-17.0)**	3.14 (1.4-7.0)**
<i>C. trachomatis</i> infection	Adjusted odds ratio <sup>a</sup> 4.35 (1.3-15.2)**	2.66 (1.1-6.3)**

Analyses are done versus delivery ≥ 37 weeks (n = 3,724)  
<sup>a</sup> 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



### Neonatal infection

Transmission rate: 50 to 70%



### Neonatal infection

Transmission rate: 50 to 70%

### Neonatal infection

Transmission rate: 50 to 70%

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

### Neonatal infection

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

### Neonatal infection

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

### Plan:

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  - > 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): 185-194. doi:10.1586/eri.10.164

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

Anna S Graseck<sup>1</sup>, Shirley L Shih<sup>1</sup>, and Jeffrey F Paupert<sup>1,†</sup>

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



## Specimens / strategies

Study (year)	Design	Sample size (n)	Control arm	Home testing rate	Control testing rate
Wassilak et al. (2005)	Randomized study of American high-velocity contraceptive users	138	Home testing (self-swab) vs. clinic (self-swab or screening using the usual medical pathway for the participant's physician)	76%	57%
Shaw et al. (2007)	Cluster-random study of American women (clinical sites vs. home-based screening)	482	Screening by clinic-based screening with self-swab at home vs. screening using the usual medical pathway for the participant's physician	67%	67%
Coak et al. (2007)	Randomized study of high-risk young heterosexual women	420	Screening by clinic-based screening	134 (32%)	141 (34%)
Lagarde et al. (2007)	Randomized study of Trinidadian women recruited from a clinic	518	Agreement for clinic-based screening with self-swab	42%	194 (37%)
Dean et al. (2007)	Randomized study of South African women recruited from a clinic and self-screening	826	Agreement for clinic-based screening with self-swab	42%	133 (16%)
Waller et al. (2007)	Randomized study of white women in an American health plan	1825	Mail-based self-report card vs. 100% clinical test (self-swab) vs. 93% clinical test (self-swab)	21%	100%
Waller et al. (2007)	Randomized study of female inmates belonging to one of three medical practices	608	Screening by clinic-based screening with self-swab vs. screening using the usual medical pathway for the participant's physician	22% (screening by self-swab)	100%
Waller et al. (2007)	Randomized study of female inmates belonging to one of three medical practices	608	Mail-based self-report card vs. 100% clinical test (self-swab) vs. 93% clinical test (self-swab)	21%	100%
Chang et al. (2007)	Cluster-random study of women in an American health plan	2000	Screening by physician screening vs. screening using the usual medical pathway for the participant's physician	10%	10%

## Specimens / strategies

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



Schoeman SA – BMJ - 2012

## Specimens / strategies

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

	Predictive value			
	Sensitivity (95% CI)	Specificity (95% CI)	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

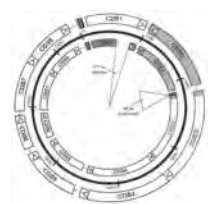
Schoeman SA – BMJ - 2012

## 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

Bébéar et al. . CMI, 2009

### Chlamydia trachomatis plasmids



**Swedish new variant *C. trachomatis* serotype 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


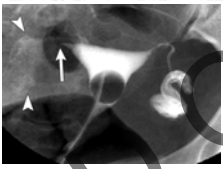
*Review Article*  
**Antichlamydial Antibodies, Human Fertility, and Pregnancy Wastage**  
*Infectious Diseases in Obstetrics and Gynecology*  
 Volume 2011, Article ID 525182, 9 pages

Annalisa I. Stephens, Mira Aubricsson, and Daner I. Schoni

- 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**  
 Annalisa I. Stephens, Mira Aubricsson, and Daner I. Schoni

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

### Indirect diagnosis - Serology

*Review Article*  
**Comparison of five commercial serological tests for the detection of anti-*Chlamydia trachomatis* antibodies**  
 D. Bond, E. Pagan, F. Grech

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	LR +	LR -
IF	83.3	95.6	65.8	98.3	18.8	0.17
ChSP90-Medic	93.3	87.4	43.1	99.2	7.4	0.08
MOMP-Medic	93.3	96.9	75.7	99.3	30.8	0.07
MOMP-RB	96.7	99.7	96.7	28.4	0.03	
StarPlus	100	89.6	49.2	100	9.5	0

### 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)  
 "Mason & Steinmeyer" © approved journal

Antimicrobial	MIC range (µg/ml)	
	<i>C. trachomatis</i>	<i>C. pneumoniae</i>
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
Solidromycin (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 Expert Opin. Pharmacother. (2012)

- **Recommended regimens**
  - Azithromycin: 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, persistence symptoms, reinfection
- **Pregnant Women**
  - Azithromycin: 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 !



The first poster is a red and white advertisement for 'CHLAMYDIA' with the text 'Durable Infection WITH NO OBVIOUS SYMPTOMS PREMIUM STI NO 2'. The second poster is an NHS advertisement with the text 'Before you get into someone else's pants' and '...make sure you do your "blat" test in Youself!'.

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