

# **Clinical Commissioning Policy: Surgical sperm retrieval for male infertility**

Reference: NHS England: 16040/P



**NHS England INFORMATION READER BOX****Directorate**

Medical	Operations and Information	<b>Specialised Commissioning</b>
Nursing	Trans. & Corp. Ops.	Commissioning Strategy
Finance		

**Publications Gateway Reference: 05527s**

<b>Document Purpose</b>	Policy
<b>Document Name</b>	Clinical Commissioning Policy 16040/P
<b>Author</b>	Specialised Commissioning Team
<b>Publication Date</b>	13 July 2016
<b>Target Audience</b>	CCG Clinical Leaders, Care Trust CEs, Foundation Trust CEs , Medical Directors, Directors of PH, Directors of Nursing, NHS England Regional Directors, NHS England Directors of Commissioning Operations, Directors of Finance, NHS Trust CEs

**Additional Circulation List**

**Description** NHS England will routinely commission this specialised treatment in accordance with the criteria described in this policy

**Cross Reference** This document is part of a suite of policies with Gateway Reference 05527s.

**Superseded Docs (if applicable)** N/A

**Action Required** N/A

**Timing / Deadlines (if applicable)** N/A

**Contact Details for further information** [england.specialisedcommissioning@nhs.net](mailto:england.specialisedcommissioning@nhs.net)

**Document Status**

This is a controlled document. Whilst this document may be printed, the electronic version posted on the intranet is the controlled copy. Any printed copies of this document are not controlled. As a controlled document, this document should not be saved onto local or network drives but should always be accessed from the intranet.

# Clinical Commissioning Policy: Surgical sperm retrieval for male infertility

First published: July 2016

**Prepared by NHS England Specialised Services Clinical Reference Group for Specialised Urology (URO)**

Published by NHS England, in electronic format only.

**Contents**

1 Introduction ..... 7

2 Definitions ..... 8

3 Aims and Objectives ..... 9

4 Epidemiology and Needs Assessment ..... 9

5 Evidence base ..... 10

6 Criteria for Commissioning ..... 18

7 Patient Pathway ..... 20

8 Governance Arrangements ..... 23

9 Mechanism for Funding ..... 23

10 Audit Requirements ..... 23

11 Documents which have informed this Policy ..... 23

12 Date of Review ..... 23

References ..... 24

## **Policy Statement**

NHS England will commission surgical sperm retrieval for male infertility in accordance with the criteria outlined in this document. In creating this policy NHS England has reviewed this clinical condition and the options for its treatment. It has considered the place of this treatment in current clinical practice, whether scientific research has shown the treatment to be of benefit to patients, (including how any benefit is balanced against possible risks) and whether its use represents the best use of NHS resources. This policy document outlines the arrangements for funding of this treatment for the population in England.

## **Equality Statement**

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities

## **Plain Language Summary**

### **About male infertility**

In conception, sperm is required to fertilise the egg.

- There are some conditions where men are unable to produce sperm, or they produce less sperm than normal.
- Sperm cells are carried in a fluid called semen - some men may have a blockage that stops the sperm being released into the semen during sexual intercourse.

Men who cannot produce or release sperm will be unable to conceive through sexual intercourse - this known as 'infertility'.

### **About the current treatment**

Treatment for male infertility is not always available - it varies between regions.

### **About the new treatment**

Surgical sperm retrieval is the process of retrieving the sperm so it can be used to fertilise an egg or be frozen for future use. Sperm is retrieved from either:

- the testicles - where sperm is produced
- the epididymis - where sperm is stored.

Retrieving sperm in this way allows patients to follow assisted reproductive techniques to try to have children with their own genetic make-up. The other options are to use donor sperm (i.e. from another male) or to adopt.

### **What we have decided**

NHS England has carefully reviewed the evidence for use of surgical sperm retrieval procedures in specific patient groups. We have concluded that there is enough evidence to make the treatment available. However, patients must have confirmed funding for the next stages of the treatment process, including freezing of the sperm (cryopreservation) and/or IVF treatment.

## 1 Introduction

This document describes the evidence that has been considered by NHS England in formulating a proposal to routinely commission surgical sperm retrieval for patients with obstructive and non-obstructive azoospermia.

Surgical sperm retrieval is the retrieval of sperm for fertilisation from the epididymis or testicles to assist conception for couples where the male partner suffers from azoospermia. The retrieved sperm is used immediately for fertilisation or stored for future fertility treatment. This enables men to father their own genetic offspring through intra-cytoplasmic sperm injection (ICSI) fertility treatment. The alternative would be to use donor sperm or to adopt.

Surgical sperm retrieval includes the following techniques:

- Percutaneous epididymal sperm aspiration (PESA)
- Microsurgical epididymal sperm aspiration (MESA)
- Testicular sperm aspiration (TESA), also described as testicular fine needle aspiration (TEFNA)
- Testicular sperm extraction (TESE)
- Microdissection testicular exploration and sperm extraction (mTESE)

In obstructive azoospermia, sperm can usually be obtained from the epididymis (PESA or MESA) and from the testis (TESA or TESE or mTESE).

In non-obstructive azoospermia, sperm needs to be obtained directly from the testis by (TESA or TESE or mTESE)

## 2 Definitions

**Azoospermia:** A lack of measurable sperm in the male's semen.

**Obstructive azoospermia:** Sperm are produced by the testes, but are unable to be found in the ejaculated semen because of a blockage to the sperm transport or absence of the vas.

**Non-obstructive azoospermia:** The testicles are either producing no sperm or very low numbers of sperm and sperm is not present in the ejaculate.

**Percutaneous epididymal sperm aspiration (PESA):** the collection of sperm through a fine needle inserted directly from the epididymis, where sperm is stored, after it is formed in the testes.

**Microsurgical epididymal sperm aspiration (MESA):** the collection of sperm with an operating microscope directly from an epididymal tubule.

**Testicular sperm aspiration (TESA):** the collection of sperm by placing a needle attached to a syringe through the skin of the scrotum and sucking out the fluid and small quantities of tissue from inside the testicle. It is also described as testicular fine needle aspiration (TEFNA).

**Testicular sperm extraction (TESE):** the collection of sperm from a biopsy or several biopsies from the testicular tissue after making an incision in the scrotal skin and usually used for non-obstructive azoospermia.

**Microdissection TESE (mTESE):** a similar technique to TESE but an operating microscope is used to identify the best tissue within the testicle which has the highest probability of containing mature sperm. This aims to cause less damage to the structure inside the testicle and reduce the volume of tissue removed, and to therefore have fewer after effects such as blood supply problems caused by tiny



blood vessels being cut. It also appears to increase the number of successful sperm retrievals.

### **3 Aims and Objectives**

The policy aims to define NHS England's commissioning approach for surgical sperm retrieval for men with azoospermia to surgically extract sperm to assist conception.

The objective is to ensure evidence based commissioning with a view to improving outcomes for men with azoospermia and their partners.

### **4 Epidemiology and Needs Assessment**

The prevalence of azoospermia is 1% in men, of whom 15%-20% have obstructive azoospermia.

In 2013, 11,712 fresh cycles of ISCI were due to only male factor infertility (Human Fertilisation & Embryology Authority, 2014) and of those, it is estimated that 10% (1,171) were due to azoospermia.

Of the patients with azoospermia, an estimated 10% (117) of patients will have had certain Y chromosome deletions meaning they were not eligible for surgical sperm retrieval. In addition, an estimated 10-20% (117-234) of patients will have chosen not to undertake surgical sperm retrieval or have looked for alternative fertility treatments. Therefore approximately 819-936 patients were eligible for surgical sperm retrieval.

There were 694 procedures of surgical sperm retrieval in England in 2013/14. The breakdown of 694 surgical sperm retrieval procedures, including some repeat procedures, is as follows:

OPCS Code	Description	Type	No. of procedures
N34.2	Collection of sperm NEC	All	35
N34.4	Microsurgical epididymal sperm aspiration	MESA	159
N34.5	Percutaneous epididymal sperm aspiration	PESA	144
N34.6	Testicular sperm extraction	TESA/TEFNA/ TESE/mTESE	356
<b>Total</b>			<b>694</b>

The number of men with azoospermia requiring surgical sperm retrieval is expected to rise slightly in future years due to increased obesity rates, greater patient awareness of surgical sperm retrieval techniques and increased access of patients to cancer treatments which result in azoospermia. However, total demand is not expected to exceed approximately 900 cases per year.

## 5 Evidence base

NHS England has concluded that there is sufficient evidence to support a proposal for the routine commissioning of PESA, MESA and TESA for males with obstructive azoospermia and mTESE for males with non-obstructive azoospermia to assist conception.

### **Evidence review summary for surgical sperm retrieval techniques for non-obstructive azoospermia (including Klinefelter Syndrome and Y chromosome deletions)**

In summary, and consistent with NICE's findings in 2013, the best method of extracting spermatozoa from the testicular tissue in non-obstructive azoospermia is uncertain due to a lack of evidence regarding the relative merits of TESA and TESE using small (5mm), multiple or large (10-15mm) biopsies. Their evidence review found that compared with TESE, TESA has a reduced rate of sperm recovery but is less invasive (level 3 evidence). (NICE 2013)

A 2008 Cochrane review (Cochrane Database Systematic Review, 2008) on techniques for surgical retrieval of sperm for azoospermic men undergoing ICSI

concluded there was insufficient evidence to recommend any specific sperm retrieval technique. The review was restricted to RCTs and results was based on two RCTs studying microsurgical epididymal sperm aspiration (MESA) and testicular aspiration techniques (TESA/TESE/mTESE).

A review of published studies up to October 2015 found some evidence that mTESE is better than TESE, but there is a lack of data on important clinical measures such as long term complication rates, viability of the retrieved sperm and pregnancy rates. The generalisability of the results are limited due to the lack of good quality studies in the review (level of evidence SIGN 2- to 3).

### **Comparison of sperm retrieval success rates of microsurgical TESE (mTESE) v conventional TESE (TESE) in men with non-obstructive azoospermia**

There are no new randomised controlled trials or good quality observational studies comparing TESE with mTESE since the last Cochrane update in 2008. The evidence comparing TESE and mTESE in men with non-obstructive azoospermia is available from three systematic reviews (Donoso et al., 2007, Deruyver et al., 2014 and Bernie et al., 2015) which are predominantly based on retrospective or prospective case series (SIGN level of evidence 2- to 3). Of the three reviews, the latest systematic review by Bernie et al. (2015) provides the most comprehensive evidence available so far comparing TESE and mTESE. This review by Bernie et al. (2015) includes the majority of studies included in the previous two reviews by Donoso et al. (2007) and Derutver et al. (2014). The systematic review by Bernie et al. (2015) is presented with a good study design, inclusion and exclusion criteria and sound methodology for data synthesis and meta-analysis. The results of this review show that mTESE was 1.5 times more likely (95% CI 1.4–1.6) to result in successful sperm retrieval compared with TESE in men with non-obstructive azoospermia.

Donoso et al. (2007) found that mTESE performs better than TESE only in patients with Sertoli-cell-only syndrome where tubules containing active foci of spermatogenesis can be identified, but this could not be verified from the systematic review by Bernie et al. (2015). The available evidence on complication rates suggests that mTESE is safer than TESE, with fewer complications including

haematoma fibrosis, and testicular atrophy (Donoso et al., 2007), however the rates varied from study to study. There is no data from any of the three systematic reviews on the viability of retrieved sperm and the information on pregnancy rates or live birth is inadequately presented to draw any conclusions.

### **Successful sperm harvesting and retrieval in men with Klinefelter syndrome**

Based on one systematic review by Mehta et al. (2012), the average overall sperm retrieval rate in patients with Klinefelter syndrome was 51%, with a range of 28%–69% at various centres, using different surgical techniques. mTESE had higher retrieval rates compared to TESE (61% vs.47%). Studies varied in their conclusions as to predictors of sperm retrieval. Positive predictors included younger age and pre-operative T levels close to or within the normal range, either at baseline or with hormone treatment (aromatase inhibitors, clomiphene citrate, or hCG). Serum LH, FSH levels and testicular volume, were not predictive of testicular spermatogenic function. Results for pre-treatment testicular histology as a predictor was variable, with some showing a positive relationship and others showing no relationship. Due to the lack of meta-analysis in the systematic review and poor quality of studies identified in the review (all were retrospective case series with no randomisation or control group with heterogeneity of laboratory methods) the generalisability of these results are limited.

### **Y Chromosomal deletions including microdeletions of Y chromosome, including in the AZFa, AZFb, AZFc and combined-region deletions**

Patients with deletions in the AZFc region, the most common microdeletion seen, are often able to have successful sperm retrieval with mTESE. In two retrospective studies with more than 100 patients with microdeletion (Stahl et al., 2010 and Park et al., 2013) the sperm retrieval rate in patients AZFc microdeletion ranged from 54.1% to 71.4% but that there was no sperm retrieved in any men with AZFa and AZFb. In patients with AZFb + c, the study by Park et al. (2013) showed a success rate of 7.1%.

Additionally, there are good clinical outcomes of fertilisation in people with AZFc deletions. A Chinese study of 143 people with Y chromosome AZFc microdeletion in ICSI cycles (Liu et al., 2013), showed the clinical success rates (transferred embryos, good embryo rates, implantation rates, clinical pregnancy rates, ectopic pregnancy rates, miscarriage rates, preterm birth rates, new-born height and weight, and birth defects) in the AZFc deletion group was similar to those with normal Y chromosomes in ICSI ( $p>0.05$ ).

In summary, there is consistent evidence that patients with deletions in the AZFc region, the most common microdeletion seen, have higher rates of successful sperm retrieval with mTESE compared to patients with in AZFa, AZFb or combined-region deletions.

### **Evidence review summary for surgical sperm retrieval techniques for obstructive azoospermia**

In summary, there is insufficient evidence to recommend one surgical sperm retrieval technique over another for men with obstructive azoospermia.

According to the NICE Clinical Guideline (2013) there is no consistent relationship between the type of surgical sperm retrieval and pregnancy rates and they found that epididymal and testicular spermatozoa yield similar fertilisation, cleavage and ongoing pregnancy rates using ICSI (evidence level 3).

The NICE review (2013) suggests that when spermatozoa cannot be recovered by one technique another one can be employed, for example, TESE after MESA. Spermatozoa obtained from testicular aspiration can be successful in achieving fertilisation and pregnancies for couples in whom epididymal aspiration failed.

### **Clinical effectiveness of PESA, TESA, MESA, cTESE and mTESE in men with obstructive azoospermia**

Obstructive azoospermia is characterised by normal testicular function (with normal sperm production), the absence of spermatozoa in semen, and genital tract

obstruction. Obstructive azoospermia accounts for approximately 15%-20% of all azoospermia cases. Obstructive azoospermia can be congenital or acquired and causes can be divided into intra-testicular, epididymal, vasal, and ejaculatory duct obstruction. Post-vasectomy obstruction and congenital bilateral absence of the vas deferens (CBAVD) are the most common causes of Obstructive azoospermia.

Testicular or epididymal sperm retrieval (combined with ICSI) is an option for men with obstructive azoospermia. The evidence of effectiveness for the above methods comes from two systematic reviews (Cochrane 2008 and NICE evidence review 2013) and a number of retrospective case series.

The Cochrane review (Cochrane review, 2008) included two RCTs. The first RCT (Yamamoto et al., 1996) compared microsurgical epididymal sperm aspiration (MESA) versus micropuncture with perivascular nerve stimulation for patients with surgically irreparable vasal obstruction (CBAVD and failed vasovasostomy). This study reported lower pregnancy (OR 0.19, 95% CI 0.04 to 0.83) and fertilisation rates (OR 0.16, 95% CI 0.05 to 0.48) in the MESA group (evidence level 1a).

Another RCT from Israel (Belenky, 2001) compared percutaneous testicular aspiration with ultrasound guidance (TESA with US) versus percutaneous testicular aspiration without ultrasound guidance (TESA) in 39 participants. There was no statistically significant difference between the two groups. TESA with US in pregnancy in three out of sixteen participants compared with four out of 23 participants (odds ratio 1.10, 95% CI 0.21 to 5.74).

The NICE review (2013) reported very low failure rates for surgical sperm retrieval methods:

- MESA: 1.7% of men (1/59) - 22% of men (2/9),
- PESA: 5% in men with failed reversed vasectomy, 11% in men with CBAVD and 15.8% to 17% of initiated cycles,
- TESA: 0%.

These methods were found to be effective in men with CBAVD and in those with failed reversal of vasectomy, the main causes of obstructive azoospermia.

Bernie et al (2015) reported the following outcome rates by various techniques:

- MESA: performed under general or regional anaesthesia with a sperm retrieval rate of 95%–100% of cases. Yield- 15–95\*10<sup>6</sup> total sperm with 15%–42% total motility, cryopreservation possible in 98%–100% of cases with an average of 5.3–7.6 vials per patient.
- PESA: performed under local anaesthesia with a sperm retrieval rate of 80%–100%. Yield-Thousands to millions of sperm with variable motility (poorly reported in most studies), cryopreservation possible in 43%–96% of cases.
- TESA (Testicular fine needle aspiration): performed under local anaesthesia with a sperm retrieval rate of 52%–100%. Yield-Hundreds of thousands to millions of sperm with variable motility (poorly reported in most studies), cryopreservation possible in 38% of cases in one study.
- TESA (Testicular large needle aspiration): performed under local anaesthesia with a sperm retrieval rate of 98%–100%. Yield-Hundreds of thousands to millions of sperm with variable motility (poorly reported in most studies), cryopreservation possible in 100% of cases in one study.
- TESA (Testicular core needle biopsy): performed under local anaesthesia with a sperm retrieval of 82%–100%. Yield-Hundreds of thousands to millions of sperm with variable motility (poorly reported in most studies), often sufficient for cryopreservation (poorly reported).
- TESE: performed under local or general anaesthesia with a sperm retrieval rate of 100%. Yield-Hundreds of thousands to millions of sperm in most cases (poorly reported in most studies), usually sufficient for cryopreservation (poorly reported).
- mTESE: performed under local or general anaesthesia with sperm retrieval rate of 100%. Yield-Hundreds of thousands to millions of sperm in most cases (poorly reported in most studies), usually sufficient for cryopreservation (poorly reported).

A study by Kovac et al. (2013), of 51 men with obstructive azoospermia undergoing PESA plus ICSI reported 100% success rate for sperm retrieval, 78% fertilization and 49% pregnancy rate. Another study by Yafi et al. (2013) of 255 men with obstructive azoospermia undergoing PESA for sperm retrieval reported a success rate of 77% and suggested that younger age was positively related to successful retrieval of motile sperm.

A recent study by van Wely et al. (2015) of 374 patients comparing MESA-ICSI (280) with TESE-ICSI (94) reported a significantly better outcome from MESA-ICSI, including the amount of sperm extracted ( $p < 0.001$ ), higher proportion of frozen cycles (60 vs 15%,  $p < 0.001$ ), higher live birth rates (39 vs 24%,  $p = 0.001$ ) and higher clinical and ongoing pregnancy rates (47 vs 39%).

**Evidence review summary for other questions considered by the review:**

**Predictive factors for successful sperm retrieval in non-obstructive azoospermia (histology, FSH, inhibin, testosterone, testicular volume)**

The evidence for predictive factors for successful surgical sperm extraction comes from a number of retrospective and prospective studies, one review article (Bernie et al., 2013) and one systematic review (Yang et al., 2015), which evaluates FSH as a predictor for sperm retrieval in non-obstructive azoospermia. Based on the review by Bernie et al. (2013), the only good predictor of successful retrieval was testicular histology but having to perform a separate surgical procedure for diagnosis limits its use, as a simultaneous sperm retrieval can be undertaken. There is no clear relationship between successful sperm retrieval and serum FSH or serum inhibin –B levels, or testicular volume. Models to calculate the predictivity rates with data crossed with other parameters (age, duration of fertility and hormonal (LH, testosterone, prolactin)) have not shown to be useful in predicting successful sperm extraction.

In a study by Hussein et al. (2013) the rate of successful sperm extraction using mTESE was compared in two groups of men with azoospermia, one study (496 males) receiving clomiphene citrate and another group of (119 males) with no clomiphene citrate treatment. Patients receiving clomiphene citrate had higher rates of successful sperm retrieval compared to those who did not receive medication (57% vs 34%). However, due to the lack of randomisation, lack of information on baseline characteristics of the two groups and possible bias due to patient selection methods, the results cannot be generalised.

In summary, there is no clear relationship between successful sperm retrieval and serum FSH or serum inhibin –B levels, or testicular volume. The only good predictor



of successful retrieval was testicular histology but the requirement of a separate surgical procedure for diagnosis limits its use.

### **Patients with varicoceles and non-obstructive azoospermia**

Evidence on the impact of surgical repair of a varicocele in patients with non-obstructive azoospermia comes from a meta-analysis of 11 studies with 233 men with clinical varicocele and non-obstructive azoospermia (Weedin et al. 2010). At a mean follow up of 13 months, motile sperm was found in 39% of study subjects; pregnancy was achieved in approximately 26% of men with sperm in the ejaculate (60% unassisted and 40% assisted with IVF).

The probability of successful varicocele repair was significantly greater for patients with azoospermia due to hypospermatogenesis or late maturation arrest than for those with Sertoli-Cell-Only (Odds Ratio 9.4; 95% CI 3.2-27.3).

### **Success rates of repeat sperm retrieval surgery in men with non-obstructive azoospermia**

The evidence for success rates of repeat sperm retrieval surgery in men with non-obstructive azoospermia is based on a very small number of retrospective case series with varying patient selection criteria and methodologies. The success rate of repeat TESE varied from 30% (Haimov-Kochman et al., 2009) to 41.6% (Vernaev et al., 2006) in the first repeat attempt and the success rate increased to 100% for two patients with six attempts (Vernaev et al., 2006), there are limitations of this evidence as only 2 out of 628 patients in the study reached six attempts, hence it is difficult to generalise.

One retrospective case series of repeat mTESE (Ramasamy et al., 2011) showed a success rate of 82%. The study identified lower follicle-stimulating hormone level and larger testicular volume to have a predictive value in determining the success of a second attempt. The findings of the study are limited by its retrospective, nonrandomized, non-controlled nature.

In summary, there is low level evidence from retrospective case series that the cumulative success rate of repeat sperm retrieval increases with increasing numbers of attempts and is higher in males who have had a previous successful attempt. The results are not substantiated by other studies, hence the replicability of these results in other patients or settings is limited.

### **Comparison of psychosocial impact of men with successful and unsuccessful surgical sperm retrieval**

No evidence was identified from the literature search to compare the psychosocial impact of men with successful and unsuccessful surgical sperm retrieval.

Congenital disorders in live births following ICSI using sperm from TESE or mTESE in non-obstructive azoospermic men

No evidence was identified from the literature search to compare the risk of congenital disorders in live births following ICSI using sperm from TESE or mTESE in non-obstructive azoospermic men.

### **Likelihood of multiple pregnancy following ICSI using surgical sperm retrieval**

No evidence was identified from the literature search to compare the risk of multiple pregnancy following ICSI using surgical sperm retrieval.

## **6 Criteria for Commissioning**

### **Inclusion Criteria:**

• Males who either:

(i) Have been diagnosed with azoospermia by a urologist with an interest in male infertility problems in a specialised urology centre with established links with an HFEA licenced facility centre; OR

## OFFICIAL

(ii) Are prior to surgery or chemotherapy that would result in infertility, and who cannot produce sufficient sperm for storage (in number or quality of sperm, as determined by an embryologist);

AND

- The patient has a reasonable likelihood of successful retrieval of motile sperm; AND
- The patient has confirmed funding for subsequent stages of the pathway (cryopreservation and/or IVF treatment); AND
- Facilities for sperm storage are available.

PESA, MESA, TESE or TESA will be commissioned for:

- Men with obstructive azoospermia who meet the inclusion criteria above
- Men prior to surgery or chemotherapy that would result in infertility who meet the inclusion criteria above

mTESE will be commissioned for:

- Men with non-obstructive azoospermia, who meet the inclusion criteria above (including patients with Klinefelter's syndrome and patients with AZFc Y chromosome deletion who have been provided information of the ethical issues by a urologist)
- Men with obstructive azoospermia where PESA, MESA, TESA or TESE has failed and they require a repeat procedure
- Men prior to surgery or chemotherapy where PESA, MESA, TESA or TESE has failed and they require a repeat procedure
- Men who have had one failed attempt with mTESE, if there is histological evidence of sperm on the testicular biopsy but no sperm found at the operation

### **Exclusion criteria:**

- Men with non-obstructive azoospermia caused by AZFa or AZFb Y chromosome deletions
- Men with obstructive azoospermia caused by vasectomy
- Men with uncontrolled or irreversible coagulopathy, uncorrected undescended testes, absent testicle, or untreated hypogonadotropic hypogonadism
- Purely diagnostic histological biopsies, without planned subsequent sperm retrieval, are excluded

**Stopping criteria:**

- After the second failed attempt at mTESE

## 7 Patient Pathway

Patients will see their GP and are offered an initial assessment, including a semen analysis. If the result of the first semen analysis is abnormal, a repeat confirmatory test will be offered in an accredited laboratory in primary care or at a hospital. If a gross spermatozoa deficiency (azoospermia or severe oligozoospermia) has been detected the repeat test will be undertaken as soon as possible.

The infertile couple's management will be discussed by a urologist with an interest in male infertility within a specialised urology centre and the urologist will either make the azoospermia diagnosis and discuss treatment options with the patient or may refer patients to a specialist MDT for alternative treatments. In difficult cases or cross referral, a MDT will make a decision about onward referral. Patients with Klinefelter's syndrome and patients with AZFc Y chromosome deletion will be provided information of the ethical issues by a urologist.

Patients are treated as part of a specialist fertility MDT that should primarily include urologists, the reproductive medicine physician and the scientific team. The reporting laboratory should meet national quality standards, as defined by NICE.

Patients prior to surgery or chemotherapy that would result in infertility, and who cannot produce sufficient sperm for storage (in number or quality of sperm, as determined by an embryologist) would be offered surgical sperm retrieval and follow the obstructive azoospermia treatment pathway.

PESA for obstructive azoospermia can be provided within HFEA-licensed units by Reproductive Medicine specialists, with subspecialty training in Reproductive Medicine, who are trained to assess azoospermic men and perform surgical sperm retrieval procedures.

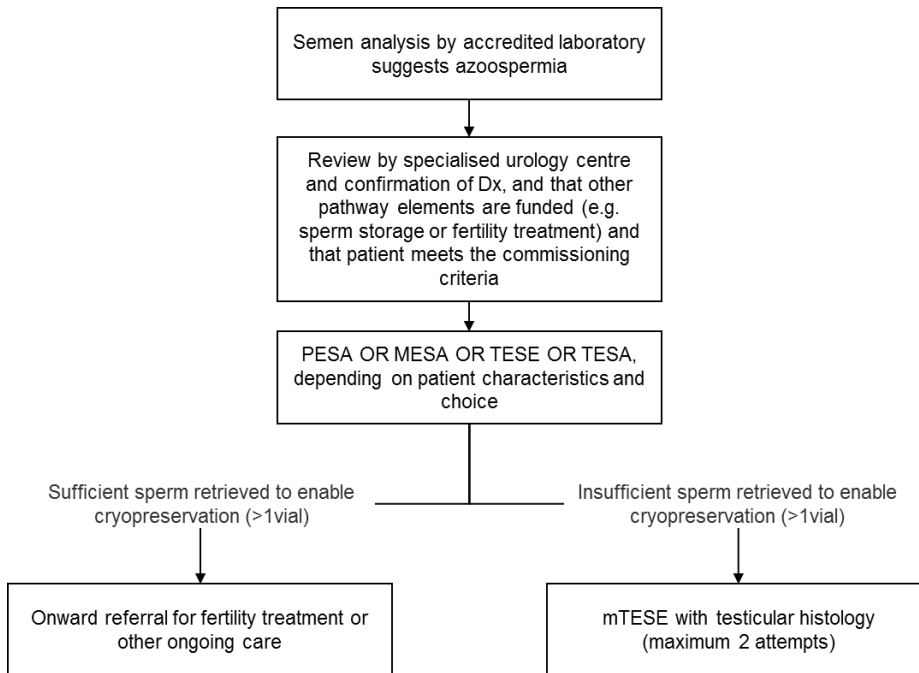
## OFFICIAL

Procedures are carried out as a day case, with the use of a local anaesthetic or under general anaesthetic, as is the case for mTESE, by individuals that have undertaken appropriate and accredited scrotal surgery training. The testicular tissue or aspiration collected is examined and patients are advised about the quality of the material and whether there is any sperm present. When sperm is present, the specimen is frozen and placed in storage for use at a later stage. These specimens are thawed and used to inject the eggs obtained during IVF treatment using the technique of ICSI. Alternatively, ICSI fertility treatment can be synchronous with the sperm retrieval for cases of non-obstructive azoospermia due to poorer freeze-thaw rates of the lower quality sperm.

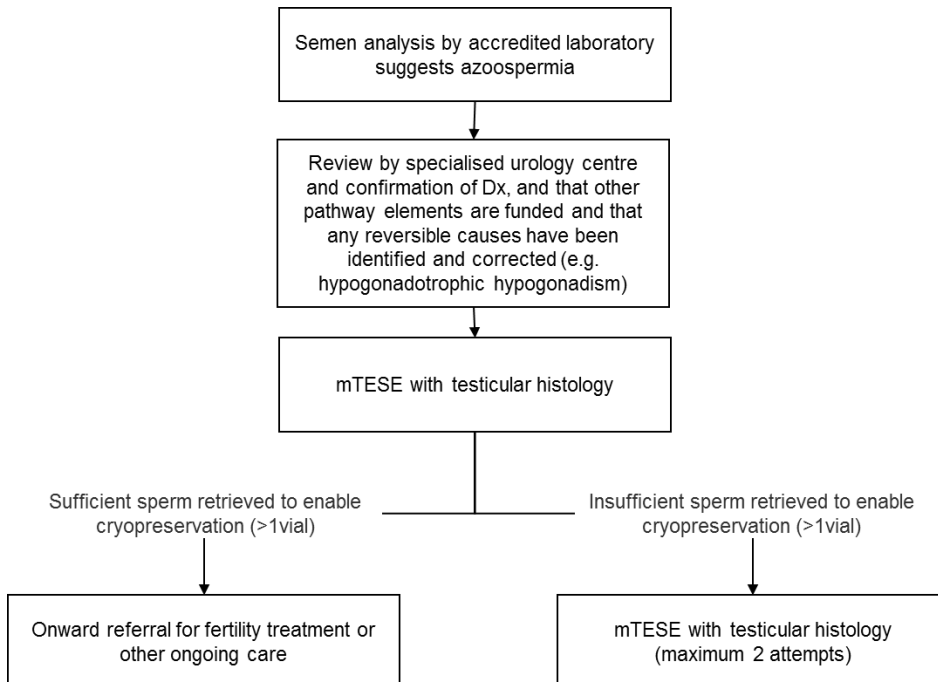
For patients who have had failed attempts at sperm retrieval with PESA, MESA, TESA or conventional TESE, mTESE will be the next treatment available. Repeat attempts of mTESE will be available to men who have had failed prior attempts with mTESE, if there is histological evidence of sperm on the testicular biopsy but no sperm found at the operation.

Following surgery, patients will have a joined-up management plan that includes a follow-up to understand if they are at risk from hypogonadism and to understand what their fertility treatment options are. If surgical sperm retrieval is unsuccessful, other fertility options available are to use donor sperm or adopt.

### Obstructive Azoospermia Pathway



### Non-obstructive Azoospermia Pathway



## **8 Governance Arrangements**

The specialist fertility MDT will include as a minimum urologist, reproductive medicine physician and embryologist.

Specialised centres must have a fertility laboratory with facilities to store sperm.

The reporting laboratory must meet National Quality standards.

Fertility centres must register with, and be governed by, HFEA.

## **9 Mechanism for Funding**

Surgical sperm retrieval will be funded by the local specialised commissioning team via a contract with the urology provider.

Cryopreservation and/or IVF treatment are commissioned by CCGs.

## **10 Audit Requirements**

As per national quality standards and HFEA audit requirements.

## **11 Documents which have informed this Policy**

National Institute for Health and Care Excellence Clinical Guideline 156 Fertility problems: assessment and treatment. 2013.

## **12 Date of Review**

This document will be reviewed when information is received which indicates that the policy requires revision.

## References

Belenky, A.; Avrech OM.; Bachar N.; Zuckerman Z.; Ben Rafael Z.; Fisch B.; Cohen M. J Clin Ultrasound. 2001; 29(6): 339-43.

Bernie, Aaron M.; Ramasamy, Ranjith; Stember, Doron S.; Stahl, Peter J.. Microsurgical epididymal sperm aspiration: indications, techniques and outcomes. Asian Journal of Andrology. 2013.

Bernie, Aaron M.; Mata, Douglas A.; Ramasamy, Ranjith; Schlegel, Peter N.. Comparison of microdissection testicular sperm extraction, conventional testicular sperm extraction, and testicular sperm aspiration for nonobstructive azoospermia: a systematic review and meta-analysis. Fertil. Steril.. 2015, 8.

Van Peperstraten, A.; Proctor, M. L.; Johnson, N. P.; Philipson, G.. Techniques for surgical retrieval of sperm prior to intra-cytoplasmic sperm injection (ICSI) for azoospermia. Cochrane Database Syst Rev. 2008.

Donoso, P.; Tournaye, H.; Devroey, P.. Which is the best sperm retrieval technique for non-obstructive azoospermia? A systematic review. Hum. Reprod. Update. 2007, Human Fertilisation & Embryology Authority, 2014.

Hussein, Alayman; Ozgok, Yasar; Ross, Lawrence; Rao, Pravin; Niederberger, Craig. Optimization of spermatogenesis-regulating hormones in patients with non-obstructive azoospermia and its impact on sperm retrieval: a multicentre study. BJU Int.. 2013.

Kovac, Jason R.; Lehmann, Kyle J.; Fischer, Marc Anthony. A single-center study examining the outcomes of percutaneous epididymal sperm aspiration in the treatment of obstructive azoospermia. Urology Annals. 2014.

Lin, Y. M.; Hsu, C. C.; Kuo, T. C.; Lin, J. S.; Wang, S. T.; Huang, K. E.. Percutaneous epididymal sperm aspiration versus microsurgical epididymal sperm aspiration for



irreparable obstructive azoospermia--experience with 100 cases. Journal of the Formosan Medical Association = Taiwan Yi Zhi. 2000.

Mehta, Akanksha; Paduch, Darius A.. Klinefelter syndrome: an argument for early aggressive hormonal and fertility management. Fertil. Steril.. 2012.

Ranjith Ramasamy, Joseph A. Ricci, Robert A. Leung, Peter N. Schlegel . Successful Repeat Microdissection Testicular Sperm Extraction in Men With Nonobstructive Azoospermia . The Journal of Urology . 2011.

Stahl PJ1, Masson P, Mielnik A, Marean MB, Schlegel PN, Paduch DA.. A decade of experience emphasizes that testing for Y microdeletions is essential in American men with azoospermia and severe oligozoospermia.. Fertil Steril. 2010 .

Valérie Vernaëve 1, 3, G. Verheyen 2, A. Goossens 2, A. Van Steirteghem 2, P. Devroey 2 and H. Tournaye 2 . How successful is repeat testicular sperm extraction in patients with azoospermia. Hum. Reprod. . 2006.

Yang, Qi; Huang, Yan-Ping; Wang, Hong-Xiang; Hu, Kai; Wang, Yi-Xin; Huang, Yi-Ran; Chen, Bin. Follicle-stimulating hormone as a predictor for sperm retrieval rate in patients with nonobstructive azoospermia: a systematic review and meta-analysis. Asian J. Androl.. 2015.