FACT SHEET ON IMMUNOLOGICAL CONTRACEPTIVES
(Antifertility 'Vaccines')

WHAT ARE IMMUNOLOGICAL CONTRACEPTIVES?

The mode of action of immunological contraceptives is based on the relationship between the immune and the reproductive systems. Most people know the immune system as the 'police of our body.' The immune system - a complex interplay between cells, molecules and organs — is our most powerful defense mechanism against infectious microorganisms, such as viruses, bacteria, parasites and fungi. Few people realize that there is another, equally important function of our immune system, the prevention of 'self' attack by the immune system, i.e. the attack on the *body's* own components. The effector mechanisms of our immune system - in particular antibodies and immune cells – are capable of attacking constituents of our body as well as foreign microorganisms. If this occurs, severe autoimmune diseases such as myasthenia gravis, forms of rheumatoid arthritis and diabetes can result.

The capacity of the immune system to protect the body from immune-mediated self-destruction is known as 'self-tolerance.' As yet little is known about how self-tolerance actually works. We do know, however, that our immune system starts to build up self-tolerance early in life. By the time we are born, our immune systems are already tolerant of most of our cell types, enzymes and hormones.

Immune-mediated contraceptives aim at temporary interference of the 'self'-tolerance to which allows successful reproduction to occur. Immune-mediated contraceptives interrupt one of three basic reproductive processes:

* production and/or maturation of human gametes, i.e. sperm or egg cells,
* fertilization, or
* implantation and/or development of the early embryo.

To disturb any of these processes, researchers encourage an auto-immune attack on the cells or molecules involved. This is done by tricking the immune system into believing these molecules are 'foreign' antigens. An altered version of the reproductive cell or molecule is linked to a 'non-self' antigen such as diphtheria toxoid or tetanus toxoid so that the whole complex is recognized as 'foreign', and the immune system responds with antibodies to the natural structure. The following reproductive cells or molecules have been identified as targets for immunological intervention.

(1) The first class of potential targets are non-pregnancy associated (reproductive) hormones which regulate the monthly ripening and release of egg cells in women and the continuous production of sperm in men. The aim of the auto-immune attack is to disturb maturation of eggs or the production of sperm.

(2) The second class of target components are our egg and sperm cells. The aim is to incapacitate them such that they become incapable of fertilization.

(3) The third class of targets are either pregnancy-associated hormones or enzymes or the early embryo itself. This group includes hCG (human chorionic gonadotrophin) regarded as the most 'promising' target antigen. Immune-mediated neutralization of this hormone prevents implantation of the early embryo. A target component of the early embryo is the trophoblast; it is from the trophoblastic cells of the early embryo that the placenta develops.

As .such there is a variety of potential immunological contraceptives[1]. The profile of action and potential adverse effects of specific types of immunological contraceptives will differ considerably depending on the role and location of the target antigen, and whether the product is developed for women or men.

WHY IMMUNOLOBICAL CWHY IMMUNOLOGICAL CONTRACEPTIVES SHOULD NOT BE DEVELOPED

1. No benefits over existing contraceptives

Although immunological contraceptives are still under development, it can already be forecast that even the best possible types will have a negative benefit risk ratio. Their most significant shortcoming is their problematic efficacy profile.

Researchers claim that they are working on a immunological contraceptive which will be reversible after one or two years. The researchers' main concern has been whether immunological contraceptives can be developed to be effective for this time period and in what percent age of women. Leaving aside the question of which of the immunological contraceptives currently under development will ever fit this description, and to what degree immunological contraceptives will be reversible after long-term use, there are a number of problems underlying the immunological mode of action:

For any immunological contraceptive there will be a lag-

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[1] See appendix I

Period (period during which the antibody titres begin to increase) after the first administration, a contraceptive phase (a period during which the antibody titre is above the effective threshold) and a waning phase. This process is inherent in the immunological response.

The first problem is thus a **lag-period** of several weeks to two to three months before the antibody titre is above the contraceptive threshold. This means that a woman must not to get pregnant during this time, or the fetus will be exposed to the effects of an ongoing immune reaction.

A second problem – even with the best possible immune contraceptive - may be the relatively high 'method failure rate**',** i.e. the rate of accidental pregnancies under best possible circumstances. As Spieler points out, "a fertility regulating vaccine . . . would have to produce and sustain effective immunity in at least 95% of the vaccinated population, a level of protection rarely achieved even with the most successful viral and bacterial vaccines" (1987). In phase II of the Indian trials the rate of 'low—responders' (i.e. women not reaching the putative effective threshold) was 20 percent.

The problems to be expected under real usage conditions are infinitively greater. The biggest problem of immune contraceptives will be their inherent unpredictability for the individual woman. First, there will be considerable variations in the duration of the lag-phase and the contraceptive phase[2]. Second, women with a predisposition to inappropriate immune responses (allergies or autoimmune diseases) might find themselves unexpectedly infertile for life. On the other hand, an unexpected low immune response may occur during times of stress, malnutrition, or with the onset of immuno—suppressive diseases such as malaria tuberculosis, and HIV infection.

Finally, it is difficult if not impossible to stop ongoing immune reactions at will**.** This greatly compounds problems if a women gets pregnant during this period or if she develops adverse effects.

Although some of these problems may be reduced by novel ways of formulating the product, in essence they will remain. The problem is not that of a particular prototype 'vaccine,' but that the immune system is an interconnected, open, regulatory system and that the magnitude and duration of immune responses

[2] For HRP's hCG formula the lag phase was 5-6 weeks; the theoretically effective phase was 2 to over 9 months; for the Indian hCG formula in phase II the lag-phase was even longer; the contraceptive phase ranged from 6 months to over two years - for the 80 percent of women who reached the contraceptive threshold.

varies depending on genetic, environmental and psychological factors.

No protection against sexually transmitted diseases

In the 1990s,a pertinent question for any contraceptive is whether it will protect users not only against pregnancy but also against sexually transmitted diseases. Research on immunological contraceptives began in 1970s, well before AIDS was known. WHO estimates that by the year 2000, more than 90% of HIV infections will occur in developing countries - and more than four fifths will be contracted by heterosexual intercourse. HIV is making a fulgurant entry on the Indian sub-continent. Is this a climate for the release of an immunological contraceptive?

It is as yet unclear whether or not immune contraceptives will speed up the course of an HIV infection. However, this is not the only concern. Eka-Esu Williams, head of the Society for Women and Aids in Africa expressed her fears at the 1992 HRP Meeting between women's health advocates and researchers, that immunological contraceptives will create a set-back to campaigns against the spread of HIV. First, injectable contraceptives will contribute to the spread of HIV via unsterile needles. Second, the predictable heavy promotion of anti-fertility 'vaccines' is likely to reverse progress in the difficult endeavour to persuade men to use condoms.

2. Considerable risks:

Immune—mediated adverse effects

One could propose to stop the risk benefit, assessment here, because according to the Declaration of Helsinki on ethics in clinical trials, a new contraceptive would need to offer significant gains over existing alternative methods to justify its development. The efficacy profile of immunological contraceptives in itself is a risk, rather than a benefit. It does not justify any of the potential risks of immunological contraceptives.

The major risks of an immune-mediated interference of the reproductive system are:
- auto-immune diseases
- allergies
- interference with diseases

On talks about autoimmune diseases if the immune reaction against body own components results in pathological effects The Indian and the Population Council's anti-hCG formulas, for example, induce an immune reaction not only against hCG, but also against

the luteinizinq hormone. They thus do interfere with the hormonal cycle. The researchers say this does not cause any of the expected problems, which are menstrual cycle disturbances in the short run and endometrial carcinoma in the long run. However, one will know the definitive answer only after long-term use in human beings. A particular problem of immunological interference with hormones is the risk of immune attack of the cells which secrete and receive the hormone, in this case whether the interference with LH may ultimatley damage the pituitary gland at the base of our brain or the ovaries. The true risks will be known only after long-term use in humans.

HRP's anti-hCG prototype does not seem to interfere with LH. But it did cause unexpected cross-reactions with cells of the pancreas and the pituitary gland. Also here, the long term effects are uncertain.

Allergies were caused by all formulas. In most cases allergies may be localized inflammatory reactions. However, with all vaccines there is a risk of potentially fatal circulatory collapse - it is doubtful that in a Third world setting one can screen out individuals at risk with an allergy test prior to administration of an immunological contraceptive.

A rather neglected question of immune contraceptives is to what degree they may interfere with pre-existing diseases. Contraceptive 'vaccines' are given rather frequently as compared to anti-disease vaccines. Their administration may result in a general push of immune processes - be it good ones or harmful ones**.** Nobody knows to what degree this may, for example, push pre-existing allergies or auto-immune diseases. Nobody knows whether e.g. this may hasten chronic liver diseases in persons with jaundice.

Risks for the fetus

Fetal exposure to the effects of immunological contraceptives is more likely than with any existing contraceptive due to the lag-period and the inherent unpredictability of immunological methods. The problem is compounded by the impossibility to 'switch off' the immune reaction. [How this will affect a pregnancy, i.e. whether this will result in repeated miscarriages or more or less visible damages to the fetus will depend on the type of immune contraceptive. Only long-term follow up of children can give us an ultimate idea of the risks of exposing fetuses to an ongoing immune reaction. Whatever the ultimate problem, the predicable high exposure of pregnancies to ongoing immune reactions is not justified by the 'benefits' of this class of contraceptives].

Abuse potential

If we conceive the benefits of contraceptives in terms of their contribution to reproductive self-determination (and not just efficacy), then we must address whether they are used to control women's fertility, rather than giving them control over their fertility. This means that the abuse potential must become a criterium of risk. benefit assessments of contraceptives. Most people understand abuse of contraceptives as forcing people to use a contraceptive against their will or without their knowledge. However, there are many, more subtle ways of pushing particular contraceptives. Women can be persuaded to 'prefer' certain contraceptives by incentives, or by misinformation about the benefits and risks. Abuse can be defined as any uninformed, misinformed or coercive provision of a birth control technology. The abuse potential can be forecast to some degree by looking at the 'design', i.e. the technology inherent features, of a contraceptive.

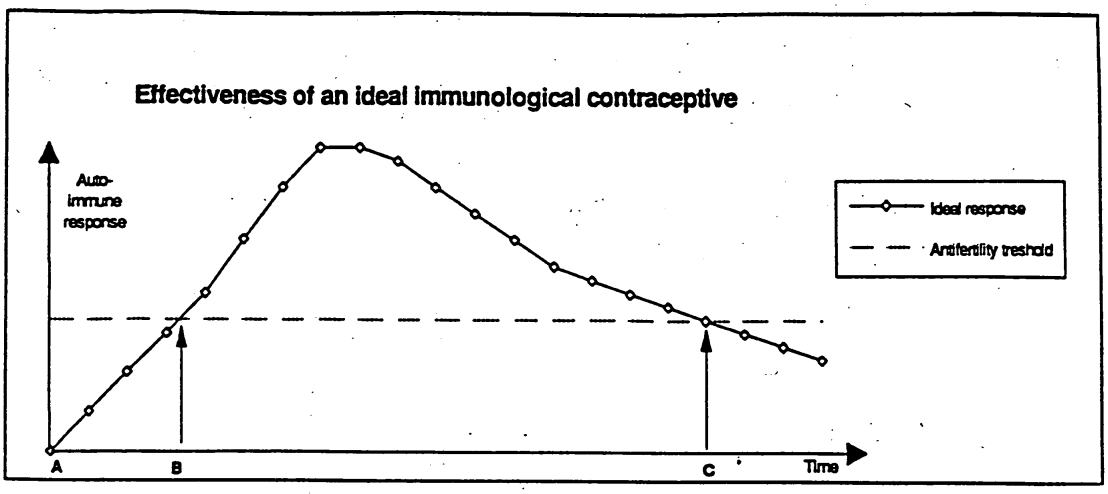
Antifertility 'vaccines have a worse abuse potential than any of the existing contraceptives for three reasons:

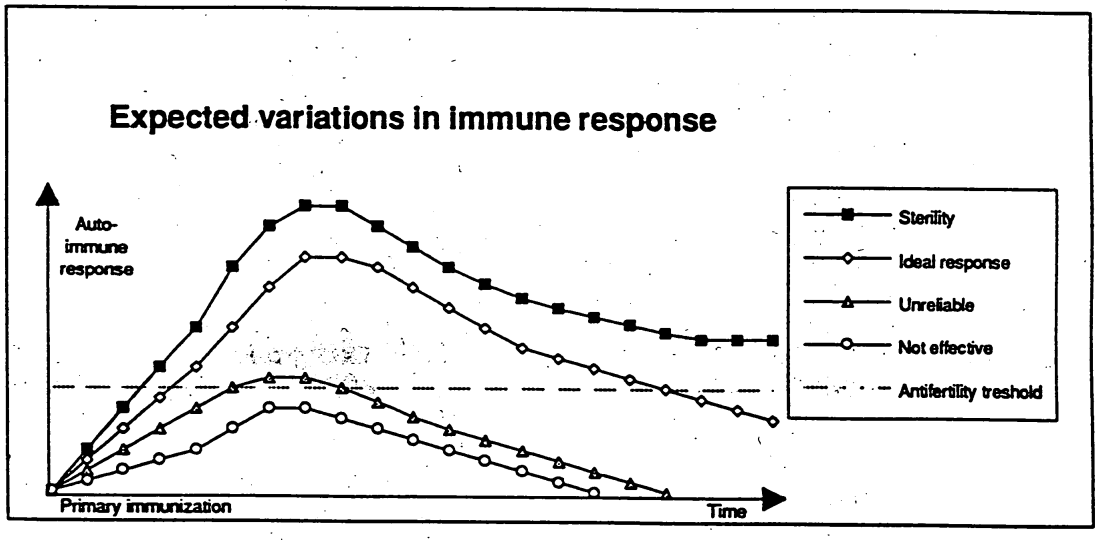
- they have a relatively long action. (Although the ultimate length of action is still unknown, duration could range from 1 year for the anti-hCG contraceptives to life-long for the anti-sperm contraceptives for women)
- they cannot be stopped by the user at will
- they can be easily administered - not only with but also without the knowledge of the user

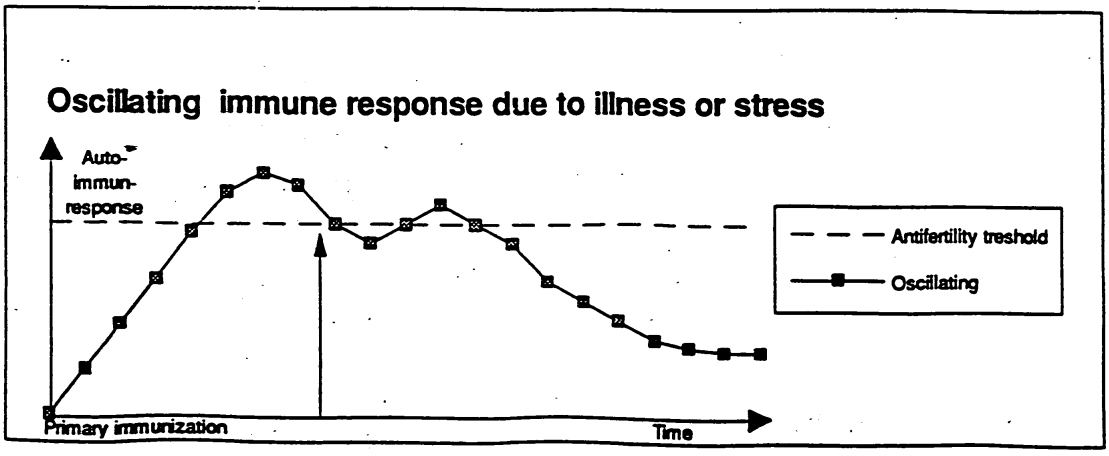
The worries about abuse of immunological contraceptives are compounded by statements of the researchers how the 'popularity' of anti-disease vaccines and injectable will help the introduction of antifertility 'vaccines'. Misinformation about the risks and benefits of immune contraceptives seems to be pre-programmed from the very conception of this particular contraceptive.

To sum up: Particularly for poor women in Third World countries the risks of immune contraceptives will outweigh any alleged benefit. Their unreliability, the impossibility to 'switch off' their action and their high abuse potential are likely to result in a decrease rather than an increase of reproductive self-determination. They will not protect against HIV, but may increase the risks of transmission. Moreover, immune contraceptives harbour a range of immune-mediated adverse effects, in particularly the risk of auto-immune diseases, allergies and a high probability of fetal exposure to ongoing immune reactions.

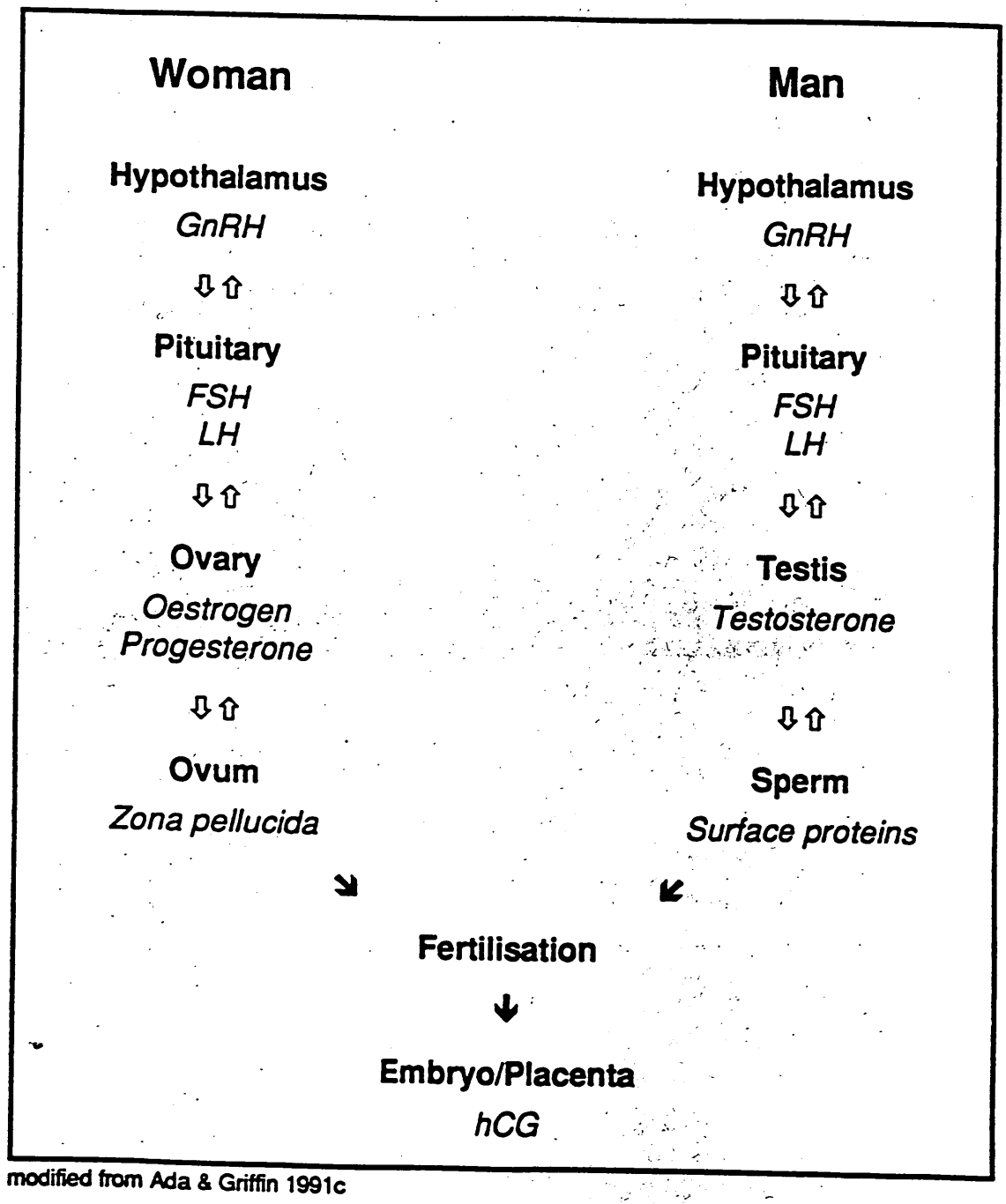
By Judith Richter, 26th October, 1993


Effectiveness of an ideal immunological contraceptive
Auto-
immune
response
Ideal response
Antifertility treshold
A
B
C
Time


Expected variations in immune response
Auto-
immune
response
Sterility
Ideal response
Unreliable
Not effective
Antifertility treshold
Primary immunization
Time


Oscillating immune response due to illness or stress
Auto-
immun-
response
Antifertility treshold
Oscillating
Primary immunization
Time

Possible target substances for immunological contraceptives



modified from Ada & Griffin 1991c