

Diabetes linked to male infertility; excess sugars in the body have direct effect on sperm quality

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Diabetes in men has a direct effect on fertility, a scientist told the 24th annual conference of the European Society of Human Reproduction and Embryology today. Dr. Con Mallidis from Queen's University, Belfast, UK, said that, despite the prevailing view that it had little effect on male reproductive function, the Belfast group had shown that diabetes caused DNA damage in sperm.

The increase in the numbers of diabetics diagnosed at a young age has coincided with worldwide concerns over male fertility, he told the conference. "But this is not simply a coincidence," he said. "We have shown for the first time that diabetes adversely influences male fertility at a molecular level."

The scientists studied semen samples from men with diabetes who were receiving insulin therapy. On initial routine microscopic examination the semen samples appeared normal, apart from a slight decrease in volume.

"But when we looked for DNA damage, we saw a very different picture," said Dr. Mallidis, adding that this is not part of a routine semen analysis. "Sperm RNA was significantly altered, and many of the changes we observed are in RNA transcripts involved in DNA repair. And comparison with a database of men of proven fertility confirmed our findings. Diabetics have a significant decrease in their ability to repair sperm DNA, and once this is damaged it cannot be restored."

Transcription is the synthesis of RNA under the direction of DNA, and is the first step towards gene expression, where the information from the gene becomes a product such as a protein translating the genetic information into a cellular function. If there are errors in transcription, there will also be errors in the function of the gene. "We were particularly interested to see a fourteen-fold decrease in the expression of a protein called ornithine decarboxylase, which is responsible for the production of spermine and spermidine, compounds responsible for cell growth that help stabilise the structure of DNA. We also found that spermatogenesis 20, a factor unique to the testis and whose function remains unknown, was greatly increased. Taken together, these factors indicate clearly that having diabetes has a direct influence on the health of semen."

Sperm DNA quality is known to be associated with decreased embryo quality, low embryo implantation rates, higher miscarriage rates, and some serious childhood diseases, in particular some childhood cancers. Over the years possible causes for sperm DNA fragmentation have been suggested but to date the exact mechanism for the damage remains unknown, say the scientists.

"We found a class of compounds known as advanced glycation end products (AGEs) in the male reproductive tract. These are formed as the result of glycation (the addition of sugar)," said Dr. Mallidis, "and accumulate during normal ageing. They are dependent on life style – diet, smoking etc – and in many diabetic complications are centrally implicated in DNA damage. We believe that they play a similar role in the male reproductive system."

The scientists intend to follow up their work by trying to determine how AGEs cause and contribute to DNA damage. They believe that they may have uncovered a new role for AGEs, and that their influence goes far beyond diabetes and its complications.

"We must now try to develop strategies to protect sperm, and to diminish the accumulation of AGEs," said Dr. Mallidis. Such strategies could involve changes in diet, disrupting a step in the formation of AGEs, or increasing the body's protection against AGEs, possibly through the use of dietary supplements.

"Finally, there is spermatogenesis 20. What does it do, how does it do it, under what circumstances and why? Why is it so greatly increased in diabetics? We need to find answers to all these questions," said Dr. Mallidis.

Source: European Society for Human Reproduction and Embryology

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