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Contents

Acronyms:

ART	Assisted Reproductive Technique
S/A	Semen analysis
NOA	Non-obstructive azoospermia
OA	Obstructive azoospermia
OAT	Oligo-Astheno-Teratospermia
mTEST	Microdissection Testicular Sperm Extraction
ICSI	Intra-Cytoplasmic Sperm Injection
IUI	Intra-Uterine Insemination
RPL	Recurrent pregnancy Loss
IVF	In Vitro Fertilization
CFTR	Cystic Fibrosis Trans-membrane conductance Regulator
VD	Vas Deferens
CBAVD	Congenital Bilateral Absence of the Vas Deferens
CUAVD	Congenital Unilateral Absence of the Vas Deferens

1. Definitions:

1.1 **Male infertility**: the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse

1.2 **Primary male infertility**: male who has never initiated a clinical pregnancy and meet the citeria of being classified as infertile.

1.3 **Secondary infertility:** a couple where the man is unable to initiate a clinical pregnancy but who had previously initiated a clinical pregnancy (with the same or different sexual partner)

1.4 **RPL**: two or more failed pregnancies.

1.5 **Azoospermia**: absence of sperms in ejaculate

1.6 **Oligospermia:** sperm concentration less than 15 million/ml

1.7 **Severe Oligospermia**: sperm concentration less than 5 million/ ml

1.8 **Pyospermia**: white blood cells more than 1 million / ml

1.9 **Hypogonadotrophic Hypogonadism:** is secondary hypogonadism

1.10 **Hypergonadotrphic Hypogonadism:** primary testicular failure with high FSH and LH

Chapter 1

2. Introduction:

Male infertility refers to the inability of a male to achieve pregnancy in a fertile female partner. Approximately 15% of couples are unable to conceive after one year of unprotected intercourse. A male factor is solely responsible in about 20% of infertile couples and informative in another 30-40%. Male factor infertility may be explained by an abnormal SA or by other sperm function defects, in the setting of a normal SA as well as functional male defects. Male infertility can be due to a variety of conditions. Some of these conditions are identifiable and reversible, such as ductal obstruction and HH. Other conditions are identifiable and treatable but not reversible, such as bilateral testicular atrophy secondary to viral orchitis. Identification of the etiology of an abnormal SA is not possible in approximately 30% of men in which case this condition is termed idiopathic male infertility. When the reason for infertility is not clear with a normal SA and partner evaluation the infertility is termed unexplained, which is found in up to approximately 25% of couples

3. Purpose:

The purpose of this guideline are to standardize the evaluation and management of the male in an infertile couple which include the following:

a. an appropriate history
b. physical exam as well as diagnostic testing
c. Medical therapies
d. surgical techniques
e. use of intrauterine insemination (IUI)/in vitro fertilization (IVF)/intracytoplasmic sperm injection (ICSI) are covered to allow for optimal patient management

4. Scope:

This guideline applies for all healthcare professions dealing with management of male infertility in Fertility center at DGKH

5. Structure:

5.1 Assessment:

5.1.1 For initial infertility evaluation, both male and female partners should undergo concurrent assessment.

5.1.2 Initial evaluation of the male for fertility should include a reproductive history.

5.1.3 Initial evaluation of the male should also include one or more semen analyses.

5.1.4 The SA should include measures of semen volume, pH if indicated, sperm concentration/sperm count, sperm motility, and sperm morphology at least two SAs obtained a month apart are important to consider, especially if the first SA has abnormal parameters

5.1.5 In couples with failed ART cycles or recurrent pregnancy losses (RPL) (two or more losses), evaluation of the male should be considered including: Evaluation of sperm DNA fragmentation and karyotype testing of the male.

5.1.6 The results from the SA should be used to guide management of the patient. In general, results are of greatest clinical significance when multiple abnormalities are present

5.1.7 Clinicians should obtain hormonal evaluation including follicle-stimulating hormone (FSH) and testosterone for infertile men with impaired libido, erectile dysfunction, oligozoospermia or azoospermia, atrophic testes, or evidence of hormonal abnormality on physical evaluation

5.1.8 Testosterone levels should be defined based upon a blood sample drawn in the morning Endocrine testing is also suggested for oligozoospermic patients, particularly, men with sperm concentrations below 10 million/mL.

5.1.9 If the fasting morning total testosterone level is low (<300 ng/dL), a repeat measurement of total and free testosterone (or bioavailable testosterone) as well as determination of serum LH, estradiol, and prolactin levels should be obtained

5.1.10 Azoospermic men should be initially evaluated with semen volume, physical exam, and FSH levels to differentiate genital tract obstruction from impaired sperm production.

5.1.11When a semen analysis shows azoospermia, a second SA should be performed at least one to two weeks later.

A low volume, acidic pH, azoospermic ejaculate can be indicative of obstruction in the genital tract. Obstructive azoospermia is suspected if the physical examination reveals testes of normal size, fully descended into the scrotum and bilaterally indurated epididymides with or without absence of the vas deferens. In these cases, FSH levels are usually less than approximately 7.6 IU/L). In contrast, when the testes are atrophied and soft, especially in the presence of FSH greater than 7.6 IU/L, the results are suggestive of spermatogenic failure rather than obstructive azoospermia.

5.1.12 Karyotype and Y-chromosome microdeletion analysis should be recommended for men with primary infertility and azoospermia or severe oligozoospermia (<5 million sperm/mL) with elevated FSH or testicular atrophy or a presumed diagnosis of impaired sperm production as the cause of azoospermia such as Klinefelter syndrome (the presence of extra X chromosomes). The most common pattern is 47, XXY but more severe cases demonstrate 48, XXXY or 49, XXXXY, Men with Klinefelter syndrome.

5.1.13 Y chromosome microdeletions are the second most common known genetic cause of infertility in the male. Azoospermia Factor (AZF) region on the long arm of the human male chromosome consists of three areas encoding genes involved in spermatogenesis (AZFa, AZFb, and AZFc). Although sperm may be found in the ejaculate of some men and through TESE in approximately 50% of men with an AZFc deletion, sperm have not been retrieved by TESE in men with complete AZFa and/or AZFb microdeletions. Partial deletions of AZFa, AZFb, or AZFc are a bit more problematic to interpret because there is no standardization of the clinical Y diagnostic test for partial deletions of AZF sub regions as men with complete deletions of AZFa and/or AZFb should not undergo TESE for ART. Men with deletions of AZFc and smaller partial deletions of AZFa and/or AZFb should be counseled that sperm may or may not be found with TESE.

5.1.14 Clinicians should recommend Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) mutation carrier testing in men with vasal agenesis or idiopathic

obstructive azoospermia, for men who harbor a CFTR mutation, genetic evaluation of the female partner should be recommended.

5.1.15 Men with increased round cells on SA (>1million/mL) should be evaluated further to differentiate white blood cells (pyospermia) from germ cells by simple assay is the o-toluidine test for cellular peroxidase (peroxidase stain) that will not stain leukocytes that have released their granules or lymphocytes, macrophages, or monocytes, which do not contain peroxidase

5.1.16 Patients with pyospermia should be evaluated for the presence of infection antisperm antibody (ASA) testing should not be done in the initial evaluation of male infertility.

a. ASA can result from events such as trauma, mumps orchitis, testis malignancy, vasal obstruction, vasectomy that disrupts the blood-testis barrier, or the patency of the male genital tract allowing sperm antigens or genital tract infections to generate ASA.
b. ASA can result in sperm agglutination in the semen. ASA may be present without sperm agglutination and, conversely, agglutination may be present due to other factors, such as the presence of E.coli in the semen.
c. IgA and IgG antibodies are the predominant antibodies found in semen, while IgM is rarely found.
d. ASA can impair sperm-ova penetration; accordingly, ICSI will negate this issue

For couples with RPL, men should be evaluated with karyotype and sperm DNA fragmentation, the DNA fragmentation testing should be considered in couples with unexplained RPL. When present, various treatments have been employed including using TESE with ICSI, antioxidant administration, donor sperm, varicocele repair, and/or frequent ejaculation.

5.1.17 Diagnostic testicular biopsy should not routinely be performed to differentiate between obstructive azoospermia and non-obstructive azoospermia (NOA). Differentiation

of obstructive azoospermia from NOA may most frequently be predicted from clinical and laboratory results without the need for surgical diagnostic biopsy. FSH levels greater than 7.6 IU/L and testis longitudinal axis less than 4.6 cm indicate an 89% likelihood of spermatogenic dysfunction as the etiology.89 Conversely, FSH levels less than 7.6 IU/L and testis longitudinal axes greater than 4.6 cm indicate 96% likelihood of obstruction as the etiology.

5.2. Imaging:

5.2.1 Scrotal ultrasound should not be routinely performed in the initial evaluation of the infertile male, the scrotum may sometimes be difficult to examine, for example in an obese patient or when the dartos muscle remains highly contracted during the physical exam. In these infrequent cases, color doppler ultrasound may be used to examine spermatic cord veins. The standard definition of a varicocele with this technique is the presence of multiple large veins greater than 3 mm in diameter and reversal of blood flow with the Valsalva maneuver.

5.2.2 Clinicians should recommend TRUS in men with SA suggestive of ejaculatory duct obstruction (EDO) (i.e., acidic, azoospermic, semen volume <1.5mL, with normal serum T, p alpable vas deferens).

5.2.3 Clinicians should recommend renal ultrasonography for patients with vasal agenesis to evaluate for renal abnormalities

5.3 .Treatment Management:

5.3.1 Varicocelectomy

a. Surgical varicocelectomy should be considered in men attempting to conceive who have palpable varicocele(s), infertility, and abnormal semen parameters, except for azoospermic men
b. Clinicians should not recommend varicocelectomy for men with non-palpable varicoceles detected solely by imaging
c. For men with clinical varicocele and NOA, couples should be informed of the absence of definitive evidence supporting varicocele repair prior to ART

3.5.2 Sperm Retrieval:

a. For men with NOA undergoing sperm retrieval, microdissection testicular sperm extraction (TESE) should be performed

b. In men undergoing surgical sperm retrieval, either fresh or cryopreserved sperm may be used for ICSI

c. In men with azoospermia due to obstruction undergoing surgical sperm retrieval, sperm may be extracted from either the testis or the epididymis

5.3.3 For men with aspermia, surgical sperm extraction or induced ejaculation (sympathomimetics, vibratory stimulation or electro-ejaculation) may be performed depending on the patient's condition and clinician's experience

5.3.4 1Infertility associated with retrograde ejaculation (RE) may be treated with sympathomimetics and alkalinization of urine with or without urethral catheterization, induced ejaculation, or surgical sperm retrieval

5.3.5 Retrograde Ejaculation is present as demonstrated by postejaculatory urinalysis, various therapies may be required. These treatments include oral sympathomimetics with alkalinization of urine. These specimens may be collected from voided urine or with urethral catheterization. Many men with lack of emission associated with spinal cord injury or psychogenic an ejaculation may also respond to penile vibratory therapy.

5.3.6 For men with persistent lack of emission despite medical therapy, then electroejaculation, or surgical sperm retrieval may be employed based on severity, clinical presentation and response to other less invasive therapy.

5.4 Obstructive Azoospermia, Including Post-Vasectomy Infertility:

5.4.1 Couples desiring conception after vasectomy should be counseled that surgical reconstruction, surgical sperm retrieval, or both reconstruction and simultaneous sperm retrieval for cryopreservation are viable options.

5.4.2 Clinician1s should counsel men with vasal or epididymal obstructive azoospermia that microsurgical reconstruction may be successful in returning sperm to the ejaculate

5.4.3 For infertile men with azoospermia and EDO, the clinician may consider transurethral resection of ejaculatory ducts (TURED) or surgical sperm extraction, the findings on TRUS suggesting obstruction include seminal vesicle anterior- posterior diameter >15mm, ejaculatory duct caliber (>2.3mm), or dilated vasal ampulla (>6mm) as well as prostatic cysts (midline or paramedian (ejaculatory duct). If a seminal vesicle aspirate reveals the presence of sperm in an azoospermic man, then TURED may be offered.

5.5. Medical & Nutraceutical Interventions for fertility:

5.5.1 A clinician may advise an infertile couple with a low total motile sperm count on repeated SA that IUI success rates may be reduced, and treatment with ART (IVF/ICSI) may be considered

5.5.2 The patient presenting with Hypogonadotropic Hypogonadism (HH) should be evaluated to determine the etiology of the disorder and treated based on diagnosis.

5.5.3 Clinicians may use aromatase inhibitors (AIs), HCG, selective estrogen receptor modulators (SERMs), or a combination thereof for infertile men with low serum testosterone

5.5.4 Clinicians may consider use of AIs for men with testosterone deficiency and elevated estradiol levels.

5.5.5 Clinically, either HCG or SERMs may be considered for testosterone optimization in men with low or normal serum LH.

5.5.6 The infertile male with hyperprolactinemia should be evaluated for the etiology and treated accordingly as the following:

a. Men with decreased libido and/or impotence and/or testosterone deficiency accompanied by a low/low- normal LH level warrant measurement of serum prolactin to investigate for hyperprolactinemia.

b. If prolactin is mildly elevated (≤1.5 times the upper limit of normal), a repeat fasting prolactin should be drawn to rule out a spurious elevation.
c. For persistently elevated prolactin levels above the normal value without an exogenous etiology, MRI is indicated.
d. Dopamine agonists are the first- line treatment for patients with pituitary prolactinomas. Transsphenoidal surgery may be considered when dopamine agonist treatment is unsuccessful or if the patient prefers surgery to life-long therapy.
e. For men with hyperprolactinemia who do not have a pituitary adenoma, management should focus on treatment of the underlying condition or factor causing the elevated prolactin (e.g., treatment of hypothyroidism, medication changes for drugs associated with elevated prolactin levels).

5.5.7 Drugs that decrease dopaminergic inhibition of prolactin secretion also cause hyperprolactinemia. These include opioid analgesics, many antipsychotics and antidepressants, antiemetics, prokinetics, and antihypertensives. Hypothyroidism, stress, elevated estrogen levels, chronic renal failure, and chest wall injuries can increase prolactin levels

5.5.8 For men with idiopathic infertility, a clinician may consider treatment using an FSH analogue with the aim of improving sperm concentration, pregnancy rate, and live birth rate

5.6 Gonadotoxic Therapies and Fertility Preservation:

5.6.1 Clinicians should discuss the effects of gonadotoxic therapies and other cancer treatments on sperm production with patients prior to commencement of therapy.

5.6.2 Clinicians should inform patients undergoing chemotherapy and/or radiation therapy to avoid pregnancy for a period of at least 12 months after completion of treatment.

5.6.3 Clinicians should encourage men to bank sperm, preferably multiple specimens when possible, prior to commencement of gonadotoxic therapy or other cancer treatment that may affect fertility in men'

5.6.4 Clinicians should consider informing patients that a SA performed after gonadotoxic therapies should be done at least 12 months (and preferably 24 months) after treatment completion

5.6.5 Clinicians should inform men seeking paternity who are persistently azoospermic after gonadotoxic therapies that TESE is a treatment option

Chapter 3

6. **Responsibilities:**

6.1 Head of Obstetrics and Gynecology Department shall:

6.1.1 Ensure that all clinicians are ware and adhere the protocol.

6.2 All clinicians shall:

6.2.1 Adhere to this protocol.

6.2.2 Request investigations related infectious diseases for patient shifting to surgery.

6.2.3The consent should be prepared before surgery.

6.2 Director of Nursing Affairs shall:

6.2 Ensure that Supervisor of Maternity child health and Wattayah Polyclinic In-Charges are aware and adhere to the protocol

6.3 Wattayah Polyclinic In-Charges shall:

6.3.1 Ensure all staff are aware and adhere to the guideline

6.4 .The Nurses shall:

6.4.1 Adhere to the guideline

6.4.2 Prepare the semen analysis result before the patient meeting clinician.

6.5 **Lab Fertility Technicians Shall**:

6.5.1 Adhere to the guideline

6.6 **The pharmacist shall:**

6.6.1 Adhere to the guideline

6.6.2 Ensure early communication and maintain validity of stock medication of male unit .

7. Document History and Version Control Table:

version	Description	Author	Review Date
1	Initial Release	1.Dr Rahma Al Ghabshi 2.Dr. Shahrokh Sakhai 3.Dr. Hesham Ghzayel	2026

8. References:

1. Male infertility Guidelines of American Urological Association and American Society for Reproductive Medicine (AUA/ASRM).

9. Annexes:

9.1 Appendix 1: Semen Parameter Table:

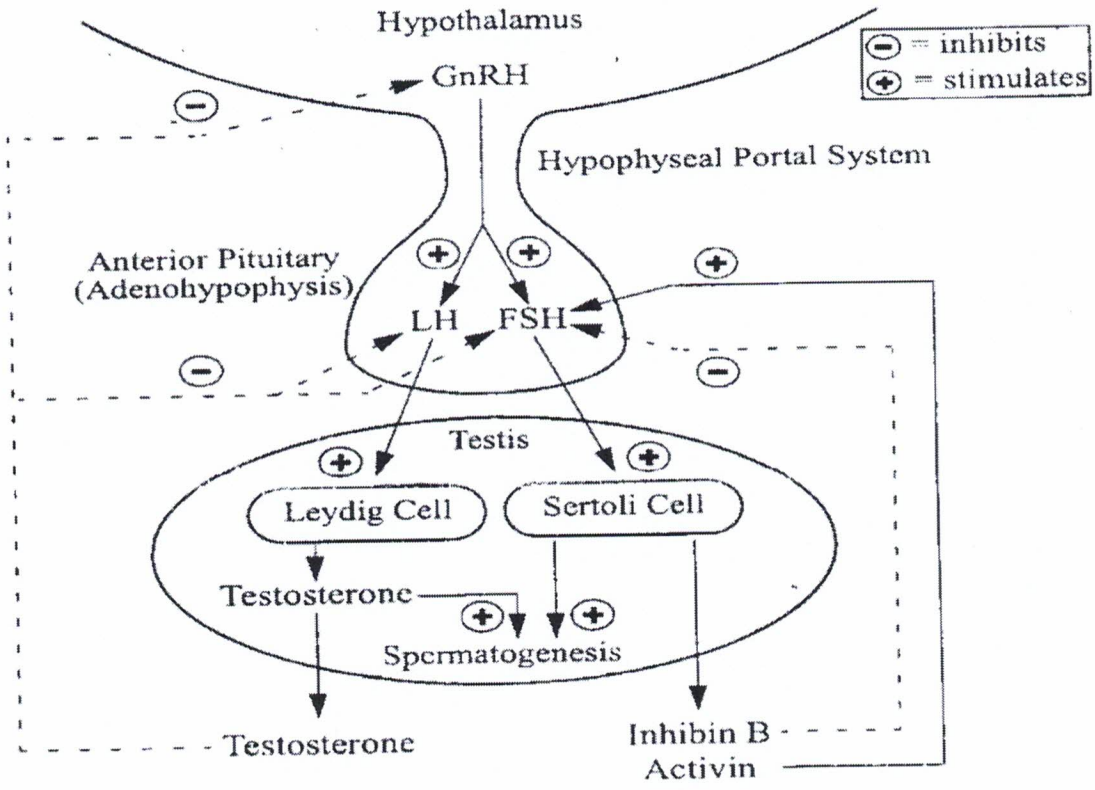
Semen Parameter	One-Sided Lower Reference Limit (Fifth Centiles With 95% Confidence Intervals)
Semen Volume	1.5 mL (1.4-1.7)
Total Sperm Number	39 million per ejaculate (33-46)
Sperm Concentration	15 million/mL (12-16 million/mL)
Vitality	58% Live (55-63%)
Progressive Motility	32% (31-34%)
Total Motility (Progressive + Non-Progressive)	40% (38-42%)
Morphologically Normal Forms	4.0% (3.0-4.0)
***Semen samples from 4500 men (men with proven fertile, with unknown fertility status and other men who were normozoospermic) from 14 countries and 4 continents were analyzed. Men described above were all fertile (Partners' time-to-pregnancy < or = 12 months) and their parameters were selected to calculate the values shown below.[17,28]**	

9.2. Appendix 2: Male Reproductive Health Physical Examination.

The goal of the physical examination is to identify potential etiologies of reproductive impairments, health ailments, or factors that can be optimized to improve health or reproductive success.

General	Body habitus as overweight obesity is associated with impaired spermatogenesis. Virilization to assess pubertal development/ androgen status Gynecomastia may be a marker for endocrine disorders
Abdominal exam	Examination of any scars from prior surgical procedures that may involve the pelvis or impact the urogenital system.
Phallus	Meatal location as hypospadias/epispadias may make semen deposition in the vagina challenging Penile plaque as Peyronie's disease may make vaginal intercourse difficult Penile lesions/ulcers/discharge may be a sign of sexually transmitted infection
Scrotum/Testes	Examination for prior scars suggesting prior scrotal surgery/trauma Location as scrotal position of the testes is important for normal function Size/consistency/contours as a majority of the testis is devoted to spermatogenesis. The exam may also reveal masses consistent with a testicular cancer
Epididymides	Shape/consistency as normal development should be identified to determine atresia that could be identified by the presence of a *CFTR* mutation. Induration/dilation could suggest obstruction. Epididymal cysts or spermatoceles may also lead to obstruction.
Vas Deferens	Shape/consistency as normal development and contour should be confirmed to rule out agenesis as may be seen in the presence of a *CFTR* mutation or aberrant Wolffian duct embryogenesis The presence/location of any vasectomy defect or granuloma should also be assessed
Digital Rectal Examination	Midline prostatic cysts or dilated seminal vesicles may assist in the diagnosis of EDO

Appendix 3: Hormone Profiles diagram

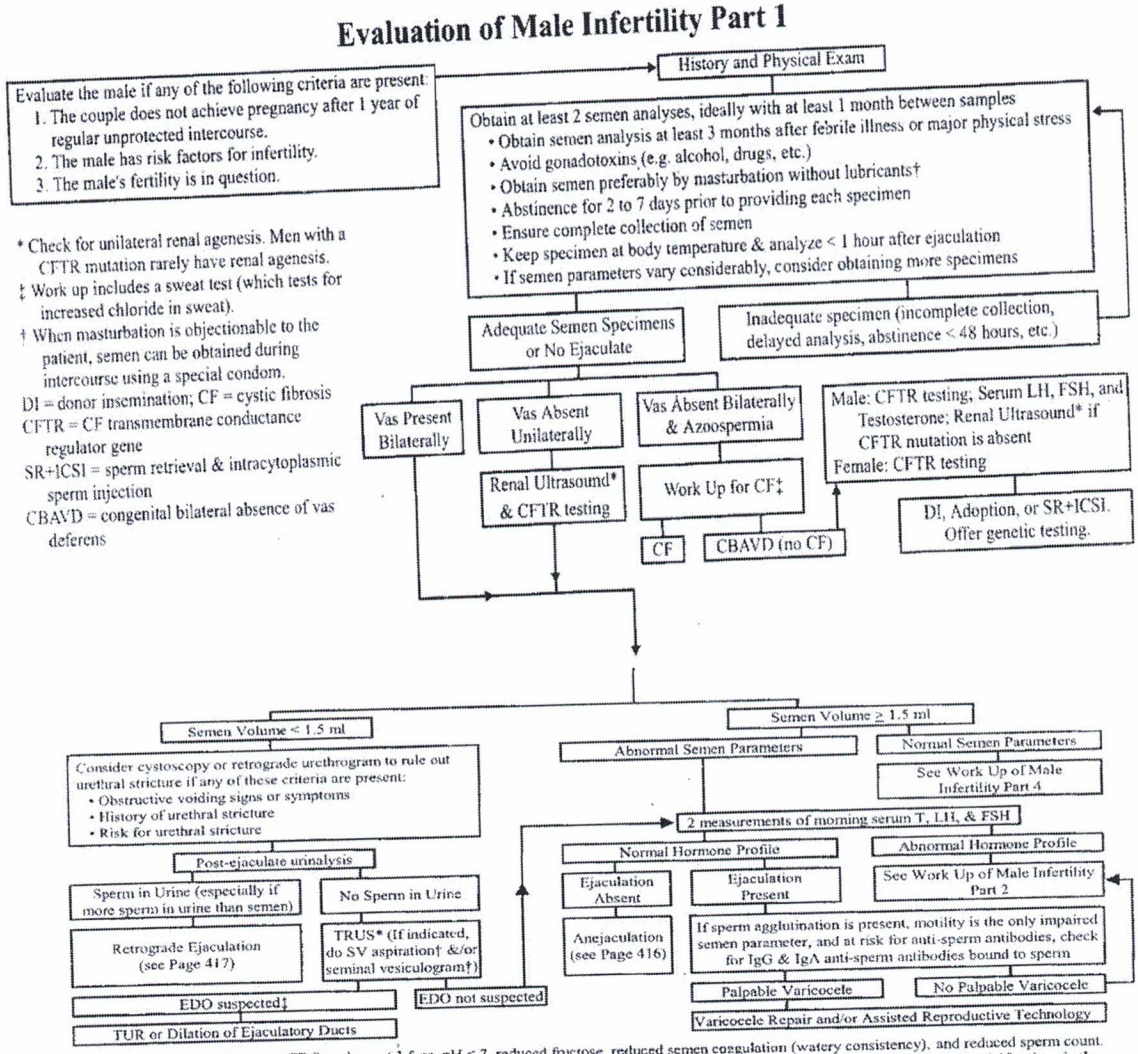


Hormone Profiles

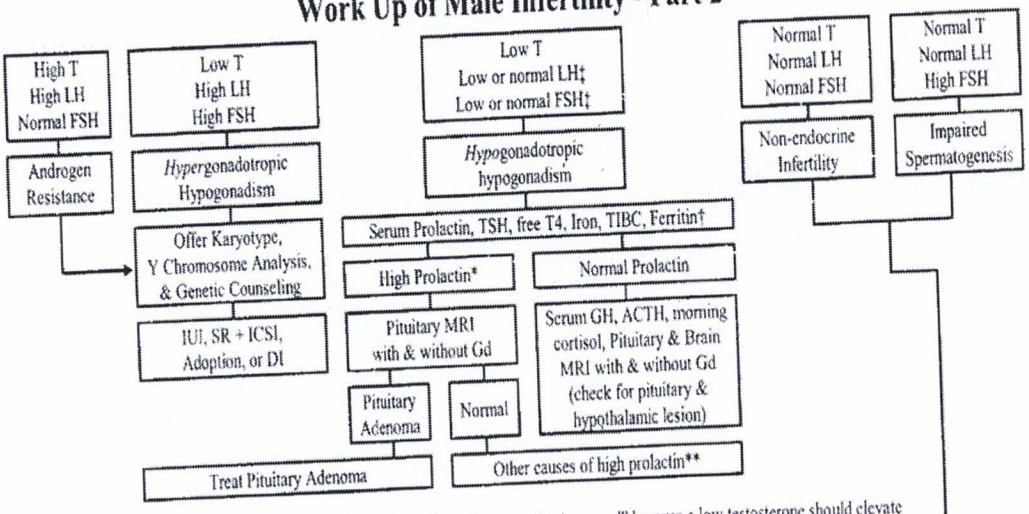
	Testosterone	LH	FSH	Prolactin
Hypogonadotropic hypogonadism	↓	↓ or N	↓ or N	N
Hypergonadotropic hypogonadism	↓ or N	↑	↑	N
Prolactinoma	↓	N or ↓	N or ↓	↑
Germ cell failure (e.g. Sertoli only)	N	N	↑	N
Androgen resistance	↑	↑	N or ↑	N

↓ = below normal; ↑ = above normal; N = Normal

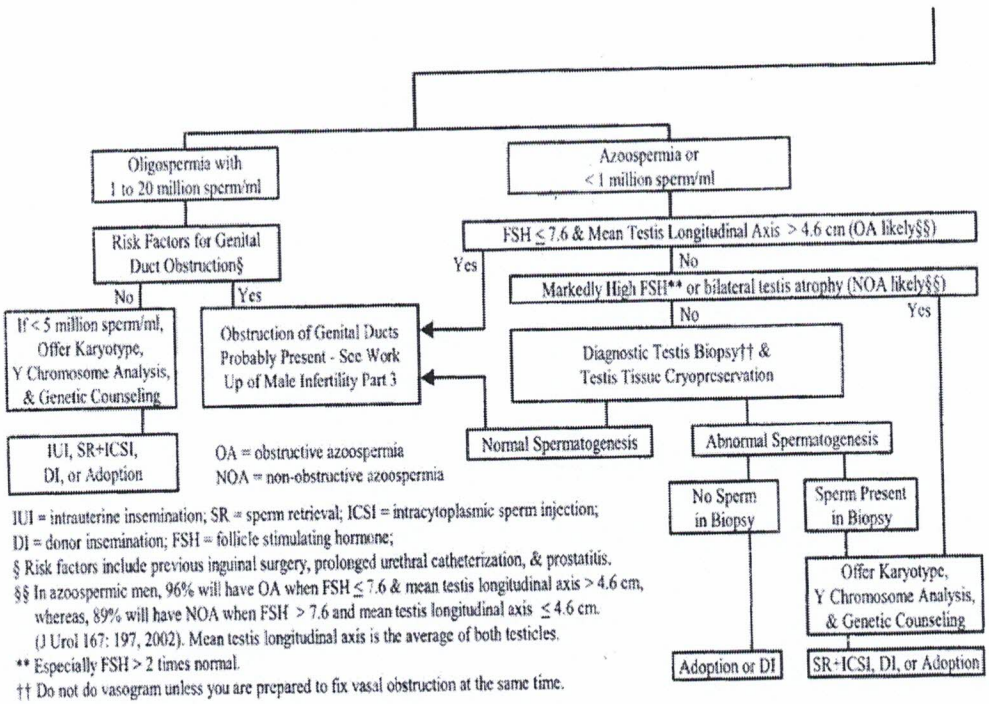
Appendix 4: management of male infertility (part 1 to part 4).



Work Up of Male Infertility - Part 2



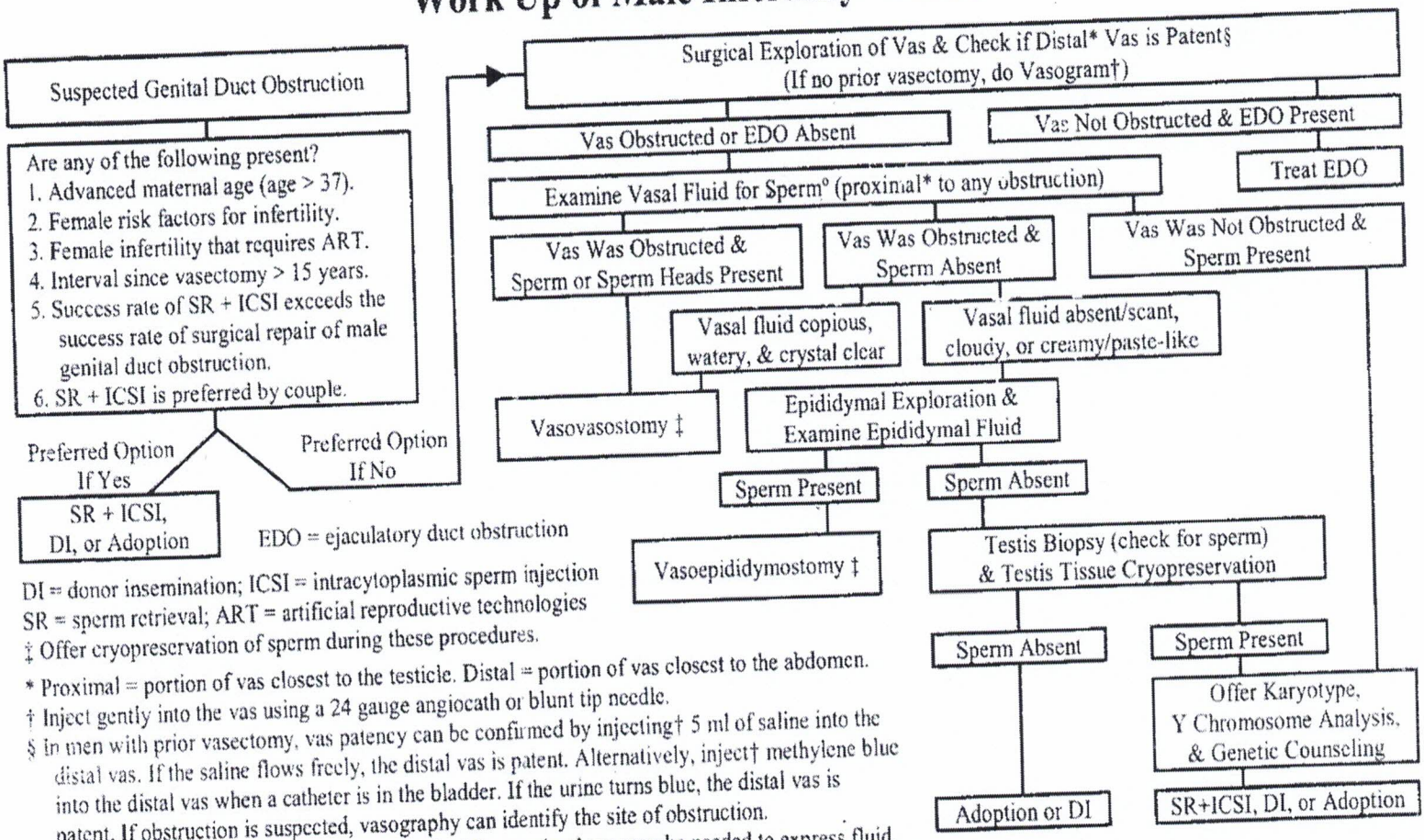
‡ In the presence of low testosterone, normal FSH and LH levels are "inappropriately normal" because a low testosterone should elevate gonadotropin levels.
† Iron, TIBC, and ferritin are obtained to check for hemochromatosis (which can impair pituitary and hypothalamic function).
* High prolactin should be confirmed with a repeat prolactin measurement.
** Conditions that can increase prolactin include renal failure, hypothyroidism, estrogen exposure, certain medications, and stress.
T = testosterone; LH = luteinizing hormone; FSH = follicle stimulating hormone; T4 = thyroxine; TSH = thyroid stimulating hormone; TIBC = total iron binding capacity; GH = growth hormone; ACTH = adrenocorticotropic hormone ; MRI = magnetic resonance imaging; Gd = gadolinium; SR = sperm retrieval; ICSI = intracytoplasmic sperm injection; DI = donor insemination; IUI = Intrauterine insemination



OA = obstructive azoospermia
NOA = non-obstructive azoospermia

IUI = intrauterine insemination; SR = sperm retrieval; ICSI = intracytoplasmic sperm injection; DI = donor insemination; FSH = follicle stimulating hormone;
§ Risk factors include previous inguinal surgery, prolonged urethral catheterization, & prostatitis.
§§ In azoospermic men, 96% will have OA when FSH ≤ 7.6 & mean testis longitudinal axis > 4.6 cm, whereas, 89% will have NOA when FSH > 7.6 and mean testis longitudinal axis ≤ 4.6 cm. (J Urol 167: 197, 2002). Mean testis longitudinal axis is the average of both testicles.
** Especially FSH > 2 times normal.
†† Do not do vasogram unless you are prepared to fix vasal obstruction at the same time.

Work Up of Male Infertility - Part 3

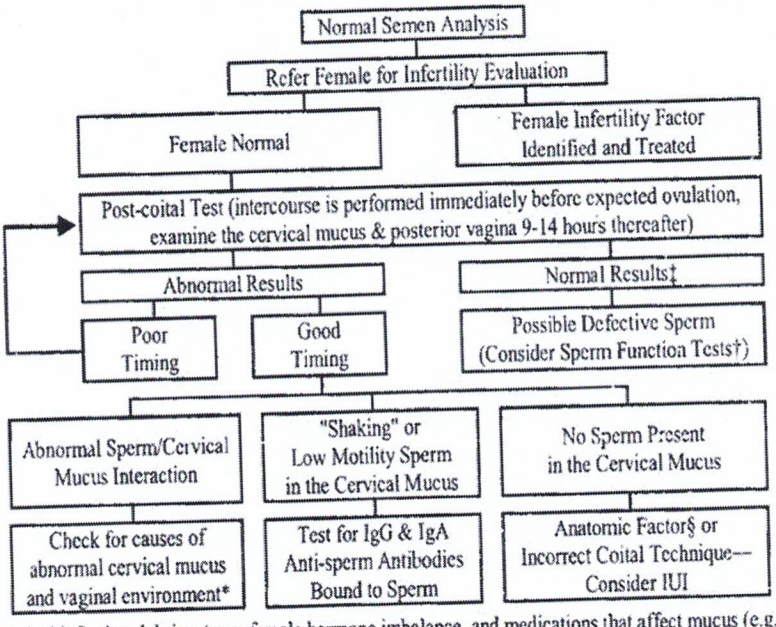


EDO = ejaculatory duct obstruction

DI = donor insemination; ICSI = intracytoplasmic sperm injection
SR = sperm retrieval; ART = artificial reproductive technologies
‡ Offer cryopreservation of sperm during these procedures.

* Proximal = portion of vas closest to the testicle. Distal = portion of vas closest to the abdomen.
† Inject gently into the vas using a 24 gauge angiocath or blunt tip needle.
§ In men with prior vasectomy, vas patency can be confirmed by injecting† 5 ml of saline into the distal vas. If the saline flows freely, the distal vas is patent. Alternatively, inject† methylene blue into the distal vas when a catheter is in the bladder. If the urine turns blue, the distal vas is patent. If obstruction is suspected, vasography can identify the site of obstruction.
° Milking &/or barbotage† (with 0.1 ml saline) of the proximal vas may be needed to express fluid.

Work Up of Male Infertility - Part 4



* Potential causes include vaginal infection, lubricant use, female hormone imbalance, and medications that affect mucus (e.g. decongestants).
† Examples include sperm penetration assay and acrosome reaction assay.
‡ The presence of sperm with rapidly progressive motility indicates a normal result.
§ Anatomic abnormalities that may impair the ability of the male to deposit semen into the posterior vagina (e.g. hypospadias, penile curvature).
IUI = intrauterine insemination