INTRODUCTION
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The world is currently in the midst of an unprecedented expansion of its human population. The control of worldwide population growth is, without doubt, one of the most urgent problems of mankind. From a demographic perspective, India may be the world's most critical country, its current population, estimated at about 950 million people is growing at about 2 per cent each year. With roughly 27 million births annually, India currently contributes one-fifth of total world population-growth, more than any other country. If the present trends continue, India's population would reach the one billion mark around the year 2000 and 2.5 billion people around the year 2040 (Conly and Camp, 1992). Beyond this compelling demographic justification, fertility reduction would have a powerful impact on the health and quality of life of India's women and children.

Although several contraceptive methods are currently available, unfortunately all of them have one or the other disadvantage in terms of their availability, acceptability, efficacy or safety. Extensive efforts are, therefore, being made to design newer strategies for contraception. Immunocontraception represents an attractive mode of fertility regulation because of its potential for safety, reversibility, efficacy and low cost. The original concept of an immunological approach to contraception arose from studies carried out in the early 1970s, when it was demonstrated that anti-sera raised against aqueous extracts of hamster ovarian tissue possessed the ability to block fertilization of hamster ova in vitro (Shivers et al., 1972). The concept of an anti-fertility vaccine has since made great progress and presently there are a number of birth-control vaccines in various stages of development.

Leading antigen candidates for fertility control vaccines belong to two different categories. The first category comprises of the hormones of the reproductive-endocrine system such as human chorionic gonadotropin (hCG), luteinizing hormone releasing hormone (LHRH) and follicle stimulating hormone (FSH). The second category, which consists of blastocyst and gamete associated antigens, includes trophoblast, sperm and zona pellucida antigens. At present, the most advanced candidate birth control vaccines are based on hCG as an antigen (Stevens, 1996) and these are the only ones to have entered human clinical trials so far. The
hCG vaccine on inoculation elicits antibodies that are capable of neutralizing hCG bioactivity which in turn leads to withdrawal of the hormonal support to the implanting embryo resulting in the abrogation of pregnancy.

At the National Institute of Immunology (NII) an anti-fertility vaccine based on the β-subunit of hCG has undergone phase I / phase II clinical trials in women where it has been found to be effective and devoid of notable side effects (Talwar et al., 1994). The vaccine formulation employs a heterospecies dimer (HSD) composed of the β-subunit of hCG linked to the α-subunit of ovine luteinizing hormone (oLH) which is then chemically conjugated to tetanus toxoid (TT) or diphtheria toxoid (DT) carriers. The β-subunit of hCG used in the HSD vaccine is currently being obtained by the dissociation of native hCG secreted in the urine of pregnant women. This process is inefficient, expensive and labor-intensive and the hCG thus obtained may be contaminated by traces of the α-subunit of hCG. This impurity may result in induction of antibodies to α-subunit which could have undesirable cross reactivity with hTSH and hFSH as these pituitary hormones and hCG share a common α-subunit (Fiddes and Goodman, 1981). In addition, chemical conjugation of βhCG to the carrier molecules has batch-to-batch variation. Thus, chimeric βhCG fused to a carrier molecule produced by recombinant DNA means has the advantage of consistency and purity, and a recombinant virus producing this fusion protein may have added advantage of being economical and relatively easy to deliver.

Earlier studies at the NII (Srinivasan et al., 1995) have established that recombinant vaccinia virus expressing βhCG on the cell surface was capable of generating high titered anti-hCG antibodies in rats. However, since vaccinia has a broad host range, there is an inherent risk of transmission of the virus from the vaccinees to unintended subjects. Secondly, immunocompromised individuals are vulnerable to infection associated with vaccinia. These concerns assume significance in view of an ever increasing numbers of immunosuppressed individuals infected with the HIV (Redfield et al., 1987). Thus it may not be desirable to use vaccinia based vectors for the purpose of immunocontraception. Hence, there is a need to
develop alternate viral expression vector systems that may be contact-transmission-safe, easy to prepare and cost effective.

Adenovirus expression vector system offers a number of unique features highly desirable for the development of a recombinant virus based birth control vaccine. First, E1-substituted adenovirus recombinants can be made that are replication-defective \textit{in vivo} and thus do not pose the risk of being transmitted from the vaccinees to unintended subjects. The apparent efficacy of adenovirus vaccines in non- or semi-permissive species suggests that enough antigen is expressed in the absence of viral replication. Second, adenovirus can be delivered by oral route in the form of enteric coated capsules. Protection is apparently related to colonization of the gastro-intestinal tract by the orally administered adenovirus and associated with the subsequent development of serum neutralizing antibodies. The popularity of adenovirus as a recombinant viral vector is largely due to the successful and safe immunization of millions of military recruits in the United States of America with enteric-coated adenovirus types 4 and 7 as a prevention against acute respiratory disease outbreaks (Top \textit{et al.}, 1971a,b; Top, 1975). These features of adenovirus vector system led us to develop and explore the potential of an E1-substituted recombinant adenovirus expressing cell surface anchored form of $\beta$hCG as an anti-fertility vaccine.

This thesis presents the construction of a recombinant human adenovirus expressing $\beta$hCG on the cell surface. This recombinant virus was capable of generating high titers of anti-hCG antibodies in experimental animals thus indicating its potential for the control of fertility.