

# Normal-looking sperm may have serious damage; scientists urge more care in selection

8 July 2008

Intracytoplasmic sperm injection (ICSI), where a single sperm is injected into an egg to fertilise it, is increasingly used to help infertile men father children. Although the sperm chosen for the procedure may appear quite normal, researchers in the US have found that many of them in fact have DNA damage, which can decrease the chances of pregnancy.

Mr. Conrado Avendaño, from the Jones Institute for Reproductive Medicine, Norfolk, Virginia, USA, and colleagues studied a group of infertile men with moderate and severe teratozoospermia, where most of the sperm looks abnormal.

He told the 24th annual conference of the European Society of Human Reproduction and Embryology today that, in this group of men, the embryologist would normally select the 'best looking' sperm for injection. "This would typically be done by analysing the sperm's shape under a microscope," he said. "A 'good' sperm by this criterion would have a regular oval head and a long straight tail. However, our research has shown that appearances can be deceptive."

Mr. Avendaño and colleagues studied sperm from ten infertile men and found that, despite appearing to be completely normal, many of them had DNA damage (DNA fragmentation). "In routine ICSI procedure, the embryologist chooses the best-looking sperm under the microscope, but it could be damaged," he said. "DNA-damaged sperm has a highly deleterious effect on the ability to achieve a pregnancy. Even if damaged sperm are used and the woman becomes pregnant, the chances of miscarrying are significantly higher."

The researchers compared levels of DNA fragmentation in sperm from the infertile group with that from fertile men. The study was performed by

a simultaneous examination of normal sperm morphology using phase contrast and DNA fragmentation by fluorescence microscopy. The sperm morphology was evaluated in 400 randomly selected cells per sample. When a sperm with normal morphology was found, the light was switched to fluorescence to determine DNA integrity. Sperm with normal morphology from the fertile group showed no evidence of DNA fragmentation. But in the infertile men, between 20 and 66% of normal-looking sperm had DNA damage.

"The origin of DNA fragmentation can be multifactorial," said Mr. Avendaño. "Oxidative stress (mainly due to reproductive tract infections) and apoptosis are the most studied, but other factors as age, smoking, exposure to air pollution and abnormal testicular warming are believed to increase the proportion of sperm DNA fragmentation."

The researchers are now applying DNA fragmentation evaluation to couples with male factor infertility. "Our preliminary results using this new evaluation method show a clear negative correlation between the percentage of DNA fragmented sperm and the embryo quality and pregnancy outcome," said Mr. Avendaño.

"Different research groups have shown that in addition to affecting normal embryonic development, fertilisation with damaged spermatozoa resulting in a live-born infant can be associated with increased chromosomal abnormalities, minor or major birth defects, and even childhood cancer," said Mr. Avendaño. "Our work has shown that normal sperm morphology alone should not be used as the unique attribute for the selection of sperm for ICSI. New methods that allow an accurate separation of sperm with intact

DNA should be sought.”

Sperm biology has received less attention since the introduction and success of the ICSI technique, say the researchers. “While the ICSI procedure bypasses the natural sperm selection, we believe that the deleterious effects of injecting a DNA-fragmented sperm should and can be avoided. Further research into sperm biology is essential if we are to avoid problems in the future,” said Mr. Avendaño.

Source: European Society of Human Reproduction and Embryology

APA citation: Normal-looking sperm may have serious damage; scientists urge more care in selection (2008, July 8) retrieved 21 January 2022 from <https://medicalxpress.com/news/2008-07-normal-looking-sperm-scientists-urge.html>

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