Frozen eggs and other marvels take "hi-tech" up a notch or 2

Momentous discoveries are moving into the clinical arena.

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As predicted in this column a year ago, 2004 saw the emergence of human oocyte cryopreservation as a hot topic. Now, it is generally agreed that human oocyte cryopreservation is a technique that can be applied to clinical practice in certain circumstances, although general application will be hotly debated pending further adequate clinical trials.

Be prepared for questions when the marketing starts

We can expect younger patients wishing to preserve reproductive capacity to ask our advice on freezing their eggs. (This technology is of limited applicability to the average reproductive-aged woman). The official position of the American Society for Reproductive Medicine is that, until more outcome data are available, it is too early to incorporate this practice into general use.

However, a growing number of assisted reproductive technology (ART) centers will be offering—and marketing—the procedure.

Related to the growing interest in preserving female fertility so that women can delay childbearing: a momentous discovery reported in 2004 suggests that our time-honored dogma on growth of new human oocytes may be wrong.

In addition, 2 laboratory studies suggest a future for assisted reproductive technologies, when every embryo is assessed for its likelihood to result in a healthy infant.

These reports demonstrate the excitement of translational research in bringing basic discoveries into the clinical arena. They highlight the incredible development of both stem cell biology and nanotechnology, and suggest how such fields are rapidly becoming relevant in the modern practice of infertility. While it is difficult to predict an accurate timeline, or certainty, of the application of these discoveries to a modern infertility practice, it is safe to say that these and similar discoveries will influence our usual practice in the foreseeable future.

FAST TRACK

More ART centers will offer and market cryopreservation

Oocytes unlimited after all?

Johnson J, Canning J, Kaneko T, Pru J, Tilly J. Germline stem cells and follicular renewal in the postnatal mammalian ovary. Nature. 2004;428:145–150.

A long-held belief is that women reach their peak oocyte number at midgestation, and that number continuously declines until oocytes are depleted, sometime after menopause. This study from Jonathan Tilly's group at Harvard Medical

School presents evidence for germline stem cells in the ovaries of mice capable of replenishing oocytes into adult life. Removal of these germline stem cells caused a rapid depletion of primordial follicles, suggesting that the primordial follicle reserve was continuously replenished from germline stem cells.

While it is quite a leap to assume that human ovaries contain similar germline stem cells, the possibility that reproductive age woman may be able to develop new oocytes is truly exciting. If such oogonial stem cells exist in women—and could be harvested and cryopreserved, as mature oocytes are now being harvested and preserved—it opens the possibility that a renewable supply of oocytes may be available for women who wish to preserve the capacity to reproduce.

Practical implications

Whether for personal use following cancer therapy or oophorectomy, or as a source of oocytes for donation to women who have lost ovarian function, the potential holds great promise. However, extensive further work is required, not the least of which is independent verification of Dr. Tilly's findings and the extension of that discovery to women.

For the practicing obstetrician/gynecologist fielding a question about "growing new eggs" from a savvy patient surfing the Net, know that the concept has a scientific basis but is definitely not ready for prime time.

FAST TRACK

Savvy Net-surfers may soon be asking Ob/Gyns about "growing new eggs"

New standard ahead for embryo assessment

In vivo assessment without injury

Kulkarni RN, Roper MG, Dahlgren G, Shih DQ, Kauri LM, Peters JL, Stoffel M, Kennedy RT. Islet secretory defect in insulin receptor substrate 1 null mice is linked with reduced calcium signaling and expression of sarco(endo)plasmic reticulum Ca2+-ATPase (SECA)-2b and -3. Diabetes. 2004;53:1517–1525.

The assessment of human embryos for their viability and the likelihood of implanting and developing into a healthy baby has been a challenge for in vitro fertilization programs worldwide. Recent interest has focused on removing single cells from embryos and performing genetic studies. However, this is expensive, time consuming, and runs the risk of damaging embryos in the process of removing single blastomeres.

This study by Kennedy and colleagues, while not immediately applicable to human ART programs, demonstrates a technique for monitoring the secretion products from individual pancreatic beta cells. Using microelectrodes placed adjacent to individually cultured beta cells, insulin secretion from each cell was estimated by measuring the number of exocytotic events in normal and IRS-1 knock-out mice. The in vivo measurement of specific secretion products from individual cells without injuring them is an exciting example of the miniaturization of clinical science.

Practical implications

The extension of this technique to the safe assessment of human embryos in vivo while they are in culture is logical and opens up an entire area of both investigation and potential clinical practice. If the metabolic activity of the individual embryos indicates the likelihood of implantation and development, then this could become a new standard in the assessment of every embryo resulting from an ART cycle.

Much work will be required to translate this exciting new technique to human embryos, but it does offer a logical

approach to the longstanding problem of embryo assessment.

Real-time assessment

Schuster TG, Cho B, Keller LM, Takayama S, Smith GD. Isolation of motile spermatozoa from semen samples using microfluidics. Reproductive Biomedicine Online. 2004;1(Jul-Aug):75–81.

One of the challenges of assessing individual human embryos in vivo is the dilution effect on any secretion products secreted from an embryo into the relatively vast amount of media in a traditional ART Petri dish. This report describes the first of a series of microfluidic devices designed to separate motile from nonmotile spermatozoa in very small volumes. Such devices can be used to isolate motile sperm from nonmotile sperm and debris for ART procedures when numbers are exceptionally low.

However, similar microfluidic devices are being developed to include tiny chambers that could be used to contain individual human embryos receiving a constant stream of nutrient media with a constant output of spent media and secretory products. In conjunction with the capacity to analyze such tiny amounts of secretory products in vivo from individual cells, this suggests a system for evaluating all human embryos in modern microchambers and continually monitoring for appropriate secretion and subsequent selection for optimal reproductive capacity.

Practical implications

The promise of real-time embryo assessment is certainly upon us, though much work needs to be done to develop these microfluidic incubation chambers before they will be clinically applicable.

For the practicing Ob/Gyn, it is useful to know that the era of preimplantation evaluation of all embryos is not far off. Whether that will translate into fewer fetal/neonatal defects remains to be seen. ■

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