Chlamydia trachomatis Female Genital Tract Infections: Memorium to Professor Per-Anders Mardh

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Chlamydia trachomatis is recognized as the most common sexually transmitted bacterial infection worldwide and the leading cause of infertility due to occlusion of the Fallopian tubes[1]. This Gram-negative bacterium is an obligate intracellular microorganism whose only natural host is humans. Due to the absence of distinctive clinical symptoms, the acquisition of a chlamydial infection often goes unrecognized in the majority of exposed women. This contributes to the continued transmission of the microbe to subsequent sexual partners, leading to development of silent epidemics. Without appropriate treatment, the organism migrates from the vagina to the cervix and then to the Fallopian tubes. The resulting induction of a local pro-inflammatory immune response results in tissue scarring that blocks the passage of ova from the ovary to the site of fertilization in the uterus[2]. There is also evidence that women with blocked Fallopian tubes due to a chlamydial infection who attempt to conceive by *in vitro* fertilization (IVF) will have a lower success rate than will women who undergo IVF for other indications. This might be due to the subsequent reactivation of a persistent form of *C. trachomatis* that remains undetected in the female genital tract and/or to the development of a humoral and cell-mediated immune response to a specific antigen, the 60kDa heat shock protein, whose amino acid sequences are conserved between this microorganism and man[3].

The often mild and unrecognized clinical consequences of a recently acquired *C. trachomatis* cervical infection, coupled with the difficulty to identify this microorganism in many clinical laboratories, results in the lack of proper identification of infected women and the initiation of appropriate treatment.

Among the many contributions of Per-Anders Mardh, who died in December 2022 at the age of 81, to the diagnosis and treatment of many sexually transmitted diseases, was his early recognition of *C. trachomatis* pathogenesis[4-7]. Although his insights were not originally accepted by the majority of scientists and physicians who worked in the field, he became the leading and tireless advocate of *C. trachomatis* as a primary cause of pelvic inflammatory disease, tubal factor infertility and other female genital tract disorders. Along with co-workers he alerted the scientific and medical communities to the increasing negative consequences of one, two or three episodes of a chlamydial infection. Based on his initial clinical findings, coupled with the subsequent development of sensitive gene amplification assays, the detection of an inapparent chlamydial genital tract infection in many women is now possible. Treatment of this infection at its early stages when it is still confined to the cervix has preserved the fertility and eliminated the development of pelvic pain and the risk of ectopic pregnancy and/or infertility in many infected women.

Unfortunately, there still remains an unmet need to make public health officials and clinicians, as well as sexualy active women, aware of the serious adverse consequences of contracting *C. trachomatis* by engaging in unprotected sexual intercourse. Ideally, nucleic acid-based testing for this microorganism after unprotected sex with a new partner, and having the test available at no charge by the country's public health service, is the best protocol to limit the spread of a chlamydial infection and avoid negative sequelae in the infected woman. There are other less costly tests to identify *C. trachomatis* in the cervix. Unfortunately, they are less sensitive than gene amplification analysis and result in the failure to detect this microbe in many cases[8]. Public health agencies should be strongly encouraged to provide the gene amplification assays for *C. trachomatis* detection and clinicians should insist on this analysis for their patients. An increased investment in the optimal testing protocol will be more than compensated by the subsequent reduced cost of infertility and pelvic pain treatments.

Through his pioneering investigations in chlamydial pathogenesis, his teaching of a great many researchers on the fundamentals of scientific investigations and his training of numerous clinicians and students on the identification and treatment of sexually transmitted infections, the scientific and medical communities owe Professor Mardh a strong debt of gratitude. He was truly a unique individual who dedicated his life to identifying the causes of sexually transmitted diseases and proposing protocols for their prevention and treatment. His sharp wit, unique insights and rare intelligence will certainly be missed, but his legacy will endure.

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Conflict of interests: nothing to declare. Funding: none.
Received on: 01/06/2013. Accepted on: 01/10/2023.

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