

# WORLD CONGRESS ON RHEUMATIC HEART DISEASE

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**Title:** Mucosal delivery of Group A Streptococcus vaccines has benefits over traditional systemic immunisation

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**Background & Aims:** Group A Streptococcus (Strep A) is the major cause of rheumatic fever and rheumatic heart disease (RHD) globally. Strep A initially infects humans through the mucosa, such as the throat, or through the skin. Adhesion and colonisation occur in these environments with the potential to lead to mucosal infections, skin and soft tissue infections, invasive diseases and post-infectious sequelae. Blocking the interaction at mucosal sites is paramount for an effective Strep A vaccine to prevent infections and post-infectious autoimmune sequelae such as RHD.

**Methods:** A study was conducted to compare sublingual (SL) and intranasal (IN) immunisation with subcutaneous (SC) immunisation for induction of mucosal and systemic immunity. BALB/c mice were immunised SL, IN or SC with a combination of protein antigens relevant to several stages of infection (SpyCEP, IL-8 protease; Cpa, pilin protein; IdeS, IgG protease; MalE, saliva survival). IgA and IgG titres were compared in mucosal samples and sera by ELISA.

**Results:** Mucosal delivery was key for mucosal IgA production, but high titres of IgG were generated by all routes of immunisation. IN and SC routes in particular were able to generate high antibody titres that had functional activity blocking IL-8 cleavage, IgG cleavage, opsonophagocytosis, and binding to HaCaT cells.

**Conclusions:** This study demonstrates the efficacy of mucosal delivery of Group A streptococcal antigens as vaccines and helps to inform thinking towards delivery of Strep A vaccines to improve the mucosal immune response.