

**S9 Immunological Aspects of Maternal Immunization**

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Immunizing pregnant women can bypass the problems of immunological immaturity in the neonate, avoid or delay active immunization of the infant in the first year of life, and prevent transmission of an infection from the mother to the neonate by providing passive protection to young infants. Optimal vaccines should induce high IgG antibody titers that reach their maximum level quickly after immunization and persist at protective levels to provide passive protection in subsequent pregnancies. Immunological aspects of placental transfer of IgG, differences in transfer of IgG subclasses, and theoretical possibilities of increasing IgG transfer to the neonate will be discussed. The theoretical possibility that maternal immunization may activate or suppress the infant's active antibody response or alter the repertoire of that response will be detailed. A role of maternal immunization in increasing breast milk antibody will also be described.

**S10 Maternal Immunization: The Two for One Group B Streptococcal Prevention Model**

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Prevention of life-threatening human infections through vaccination is a remarkable achievement in medicine. Extension of this concept to a "two for one" model, in which maternal immunization accomplishes protection of newborn and young infants, was the basis for the conquest of tetanus neonatorum. Group B *Streptococcus* (GBS) causes substantial morbidity among pregnant women and their newborns. Prevention of these GBS perinatal infections through maternal immunization is possible theoretically since maternally derived antibody (Ab) protects against neonatal GBS infection and >95% of infants acquire disease by age 3 months (an age at which passively acquired Ab persists). Previously, immunization of pregnant women with type III GBS capsular polysaccharide resulted in transplacental passage of type III-specific Ab in concentrations exceeding protective levels through age 2 months in sera of infants born to vaccine responders. However, GBS polysaccharides have had variable immunogenicity. Vaccine response rates in 194 healthy adults type Ia, II or III polysaccharides were 56%, 92% and 70%, respectively. Recent testing of new GBS vaccines, in which type Ia, Ib, II, III or V polysaccharides are conjugated to tetanus toxoid, indicates good tolerance in non-pregnant women, with minimal reactogenicity. The geometric mean serum concentrations of IgG-specific Ab 2, 4, 8 and 26 weeks after immunization were significantly higher than those after immunization with unconjugated polysaccharides. More than 90% of subjects developed >4-fold increases in Ab and at mean serum concentrations that exceed protective levels 10- to 20-fold. Persistence of Ab 2 years after immunization suggests that conjugate vaccine-induced immunity is durable. Providing passive immunity to young infants through maternal immunization should achieve a substantial reduction in GBS disease in young infants and pregnant women.

**S11 Maternal Immunization: Prevention of Respiratory Disease**

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Maternal immunization can enhance passive immunity of infants to agents that produce life-threatening infections of the respiratory tract. Inactivated vaccines given in the third trimester of pregnancy pose no known risk to the woman or to her fetus. Immunization during pregnancy may provide protection for the woman as well as her offspring. Influenza vaccine is an example of a currently recommended vaccine that provides this double benefit. Studies have shown that naturally acquired maternal antibodies to respiratory syncytial virus (RSV) will protect full-term infants during the first months of life and that passive immunization with RSV immunoglobulin will reduce risk of lower tract disease for high risk infants. Boosting maternal RSV antibodies with subunit vaccines should enhance natural passive immunity. Maternal immunization with pneumococcal vaccines not only increases serum antibodies transferred to the infant but also increases breast milk antibody. Studies have suggested that breast milk antibody may affect the acquisition of nasopharyngeal carriage and thus prevent serious infections in the first months of life.

**S12 Overview of Immunomodulators and Adjuvants**

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Many vaccines presently under development and testing are composed of synthetic, recombinant, or highly purified subunit antigens. Vaccines composed of these subunit antigens are often considered to be safer than whole-inactivated or live-attenuated vaccines. However, vaccines containing purified subunit antigens are often less immunogenic than traditional vaccines. Immunological adjuvants are agents that enhance specific immune responses to vaccines. Formulation of vaccines with potent adjuvants is an attractive approach for enhancing immune responses to subunit antigens. Adjuvants have diverse mechanisms of action and should be selected for use based on the route of administration and the type of immune response (antibody, cell-mediated, or mucosal immunity) desired for a particular vaccine. Adjuvant mechanisms of action include: 1) increasing the biological or immunological half-life of vaccine antigens; 2) improving antigen delivery and presentation; and 3) inducing the production of immunomodulatory cytokines. Through modulation of cytokine responses, adjuvant formulations can be designed to favor the development of Th1 (type 1) or Th2 (type 2) immune responses to vaccine antigens. Novel adjuvants are presently undergoing preclinical and clinical testing with experimental vaccines including vaccines against HIV-1. Standardized preclinical adjuvant safety tests are also under development.