Swimming against the stream: modern-day challenges to male reproductive health

The effects of a mother’s age, health and habits upon her offspring are well documented. However, far less attention has been paid to fathers. Dr Bernard Robaire, Professor at McGill University, Montreal, Canada, believes male reproductive health may be just as important for future generations as that of females, with a father’s age, health and exposure to chemicals all having an impact on the quality and genetic makeup of his sperm – and ultimately the fitness of his children.

Women today are showered with advice regarding their reproductive health and the health of their future children. Some of the stories you hear typically include: ‘older mothers are more at risk of fetal abnormalities’; ‘don’t drink alcohol, smoke, or eat soft cheese during pregnancy’; ‘take folic acid when you’re trying to conceive’; ‘avoid exposure to chemicals such as pesticides’, etc. This is all good advice, of course, but how about the fathers – do they get off scot-free? Well, not for much longer! Dr Bernard Robaire’s research is set to overturn the predominant view that a man’s age, health and habits have little impact upon his future offspring. Bad news for fathers-to-be, perhaps, but good news for the accuracy of reproductive health guidelines.

Sperm are continuously produced throughout a man’s life – at a rate of about 1000 every time his heart beats that divide to produce sperm – and sperm nurse cells (‘Sertoli cells’), which regulate the process, under the control of sex hormones such as testosterone. As sperm mature they pass through the tubules and are stored until they are ready to be released. It was previously thought that their constant manufacture rendered sperm relatively immune to the kind of damage that can accumulate in a woman’s eggs over her lifetime. However, Dr Robaire’s research and that of his colleagues have shown that this is not the case. Exposure to drugs (therapeutic or otherwise), smoking, environmental chemicals, and conditions such as obesity, are now known to have negative effects on a man’s sperm, and, therefore, his children, and these effects may cumulate with age.

Dr Robaire’s research aims to find out exactly how these effects are manifested. His team members are investigating how the components of the male reproductive system, and the different processes involved – hormone production and reception, sperm production, maturation and storage – are impacted by a range of possible environmental factors, and are looking to characterise the molecular mechanisms that mediate these effects.

The Age Effect
In today’s society, men and women alike are increasingly delaying parenthood until later in life. Now it seems that this may not be such a good plan. Dr Robaire’s animal studies have shown that the progeny of older male rats have lower weights and are more likely to die in the neonatal period than those of younger fathers. When their sperm were examined, the...
offspring of the older rats were found to have greater levels of damage to their genetic material, DNA. In humans, older men are reported to have testes containing slower sperm, and a higher proportion of these are abnormal. They also show higher rates of infertility, and their partners take longer to get pregnant and are more likely to miscarry. Increasing numbers of studies have linked paternal age with higher rates of diseases with a complex genetic component, such as autism, ADHD, schizophrenia, and bipolar disorder.

There is mounting evidence linking paternal age with chromosomal and genetic changes in offspring, increasing the risk of breast cancer, heart defects, and developmental, behavioural and neurological disorders. Furthermore, dominant genetic disorders such as achondroplasia, the most common form of dwarfism, are shown to be more common in the children of older fathers. These genetic changes have been connected to defects in the cellular mechanisms for repairing damaged DNA, which are essential in cells undergoing genetic recombination such as sperm cells. Dr Robaire’s research has, in turn, linked these failings to defects in the body’s defence against oxidative stress, which can cause mutations in the genetic material. His studies in mice even suggest a possible preventative measure—an antioxidant molecule—which seems to halt the losses associated with increased oxidative stress during ageing.

His current grant, supported by the Canadian Institutes of Gender and Health under the Canadian Institutes of Health Research, brings together a team of researchers with complementary expertise, aiming to explore the whole spectrum of impacts of age in the sperm stem cells themselves, in the environment provided by the seminiferous tubule, or both.

The seminiferous tubule of the testis contains a complex of epithelial cells that produce sperm. These cells are constantly renewing, and the sperm that are produced are transferred to the epididymis, where they mature. The seminiferous tubule is a dynamic structure, where the population of sperm changes continuously, and the cells in the tubule are constantly dividing. The cells in the tubule are maintained by two types of primary germ cells, the spermatogonia and the spermatocytes, which undergo meiotic division to produce haploid spermatids. The spermatids then undergo the process of spermiogenesis, where they mature into spermatozoa, which are then transferred to the epididymis.

There is a debate as to whether the number of sperm produced actually decreases with age, but there is little doubt that the quality of sperm does go down as men age. By quality I include sperm motility, their appearance and the integrity of their DNA and its packaging. Is there a relationship between the different factors that affect sperm quality? For instance, does the effect of chemicals on sperm cumulate as men age? Few studies have looked at a combination of factors such as age, obesity, or exposure to chemicals that could affect sperm. However, there is no reason to think that these would not be cumulative. Could a combination of factors, such as age, obesity, or exposure to chemicals, affect sperm quality?

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