What are the consequences of sexually transmitted infections on male reproduction?

F.R. Ochsendorf

Sexually transmitted infections/diseases (STI) are caused by organisms sharing the following properties: 1) very sensitive to physical/chemical factors, hence only transmittable by direct contact, 2) only infectious for humans, 3) colonizing the genital region, 4) often causing only mild symptoms and 5) not leading to immunity. As a consequence concurrent infections with different STD-agents may occur at the same time (Table 1).

Mechanism of damage

Fertility may be impaired by organ damage due to the organism itself, cell damage via mediators of inflammation, inflammatory obstruction of the excurrent ductal system, or binding to spermatozoa. Thus, with respect to the impact on male reproductive system, chronic or inadequately treated STI's are more relevant than the acute infections.

Relevance

The difference in the prevalence of STI's in different regions of the world as well as the access to their adequate diagnosis and treatment explain conflicting data on the relevance of these infections in male infertility. In western countries STI's only account for a minority of inflammatory damage in the reproductive tract. However, In other parts of the world STI's can severely impair male fertility: men with a history of penile discharge, painful micturition and genital ulcers, who did not seek adequate treatment for these symptoms, are more likely to be infertile than men without these symptoms or are adequately treated. Recently it was shown that 18.7% of semen samples (45/ 241) of asymptomatic men seeking infertility investigation contained DNA from STI-pathogens (e.g., CMV, HPV, HSV, HHV6, EBV, C. trachomatis). There was no difference in prevalence between samples with or without leukocytospermia. The presence of STI-DNA in semen samples was found to be associated with impairment in semen parameters (e.g., concentration, motile sperm concentration, total sperm count and neutral alpha-glucosidase concentration). However it has to be kept in mind that the presence of a germ does not necessarily mean "infection", as the pathogen may just colonize the tissue without causing a clinical infection with pathological sequelae. This fact may also explain some conflicting data in the literature. Another impact of STI's is their potential to increase the rate of

HIV-transmission. Thus, adequate diagnosis and treatment of STI's is not only relevant for the prevention of long-term negative consequences for fertility but also for the prevention of HIV-spreading.

Relevant infections

Various common pathogens that can be isolated in the male reproductive tract are listed in Table1. Currently, literature supports the association of a significant negative impact on male fertility with infection of gonococci and HIV, while the roles of other pathogens such as *chlamydia trachomatis*, *ureaplasma urealyticum*, HSV, HPV and *trichomonas vaginalis* in impairing male fertility remain controversial.

Bacteria and protozoa

A review of the literature could not demonstrate a general link between urethritis and male infertility. Gonorrhoea, however, can cause urethral strictures as well as a strong impairment of testicular functions. In female, *C. trachomatis* infection can impair fertility by tubal obstruction. On the other hand, its impact on male fertility remains to be established although some epidemiological data points to the risk of subfertility in men (and women) with a past *C. trachomatis* infection, The exact role of Mycoplasmae, i.e. *M. hominis, Ureaplasma urealyticum* and *M. genitalium* has still to be elucidated. *U. urealyticum* may cause infertility via deleterious effects on sperm chromatin and DNA integrity, leading to impairment of embryo development. *Trichomonas vaginalis* was more often found in infertile men than in fertile controls; however, no effect on motility or sperm-mucus interaction has been demonstrated (Soper 2004).

Viruses

At present the clinical relevance of viruses as a cause of male infertility is largely unknown. Cytomegalovirus (CMV) and human herpes virus type 6 (HHV-6) were demonstrated in semen without an association with impaired semen parameters. The data on the relevance of herpes simplex virus (HSV) as well as human papilloma virus (HPV) and their associations with sperm parameters are conflicting (Ochsendorf 2006).

HIV. Infected leukocytes are the most relevant source of human-immunodeficiency virus (HIV) in the male reproductive tract. In AIDS patients oligozoospermia, azoospermia, orchitis and hypogonadism were reported. Spermatozoa morphology is particularly impaired with progression of the disease. Disturbed function of the seminal vesicles and prostate gland may explain the decrease in semen volume and increase in ejaculate viscosity. With the latest advances in drug-therapies, HIV infection is considered a chronic disease. The safety of both the uninfected partner and the potential

offspring are of particular concern. In a sero-discordant couple the risk of acquiring HIV is dependent on the viral load in semen. Depending on the semen quality, spermatozoa can be used for intrauterine insemination, IVF or ICSI after adequate preparation of the ejaculate. The semen has to be washed free of HIV by a gradient technique and the success of this procedure has to be controlled prior to use. A thorough counselling of both partners on the therapeutic options, psychosocial and economic aspects with respect to their sexual health and reproductive health is thus necessary.

Table 1: Sexually transmitted infections: pathogens and relevance for male fertility; + = clinical relevance demonstrated; ? = relevance possible but not yet proven

Disease	Pathogen	Relevance for infertility
Bacteria		
Gonorrhoea	Neisseria gonorrhoea	Male + Female +
Chlamydia infection	Chlamydia trachomatis (D-K)	Male ? Female +
Urethritis (due to)	Ureaplasma urealyticum	May impair motility, sperm chromatin ?
Syphilis	Treponema pallidum	Co-factor for transmission of HIV Gummatous testicular lesions: + Female +
Chancroid	Haemophilus ducrey	-
Lymphogranuloma venereum	Chlamydia trachomatis (L1-L3)	-
Granuloma inguinale	Calymmatobacterium granulomatis	-
Viruses		
AIDS	HIV	Male +
Mononucleosis	CMV	-
Asymptomatic infection	HSV	Impaired semen quality ?
Asymptomatic infection	HPV	Impaired semen quality ?? Asthenozoospermia
Asymptomatic infection	Adenovirus	Infertility ?
Mumps	Mumps virus	Testicular atrophy +
Protozoa		
Urethritis (Prostatis, Epididymitis) due to	Trichomonas vaginalis	? controversial
Yeasts		
Balanitis, Urethritis (due to)	Candida albicans	-

Handbook of Andrology – What are the consequences of sexually transmitted infections on male reproduction?

Suggested reading

Bezold G, Politch JA, Kiviat NB, Kuypers JM, Wolff H, Anderson DJ. Prevalence of sexually transmissible pathogens in semen from asymptomatic male infertility patients with and without leukocytospermia. Fertil Steril. 2007; 87: 1087-1097.

Dejucq N, Jégou B. Viruses in the mammlian male genital tract and their effects on the reproductive system. Microbiol Mol Biol Rev. 2001; 65: 208 - 231.

Karinen L, Pouta A, Hartikainen AL, et al. Association between Chlamydia trachomatis antibodies and subfertility in the Northern Finland Birth Cohort 1966 (NFBC 1966), at the age of 31 years. Epidemiol Infect. 2004; 132: 977-984.

Ness RB, Markovic N, Carlson CL, Coughlin MT. Do men become infertile after having sexually transmitted urethritis? An epidemiologic examination. Fertil Steril. 1997; 68: 205-213.

Ochsendorf FR. Reproductive tract infections/sexually transmitted diseases. In: Schill WB, Comhaire FH, Hargreave TB, eds. Andrology for the clinician Berlin - Heidelberg - New York Springer. 2006: 125 – 130.

Okonofua F, Menakaya U, Onemu SO, Omo-Aghoja LO, Bergstrom S. A case-control study of risk factors for male infertility in Nigeria. Asian J Androl. 2005; 7: 351-361.

Paavonen J, Eggert-Kruse W. Chlamydia trachomatis: impact on human reproduction. Hum Reprod Update. 1999; 5: 433-447.

Reichart M, Kahane I, Bartoov B. In vivo and in vitro impairment of human and ram sperm nuclear chromatin integrity by sexually transmitted Ureaplasma urealyticum infection. Biol Reprod. 2000; 63: 1041-1048.

Soper D. Trichomoniasis: under control or undercontrolled? Am J Obstet Gynecol. 2004; 190: 281-290.

van Leeuwen E, Prins JM, Jurriaans S, et al. Reproduction and fertility in human immunodeficiency virus type-1 infection. Hum Reprod Update. 2007; 13: 197-206.