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The HSD-hCG Vaccine Prevents Pregnancy in Women: Feasibility Study of a Reversible Safe Contraceptive Vaccine

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Abstract

PROBLEM: To develop a vaccine for reversible control of fertility in women.

MATERIALS AND PROTOCOLS: Purified β subunit of hCG annealed to purified alpha subunit of ovine LH linked chemically to tetanus toxoid (TT) and diphtheria (DT); vaccine employed at 300 μg gonadotropin equivalent per injection adsorbed on alhydrogel with 1 mg SPLPS added in the first injection; Phase I safety trials in 47 women with elective tubal ligation; Phase II efficacy studies in 148 proven fertile women (2 children), sexually active, desirous of family planning using IUD; IUD removed when anti-hCG titres exceed 50 ng/ml hCG bioneutralization capacity; boosters given to maintain above threshold antibody levels; post coital tests conducted in 8 volunteers; sera of protected women analysed for immuno-determinants recognized by competitive enzyme immunoassays employing a panel of monoclonal antibodies and by direct binding to synthetic peptides; recombinant vaccines expressing phCG as a secreted product or as a fused protein anchored on membrane.

RESULTS: Immunization was well tolerated with no significant changes in endocrine, metabolic and hematological indices. Normal ovulatory cycles were maintained as indicated by menstrual regulation. The vaccine was highly effective in preventing pregnancy (1 pregnancy in 1224 cycles) at and above antibody titres of 50 ng/ml. Antibodies declined in course of time in absence of boosters, with conceptions occurring below 35 ng/ml titres indicating regain of fertility. Ability of antibodies to prevent pregnancy was confirmed by post coital tests. High avidity ($10^{10}M^{-1}$) and other characteristics of antibodies generated by the vaccine are described and compared with those induced by two other hCG vaccines having undergone Phase I trials. The antibody response of the HSD vaccine in humans is characterized predominantly to an epitope recognized by the monoclonals 206 and P_3W_{80}. The antibodies had low or no reactivity with the carboxy terminal peptide and 38–57 region peptide. Live recombinant vaccines expressing βhCG as a membrane anchored peptide generated antibody response to hCG in all animals following a single injection.

CONCLUSIONS: Reversible fertility control is feasible with the HSD-hCG vaccine without impairment of ovulation or disturbance of menstrual regularity. Suggestions have been made for further optimization of the vaccine, which include replacement of TT and DT by a

> panel of T non B determinants communicating with the entire MHC spectrum and development of recombinant vaccine expressing phCG along with membrane anchored carrier.