Keynote Lecture XVI
Human Reproduction and Oxidative Stress

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Eric Jauniaux qualified in Medicine in 1986 from the Free University of Brussels. After 5 years of part-time research on the pathophysiology of early Human Pregnancy he was awarded a PhD degree from the same University. Following clinical and research posts at the Academic Hospital Erasme (Universite Libre de Bruxelles) and King's College Hospital (University of London) he was accredited Specialist in Obstetrics and Gynaecology in June 1992 and was appointed Lecturer in Fetal Medicine at King's College London Medical School. In November 1994, he was appointed Senior Lecturer in Obstetrics and Gynaecology at University College London and became Reader in 1998. In October 2002 he was awarded the title of Professor in Obstetrics and Foetal Medicine at the Royal Free and University College London School of Medicine.

His main research interests include Placental and Foetal Developmental Physiology, Early Human Pregnancy, Placental Related Pregnancy Disorders, Pathophysiology of Miscarriage and Preeclampsia and Placental Transfers.

Professor Jauniaux is the author/co-author of more than 250 peer-reviewed publications and the editor/co-editor of six textbooks on prenatal diagnosis, physiology of early pregnancy, ultrasound/imaging technique in Obstetrics and Gynaecology, Embryonic therapy and Cancer and Pregnancy. He is the member of the editorial board of 6 international journals and the co-founder of Reproductive Biomedicine On line (www.RBMonline) of which he is currently the Pregnancy Editor. He has been the Laureate of 3 Belgian national scientific prizes and 3 international prizes (Alexander Fleming Award 1989; Spa Foundation Award 2001 and International Federation of Placental Association Award 2002).

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Evolution from unicellular life in the oceans to multicellular life on land has been associated with remarkable metabolic changes linked to the increasing demand for energy that a multitissular body requires to live, grow and reproduce. Energy transformation of dietary proteins, carbohydrates and fats occurs mainly in the mitochondria of animal cells through a series of oxidation-reduction reactions, and the energy released in these reactions is used to phosphorylate adenosine diophosphate (ADP), so generating adenosine triphosphate (ATP). The final step of this process requires oxygen (O_2) as an electron recipient, and the entire process is known as oxidative phosphorylation. ATP is pivotal as the storage form of the chemical energy required to drive many biochemical reactions in the cell, in particular protein biosynthesis, active transport of molecules through cellular membranes, and muscular contractions.

Most of the O_2 used during the oxidation of dietary organic molecules is converted into water, but a significant amount (1-2%) of the O_2 consumed is diverted into highly reactive O_2 species (ROS), mainly the superoxide (O_2), hydroxyl (OH), peroxyl (RO_2) and hydroperoxyl (HO_2) anions. Thus ROS are constantly formed as a by-product of aerobic respiration and other metabolic reactions. If generation of ROS exceeds the cellular defences, however, indiscriminate damage can occur to proteins, lipids and DNA, resulting in oxidative stress. The consequences may range from the activation of stress-response proteins through to apoptosis or necrosis. There now appears to be a consensus that culture in a low oxygen environment enhances the blastulation rate in many species, and that metabolism becomes increasingly anaerobic during this phase of development. More recent

data indicate that even after implantation the same conditions prevail in the human. This may confer benefits on the embryo by minimising both the risk of damage to DNA, and of disruption of signalling pathways and gene expression by reactive oxygen species generated during aerobic metabolism. Only once the principal stages of organogenesis are complete are significant quantities of oxygen delivered, and this corresponds with the start of a phase of rapid growth.

The O_2 tension in the oviduct and uterus of most mammalian species has been found to range between 11 and 60 mmHg, which corresponds to approximately 1 to 9% O_2. These data indicate that the earliest stages of development take place *in vivo* under a low O_2 concentration compared to atmospheric conditions of 21% O_2 (98 mmHg). The human fetus is no exception to this universal rule, and the PO_2 measured within the human placenta *in vivo* is <20 mmHg at 7-10 weeks gestation. It subsequently rises to >50 mmHg at 11-14 weeks as the maternal intraplacental circulation becomes fully established. Similarly low values have been reported within the fetus. At 13-16 weeks the PO_2 in the fetal blood is 24 mmHg, whereas during the second half of pregnancy that in the umbilical vein ranges between 35 and 55 mmHg. These values are relatively low compared to the PO_2 values found in the maternal circulation, suggesting that there is a significant O_2 gradient between the maternal and fetal tissues throughout pregnancy.