Short title: Experimental Gonorrhea skin patch vaccine

Gonococcal microparticle vaccine in dissolving microneedles induced immunity and enhanced bacterial clearance in infected mice

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Abstract:
There is an alarming rise in the number of gonorrhea cases worldwide. *Neisseria gonorrhoeae*, the bacteria that causes gonorrhea infection, has gradually developed antimicrobial resistance over the years. To date, there is no licensed vaccine for gonorrhea. This study investigates the *in vivo* immunogenicity of a whole-cell inactivated gonococci in a microparticle formulation (Gc-MP) along with adjuvant microparticles (Alhydrogel®- Alum MP and AddaVax™ MP) delivered transdermally using dissolving microneedles (MN). The proposed vaccine formulation (Gc-MP+ Alum MP+ AddaVax™ MP) was assessed for induction of humoral, cellular, and protective immune responses *in vivo*. Our results show the induction of significant gonococcal-specific serum IgG, IgG1, IgG2a, and vaginal mucosal IgA antibodies in mice immunized with Gc-MP+ Alum MP+ AddaVax™ MP and Gc-MP when compared to the control groups receiving blank MN or no treatment. The serum bactericidal assay revealed that the antibodies generated in mice after immunization with Gc-MP+ Alum MP+ AddaVax™ MP were bactericidal towards live *Neisseria gonorrhoeae*. Gc-MP+ Alum MP+ AddaVax™ MP and Gc-MP-immunized mice showed enhanced clearance rate of gonococcal bacterial infection post challenge. In contrast, the control groups did not begin to clear the infection until day 10. In addition, the mice which received Gc-MP+ Alum MP+ AddaVax™ MP showed enhanced expression of cellular immunity markers CD4 and CD8 on the surface of T cells in the spleen and lymph nodes. Taken together, the data shows that microneedle immunization with whole-cell inactivated gonococci MP in mice induced humoral, cellular, and protective immunity against gonococcal infection.