

## TESTIS BIOPSY

Testis biopsy was first performed in the 40s and we continue to rely on testis biopsies not only to diagnose but also to manage (please also see sperm aspiration & extraction) men with infertility.

### Testis biopsy may be indicated in the following situations:

1. Azoospermic men with normal testes and FSH with or without physical evidence of obstruction: biopsy with an operating room “wet prep” will help to differentiate obstruction vs. reduced production; if it is the former, exploration and reconstruction can proceed immediately.
2. Azoospermic men with abnormal production: in men with elevated FSH and small testes, biopsy will likely reveal 1 of 3, or a mixture of, histological findings. These are Sertoli cell only, maturation arrest and hypospermatogenesis. In the absence of a treatable cause, these conditions can only be managed with TESE and IVF/ICSI.
3. Oligospermia: in men with severe oligospermia, a normal testis biopsy lends supportive evidence for partial obstruction although this is an infrequent indication.
4. Testicular sperm extraction, TESE: sperm may be extracted directly from testis tissue and used for IVF/ICSI. In men with normal spermatogenesis and obstructions (obstructive azoospermia, OA), aspiration may suffice. In men with production defects (non-obstructive azoospermia, NOA), a trial of TESE may be performed prior IVF/ICSI to see whether sperm extraction is possible. TESE success rate varies depending on the histology; on average, 30 to 50% of men with NOA may have extractable sperm.
5. Microscopic testicular sperm extraction, micro-TESE: in contrast to routine biopsy/TESE during which a small portion of testis tissue is removed and then submitted for processing in the laboratory, micro-TESE attempts to identify pockets of sperm production in the testis prior to removal. This is performed with the aid of an operating microscope to differentiate sperm containing tubules from the empty ones. These tubules tend to be different in color and diameter to allow for selective excision. Micro-TESE is more involved than routine biopsy since we need to fillet open the testis in order to separate the tubules for microscopic inspection. It is time consuming and with higher expense. Yield has been consistently higher than routine biopsy. This procedure is reserved for men with NOA only.
6. Testis mapping: some investigators have examined the concept of doing multiple biopsies or needle aspirations in order to find pockets of spermatogenesis in NOA men. The rationale is that despite the overall appearance of the biopsy, minute but full sperm production may be randomly present. This approach has essentially been replaced with the advent of micro-TESE.

### Testis Histology:

1. Normal Testis: spermatogenesis is a complicated process involving the constant evolution of germ cells taking on different size, shape and form at each step. The chromosome content also needs to be halved during this extremely delicate process with rapidly dividing but slowly maturing cells eventually forming the mature spermatozoa. The overall length of time from start to finish including transit through the epididymis is 90 days. In a normal biopsy, one should expect richly populated tubules with germ cells at various developmental stages all the way to maturity.
2. Sertoli Cell Only/Germ Cell Aplasia: SCO describes the finding of tubules containing only the supporting cells but no germ cells. Leydig’s cells, or the testosterone secreting cells are typically normally located amongst the tubules. A number of conditions can lead to SCO; these include



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radiation or chemotherapy, toxins and genetic causes. Some will exhibit other features such as scarring or abnormal Leydig's cell aggregates depending on the underlying cause such as mumps or excess sex chromosomes.

3. Maturation Arrest: MA describes the finding of tubules containing incomplete germ cell development such that no mature sperm are formed. The developmental arrest may be early or late and is often seen in conjunction with hypospermatogenesis. Attempts at extracting the incompletely developed sperm for IVF/ICSI have resulted in live births but the overall success is very low at less than 10%.
4. Hypospermatogenesis: HS describes the finding of complete germ cell development but at reduced rate. The reduction may lead to either low or zero sperm count. TESE for NOA is best in this condition.
5. Carcinoma In Situ: CIS describes the presence of individually scattered cancer-like cells in the tubules. Most testis cancers arise from the germ cells and CIS represents a pre-malignant condition. CIS is not frank cancer but is capable of developing into one if untreated. Most men with CIS have low or zero sperm count.