

## **PERICONCEPTIONAL DETERMINANTS OF HEALTH**

**N.S. Macklon**

*Chair, Department of Obstetrics and Gynaecology, Division of Human Development and Health, University of Southampton*

Over the past three decades, assisted reproductive technology has made startling progress with respect to clinical protocols, pharmaceutical drugs, embryology, treatment of male infertility, pre-implantation genetic diagnosis and quality management systems. We have seen pregnancy rates rise from single figures to those that exceed natural conception while at the same time reducing multiple pregnancy rates to below 5% by performing single embryo transfer. We have revolutionized the way assisted reproductive technology is practiced and are rightly proud of all that we have achieved for our patients.

Yet a number of challenges remain to be addressed. While we have learnt to control everything within the clinic, ranging from clinical to laboratory to administrative procedures, wrapped them in quality management systems and undertaken detailed surveillance of all aspects of the operation, we have yet to control the most important determinants of success: the characteristics of our patients. And as we enter the second generation undergoing IVF, the patients we treat are very different to those who sought treatment three decades ago. Clinics are increasingly seeing women approaching and exceeding their 40's seeking assistance to become pregnant. Not only does this affect the efficacy of fertility therapies, it also means that more of our fertility patients will have co-morbidities which can impact on IVF and vice versa. Unfortunately, age is not amenable to our interventions. However, many other features of the new patient population are. The epidemic of obesity is upon us and it is rare to see somebody in many clinics where the body mass index is below 25. Young women continue to smoke heavily, and we know that sperm counts are decreasing in some parts of the world, largely due to environmental and lifestyle factors. The changing demographics of our patients, in combination with the new indications for ART such as fertility preservation for cancer patients and PGD for carriers or sufferers of serious inherited disease present us with new clinical challenges. In addition, the improved prognosis associated with some serious medical conditions mean that many patients who would have never had children are approaching us after controlling their serious heart disease or diabetes or cystic fibrosis.

The new imperative to focus on the preconceptional phase when planning fertility treatments is clear, and made more urgent by an increasing understanding that pregnancy outcomes, and indeed long term health are significantly influenced by the preconceptional health. This question has been brought into focus in recent years by research which has demonstrated the validity of the so-called 'Barker Hypothesis'. This theory states that the nutritional environment of the embryo and foetus affects its risk of developing cardiovascular and other health problems later in life. The question therefore rises whether environmental factors associated with periconceptional development (including culture conditions in IVF) may disrupt processes crucial for fetal growth and development. The in-vivo nutritional environment at the time of conception has been shown to influence further development. More recent studies have shown that dietary content at the time of conception and during pregnancy is associated with an altered birth weight, and other determinants of long-term health.

In conclusion, those of us working in Assisted Reproduction should understand that successful IVF is not just about having the best clinical and laboratory protocol and the highest trained staff. It is about helping patients as individuals to assess their risks from their genetic and environmental background, and to adjust in an appropriate way that maximizes their chances of becoming pregnant, and having a healthy child .