IMMUNOCONTRACEPTION

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IMMUNOCONTRACEPTION

General issues

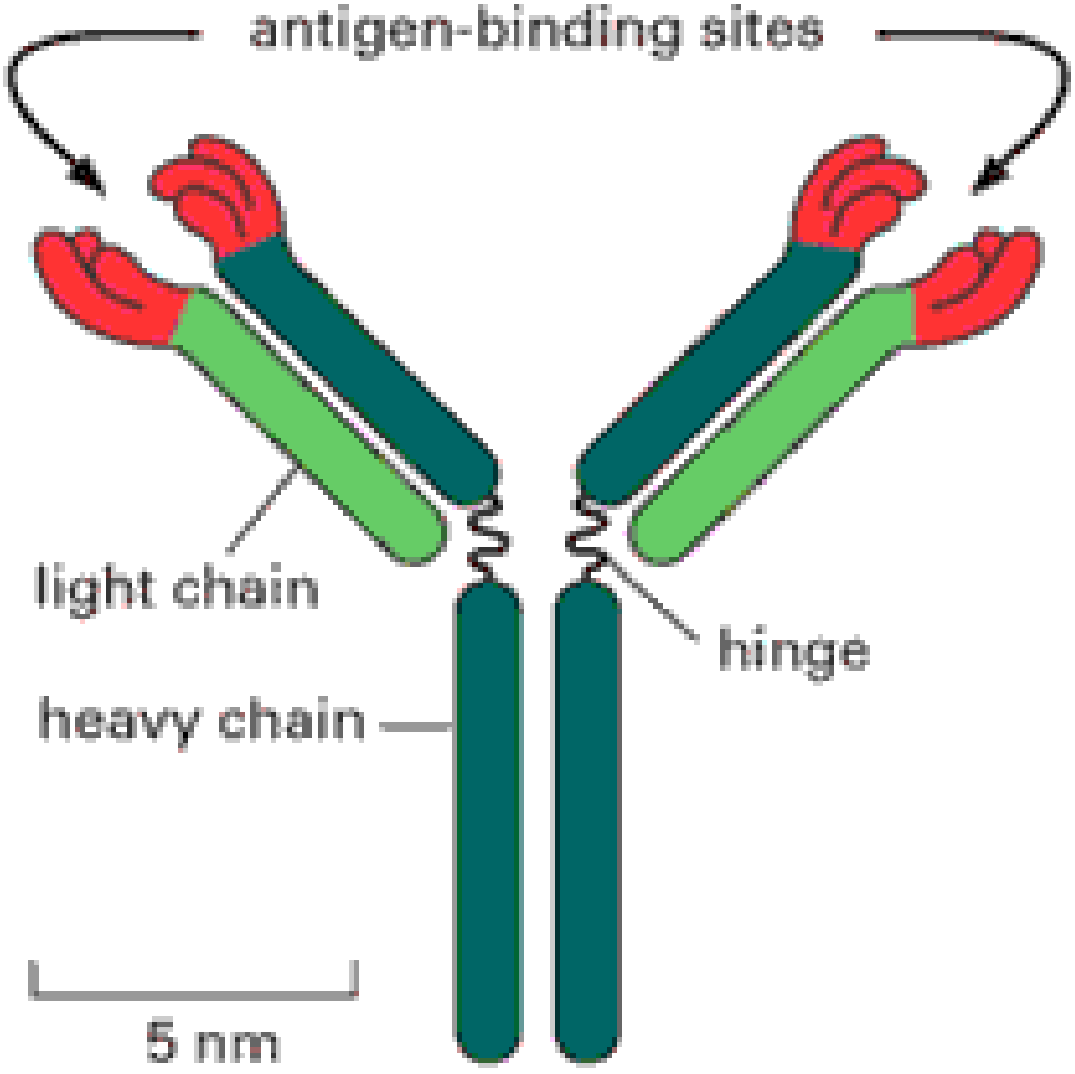
Biomedical issues

WHAT IS IMMUNOCONTRACEPTION?

The use of the body's natural immune defence mechanisms to provide protection against an unplanned pregnancy.

It requires the production of a controlled, time-limited and non-pathogenic immune response to components of the reproductive process.

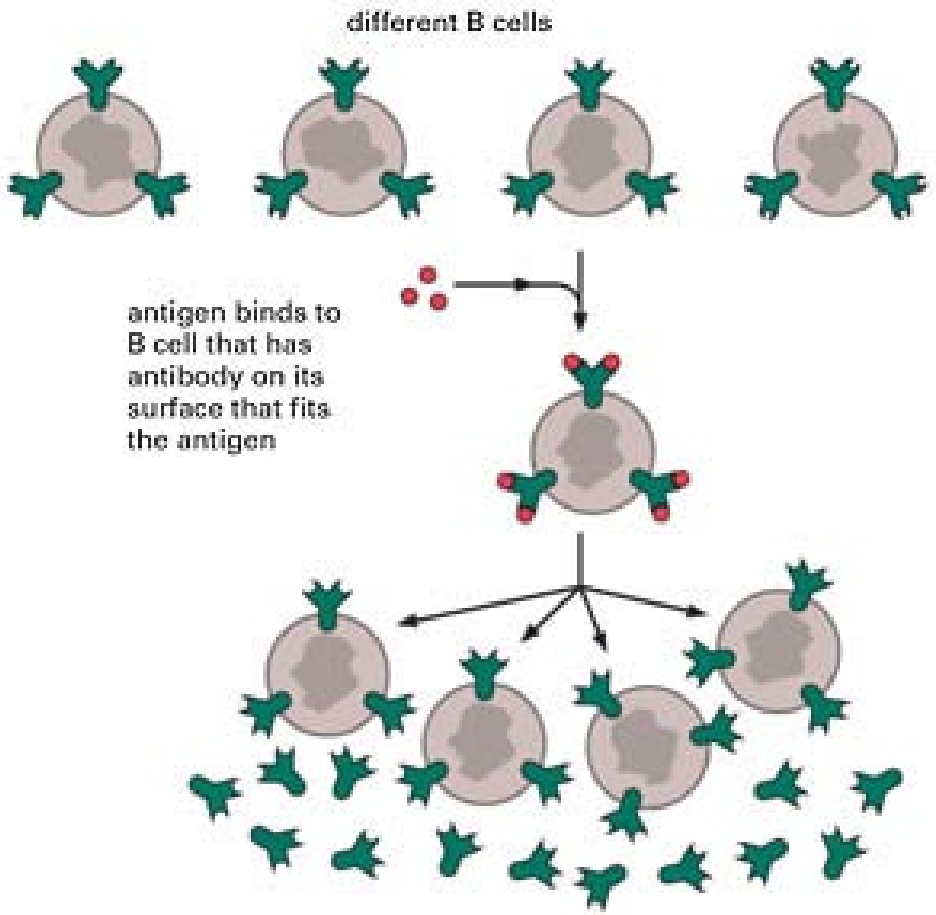
THE ANTIBODY MOLECULE



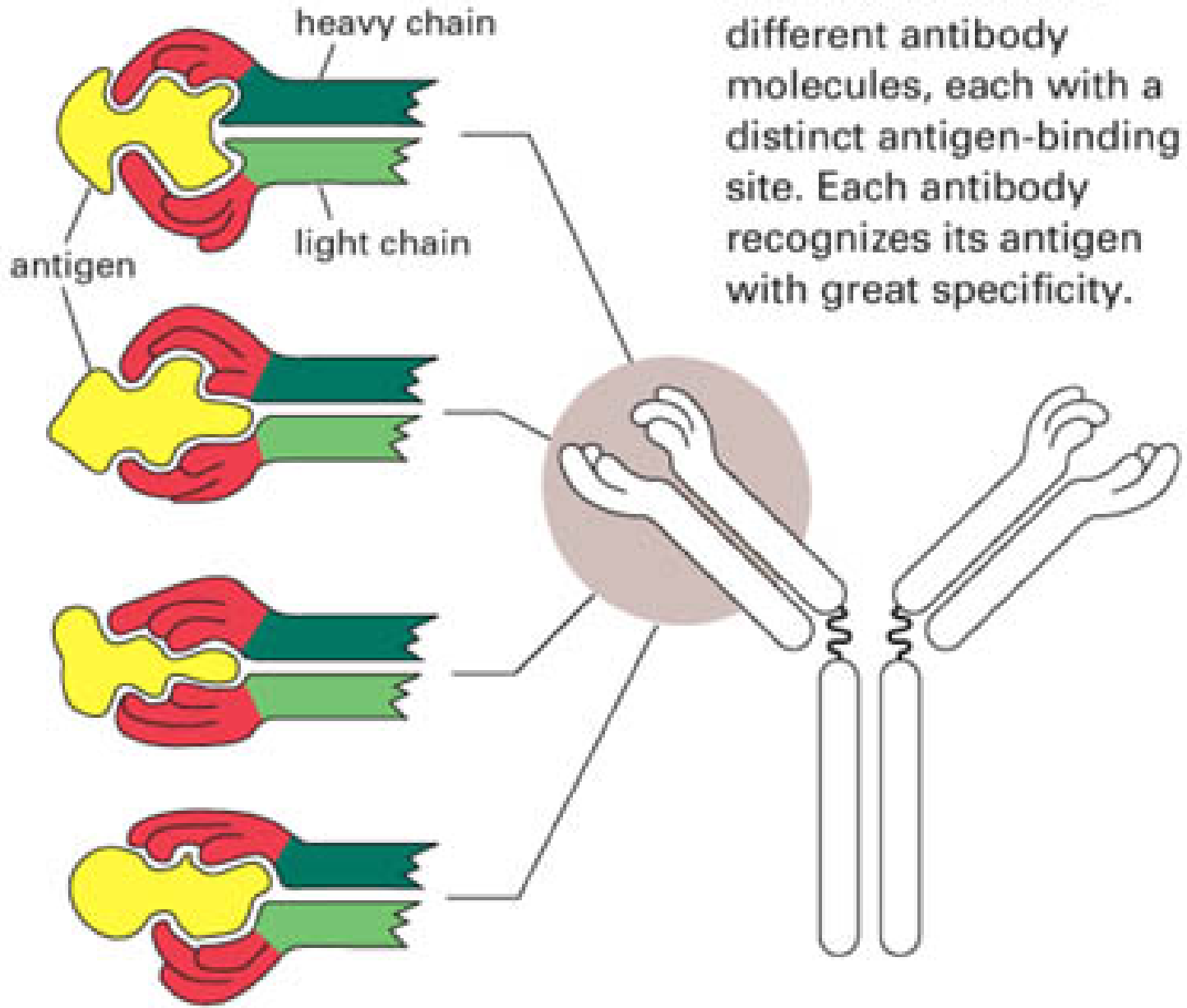
Antibodies are proteins that bind very tightly to their targets (antigens). They are produced in vertebrates as a defense against infection. Each antibody molecule is made of two identical light chains and two identical heavy chains, so the two antigen-binding sites are identical.

B CELLS

Antibodies are made by a class of white blood cells, called B lymphocytes, or B cells. Each resting B cell carries a different membrane-bound antibody molecule on its surface that serves as a receptor for recognizing a specific antigen. When antigen binds to this receptor, the B cell is stimulated to divide and to secrete large amounts of the same antibody in a soluble form.



ANTIBODY SPECIFICITY



An individual animal can make billions of different antibody molecules, each with a distinct antigen-binding site. Each antibody recognizes its antigen with great specificity.

WHO WOULD BE ABLE TO USE IMMUNOCONTRACEPTION?

Intended for the use of women and men, throughout their reproductive lives, for them to

- **delay or postpone first pregnancies;**
- **space pregnancies at intervals beneficial to the health of the mother and her infants;**
- **provide comparatively long-lasting but not permanent protection on the attainment of the desired family size.**

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Reasons for development

To provide an additional option to current or potential users of family planning methods and services

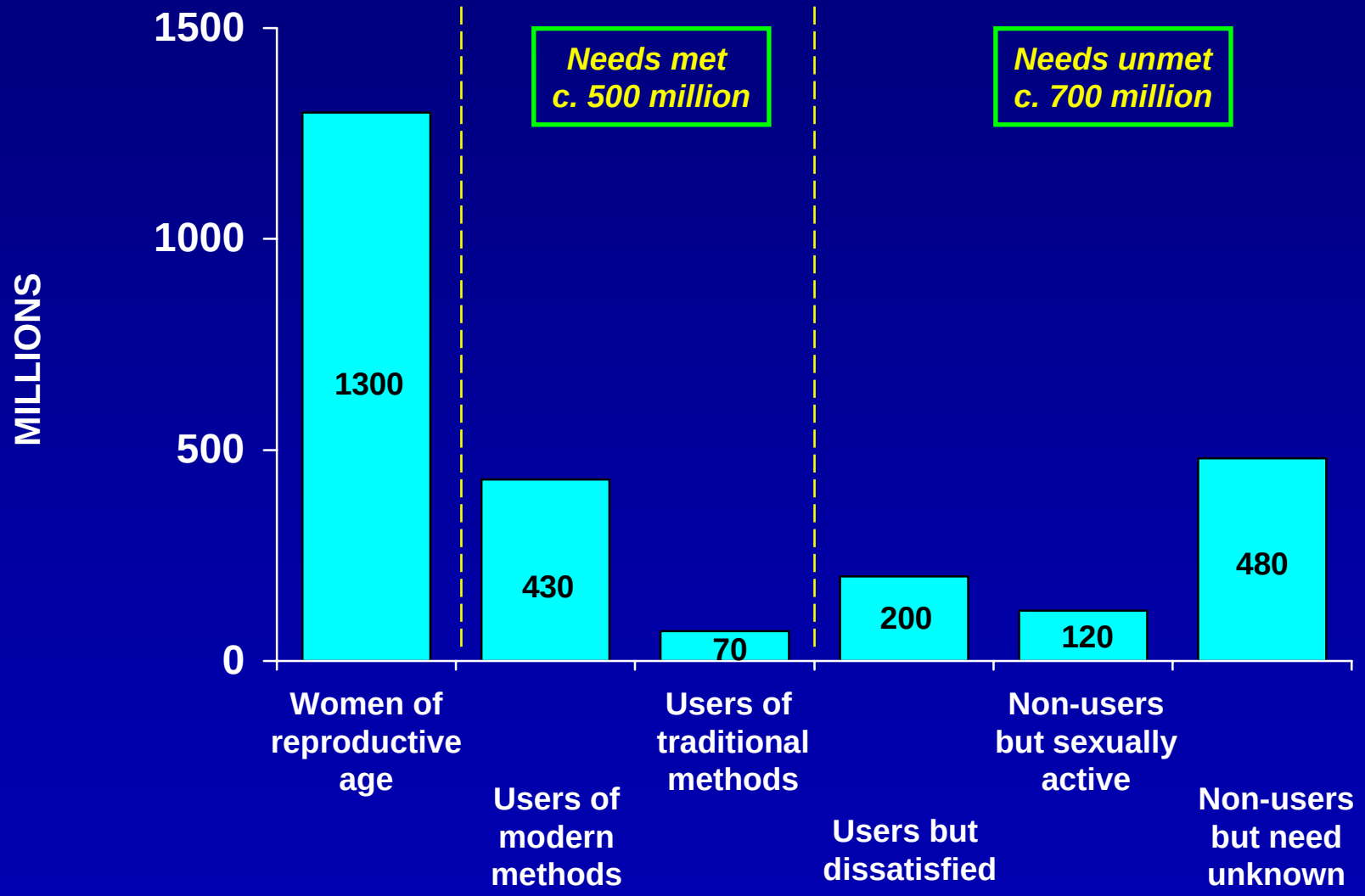
To address an unmet need in reproductive health

GLOBAL ESTIMATES OF UNMET REPRODUCTIVE HEALTH NEEDS

Category of unmet reproductive health need	Millions (world wide)
Couples with unmet family planning needs	***120***
Infertile couples	60-80
Unsafe abortions	20
Maternal deaths	0.5
Incidence of maternal morbidity	25
Perinatal mortality	7.2
Infants with low weight at birth	23
Infant deaths	8.4
Cumulative total of HIV infections by the year 2000	30-40
Cumulative total of AIDS cases by the year 2000	12-18
Curable sexually transmitted diseases (new cases)	298
Female genital mutilation *	85-110

Total number Annual number

CONTRACEPTIVE USE AND UNMET NEED



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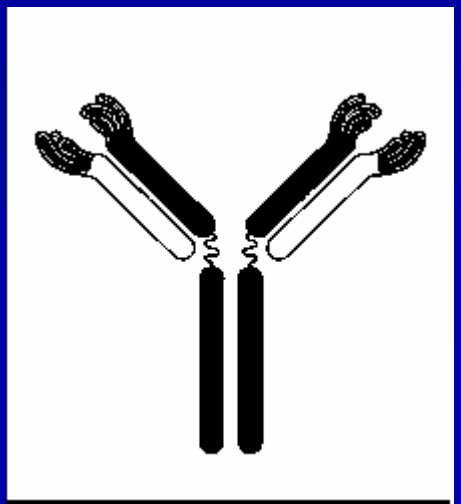
What are the advantages of immunocontraceptives ?



ADVANTAGES OF IMMUNOCONTRACEPTIVES

- lack of endocrine or metabolic side-effects;
- do not require insertion of an implant or device;
- provide long term but not permanent protection;
- do not require storage or disposal by the user;
- use is independent of coitus;
- permit confidentiality of use;
- low annual cost to users and services.

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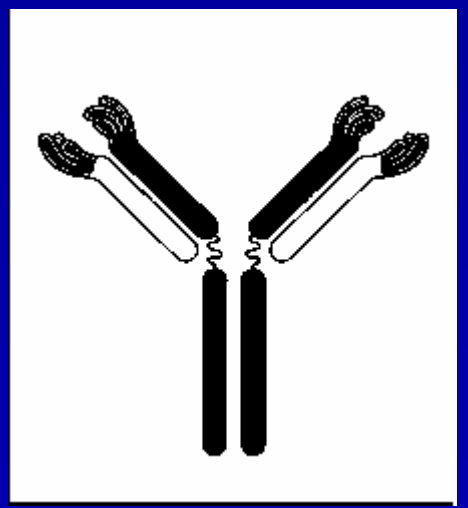
What are the disadvantages of immunocontraceptives ?



DISADVANTAGES OF IMMUNOCONTRACEPTIVES

- delay between administration and attainment of effective immunity;
- individual variations in immune responses and, therefore, in level and duration of effectiveness;
- cannot be ‘turned off’ on demand;
- not a barrier to sexually-transmitted infections;
- alleged abuse potential.

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General issues

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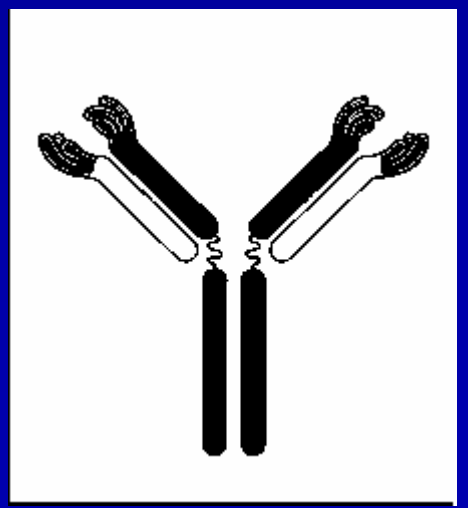
Where and how would immunocontraceptives work ?



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Possible points of intervention

Hypothalamus - **GnRH**

Pituitary - **FSH and LH**

Gonads - **progesterone, estrogen and testosterone**

Gametes - **ovum and sperm**

Pre-embryo - **structural and endocrine components**

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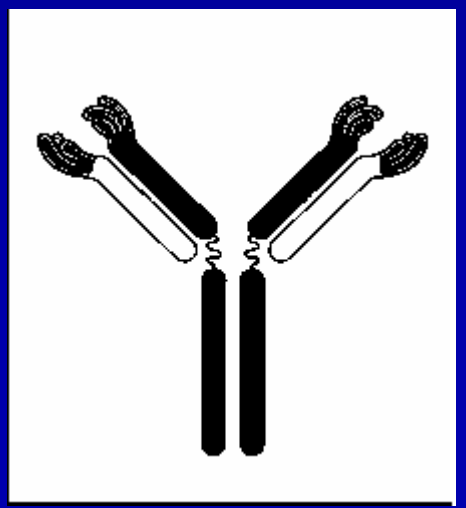
What is the current status of development of prototype immunocontraceptives ?



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GnRH immunocontraceptive

Various veterinary trials to control feral animal populations and for immunological castration

Clinical trial conducted in postpartum women to prolong anovulation

Clinical trial conducted in men with prostatic cancer

Clinical trial underway in normal men

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FSH immunocontraceptive

Phase I clinical trial conducted in normal men to assess immunogenicity and to assess effect on spermatogenesis

Prototype preparation found to be only weakly immunogenic, some reduction in sperm numbers and motility but no significant effect on semen parameters

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Steroid immunocontraceptives

Several studies carried out in laboratory animals but no known clinical trials conducted to date

Gamete immunocontraceptives

Several studies carried out in laboratory animals but, again, no known clinical trials conducted to date

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hCG immunocontraceptive

Several types and formulations of hCG-based immunocontraceptives have been studied extensively in preclinical studies and clinical trials sponsored by:

National Institute of Immunology, Delhi, India
Population Council, New York, USA
World Health Organization, Geneva, Switzerland

HCG IMMUNOCONTRACEPTIVE

National Institute of Immunology, Delhi, India

Composition:

heterospecies dimer of beta-hCG:alpha-oLH, tetanus toxoid, diphtheria toxoid, LPS, alum

Current status:

Phase I clinical trial completed
Phase II clinical trial completed
Phase III clinical trial pending long-term safety studies

HCG IMMUNOCONTRACEPTIVE

Population Council, New York, USA

Composition:
beta-hCG, tetanus toxoid, alum

Current status:
Phase I clinical trial completed
No further studies planned

HCG IMMUNOCONTRACEPTIVE

World Health Organization, Geneva, Switzerland

Composition:

hCG-specific peptides, diphtheria toxoid, muramyl dipeptide, slow-release copolymer matrix, water-in-oil emulsion vehicle

Current status:

GMP material prepared; Phase I clinical trial approved by regulatory authorities and awaiting funding

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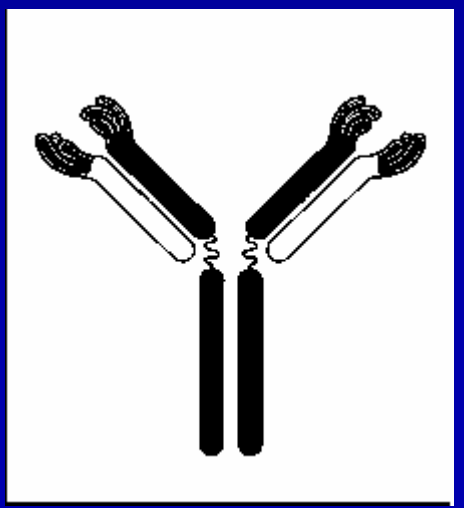
Important points to remember !



IMPORTANT AND FUNDAMENTAL DIFFERENCES BETWEEN ANTI-DISEASE VACCINES AND IMMUNOCONTRACEPTIVES

ANTI-DISEASE VACCINES	IMMUNOCONTRACEPTIVES
• designed to provide long-term, ideally life-long, protection against life-threatening or debilitating diseases;	• designed to provide long-term but not permanent protection against unplanned pregnancy;
• often the only method of protection against such diseases;	• other methods of birth control available;
• directed against an immunologically foreign pathogen;	• directed against a non-pathogenic cell or hormone;
• vaccine-induced immunity often boosted by sub-clinical infection or exposure to the pathogen.	• vaccine-induced immunity not boosted by re-exposure to the target antigen or by pregnancy.

FUTURE RESEARCH NEEDS AND ISSUES TO BE ADDRESSED

- final product development;
- assessment of safety of long-term use;
- assessment of acceptability of the approach;
- definition of mechanism(s) of action;
- reversal of contraceptive effect on demand;
- clarification and debate of socio-political issues.

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The overall objective:

to increase the choice of family planning methods available to individuals and couples world wide