Summary

Yuji Taketani, Tokyo

The interrelationship between endometriosis and infertility is very complex and will require continuing investigation. Nevertheless, the Fourth Japan Conference on Endometriosis, held on April 28th, 2001, at Hakone, Japan, was successful in advancing our understanding of the mechanisms of infertility with endometriosis. This in turn will lead to more treatment options and better clinical management of infertile women.

The first presenter, Dr. Craig Witz (University of Texas Health Science Center) discussed general aspects of endometriosis-related infertility to help us look more clearly at this enigmatic disease. However, the precise relationship between endometriosis and infertility remains controversial.

Dr. Hiroshi Suginami (Kyoto National University) emphasized the significance of performing as complete a laparoscopic resection of endometriotic tissue as possible. Data from both complete and incomplete surgery groups showed similar fecundity rates up to day 400. After day 400, there was no elevation in cumulative pregnancy rate in the incomplete surgery group. Dr. Suginami's message may be that both the presence of endometriosis itself, *per se*, and adhesive lesions can be a cause of infertility in endometriosis. He recommended use of the laparoscopic anterior rectum slicing (LARS) procedure to remove deep rectal endometriosis and deeply invading pelvic endometriosis.

Assistant Professor Tomio Iwabe (Tottori University) measured IL-6 and TNF- α levels in peritoneal fluid from women with and without endometriosis and found that levels of both cytokines were elevated in patients with endometriosis. There was a positive correlation between levels of IL-6 and active red lesions. In addition, IL-6 decreased the motility of human sperm and inhibited the

development of mouse embryos. Dr. Iwabe feels that increased levels of IL-6 in the peritoneal cavity may contribute to endometriosis-related infertility.

Assistant Professor Takashi Murakami (Tohoku University) investigated anatomical and biological factors associated with subsequent conception and found two important factors: bilateral ovarian adhesions may interfere with fertility; and serum TNF- α levels may predict subsequent pregnancy. However, he was unable to find a predictable method that simultaneously combined both factors.

Pregnancy rates in women with bilateral adhesions and at least one patent tube were lower than rates in women with unilateral or no tubal adhesions, according to a study conducted by Assistant Professor Yutaka Osuga (University of Tokyo). In patients with unilateral adhesions, pregnancy rates were highest in those with mild endometriosis and lowest in those with moderate or severe endometriosis. However, similar women without endometriosis had pregnancy rates in between those of these two groups. Patients with no tubal adhesions had similar pregnancy rates regardless of degree of endometriosis.

In a related study investigating tubal status and infertility, Assistant Professor Akira Fujishita (Nagasaki University) focused on the site of the endometriotic foci in relation to pregnancy outcome, highlighting the role of tubal adhesion as a crucial factor in reducing fertility. He reported that expectant, medical, or surgical therapy of ovarian endometrioma improved the pregnancy rate, although there was no difference among treatment methods. However, his data seems in part inconsistent with Dr. Suginami's data, leaving the issue of how to handle endometriosis in infertile women still an open matter.

Assistant Professor Hidekazu Saito (Yamagata University) found that changes in cell cycle kinetics assessed by flow cytometry and measurement of DNA in individual granulosa cells may be related to the state of follicular growth and oocyte maturation. He reported that endometriosis induced apoptosis and oxidative stress and altered the cell cycle in granulosa cells. This suggests that an increased frequency of apoptosis may give us a hint with regard to the mechanism of infertility with endometriosis.

In the final presentation, Dr. Witz introduced novel concepts concerning the pathogenesis of endometriosis. He provided evidence for the passage of endometriotic cells through the mesothelial component. In his theory, first there is retrograde menstruation that sheds sheets of

viable endometrial epithelial stromal cells that attach over the periphery of the mesothelial cells and spread into the underlying extracellular matrix. By 24 h, the mesothelial cells begin to grow back over the endometrial cells. This theory explains why endometrial cells are not seen growing on the mesothelium at biopsy. Although this may explain the initial event, additional complicated forces during the progression of endometriosis may be at play.

We hope that the basic science and clinical information and related debate featured in this supplement will be a milestone in determining the future direction of the study of endometriosis. We must continue to provide avenues for the exchange of ideas in order to understand the etiology of endometriosis and thereby provide optimal treatment for women suffering from this disease.