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FOREWORD

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An Update on Male Infertility: Factors, Mechanisms and Interventions

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In 1677, A. Leeuwenhoek placed a drop of his semen on a glass slide and viewed under his ground-breaking compound light microscope. He was immediately struck by the tiny 'animalcules' he found wriggling inside. Since that pioneering observation, the light microscope has remained a central instrument for evaluation of semen from animals and men exposed to numerous lifestyles, medical and industrial environments.

This Special Issue on 'An Update on Male Infertility: Factors, Mechanisms and Interventions' provides a comprehensive update on various important aspects of male infertility from the researcher's and the clinician's perspective, clearly showing the great advancement of optical and biochemical probes into male reproductive physiology. It is to be noted that all contributions of this Special Issue have referenced light microscope data far advanced from Leeuwenhoek's first look.

This Special Issue provides a comprehensive appraisal of a current hot topic, namely, the role of reactive oxygen species (ROS) in male reproduction. ROS act as molecular mediators of signal transduction pathways that trigger morphological changes and moderate factors involved in fertilisation. Besides spermatozoa, leukocytes and infections of the male genital tract are potent endogenous sources of ROS. On the other side of the coin, oxidative stress causes significant damage to the integrity of spermatozoon, including the all-important integrity of the male genome. Oxidative biomarkers have been used to study male infertility, predict pregnancy outcomes and reduce ROS damage in ART-based protocols.

Since our introduction of the concept of sperm DNA fragmentation and the SCSA test in 1980 (Evenson et al., 1980), three other sperm DNA fragmentation (SDF) tests have been established. Hundreds of SDF manuscripts have been published clearly showing the negative consequences of damaged DNA to fertilisation and embryo/foetal development. The landmark study of 187 couples without known infertility factors, and who were counselled for timed intercourse and followed for twelve menstrual cycles, clearly showed that %DFI and %HDS were significantly ($p < .01–.001$) related to pregnancy outcomes (Evenson et al., 1999). ROS accounts for almost 80% of SDF resulting from inflammation, infection or in various diagnosis of male infertility. Oxidative base lesions resulting from ROS can produce genetic and epigenetic mutations in offspring with significant impacts on long-term health. The egg has limited capacity to repair SDF following fertilisation.

Sperm motility is mandatory for natural fertilisation and since ROS damages not only DNA but also cell and mitochondrial membranes, this explains the high degree of relationship between SDF and motility measures. Defects in mitochondrial function impair the energy needed for sperm motility. Spermatogenesis comprises the most complex differentiation pathways in animal and human biology. These pathways are highly sensitive to numerous intrinsic and extrinsic factors. This Special Issue gives an in-depth look into how abnormal factors of spermatogenesis impacts DNA damage related to infertility and miscarriage, and probes into the various aetiologies of sperm DNA damage, its clinical assessment and resulting implications.

SCSA Diagnostics: www.SCSAtest.com

During the past six decades, human sperm quality has decreased, including an approximate 50% decrease in sperm count. This significant decrease of sperm quality may be related to various factors, which are well discussed in this Special Issue. Common lifestyle practices that are not conducive to male reproductive health may impede spermatogenesis and/or steroidogenesis resulting in oxidative stress. The extent to which obesity, a disease with rising global prevalence, impacts the male reproductive system and fertility is certainly a matter for concern. Interactions between genetics and epigenetics, lifestyle factors including obesity, and environmental factors may exert a significant influence on male fertility.

Intake of environmental contaminants permeates the entire spectrum of male reproductive organs from embryo development to adult testis function. While many reproductive toxicology studies show that the classical semen parameters of sperm count, motility and morphology are affected by toxins, one example here showed that coal energy plant air pollution caused pathological levels of SDF without effect on WHO classical semen parameters (Rubes et al., 2005). This observation suggests that if a couple remains infertile while the classical semen parameters are in the normal range, it is prudent to measure for sperm DNA fragmentation as a potential cause of infertility/ miscarriage.

Varicoceles are commonly found in infertile men and give rise to sperm DNA damage to levels not compatible with normal pregnancy outcomes. In terms of the treatment of varicocele, varicocele repair can significantly reduce the level of SDF. Varicoceles not only give rise to sperm DNA damage but also highlights the role that proteomics plays in identifying potential sperm and seminal plasma biomarkers in varicocele-mediated male infertility.

The reviews in this Special Issue clearly show that oxidative stress plays a significant role in the pathophysiology of male infertility including sperm DNA fragmentation. Common knowledge that oxidative stress damages sperm DNA and other semen parameters has spawned a huge over-the-counter nutraceutical market for males seeking pregnancy. Whether these various treatments are, or are not, a viable option is still an area in need of further investigation.

While many questions remain, readers of this update on factors, mechanisms and interventions for male factor infertility will gain valuable insights into the mechanisms involved in the pathophysiology of male infertility, and patient management in the infertility clinic.

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