

# Influence of Serum Progesterone Levels at the Time of hCG on the Release of Ova During hMG Cycles

*Jerome H. Check, M.D.  
Harriet G. Adelson, B.S.  
Julie Stern, B.A.  
Carolyn Lauer, ClSup(NCA)*

University of Medicine and Dentistry of New Jersey  
Robert Wood Johnson Medical School at Camden  
Cooper Hospital/University Medical Center  
Department of OB/GYN  
Division of Reproductive Endocrinology & Infertility  
Camden, New Jersey

**ABSTRACT:** A study was designed to monitor release of ova by sonography in hMG-treated patients following hCG and to determine if failure to release ova correlates with critically low or high progesterone levels. This was a retrospective study of 292 consecutive patients treated with hMG. The requirement for treatment was that hCG be given when at least one follicle attained a 17-mm diameter with a serum estradiol level of at least 200 pg/mL per mature follicle. If the serum progesterone assay was  $\geq 1.8$  ng/mL, then hCG would be given as long as there was at least one dominant follicle and a serum estradiol level  $>200$  pg/mL. The patients were divided into four groups for study based on the progesterone level at the time of hCG administration. There were no statistically significant differences in the ability to achieve ova release whether serum progesterone was very low or close to 2 ng/mL when hCG was given. The rise in the progesterone level prior to ovulation has been proposed to enhance egg release. However, the data presented herein do not support the necessity for a critical level of serum progesterone at the time of hCG injection in hMG-treated women.

## INTRODUCTION

**D**URING THE NORMAL OVULATORY cycle, a mid-cycle rise progesterone precedes ovum release. When a woman is treated with human menopausal gonadotropins (hMG), human chorionic gonadotropin (hCG) is generally required to achieve ova release, since the high serum estradiol levels may inhibit the normal luteinizing hormone (LH) surge need-

ed to trigger the rupture of the egg out of the follicle; or the inhibition may be related to nonsteroidal factors.

The LH surge is predominantly responsible for the rise in the serum progesterone level prior to ovulation. The normal monitoring of hMG to determine when hCG should be given involves measuring follicular size and number by sonography and by the level of serum estradiol. We generally seek at least one lead follicle of 17 mm

diameter, with 200 pg/mL estradiol per mature follicle.

A study was designed to monitor release of the ova by sonography in hMG-treated patients following hCG, and to determine if the failure to release ova correlates with a critically low or high progesterone level.

## MATERIALS AND METHODS

In this retrospective study of 292 consecutive hMG-treated patients who were either anovulatory or had luteal phase defects associated with immature follicles [1], the patient's cycles were monitored by pelvic sonography and serum estradiol, progesterone, and LH levels. The requirement for treatment was that hCG be given when at least one follicle attained a 17-mm diameter [2, 3] with a serum estradiol level of at least 200 pg/mL per mature follicle [4]. Serum estradiol assay was performed by radioimmunoassay (RIA) utilizing a solid-phase methodology (Diagnostic Products, Los Angeles). Serum progesterone and LH levels were measured by competitive binding RIA and double-antibody RIA (Amersham, Arlington Heights, IL), respectively. Pelvic sonography was performed utilizing the full-bladder technique on an ATL Ultramark 4 (Advanced Technology, Bothell, WA) with a 3.5-MHz transducer. The decision when to use hCG was influenced by the serum progesterone assay only as follows: if the serum progesterone was  $\geq 1.8$  ng/mL, especially if this was accompanied by a spontaneous LH surge, then 10,000 units hCG would be given as long as there was at least one dominant-sized follicle with serum estradiol  $>200$  pg/mL, even if multiple follicles were present and the serum estradiol was not  $>200$  pg/mL per mature follicle [5].

For example, if there were three dominant follicles of 15 mm, 16 mm, and 18.5 mm diameter, and serum estradiol was 280 pg/mL, additional hMG would normally be given until a minimum serum estradiol level of 600 pg/mL was achieved; but if serum progesterone was approaching a level of 2 ng/mL, hCG would be given at this point to prevent premature luteinization.

Release of the ovum was determined by pelvic sonography obtained three days after the follicle attained maturity. Release was defined as a collapse of the follicle by at least 5 mm. If the serum

progesterone level failed to rise above 2 ng/mL, another hCG injection of 5,000 units was given and a repeat ultrasound was performed two days later. Because of the known adverse effect of premature luteinization, any patient whose progesterone level reached 2 ng/mL before a minimum serum estradiol level of 200 pg/mL was achieved was eliminated from the study.

The patients were divided into four groups: (1) positive release, (2) questionable release (questionable release was defined as a follicle becoming smaller but not by a full 5 mm), (3) release with two hCG injections, and (4) non-release. The four patients groups were further subdivided according to the serum progesterone levels at the time of the first hCG injection: (a) 0.1–0.5 ng/mL, (b) 0.6–0.9 ng/mL, (c) 1.0–1.5 ng/mL, and (d)  $\geq 1/6$  ng/mL.

## RESULTS

The results are shown in Table I. Chi-square analysis showed no statistically significant differences in the ability to achieve release related to the progesterone level at the time of hCG administration.

## DISCUSSION

One of the proposed functions of the rise in progesterone levels prior to ovulation is to enhance the activity of proteolytic enzymes responsible, together with prostaglandins, for digestion and rupture of the follicular wall [6, 7]. Since with hCG therapy the physician controls when the "LH" surge occurs (hCG injection), the possibility exists that by not waiting until there is a progesterone surge, oocyte release may not occur. Perhaps in some cases an inadequate progesterone surge would occur and a small dose of progesterone might then be needed to achieve egg release. Only 14 patients in the higher progesterone group had premature LH surges, so we do not think the LH levels themselves help to explain the data.

However, the data presented herein do not support the necessity for a critical level of serum progesterone at the time of hCG injection. This is not to negate fully the need for serum progesterone monitoring along with estradiol measurements and sonography. It is still important to recognize the fact that a serum progesterone level approach-

**TABLE I**  
Type of release.

| Serum Progesterone Range (ng/mL) | Positive    | Questionable | 2 hCG Injections | Non-release |
|----------------------------------|-------------|--------------|------------------|-------------|
| 0.1-0.5 (n=284)                  | 171 (60.2%) | 77 (27.1%)   | 20 (7%)          | 16 (5.6%)   |
| 0.6-0.9 (n=126)                  | 82 (65.1%)  | 29 (23.0%)   | 10 (7.9%)        | 5 (4.0%)    |
| 1.0-1.5 (n=51)                   | 34 (66.6%)  | 11 (21.6%)   | 1 (2%)           | 5 (9.8%)    |
| ≥1.6 (n=31)                      | 14 (45.2%)  | 14 (45.2%)   | 1 (3.2%)         | 2 (6.5%)    |

ing 2 ng/mL would prompt an earlier injection of hCG in some circumstances; had the serum progesterone level not been known, more hMG—and not hCG—would have been administered.

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Address reprint requests to:  
Jerome H. Check, M.D.  
7447 Old York Road  
Melrose Park, PA 19126