



MALE INFERTILITY GENETICS

A number of genetic conditions may be associated with male infertility:

1. *Known syndromes and conditions with male infertility:* Syndromes such as Noonan's, Prune belly, Myotonic dystrophy, Kallman's, Sickle Cell anemia among others are known to be associated with impaired fertility. These men will have their diagnoses already established and such conditions typically do not apply to otherwise healthy men with infertility concerns.
2. *Cystic Fibrosis/Congenital Bilateral Absences of the Vas Deferens, CF/CBAVD:* CF is an inherited condition with mainly pulmonary and pancreatic dysfunctions. Affected individuals inherit the CF genes from both parents who are carriers who are not affected. Some male carriers may manifest with the absence of one or both vas deferens. Others may have congenital obstructions at the junction of the epididymis and vas. They should be checked for the CF carrier state and if positive, the spouse likewise needs to be assessed prior to the decisions to proceed with IVF.
3. *Chromosomal abnormality:* Numerical or structural abnormalities of the chromosomes may be seen in up to 14% of men with NOA. In the past, offspring inheritance was not a concern since these men were considered infertile. Given the advances in IVF and sperm extraction, it is now possible to overcome these obstacles and allow these men to procreate. This in turn raises the concerns of propagating abnormal genetics to the offspring with abnormal births. Genetic testing is highly recommended in all men with severe male factor infertility prior to consideration for IVF/ICSI.
4. *Y-chromosomal microdeletion, AZF/DAZ deletion:* We are just now beginning to understand the genetic control of male infertility; much is yet to be learned. It appears that part of the male (Y) chromosome is critical in spermatogenesis. DNA deletion in this region is found in up to 13% of men with NOA and to a lesser extent, men with severe oligospermia. Testing for this condition is also recommended. AZF/DAZ deletion appears to affect fertility only and the origin of this deletion is probably either during the father's sperm development or at some time following fertilization. ICSI infants with microdeletion similar to their fathers have been reported.

We have learned much about the genetic control of male reproduction but much is still unknown. We still do not have explanations for the majority of men with NOA or severe oligospermia; the term "idiopathic" or "unexplained" simply reflects this lack of understanding. ICSI can now overcome some of these problems and although we believe that ICSI-derived babies are just as healthy, the full implication of these advanced techniques is not fully known at this time.