

Urogenital diagnostic investigations in Men

Testing for IgA antibodies
against
Chlamydia trachomatis
in seminal fluid



***C. trachomatis* as a microorganism causing urogenital infections in men**

Urethritis, prostatitis, epididymitis and other infections of the male genital tract can be caused by *C. trachomatis* (1, 2).

The prevalence of *C. trachomatis* in asymptomatic men varies with age (3). The prevalence of this microorganism reaches its highest level of about 8% before the age of 25 years.

Consequences of *C. trachomatis* infection in men

- **Disorders of sexual function**

Inflammatory reactions induced by *C. trachomatis* may cause obliterative lesions in the seminal tract. In extreme cases there may be occlusive azoospermia (4).

- **Impaired fertility**

Inflammatory reactions induced by *C. trachomatis* lead to activation of leucocytes, and by liberating oxygen radicals, proteases and cytokines these activated leucocytes can depress sperm motility and interfere with the acrosome reaction. Fertility is likely to be impaired (7, 8).

- **Transmission of the pathogen**

The pathogen may be carried by infected spermatozoa into the female upper genital tract (9).

***C. trachomatis* diagnostic investigations in men**

Direct demonstration of the pathogen in urethral smears and/or urine:

Problem:

- microorganisms that have already ascended into the prostate, seminal vesicles or epididymis will escape detection
- false negative results

Demonstration of serum IgG and IgA antibodies against *C. trachomatis*:

Problem:

- the immune response is detectable only after seroconversion
- delay between onset of infection and immune response

NEW:

Detection of IgA antibody against *C. trachomatis* in seminal plasma:

Advantage:

- the local immune response is detectable even when the pathogen has ascended into the seminal tract
- a link between direct microscopy and serology

Clinical relevance of diagnosis by IgA antibodies versus *C. trachomatis* in seminal fluid

IgA antibodies against *C. trachomatis* in seminal plasma

- are associated with inflammatory reactions(10)
- are accompanied by increased formation of antibodies against spermatozoa (11)
- point to the likelihood of impaired fertility(12).

Detection of *C. trachomatis* antibodies in seminal plasma*:

Semen donors and subfertile men were tested in parallel for IgG and IgA antibodies against *C. trachomatis* in the serum and also for IgA antibodies against *C. trachomatis* in the seminal plasma. None of these men had any symptoms pointing to infections of the urogenital tract.

		Semen donors (n=116)	Men with impaired fertility (n=171)
Seminal fluid analysis (WHO)		Normozoospermia	Variable
positive microscopic detection of <i>C. trachomatis</i> in urine and/or urethral smear		0 %	4,7 %
antibodies against <i>C. trachomatis</i> in serum	IgG	n.d.	17,0%
	IgA		12,3%
in seminal plasma	IgA	9,5%	26, 9%¹⁾

Correlation between IgA in serum and in seminal plasma in subfertile men (n=171).

		Seminal plasma IgA		
		+	-	
Serum IgA	+	15	6	21 (12.3%)
	-	31	119	
		46 (26.9%) ²⁾		171

¹⁾IgA-frequencies in seminal plasma differ significantly (p<0,05) between semen donors and men with impaired fertility.

²⁾IgA-frequencies in serum and seminal plasma differ significantly (p<0,001).

*Schuppe et al. (2000), IVth European Chlamydia Congress Helsinki

Conclusions:

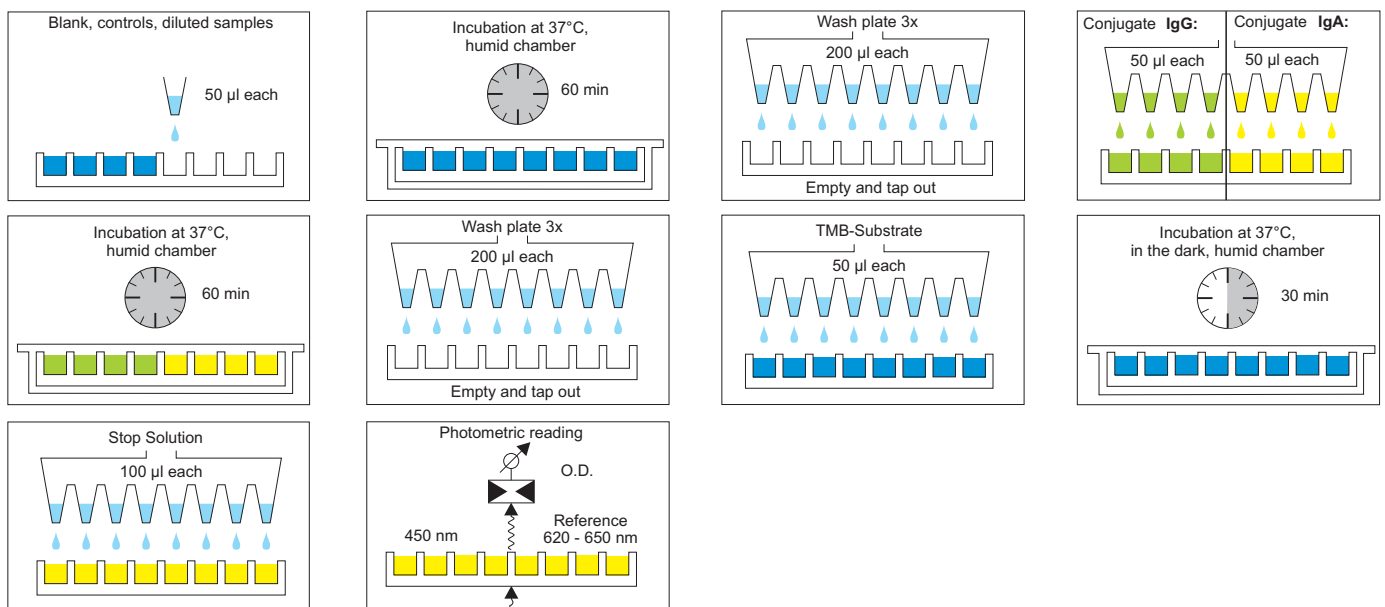
- the extent of *C. trachomatis* infection in the male urogenital tract cannot be established simply by direct microscopic demonstration of the pathogen
- the serological results reflect only a part of the immune response
- secretory IgA against *C. trachomatis* in the seminal fluid is detectable even before seroconversion, because it is an early immune response on the part of the mucosa
- the presence of secretory IgA against *C. trachomatis* in the seminal fluid suggests an increased likelihood of subfertility
- taken in conjunction with the clinical and spermatological findings, secretory IgA against *C. trachomatis* can be helpful in making decisions on therapy

Testing for secretory IgA in seminal fluid with the *C. trachomatis*-IgA-pELISA medac

1. Proceeding of the ejaculate:



2. Test procedure:



3. Cut off calculation:

$$\text{Cut off} = \text{mean OD negative control} + 0,05$$

References:

1. Nickel JC. Chronic Prostatitis: An Infectious Disease? *Infect Urol* 2000; 13(2): 31-38
2. Weidner W, Krause W, Ludwig M. Relevance of male accessory gland infection for subsequent fertility with special focus on prostatitis. *Hum Reprod Update* 1999; 5(5): 421-32
3. Petersen EE, Clad A, Mendel R, Prielwitz J, Hintz K. Prevalence of chlamydial infections in Germany: Screening of asymptomatic women and men by testing first void urine by ligase chain reaction (LCR). In: *Chlamydia Research*. Angelika Stary (ed.). Proceedings of the Third Meeting of the European Society for Chlamydia Research, Vienna, Austria, 11.-14. September, 1996: p. 415
4. Strowitzki T unter Mitarbeit von Korell M, Thaler CJ, Wolff H (Hrsg.). Männliche Sterilität. In: *Ungewollte Kinderlosigkeit*. Stuttgart: Fischer, 1996: 43-52
5. Keck C, Clad A, Naudascher I, Schmidt S, Neulen J, Breckwoldt M. Korrelation zwischen Seminalparametern und Chlamydia trachomatis spezifischen Antikörpern bei infertilen Männern. *Geburtsh u Frauenheilk* 1997; 57: 71-74.
6. Keck C, Gerber-Schafer C, Clad A, Wilhelm C, Breckwoldt M. Seminal tract infections : impact on male fertility and treatment options . *Hum Reprod Update* 1998; 4(6): 891-903
7. Wolff H. The biologic significance of white blood cells in semen. *Fertil Steril* 1995; 63(6): 1143-57
8. Wolff H, Neubert U, Zebhauser M, Bezold G, Korting HC, Meurer M. Chlamydia trachomatis induces an inflammatory response in the male genital tract and is associated with altered semen quality. *Fertil Steril* 1991; 55(5): 1017-9
9. Erbenig T. Ultrastructural observations on the entry of Chlamydia trachomatis into human spermatozoa. *Hum Reprod* 1993; 8(3): 416-21
10. Ochsendorf FR, Ozdemir K, Rabenau H, Fenner T, Oremek R, Milbradt R, Doerr HW. Chlamydia trachomatis and male infertility: chlamydia-IgA antibodies in seminal plasma are C. trachomatis specific and associated with an inflammatory response. *Eur Acad Dermatol Venereol* 1999; 12(2): 143-52
11. Witkin SS, Munoz MG, Jeremias J. The 60 kDa heat shock protein in human semen: relationship with antibodies to spermatozoa and Chlamydia trachomatis. *Hum Rep* 1996; 11(12): 2600-2603
12. Suominen J, Gronroos M, Terho P, Wichmann L. Chronic prostatitis, Chlamydia trachomatis and infertility. *Int J Androl* 1983; 6(5): 405-13
13. Schuppe HC, Bispink G, Peet DJ, Propping D, Böttcher M, Dettlaff S. The significance of antibodies against C. trachomatis in seminal plasma. IVth European Chlamydia Congress, 2000 Helsinki, in print.