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Opinion

# A unique genetically engineered vaccine against human chorionic gonadotropin that prevents pregnancy without impairment of ovulation, hormonal profiles, and menstrual regularity

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ABSTRACT

A brief overview is given of a vaccine that is competent to prevent pregnancy without any disturbance of normal ovulation, normal making of sex steroids, and menstrual regularity. It requires periodic intake and offers full privacy of use to the women. In order to render it reproducible on large scale, it has been made as a recombinant vaccine. To our knowledge, this is the first and only potential Birth Control vaccine at present in the world. This vaccine received the precious support from the International Committee on Contraception Research of the Population Council New York with clinical trials conducted in Finland, Sweden, Chile, and Brazil under eminent clinicians showing its safety and reversibility. Phase II trials in 3 major Institutions showed that it prevents unwanted pregnancy in sexually active women at antibody titers of 50 ng/ml and above. Fertility is regained with decline of antibody titers, and progeny born to previously immunized women is normal developmental land marks and cognitive ability with respect to their siblings.



## 1. Introduction

Human chorionic gonadotropin (hCG) emerges as a product of early embryo[1] and is not made in any significant amounts by any organ of a healthy non-pregnant female. This is the rationale of detecting its presence as diagnostic test of pregnancy. It plays a crucial role in implantation of the embryo onto the endometrium. Marmoset embryos exposed to anti-hCG antibodies fail to implant, whereas those exposed to irrelevant antibodies implant perfectly.[2] It is thus an ideal target for immuno-intervention for control of fertility.

### 1.1. Chemistry and structure

hCG is composed of 2 subunits, α and β. Alpha subunit of hCG is identical to the alpha subunits of 3 other pituitary hormones, TSH, FSH, and LH. The beta subunit confers

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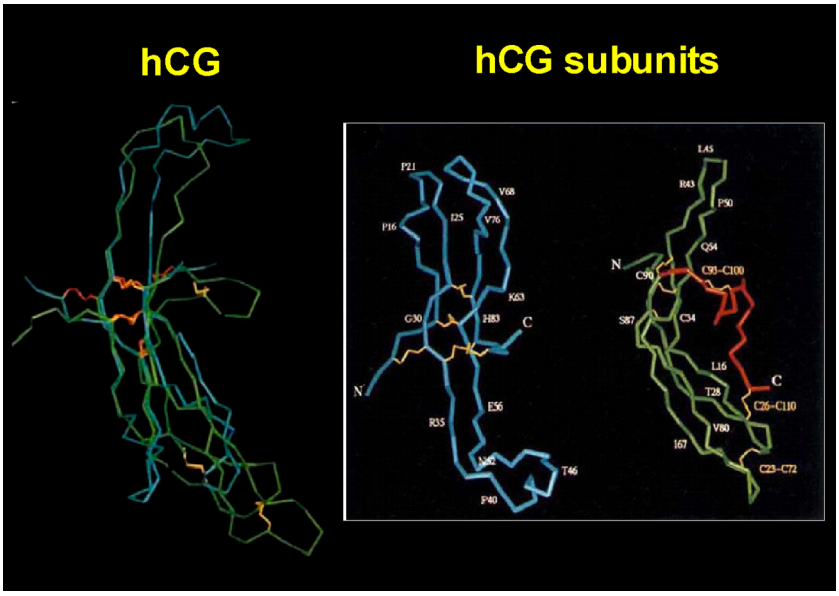


**Fig. 1 – Structures of hCG and its α and β subunits [from 3].**

**Table 1 – hCG neutralization potency of anti-βhCG and anti-HSD antisera generated in rats and bonnet monkeys [from 5].**

| Animal description | Immunogen[a] | hCG binding capacity Mean ± S.E.M. (pg) (*I*) | hCG neutralization potency Mean ± S.E.M. (pg) (*B*) | *B*/*I* × 100 |
|---|---|---|---|---|
| Rat (*n* = 6) | β hCG-TT/CHB | 27.1 ± 1.7 | 17.1 ± 1.2 | 63 ± 1.5 |
| Rat (*n* = 6) | HSD-TT/CHB | 32.5 ± 1.4 | 26.1 ± 0.8 | 80 ± 2.3 |
| Bonnet monkey (*n* = 5) | β hCG-TT/CHB | 22.2 ± 2.3 | 10.1 ± 1.8 | 44 ± 3.7 |
| Bonnet monkey (*n* = 5) | HSD-TT/CHB | 21.4 ± 1.9 | 14.0 ± 1.4 | 65 ± 1.9 |

[a] Rats received three injections of 10 μg gonadotropin equivalent adsorbed on alum at monthly intervals. SPLPS (200 μg) was included in the first injection only. Bleeds were tested 1 week after last immunization. Bonnet monkeys (*Macaca radiate*) were given three injections of 50 μg gonadotropin equivalent adsorbed on alum at monthly intervals. SPLPS (1 mg) was included in the first injection only. Bleeds were tested 2 weeks after last immunization.

identity to these 4 hormones. The beta subunit of hCG is 145 amino acids long, the terminal 35 amino are additional to those present in β-hLH. The structures of α and β subunits of hCG and the way they are linked have been elucidated.[3] Fig. 1 shows the structure of hCG and its subunits.

## 2. Making of a vaccine against hCG

Given that the alpha subunits are common to 3 other pituitary hormones, it was obvious not to employ the whole hormone but to employ β-hCG as the antigen. Women are, however, immunologically tolerant to hCG, given that hCG is made in fairly large amounts at not only in early stage but also throughout the entire duration of pregnancy. To render it immunogenic, we linked it to a carrier, the tetanus toxoid (TT). TT is a low-cost, useful vaccine available in unlimited amounts. The conjugate of β-hCG-TT elicited antibodies against not only hCG,[4] but also against tetanus preventing antenatal deaths occurring in large numbers due to tetanus infection following delivery in aseptic conditions. Fig. 2 shows the antibody response in one of these women immunized with βhCG-TT vaccine.[4]

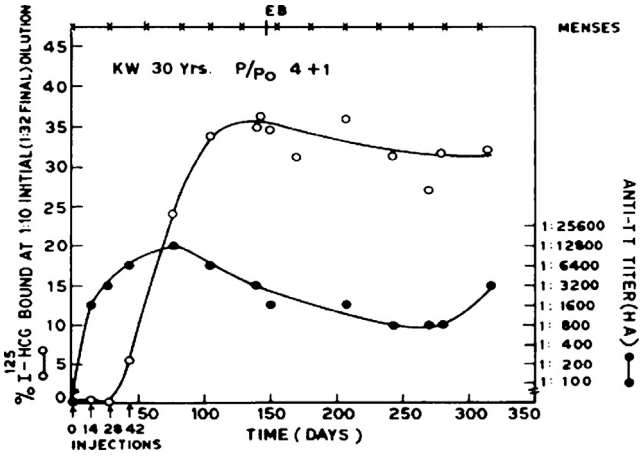


**Fig. 2 – Kinetics of antibody titers against hCG and tetanus in a woman KW 30 years old with 4 children and 1 termination of pregnancy. ×s at the upper abscissa indicates the menstruation days, which remained regular post-immunization [from 4].**