

IMMUNOCONTRACEPTION

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IMMUNOCONTRACEPTION

General issues

Biomedical issues

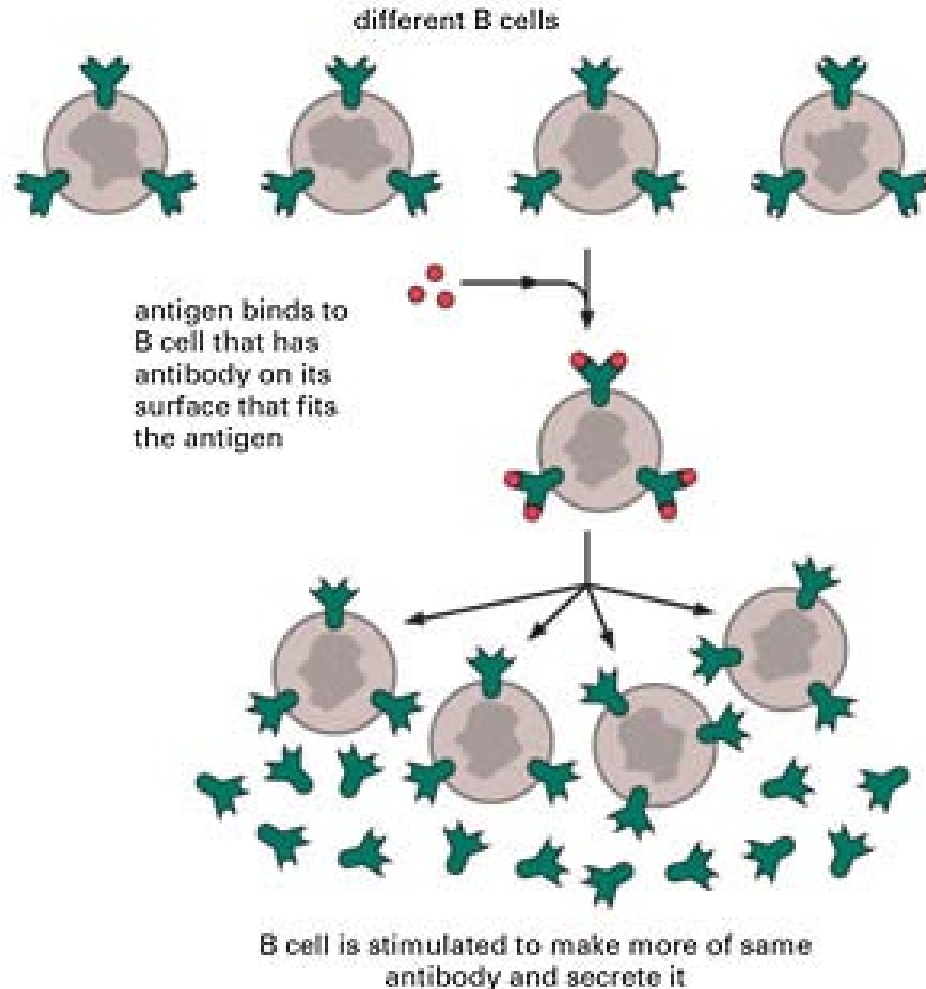
WHAT IS IMMUNOCONTRACEPTION?

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

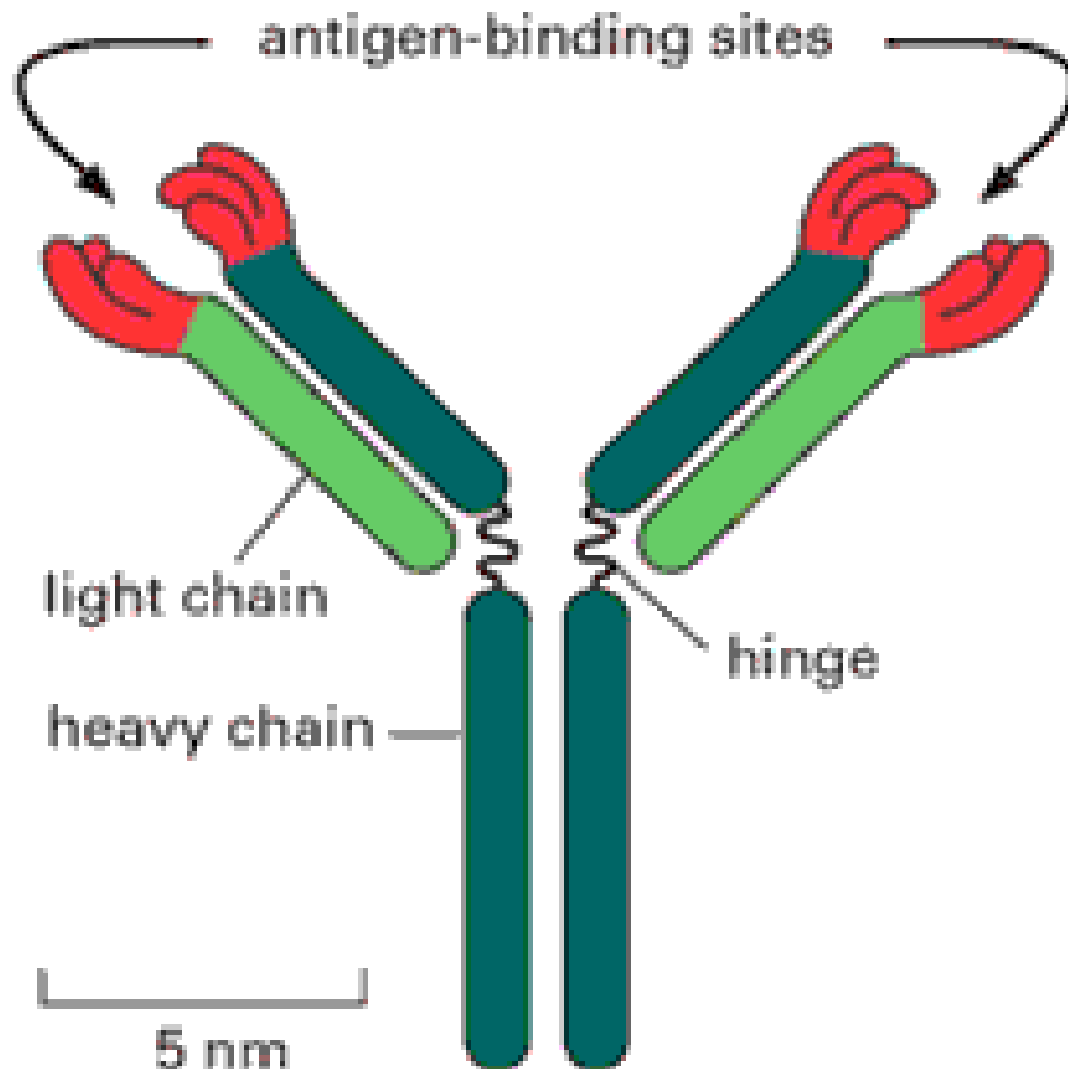
It requires the production of a controlled, time-limited and non-pathogenic immune response to components of the reproductive process.

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.



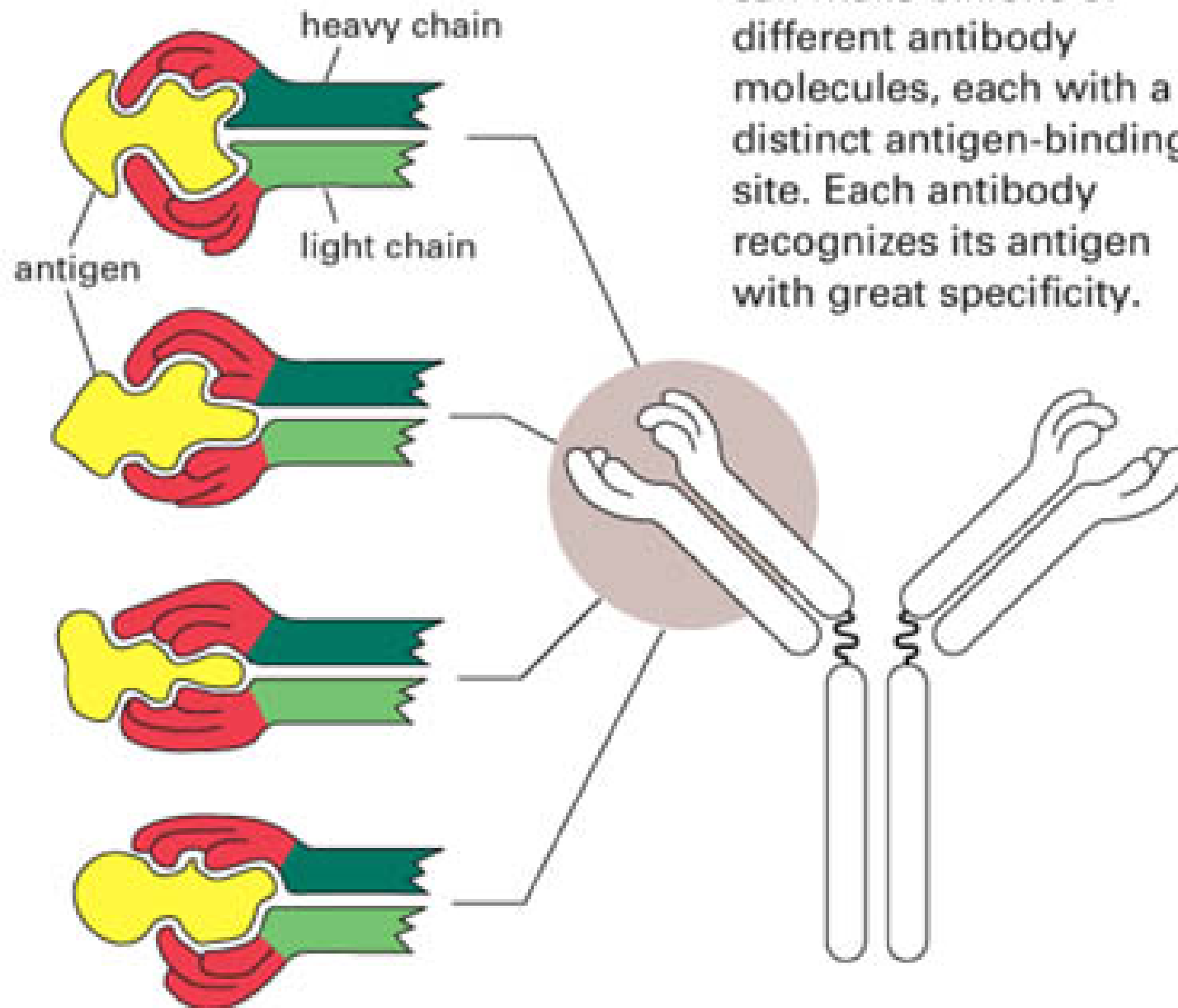
THE ANTIBODY MOLECULE



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.

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.



IMPORTANT AND FUNDAMENTAL DIFFERENCES BETWEEN ANTI-DISEASE VACCINES AND IMMUNOCONTRACEPTIVES

ANTI-DISEASE VACCINES

- designed to provide long-term, ideally life-long, protection against life-threatening or debilitating diseases;
- often the only method of protection against such diseases;
- directed against an immunologically foreign pathogen;
- vaccine-induced immunity often boosted by sub-clinical infection or exposure to the pathogen.

IMMUNOCONTRACEPTIVES

- designed to provide long-term but not permanent protection against unplanned pregnancy;
- other methods of birth control available;
- directed against a non-pathogenic cell or hormone;
- vaccine-induced immunity not boosted by re-exposure to the target antigen or by pregnancy.

WHO WOULD BE ABLE TO USE IMMUNOCONTRACEPTION?

Intended for use by 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

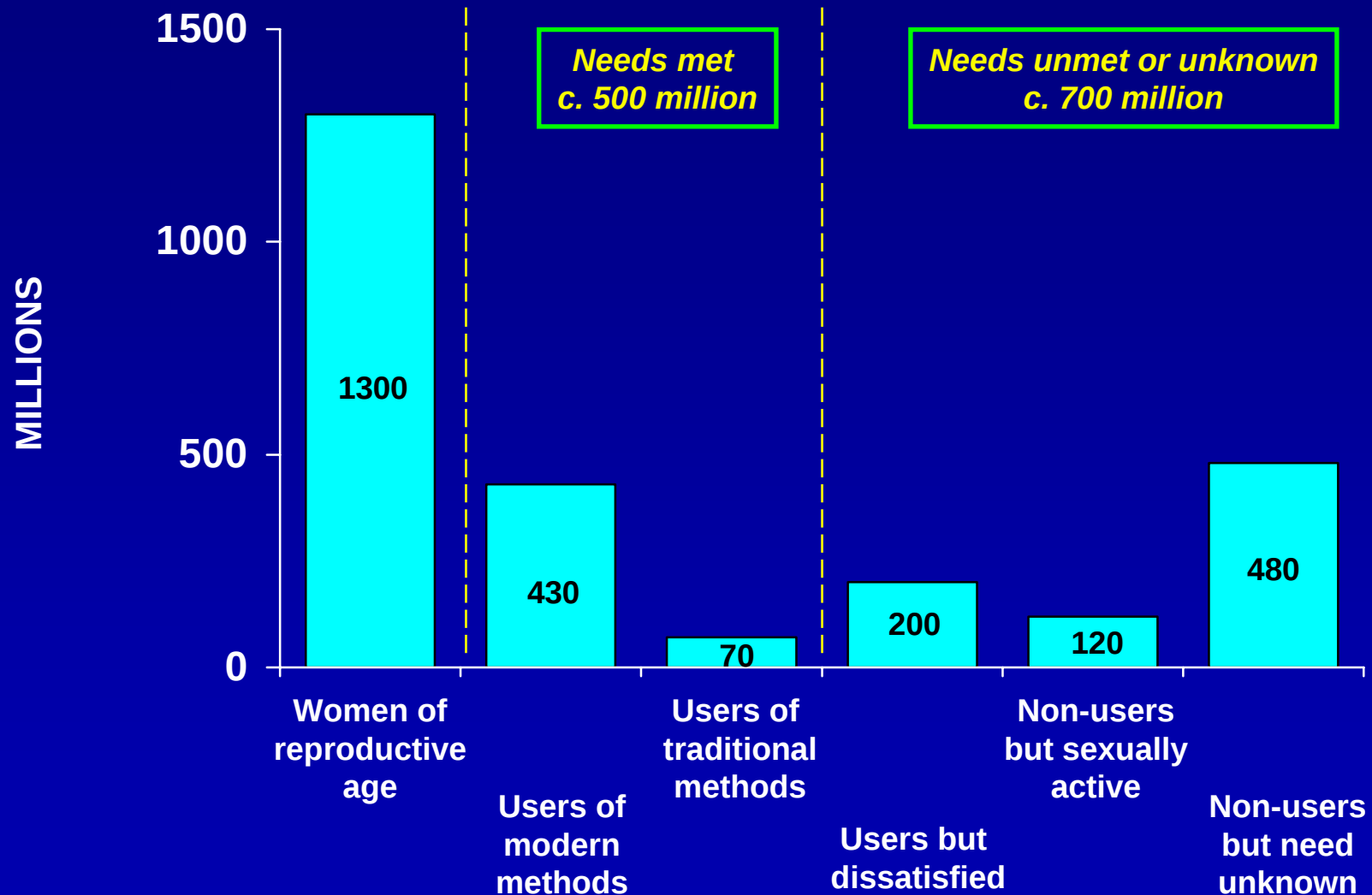
GLOBAL ESTIMATES OF UNMET REPRODUCTIVE HEALTH NEEDS

Category of unmet reproductive health need	Millions (world wide)
<i>Couples with unmet family planning needs</i>	<i>120</i>
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

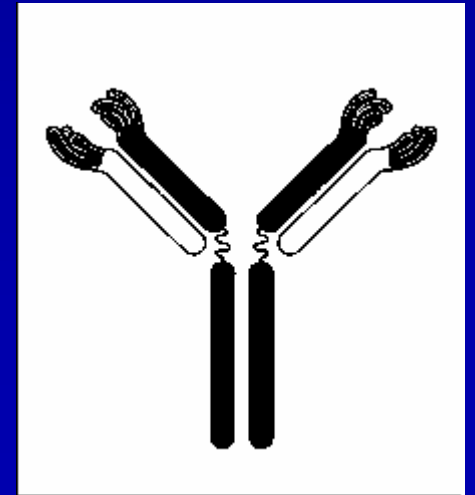
Annual number

CONTRACEPTIVE USE AND UNMET NEED



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What are the **advantages** of immunocontraceptives ?

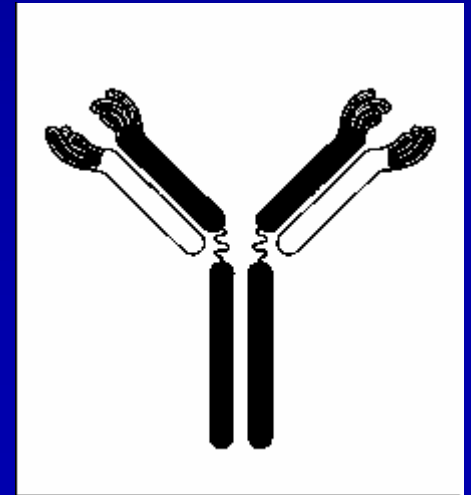


ADVANTAGES OF IMMUNOCONTRACEPTIVES

- **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;
- Need for periodic injections;
- 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/HIV;
- Alleged abuse potential and other socio-political issues.

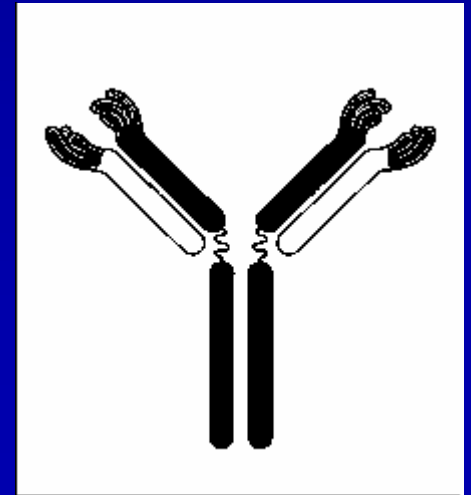
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General issues

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Where and how would
immunocontraceptives work ?



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Possible points of intervention

Hypothalamus - GnRH

Pituitary - FSH and LH

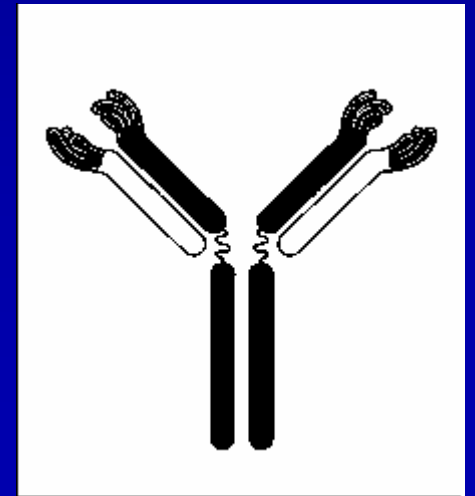
Gonads - progesterone, estrogen and testosterone

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 in healthy 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

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Gamete immunocontraceptives

Some cell surface antigens are unique, tissue-specific, immunogenic and accessible to antibodies:

- Zona pellucida antigens: used in animal control
- Sperm antigens: naturally-occurring antibodies lead to infertility

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 pre-clinical 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

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**

