A chlamydia vaccine on the horizon

For the first time, a vaccine against chlamydia has completed a clinical Phase 1 trial

Development of a vaccine against chlamydia is an international priority, but the complex lifestyle of the pathogen has made vaccine development challenging. For the first time a vaccine has completed a clinical phase 1 trial, with promising results published in The Lancet Infectious Diseases: https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(19)30279-8/fulltext.

Why do we need a vaccine?

The World Health Organization (WHO) estimates that more than one million new infections with the four curable sexually transmitted diseases – chlamydia, gonorrhea, syphilis and trichomoniasis – are acquired each day. With around 131 million annual infections, chlamydia remains the most common sexually transmitted bacterial disease. Chlamydia is primarily a disease in young adults, with highest incidence of infections observed in adolescents and young adults. However, since three in four infections remain asymptomatic, the actual incidence is likely to be underestimated.

Untreated and repeated infections are the main drivers of chlamydia-associated morbidity. One in every six infected women develops ascending infection and pelvic inflammatory disease, which contributes to chronic pelvic pain and is a leading cause of tubal factor infertility and ectopic pregnancy. *C. trachomatis* infection is strongly associated with increased susceptibility to other sexually transmitted diseases, particularly gonorrhoea and HIV. Infection during pregnancy poses a risk of adverse outcomes such as miscarriage, stillbirth and preterm birth by either direct foetal infection, placental damage, or severe maternal illness. In men, *C. trachomatis* mainly causes epididymitis, and in both men and women infections can trigger reactive arthritis in a minority of cases.

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Vaccination may be the best way to tackle the epidemic, as national treatment programmes have largely failed to curb the epidemic, despite availability of diagnostic tests and effective antibiotic treatment. Previous studies have suggested that people infected with chlamydia develop either partial or temporary natural immunity to the pathogen, but no previous vaccines for genital chlamydia have reached clinical trials.

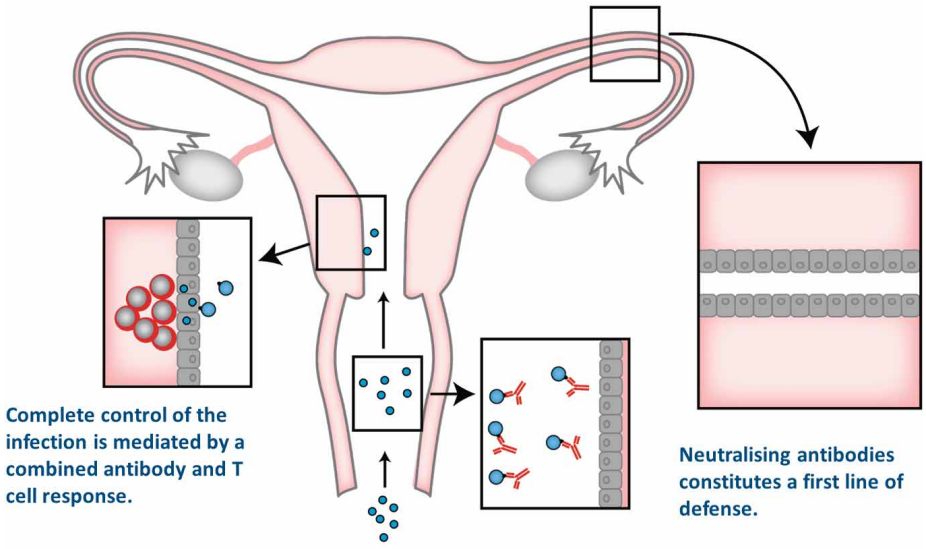
Chlamydia trachomatis: a pathogen with a complex lifestyle

Chlamydia is caused by an infection with the bacterium *C. trachomatis*. Much like a virus, the bacterium relies totally on its host to survive and replicate. *C. trachomatis* has two developmental forms: a small (0.3 microns) non-replicating infectious form, which, after attachment, is internalised into the host cell and instantly reorganised into a metabolically active; and a replicating form of almost triple the size. After completion of a replicative cycle, it reorganises into the infectious form again and is released from the host cell.

If the bacteria are not controlled by the immune system, they may ascend to infect the fallopian tubes and can cause major damage leading to pelvic inflammatory disease, scarring and occlusion.

How does the vaccine work?

At Statens Serum Institut, our vision is a vaccine that targets the bacterium immediately after it



enters the genital tract. We have designed a vaccine that elicits both cell-mediated and humoral immunity. The first line of defence is mediated by neutralising antibodies, to reduce initial infectious load; and once the bacteria are intracellular, they will be targeted by a bactericidal cell-mediated immune response.

After completion of an extensive discovery programme in the search for vaccine candidates, a first-generation vaccine candidate (CTH522), based on the major outer membrane protein of the *C trachomatis* bacterium, has now completed clinical phase 1 trial testing.

The trial aimed to assess the safety and ability to provoke an immune response of the CTH522 chlamydia vaccine. 35 women, not infected with chlamydia, were included in the trial. The vaccine was safe; and all women in the trial developed an immune response against chlamydia.

During the trial, blood samples were collected which showed that all vaccinated women had generated specific antibodies and T-cells targeting chlamydia. Local immunity in the genital tract is important to stop the infection as quickly as possible; and during the trial high levels of antibodies were found in mucous secretion, including the special mucosal antibody IgA, which effectively can block chlamydia early in the course of infection.

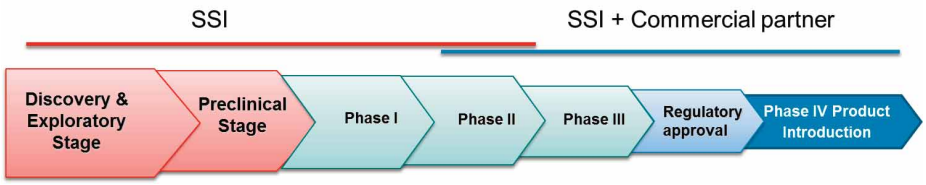
International collaborations

The TracVac consortium works towards eliminating the global problem of blinding trachoma through the development of a vaccine. TracVac has two main objectives. The first main objective is to generate a vaccine that protects against the bacterial strains causing ocular Chlamydia trachomatis infections. The second objective is to develop an immunization protocol for optimal mucosal immunity. Read more at www.trachoma-vaccine.org.

VacPath aims to establish a much-needed technological infrastructure in Europe along with educating and training young scientists by promoting the development of innovative, protective and safe vaccines for future clinical use. Please visit https://vacpath.eu/ for more information.

Future development

Several more years of research and clinical development are needed before this vaccine is marketed. SSI is planning the next stage of research, a phase 2A study, to be performed in collaboration with researchers at Imperial College London. Once this trial is finished, an efficacy trial is planned. This would be a placebo-controlled trial, meaning that half the subjects would receive the active vaccine and half would receive a placebo vaccine. Such a study would be performed in groups already at risk of infection; and the trial would need to be large enough to detect a difference in the number of detected infections between those on active or placebo vaccine (estimated between 500 to a couple of thousand).



Statens Serum Institut's Centre for Vaccine Research (CVR) consists the of Department of Infectious Immunology and Vaccine Development. The Centre is unique in its composition as it includes not only a basic and translational research department but also GMP facilities, animal testing facilities and expertise which enables accelerated development of new vaccines and diagnostics.

In collaboration with industrial partners, researchers at CVR have developed novel TB diagnostic tests (IGRA assays) that are in widespread worldwide clinical use today. Recently SSI developed a modern version of the Tuberculin test – C-TB®. SSI has entered into a partnership with Serum Institute of India Pvt Ltd. who will be producing and distributing the test.

CVR currently has one TB vaccine in late stage clinical testing, two different liposomal adjuvant formulations (CAF®01 and CAF®09b), as well as a Chlamydia vaccine: more details can be found at https://en.ssi.dk/research/center-for-vaccine-research/center-for-vaccine-research.

Further development of the vaccine would involve SSI entering into a partnership with commercial partner for production and distribution of the vaccine.

Long term goal

Should the vaccine make it successfully through clinical testing and become licensed for distribution, we envision its being administered to adolescents, possibly alongside the HPV vaccine.

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