

## A New Methodology to Evaluate Beta 3 Integrin as a Marker for Uterine Receptivity

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### Objective

The presence of the beta3 integrin molecule in the endometrium may play an important role for embryo implantation. This study evaluates a new method using beta3 integrin as a marker for uterine receptivity in women with two unsuccessful in vitro fertilization (IVF) cycles. Live birth rates were compared between patients treated for absence of beta3 integrin and patients with positive expression of beta3 integrin.

### Design

Randomized retrospective study.

### Materials and Method

Study group: 105 patients with two unsuccessful IVF cycles following transfer of good quality day 3 embryos (6 to 8-cells). All patients underwent infertility evaluation, including assessment of semen quality, ovarian reserve, tubal patency, and hysteroscopy.

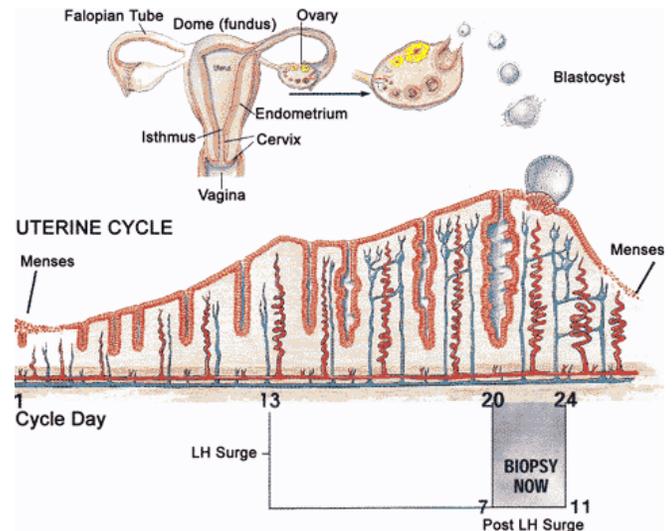
The patients followed a hormone replacement therapy (HRT) protocol to eliminate possible luteal phase defect (LPD) and were biopsied in the postovulatory phase between day 8 and 10. The timing of the biopsy was determined by counting the number of days from the start of progesterone.

Each biopsy tissue was collected in 10% formalin buffer solution and sent for histological dating of the endometrium. A 4-5 micron thick section of paraffin imbedded tissue was prepared, fixed on slide, and de-waxed. Immunohistochemical (IHC) staining was performed using monoclonal antibody MCA728 by Serotec, which is specific to the beta3 subunit of integrin. This antibody had been evaluated by flow cytometry.

The tissue was incubated with a primary antibody MCA728, which reacts in the presence of the beta3 integrin antigen. Incubation with a secondary antibody will bind to the antigen/antibody complex. A chromogen Diaminobenzidine by Serotec, which reacts with the antigen antibody complex, was added. The presence or absence of brown precipitate on epithelial cells was noted to identify the expression or absence of beta3 integrin.

### Result

35/105 patients (33%) lacked beta3-integrin expression. After various treatments, the live birth rate in this group was 60% (n=21).  $P = 0.0001$ , Chi-square and Freedman Anova analysis. 11/35 patients (30%) had type I defect showing endometrial dating is out of phase and without beta 3-integrin-expression. Out of 6 patients who underwent treatment for type I defect, 3(50%) had a live birth. 24/35 patients (70%) demonstrate type II defect showing endometrium is in phase but lacks beta3 integrin expression. 19 patients went through treatment for type II defect and 18(95%) patients had a live birth.



70/105 patients (67%) demonstrated beta3 integrin expression. From this group 61(87%) had a live birth.

*Conclusion*

Beta3 integrin is a precursor of fibronectin, which plays an essential role in adhesion and motility of cells. Patients with at least two failed ART cycles; evaluating uterine receptivity is an important step for future management. This study supports the published data for evaluation of uterine receptivity. The presence of beta3 integrin is important for the implantation of embryos. If beta3 integrin expression is absent, patients may respond to various treatments and achieve a live birth.