

Professor Ariel Weissman graduated the Hadassah-Hebrew University Medical School in 1988. In 1994 he completed his residency in Obstetrics and Gynecology at the Kaplan Medical Center, Rehovot, where he spent another two years working as a senior physician at the IVF unit. Prof. Weissman then pursued a 2-year research and clinical fellowship with Prof. Bob Casper at the Division of Reproductive Sciences, Department of Obstetrics and Gynecology, University of Toronto, Toronto, Canada. His main focus of research was transplantation of human ovarian tissue in immuno deficient mice. Upon returning to Israel in 1998, Prof. Weissman joined the IVF unit at the Department of Obstetrics and Gynecology, Wolfson Medical Center, Holon, Tel Aviv University Sackler Faculty of Medicine where he currently holds a position of an associate Professor. Together with David Gardner PhD, Colin Howles PhD, and Zeev Shoham M.D., Prof. Weissman has published the “*Textbook of Assisted Techniques: Laboratory and Clinical Perspectives*”, which is one of the leading books in the field of ART.

## Ultrasound-guided embryo transfer

The chances for embryo implantation following IVF depend on the complex equation  $IR = EQ * UR * TE$  (implantation rate=embryo quality\*uterine receptivity\*transfer efficiency). For many years little attention has been given to the blind and relatively simple transfer procedure, which was guided mainly by clinical touch. We have now become aware to the significant differences in pregnancy rates observed with different individuals performing embryo transfers (ET) in the same program, and it has been estimated that poor ET technique may account for as much as 30% of all failures in ART.

Consequently, more focus has been given to the transfer procedure, and many studies have been conducted in order to characterize variables and technical aspects of ET success or failure. One of the most studied topics with regard to ET is the use of ultrasound for its guidance. Ultrasound guidance during ET has many potential advantages such as facilitation of placement of soft catheters, confirmation that the catheter tip is beyond the internal os in cases of an elongated or wide canal, avoidance of touching the fundus or disrupting the endometrium by the catheter tip, and the full bladder required to perform transabdominal ultrasound guidance is itself helpful in straightening the cervical-uterine angle in cases with sharply anteverted uterus.

To date, several randomized prospective trials have been conducted in order to evaluate the influence of US-guided ET on cycle outcome. Despite many differences in methodology, the majority of these studies suggest a clear and significant benefit for US-guided transfers. Catheters with an echo-dense tip, which are more readily detectable by ultrasound, have been recently introduced but their role and contribution to success remain questionable. Further modifications in US-guided ET application include: measurement of the utero-cervical angle prior to transfer, development of transvaginal ultrasound guidance transfer techniques, and the use of three-dimensional ultrasound during ET. While previously transabdominal US-guidance was reserved mainly for the difficult transfer it is now emerging as a widespread powerful clinical tool. The ultrasound machine is therefore most likely to become standard in the transfer room.

## **GnRH Antagonists in clinical practice**

The recent introduction of GnRH antagonists may offer several advantages over standard GnRH agonist protocols to both patients and clinicians. GnRH antagonists act by mechanism of competitive inhibition, which leads to an immediate arrest of gonadotropin secretion, thus avoiding the flare-up effect. While agonist and antagonist preparations appear to be equally effective in prevention of premature LH surges, applying GnRH antagonists for controlled ovarian hyperstimulation in ART results in a significant reduction in the duration of GnRH analogue treatment and reduces the amount of gonadotropins required for stimulation. Other potential benefits of antagonist use include avoidance of estrogen deprivation symptoms (hot flushes, sleep disturbances, headaches and mood swings) that are frequently observed during the pre-stimulation phase of the long protocol, and a potential to reduce the risk for severe OHSS.

Whether the above medical and practical advantages justify a switch from the routine treatment of the ART patient from the 'gold standard' (long GnRH-a protocol) to the new antagonist preparations depends on whether the clinical outcome using both protocols is equivalent. In a recent meta-analysis of randomized controlled trials comparing long agonist with antagonist protocols in ART there were significantly fewer clinical pregnancies in those treated with GnRH antagonists (OR 0.79; CI 0.63-0.99; Al-Inany and Aboulghar, Cochrane Library 2002).

More experience and more studies are needed before the above findings can be ruled out or confirmed. Many questions regarding antagonist prescribing remain unanswered:

1. What is the optimal protocol for antagonist usage: can flexible and individually tailored antagonist protocols improve the results?
2. What should be the standard monitoring regimen during antagonist cycles: should daily progesterone or LH measurements be included (thus adding to the cost) in all cycles?
3. Which gonadotropin or gonadotropins combination should be used in antagonist protocols? Is it recombinant FSH alone, or should LH be added as well? If so, which form and how much of LH should be administered? hMG, recombinant LH, hCG? At what stage of stimulation should LH administration commence?
4. What is the significance of LH rise prior to antagonist administration?
5. What is the significance of progesterone rise during antagonist administration?
6. What is the significance of an estradiol drop following the initiation of antagonist therapy?
7. Should antagonist protocols be offered to all ART patients or there are subgroups of patients who may be more likely to benefit? Is it the low responders or perhaps the high responders?

While most of us are still at different stages of 'climbing' the learning curve for antagonist use, a plethora of new information has recently emerged that offers partial answers to the above complex questions.