BASIC HISTORY TAKING AND INVESTIGATION (MALE AND FEMALE)

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Outline

Timing for evaluation;

History taking in female;

Physical examination in female;

Investigations in female;

History taking in male;

Physical investigation in male;

Investigation in male

WHO/WHEN TO INVESTIGATE?

Failure to conceive naturally after at least 12 months of regular, unprotected sexual intercourse

After 6 months for couples in which the female partner is older than 35 years

Evaluation and treatment before 12 months might be considered on the basis of medical history and physical examination

> 40 years without delay.

Start evaluation within the shortest period or earlier if:

Amenorrhea/oligomenorrhea

Chemotherapy/radiotherapy

Sexually transmitted diseases/Pelvic inflammatory disease

Abdominal/pelvic surgery

Endometriosis/adenomyosis

Women whose male partner has a history of groin or testicular surgery, adult mumps, impotence or other sexual dysfunction, chemotherapy and/or radiation, or a history of subfertility with another partner

Why to investigating?

To detect potential cause(s) of infertility –availability of sperm, eggs, integrity of the genital tract

To estimate prognosis

To plan treatment such as Medically Assisted Reproduction

History taking

Duration;

Primary or secondary infertility;

Previous consultations;

Fertility history	**Current conception attempts** • Length of time of unprotected intercourse • Coital frequency • Use of ovulation monitoring • Partner status and are they contributing sperm or oocytes to the patient's reproductive efforts • Presence of sexual dysfunction, including: - Decreased libido - Erectile dysfunction - Ejaculatory dysfunction - Dyspareunia - Vaginismus **Prior fertility history** • History of previous conception attempts • Prior periods of intercourse without contraception or with low efficacy contraception • Any prior fertility evaluation or treatment	• Patient may incorrectly identify attempts at pregnancy as only conscientious efforts for conception, rather than periods of active sexual activity without contraception. • Coital frequency may change over time. • If using urine LH kits, assess whether patient has been successful in detecting ovulatory surges. • If using a fertility tracking app, discuss its limitations in accurately predicting the fertile window (10).

Gynecologic history	**Menstrual history** • Age at menarche • Cycle length (range), duration, and amount of bleeding • Presence of intermenstrual bleeding • Presence of dysmenorrhea • Presence of molimina **General gynecologic history** • Cervical screening history including related treatments • Contraceptive use including type and duration • Sexually transmitted infections and/or pelvic inflammatory disease • Dyspareunia or chronic pelvic pain • History of abnormal cervical screening (pap smear ± human papillomavirus testing)	• If menses onset <8 years of age or >14 years of age, was evaluation performed and were menses ever achieved spontaneously? (11, 12) • If menstrual interval is <21 days or >35 days or there is a significant variation in range, perform a review of systems including: - Thyroid symptoms - Hirsutism - Visual field defects - Galactorrhea - Stressors - Dietary and exercise habits - Vasomotor symptoms • If abnormal menstrual bleeding, were any investigations performed and was a diagnosis made? • Have any surgical cervical excision procedures been performed?

Obstetrical history	• Total number of pregnancies and outcomes, including: (13) - Biochemical miscarriage - Clinical miscarriage - Pregnancy of unknown location - Terminations - Ectopic pregnancy - Stillbirth - Live birth • Conceived with current vs. prior partner(s) • Details of any fertility treatment required • Obstetrical complications, including: - Gestational diabetes - Hypertensive disorders - Preterm delivery - Placental disease - Intrauterine growth restriction • Congenital disease or birth defects in offspring	• If outcome other than live birth, inquire about related evaluations.

Medical history	**Past medical and surgical history** • Medical disorders with particular attention to endocrine, autoimmune, genetic, psychiatric, or malignant disorders (14–15) • Endocrine history should include evaluation of the thyroid, and the presence of galactorrhea and hirsutism • Prior hospitalizations • Surgical procedures **Medications and allergies** • Use of gonadotoxic medications or radiotherapy • Current medications including any supplements • Known drug allergies and type of reaction	• If diagnosed with an endocrine disease, what is the status of the disease, including medications and last hormonal testing?

Continued.

	Routine assessment	Additional considerations
Family history	• Any family members with known history of: - Inherited disorders - Endocrinopathies - Birth defects - Developmental delay - Infertility - Early menopause (<40 years of age) - Multiple spontaneous abortions - Heritable cancer syndromes	• If known or suspected history of inherited disorder, construct family pedigree and assess whether patient had carrier testing. Consider referral to a genetic counselor. • If family history of developmental delay, assess whether the individual was evaluated for Fragile X syndrome. • If family history of infertility, assess whether there was a known associated diagnosis. • If family history of early menopause, assess whether there was a known autoimmune or genetic cause.
Social history	• Occupation and potential exposure to toxic agents • Use of tobacco, alcohol, or recreational drugs • History of psychological, physical, and/or sexual trauma • Gender identity • Race and ethnicity • Diet and exercise habits	

Male history - if applicable	• Fertility history (5, 6) • Urologic history • Medical and surgical history (including endocrine history) • Current medications including any supplements • Exogenous steroid use • Sexual dysfunction (16) • Social history • Family history

ASRM. Fertility evaluation of infertile women. Fertil Steril 2021.

Physical examination

The infertility physical examination should be targeted to detect pathology that specifically impacts fertility or reproductive potential.

Examination	When to consider	Evaluate for	Additional considerations
Skin examination	• Polymenorrhea • Oligomenorrhea • Amenorrhea • Signs or symptoms of androgen excess (e.g., hirsutism, acne, scalp hair loss)	• Hirsutism • Acne • Androgenic alopecia • Acanthosis nigricans	• Evaluate for evidence of biochemical androgen excess (hyperandrogenemia); and similar/mimicking disorders including thyroid dysfunction, hyperprolactinemia, and 21-hydroxylase deficient nonclassic adrenal hyperplasia.
Thyroid examination	• Abnormal thyroid function tests • Goiter	• Thyroid texture and size and the presence of nodularity, tenderness, or cervical adenopathy	• Refer for a thyroid ultrasound if the patient reports rapid growth of the thyroid or if the examination identifies nodularity, asymmetry, or tenderness. • Referral to a specialist. • Fine-needle aspiration may also be indicated based on examination and ultrasound findings.
Breast examination	• Breast pain • Breast mass • Nipple discharge	• Palpable tenderness • Masses • Skin changes • Expressed or spontaneous nipple discharge • Nearly all breast abnormalities without a known cause should be imaged	• Refer for breast ultrasound. Ultrasonography is the preferred initial modality in women <30 years of age and diagnostic mammography is preferred in women ≥30 years of age (17).
Speculum examination	• Dyspareunia • Postcoital spotting	• Vaginal and cervical abnormalities • Lesions • Cervical polyps	
Bimanual pelvic examination	• Not routinely indicated for the evaluation of infertility	• Tenderness • Rectovaginal masses or nodularity • Uterine masses • Ovarian masses	• A bimanual pelvic examination will rarely add clinical information to the infertility evaluation that cannot be assessed with pelvic ultrasound. Perform as an adjunct to ultrasound when a tactile examination may add additional useful information to the evaluation. The consideration of a bimanual examination may be influenced by the availability of resources for affordable ultrasonography.

Investigations

Ovulatory status;

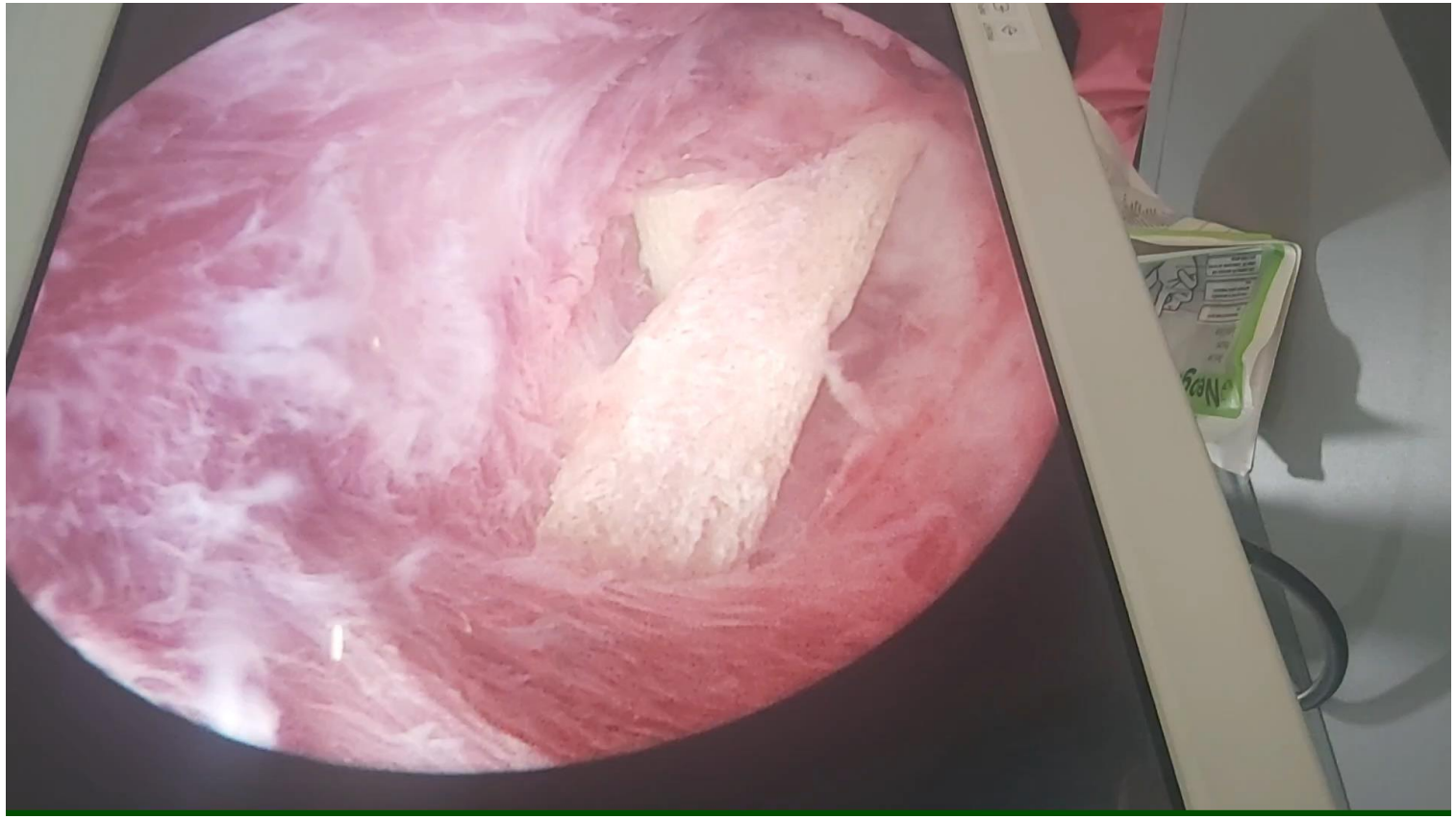
The structure and patency of the female reproductive tract;

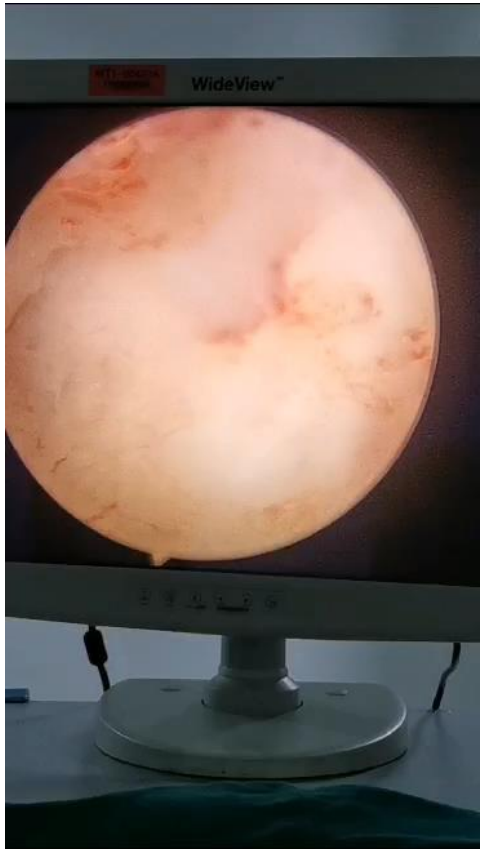
Semen evaluation of the male partner.

	Potential routine tests	Tests not routinely recommended	Other considerations
Ovulation	• Menstrual historyIf indeterminant, consider: • Luteal progesterone • Ovulation predictor kits • Transvaginal ultrasound	• Basal body temperature • Endometrial biopsy	• A menstrual history is adequate to establish an ovulatory menstrual pattern. Additional ovulation testing is not required when the history is clearly abnormal or normal. If the menstrual history is clearly abnormal, additional testing to determine the cause is indicated.
Ovarian reserve	• Antimüllerian hormone • Antral follicle count • Basal follicle-stimulating hormone and estradiol	• Inhibin B • Clomiphene citrate challenge test	• Ovarian reserve is a poor predictor of fertility but can be used to guide fertility treatments.
Other endocrine systems	• Thyroid-stimulating hormone	• Prolactin • Androgen measures	• Prolactin is indicated in women with galactorrhea, or oligomenorrhea. • If the thyroid-stimulating hormone is abnormal, assessment of free T4 and thyroid autoantibodies is warranted. • If signs of androgen excess or oligomenorrhea, check serum total and free testosterone, and 17 hydroxyprogesterone. • If testosterone is >200 ng/ml, ultrasound of the ovaries and computed tomography of the adrenal glands to exclude androgen-secreting neoplasm.

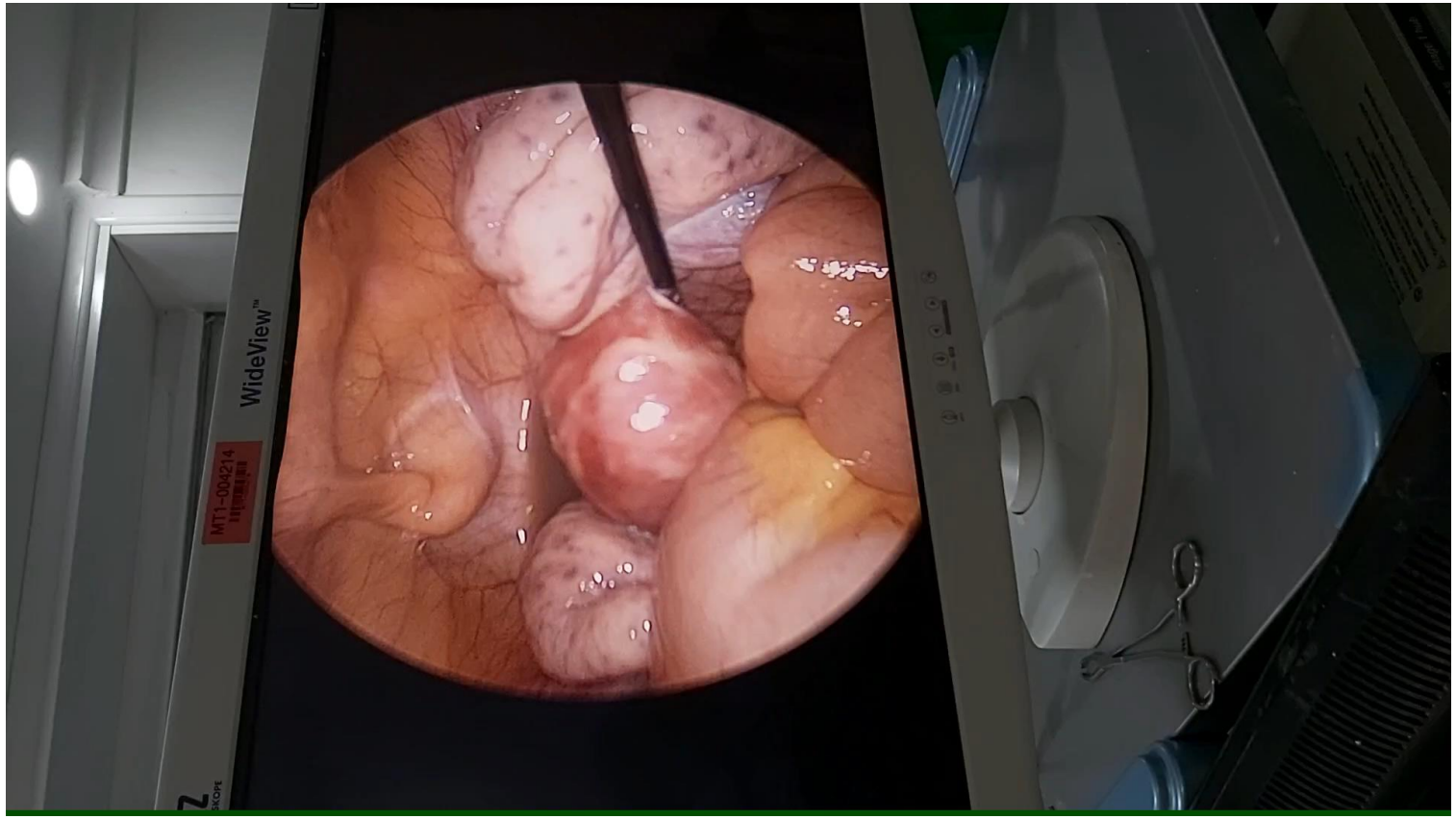
Uterus	• Transvaginal ultrasonography • Saline infusion ultrasonography • Hysterosalpingography • Hysteroscopy	• Magnetic resonance imaging	• Magnetic resonance imaging may be indicated as follow-up to further evaluate abnormalities found by other imaging modalities.
Fallopian tube patency	• Hysterosalpingogram • Hysterosalpingo-contrast sonography • Chlamydia antibody test	• Laparoscopy with chromopertubation	• Laparoscopy with chromo-pertubation is appropriate if the surgery is already being performed for a separate indication. • A positive chlamydia antibody test may require further eval-uation to confirm that the tubes are non-patent.

Hysteroscopy diagnostic




WideView™

Laparoscopy



Infertility tests that should not be routinely ordered, unless specifically indicated (33).

- Laparoscopy for unexplained infertility
- Advance sperm function testing (e.g., DNA fragmentation testing)
- Postcoital testing
- Thrombophilia testing
- Immunologic testing
- Karyotype
- Endometrial biopsy
- Prolactin
- Progesterone
- Estradiol
- Follicle-stimulating hormone
- Luteinizing hormone

ASRM. Fertility evaluation of infertile women. Fertil Steril 2021.

Male infertility – history taking

Multi-disciplinary approach.

Evaluate the couple if there's one.

Primary or secondary male infertility should be assessed in the same way.

Infertility history

- Duration of infertility
- Previous pregnancies and outcomes (primary vs

secondary infertility)

- Partner's fertility history
- Previous fertility investigation and treatment

Sexual history

- Libido
- Erectile dysfunction
- Ejaculatory dysfunction
- Type of lubricants
- Frequency and timing of coitus
- Sexually transmitted disease

Medical history

- Cryptorchidism
- Timing of puberty
- Anosmia
- History of testicular torsion
- History of testicular trauma
- Diabetes
- Neurological conditions (spinal cord injury, multiple

sclerosis)

- Infections (urinary infections, epididymitis or prostatitis,

tuberculosis, mumps orchitis, recent febrile illness)

- Renal disease
- Cancer

Surgical history

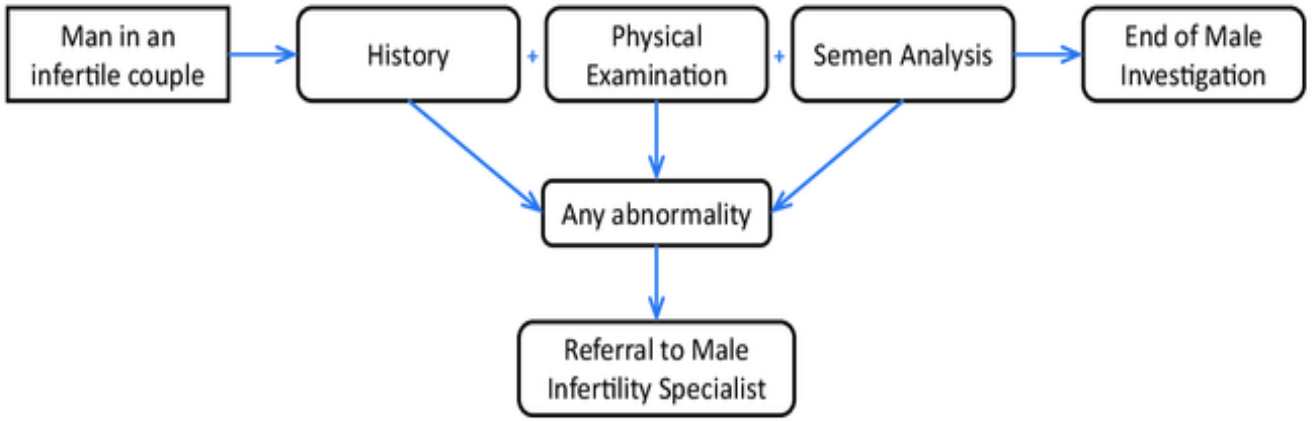
- Orchidopexy
- Retroperitoneal or pelvic surgery
- Herniorrhaphy
- Vasectomy
- Bladder neck or prostatic surgery

Gonadotoxin exposures

- Medications (endocrine modulators, antihypertensives, antibiotics, antipsychotics)
- Environmental (pesticides, heavy metals)
- Chemotherapy or radiotherapy
- Lifestyle (obesity, tobacco, vaping, recreational drugs, anabolic steroids)

Family history

- Infertility
- Cystic fibrosis
- Androgen receptor deficiency



History: including, but not limited to;

1. Medical illness and medications
2. Surgical interventions in the past
3. Sexual ability/limitation
4. Cryptorchidism, scrotal infections
5. Testosterone/anabolic usage
6. Lifestyle factors (see PICO 4)
   a. obesity
   b. smoking
7. Supplement usage (see PICO 5)
   a. vitamins
   b. oral antioxidants
8. History of malignancy (see PICO 7)

Physical: including, but not limited to;

1. Overall body habitus
   a. obesity
   b. muscular development
   c. virilisation
2. Testes
   a. location, size, consistency
3. Ductal structures (vas, epididymis)
   a. presence/absence
   b. normal/obstructed
4. Spermatic cord
   a. varicocele (PICO 8)
   b. hydrocele

Laboratory: including, but not limited to;

1. Semen analysis
2. Hormonal assays, if necessary
3. Genetic assays, if necessary
   a. Karyotype (PICO 6)
   b. YCMD (PICO 6)
   c. CFTR analysis (PICO 6)

Physical examination

Include an assessment of body habitus, secondary sexual characteristics, and genitalia. (body hair, obesity, gynecomastia).

Body habitus helps to look for endocrinopathies, klinefelter, hyperprolactinemia.

Cont…

The genital examination should begin with the phallus, carefully assessing for penile curvature, plaques, epispadias, or hypospadias, all of which can impair semen deposition in the vaginal vault.

The testicles should be examined for presence, size, and consistency.

The epididymides should be palpated to assess for enlargement that might indicate distal obstruction.

The spermatic cords should be assessed in the supine and standing positions, allowing for the detection of a varicocele.

The prostate should be assessed for size and consistency.

Scrotal ultrasonography can be useful for diagnosis of hydrocele, dilated epididymis, or inguinal testis.

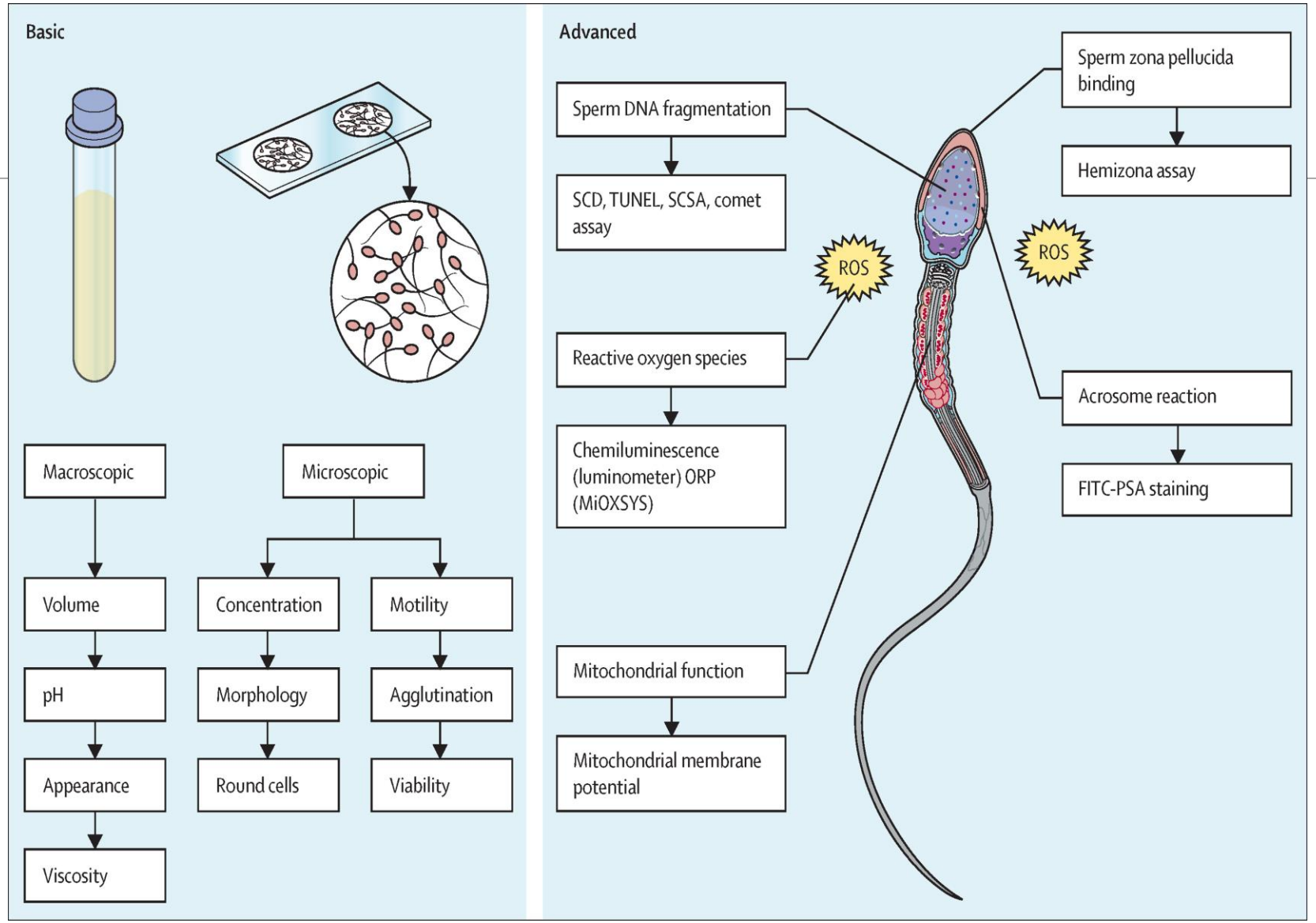
Although digital rectal examination is not routinely done, it is indicated in men with low ejaculate volume.

Semen analysis

Remains the cornerstone for evaluating male infertility

One vs two semen analyses

Depending on the results, further andrological assessments and procedures might be recommended.


Basic
Macroscopic
Volume
pH
Appearance
Viscosity
Microscopic
Concentration
Morphology
Round cells
Motility
Agglutination
Viability
Advanced
Sperm DNA fragmentation
SCD, TUNEL, SCSA, comet assay
Reactive oxygen species
Chemiluminescence (luminometer) ORP (MiOXSYS)
Mitochondrial function
Mitochondrial membrane potential
ROS
ROS
Sperm zona pellucida binding
Hemizona assay
Acrosome reaction
FITC-PSA staining

Semen parameter	WHO 1980	WHO 1987	WHO 1992	WHO 1999	WHO 2010
Volume (mL)	ND	≥2	≥2	≥2	1.5
Sperm count (10^6/mL)	20–200	≥20	≥20	≥20	15
Total sperm count (10^6)	ND	≥40	≥40	≥40	39
Total motility (% motility)	≥60	≥50	≥50	≥50	40
Progressive motility (%)	≥2	≥25	≥25 (grade a)	≥25% (grade a)	32 (grade a+b)
Vitality (% alive)	ND	≥50	≥75	≥75	58
Morphology (% normal forms)	80.5	≥50	≥30	14	4

WHO: World Health Organization; ND: not defined.

Adapted from the article of Esteves et al (Urology 2012;79:16-22) [28] with original copyright holder's permission.

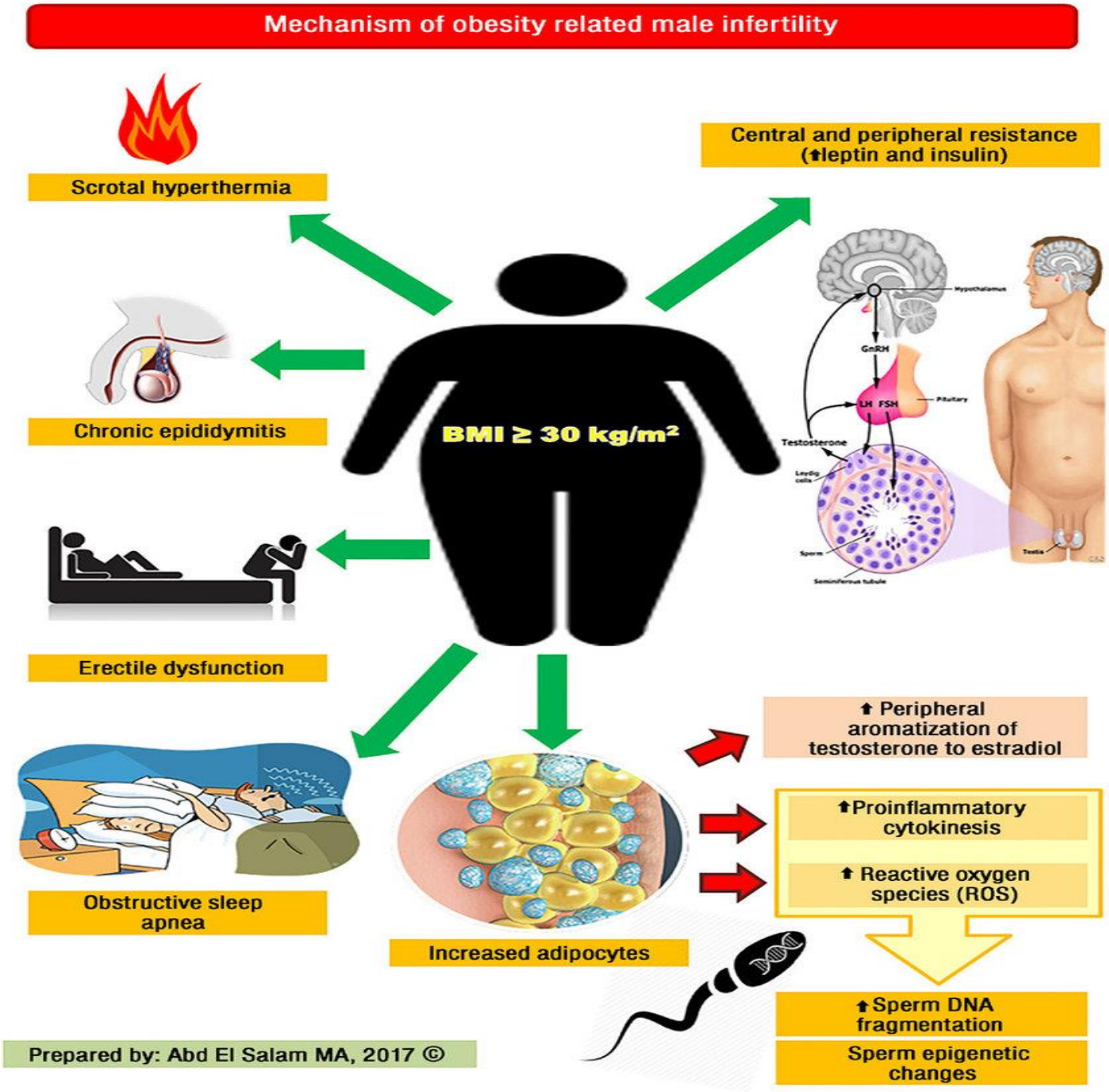
Parameter	WHO 1999	WHO 2010	% Decline
Volume (mL)	2	1.5	25
Concentration (million/mL)	20	15	25
Motility, %	50	40	20
Normal forms, %	14	4	71
Live forms, %	60	58	3

	WHO 2010	WHO 2021
Semen volume (mL)	1.5 (1.4–1.7)	1.4 (1.3–1.5)
Total sperm number (10^6 per ejaculate)	39 (33–46)	39 (35–40)
Total motility (%)	40 (38–42)	42 (40–43)
Progressive motility (%)	32 (31–34)	30 (29–31)
Non progressive motility (%)	1	1 (1–1)
Immotile sperm (%)	22	20 (19–20)
Vitality (%)	58 (55–63)	54 (50–56)
Normal forms (%)	4 (3–4)	4 (3.9–4)

Some facts…

A study of 744 men with infertility revealed that 15·4% of men who met the criteria suggestive of pre-diabetes were at increased risk of hypogonadism, higher sperm DNA fragmentation, and non-obstructive azoospermia. *Zegers-Hochschild et all, Fertil Steril 2017*

Men who are oligozoospermic are more likely to have metabolic syndrome than men who are normozoospermic. *Ferlin et all, Eur Urol Focus 2019*


Mechanism of obesity related male infertility
Scrotal hyperthermia
Central and peripheral resistance (⬆leptin and insulin)
Chronic epididymitis
BMI ≥ 30 kg/m²
Erectile dysfunction
Obstructive sleep apnea
Increased adipocytes
⬆ Peripheral aromatization of testosterone to estradiol
⬆Proinflammatory cytokinesis
⬆ Reactive oxygen species (ROS)
⬆Sperm DNA fragmentation
Sperm epigenetic changes
Prepared by: Abd El Salam MA, 2017 ©

Infection and infertility

The prevalence of male urogenital tract infection was reported to be as high as 35% in a study of more than 4000 men with infertility. *Henkel et all, Asian J Androl 2007*

A cross-sectional study of 1689 men revealed that 20% of men with primary infertility had asymptomatic semen infections, which were associated with impaired sperm concentrations. *Boeri et all, Fertil Steril 2020*

Prostatitis, a common urogenital disease caused by Escherichia coli, can have detrimental effects on various sperm parameters. *Condrelli et all, J Endocrinol Invest 2017.*

Among sexually active men younger than 35 years, Chlamydia trachomatis and Neisseria gonorrhea are the most common pathogens to cause epididymitis. *World Health Organization,2010.*

E coli is the predominant pathogen found in men older than 35 years who have infertility. *World Health Organization,2010.*

One in six men with infertility has erectile dysfunction, or premature ejaculation, or both.

Cannabis, the most frequently used recreational drug, negatively effects male fertility by inhibiting the hypothalamic–pituitary–gonadal axis, spermatogenesis, and sperm function. *Sansone et all, Reprod Biol Endocrinol 2018*

Hormonal profile

international societies recommend 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. (ASRM, EUA).

If total testosterone concentration is found to be low, a more thorough endocrine evaluation is recommended. (LH, Prolactin…).

Genetic testing

Genetic abnormalities related to male infertility affect about 15% of men with infertility. *ASRM,2020*

Genetic testing is also important for predicting the success of sperm retrieval (karyotyping, Y chromosome microdeletion, Cystic Fibrosis).

CONCLUSION

Infertility is a prognosis based diagnosis

Tests should identify problems and /or aid treatment

Understand test accuracy

Incomplete diagnosis versus unnecessary testing

The need for flexibility

References

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- *Male infertility, 2020, the Lancet journal;*
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