Mini symposium
Long-term effects on offspring of early exposure to biological and external factors

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Introduction

This mini-symposium aims to review and analyse the long-term effects on offspring of gamete, conceptus, embryo and fetus exposure to biological, chemical and physical factors. Each one of the five articles included in this mini-symposium provides not only a description of the potential long-term effects but also proposes physiological, cellular and/or molecular explanatory mechanisms. In particular, this mini-symposium deals with the long-term effects on offspring of gamete ageing, intrauterine exposure to deficits in nutrition and gestational diabetes, premature labour and exposure of parents, gametes, concepti, embryos and/or fetuses to different external agents including medications, social drugs, radiations, culture media, conceptus biopsy, conceptus splitting, environmental pollutants and chemotherapy agents.

A variety of assisted reproduction technologies in the cow and the sheep including conceptus culture, nuclear cloning, conceptus–somatic cell co-culture, asynchrony between transferred concepti and the uterus, and early progesterone treatment in early pregnancy can lead to the production of large offspring, the so-called ‘large calf/lamb syndrome’ (for reviews, see Seamark and Robinson, 1995; Leese et al., 1998; Rieger, 1998). Although this syndrome has not been observed in humans, concern has been raised recently about assisted reproduction techniques. As discussed by Prof. Auroux, gamete cryopreservation may lead to numerical and/or structural chromosomal anomalies in offspring. Cryopreservation of concepti may also affect the quality of offspring. Although the studies performed so far in children born from cryopreserved concepti have not evidenced pathological conditions in offspring, animal studies show increased fetal mortality, reduced fetal weight and changes in morphophysiological, sensorimotor and behavioural traits during pre-weaning development, adulthood and senescence. Likewise, it is worth to note that ICSI babies have higher rates of chromosome anomalies, mainly of the sex chromosomes, and likely congenital malformations (Kurinczuk and Bower, 1997; Ménézo et al. 2000) when compared to spontaneous pregnancies.

Just like a biochemical or molecular pathway, any insult to the organism at early stages of development may have worse consequences for later life than similar insults at later stages of development because a higher number of downstream traits may be affected. There is a continuum of offspring anomalies that potentially may arise from early exposure to harmful factors. They go from subtle deficiencies in behaviour and/or intelligence, decreased reproductive fitness and/or increased morbidity and/or mortality of otherwise normal-looking individuals to the immediate death of the affected conceptus, embryo or fetus. Intermediate phenotypes may display major or minor congenital malformations and/or severe deficiencies in behaviour and/or intelligence. Although the physiological, cellular and molecular mechanisms involved in the origin of most of the anomalous phenotypes remain unknown, it appears that both/either genetic and/or epigenetic changes may explain their occurrence.

There is no doubt that, in addition to the sometimes devastating psychological effects on the affected families and/or individuals, many of these anomalies may cause enormous economical burdens to society and families into which an affected individual is born. Unfortunately, many exposures of gametes, concepti, embryos and fetuses to biological, chemical and/or physical factors are inevitable. However, the negative effects on offspring of factors such as social drugs and gamete ageing could be easily prevented by efficient diffusion of the potential risks and the steps couples wishing to achieve pregnancy as well as pregnant women should take to guarantee a correct fertilization and/or development of the resulting concepti, embryos and/or fetuses. The use of animal models to analyse the long-term effects on offspring of early exposure to potentially harmful agents and/or new technologies should always precede any clinical application in human beings. Although many studies are needed to uncover the mechanisms involved, the tip of the iceberg that at the present time can be discerned clearly shows that not only the genotype but also the phenotype of a particular individual may be determined or programmed, at least in part, at early stages of the life cycle, i.e. in concepti, embryos and/or fetuses, or even before conception, i.e. in fertilizing gametes.

References


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