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Chlamydia trachomatis as a risk factor for infertility in women and men, and ovarian tumor development

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## Akademisk avhandling

som med vederbörligt tillstånd av Rektorsämbetet vid Umeå universitet för avläggande av medicine doktorsexamen framläggs till offentligt försvar i Sal B, By 1D, 9 tr., Tandläkarhögskolan, fredagen den 29 maj, kl. 13:00. Avhandlingen kommer att försvaras på svenska.

Fakultetsopponent: Professor Jorma Paavonen, Institutionen för Obstetrik och Gynekologi, Helsingfors universitet, Helsingfors, Finland.



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# Chlamydia trachomatis as a risk factor for infertility in women and men, and ovarian tumor development

#### Abstract

**Background:** Chlamydia trachomatis in women is a risk factor for tubal factor infertility and extra uterine pregnancies, but the impact of a *C. trachomatis* infection on male fertility is unclear. It is also hypothesized that persistent infection with *C. trachomatis*, or other microorganisms, might initiate/promote ovarian tumor development. The aims of the thesis were to study whether *C. trachomatis* serum antibodies in women and men had an impact on infertility diagnoses, semen characteristics, pregnancy rates and pregnancy outcomes; furthermore, to explore associations of *C. trachomatis*, and *Mycoplasma genitalium*, plasma antibodies with epithelial ovarian cancer and borderline ovarian tumors, as well as the presence of *C. trachomatis* bacteria, and other microorganisms, in ovarian tissues.

**Materials and methods:** Papers I and II: 244/226 infertile couples were tested for serum *C. trachomatis* IgG, IgA, IgM and chlamydial Heat Shock Protein 60 (cHSP60) IgG antibodies. *C. trachomatis* IgG positive couples were also tested for *C. trachomatis* DNA in a urine sample. The follow-up period was 14-54 months. 244 spontaneously pregnant women were also tested for serum *C. trachomatis* IgG antibodies. Papers III and IV: Plasma samples from 291 women with epithelial ovarian cancer, borderline ovarian tumors and benign conditions, and plasma samples from 271 healthy controls, were analyzed for *C. trachomatis* IgG, IgA and cHSP60-1 IgG and *M. genitalium* IgG antibodies. Ovarian tissues from 186 women with benign ovaries, borderline ovarian tumors and epithelial ovarian cancer, as well as tissues from the contra lateral ovary in 126 women, were analyzed for the presence of *C. trachomatis*, *M. genitalium*, *Neisseria gonorrhoeae*, HPV and the polyoma viruses BKV and JCV with nucleic acid amplification tests.

**Results:** Papers I and II: The prevalence of *C. trachomatis* IgG antibodies was higher among infertile than fertile women, and there were 9 couples with ongoing *C. trachomatis* infections. In men, *C. trachomatis* IgG and IgA antibodies were associated with a reduced likelihood to achieve pregnancy for the couple, as well as lower sperm concentration, reduced sperm motility and vitality, increased teratozoospermia index and the occurrence of leukocytes. *C. trachomatis* IgG and cHSP60 IgG antibodies in infertile women were associated with tubal factor infertility, but not with reduced pregnancy rates or outcomes. Paper III: cHSP60-1 IgG antibodies were associated with ovarian cancer belonging to the postulated type II pathogenetic pathway, when plasma samples obtained more than one year prior to diagnosis were analyzed. *M. genitalium* IgG antibodies were associated with borderline ovarian tumors; however a statistical type 1 error cannot be excluded. Paper IV: None of the microorganisms studied were found in the ovarian tissue samples.

**Conclusions:** *C. trachomatis* IgG and IgA antibodies in the man substantially decreases the chances of the infertile couple to achieve pregnancy, and are associated with subtle negative changes in semen characteristics. *C. trachomatis* IgG and cHSP60 IgG antibodies in the woman are risk factors for tubal factor infertility. Prospective plasma cHSP60-1 IgG antibodies are associated with type II ovarian carcinomas, but *C. trachomatis* bacteria, or the other microorganisms studied, could not be detected in benign, borderline or malignant ovarian tissues.

**Keywords:** Antibodies; borderline tumors; *Chlamydia trachomatis*; cHSP60; DNA; infertility; ovarian cancer; pregnancy rate; RNA; semen characteristics.

Full text - link

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