

## Current status of subfertility care: Time to rationalize treatment options

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Assisted conception treatment has been widely available throughout the world for more than two decades, but the success rate of this technology in terms of rates of live births per cycle is still low. Conventional in-vitro fertilization (IVF) usually involves the use of ovarian stimulation. Stimulated IVF is currently popular because initial studies showed that this treatment resulted in improved success rates. It is perhaps only during the past few years that the negative aspects of stimulated IVF have been recognized. The effect of ovarian stimulation on short-term (ovarian hyperstimulation syndrome) [1] and long-term (cancer risk) [2] health of women, on chromosomal abnormalities in oocytes and embryos [3,4], and on endometrial status [5] have been recognized. IVF with ovarian stimulation is also associated with increased incidence of multiple pregnancy and premature birth [6], which has financial repercussions. It is time to reconsider the need for extensive ovarian stimulation in IVF cycles. In view of the long-term effects of ovarian stimulation on the health of women, research and clinical practice should surely be directed towards using less ovarian stimulation or even none at all.

Another aspect of assisted conception technology that needs re-evaluation is the extent of gamete manipulation (intracytoplasmic sperm injection, assisted hatching, etc.) that is currently used, and whether IVF is overused for certain types of infertility that may just require simple, inexpensive therapies. A recent study by Goverde *et al.* [7] has demonstrated that intrauterine insemination in spontaneous cycles should be the first-choice treatment in couples with idiopathic or male subfertility.

Advances have revolutionized ovarian stimulation protocols. In the present issue, Salha and Balen (pp. 201–206)

reviewed newer concepts in ovarian stimulation strategies. The use of gonadotrophin-releasing hormone antagonists to block the spontaneous luteinizing hormone surge is an important milestone [8]. It is a more physiological approach than the agonist protocols. Further studies are required to determine whether less stimulation may achieve similar success rates. The priming of ovarian follicles with human chorionic gonadotrophin during spontaneous cycles, and in-vitro maturation and fertilization of oocytes seems to be promising [9]. It also seems an opportune time to revisit natural cycle IVF. Cumulative pregnancy and live birth rates after a series of natural cycle IVF seem to compete favourably with super-ovulation IVF. The advantages of natural cycle IVF are that it could be offered in subsequent cycles and that it is more cost-effective (Nargund *et al.*, unpublished data).

Management of male subfertility with assisted conception technology has given hope to many couples who could not have children in the past. An extensive review of current and future role of genetics in male infertility is provided by Hargreave in the present issue (pp. 207–219). Genetic information on sperm seems to be fundamental to the understanding and treatment of male subfertility. The effect of mechanical damage introduced by intracytoplasmic sperm injection on the development of the embryo has not been evaluated because of the lack of an alternative and comparable procedure. It is therefore difficult to assess the genetic risks of transmitting damaged genes and defective chromosomes from the father to the offspring in the absence of an animal-based experimental system. It may be necessary to establish an alternative system of producing the embryo by electrofusion of in-vitro decondensed and remodelled sperm nucleus with oocyte. The role of counselling in the management of couples with chromosomal abnormalities in infertile men is important. Long-term follow up of children born as a result of assisted conception technology is needed.

The use of ultrasound scanning for follicular and endometrial monitoring is pivotal in management of assisted conception cycles. The advent of colour Doppler with pulsed Doppler and power Doppler technology has added a new dimension to our understanding of follicular recruitment, maturity and endo-

metrial receptivity in spontaneous and stimulated cycles [10–13]. Recent technology using 3-dimensional ultrasound has allowed us to obtain volume measurements, and the addition of power Doppler has made the technique more informative, particularly in women with polycystic ovarian syndrome or intrauterine anomalies, and in assessing fallopian tubal patency [14–17]. The art of ultrasound and the science of reproductive physiology are brought together to understand angiogenic and morphological changes which occur within the reproductive tract, information that is useful in providing optimal care.

Finally, the role of cost-effective and evidence based care has clearly been demonstrated by Daya (pp. 227–231). Funding of subfertility is inadequate in most health care systems. It is only recently that the treatment of subfertility has been recognized as a health need rather than a social need. Couples who experience subfertility suffer from psychological consequences, which in most cases are not expressed adequately due to the nature of the condition.

There is also an urgent need to evaluate the cost of investigation of subfertility. As medical professionals, we suffer from constant frustration of not being able to treat couples due to lack of funding. Ethical and moral dilemmas in this field continue to dominate, while we make slow but steady progress in improving subfertility care.

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