وزارة الصحـــــــة
Ministry of Health

Document Title	**Infertility Management Guideline**
Document Type	**Guideline**
Directorate/Institution	Department of Woman and Child Health (DWCH)
Targeted Group	Healthcare providers in primary, secondary and tertiary healthcare institutions providing services for infertile couples
Document Author	Team for Developing the Infertility Management Guideline
Designation	Team for Developing the Infertility Management Guideline
Document Reviewers &	1. Dr. Jamila Al-Abri - 2. Dr. Badriya Al Rashdi, 3. Dr. Fatma Al Hinai,
Designation	1. Director, DWCH 2. Senior Consultant, Family Medicine and Community Health, Director General of Primary Health Care 3. Head - Woman Health Section, DWCH
Release Date	**2023**
Review Frequency	**5 years**

Validated by		**Approved by**	
Name	Dr. Qamra Al Sariri	Name	Dr. Badriya Al Rashdi
Designation	Director General of Quality Assurance Center	Designation	Director General of Primary Health Care
Signature		Signature	
Date	29 November 2023	Date	12th/Oct/2023

Sultanate of Oman

Ministry of Health

INFERTILITY MANAGEMENT GUIDELINE

THIRD EDITION

2023

Department of Woman & Child Health

Directorate General of Primary Health Care

ACKNOWLEDGEMENT

First and foremost, we would like to thank Dr. Yasmin Al Lawati, the former director of Department of Family & community Health, who was behind the establishment of infertility program in Oman.

With grateful thanks to all contributors from different departments and health care institutions who have contributed to this manual.

Contributors

Dr. Nawal Al Rashdi	Director of Department of Health Education
Dr. Fatma Al Hinai	Head of Woman health Section, Department of Woman and Child Health, Directorate General for Primary Health Care (DGPHC)
Dr. Omaima Abdul Wahab	Senior Medical Officer-Woman Health Section Department of Woman and Child Health
Dr. Badryia Al Qassabi	Specialist Family Medicine- Women and Child Health section
Dr. Fathiya Al Qassabi	Senior Consultant Family Medicine
Mr. Salam Al Rashdi	Head of Diagnostic Laboratory
Dr. Rahma Al Ghabshi	Senior Consultant Obstetrics & Gynecology - Khoula Hospital
Dr Azhar Tag El Din	Senior Specialist Obstetrics & Gynecology - Khoula Hospital
Dr. Muna Al Badi	Consultant Obstetrics & Gynecology - Ibri Hospital
Dr. Said Al Mamari	Senior Consultant Urology - Royal Hospital
Dr. Abdulla Al Taie	Senior Consultant Dermatology - Al Nahdha Hospital
Dr. Ali Al Maqbali	Consultant Endocrinology - Royal hospital
Dr. Nasser Al Adawi	Senior Specialist Dermatology Directorate General for Health Services - South Batinah
Dr. Saif Al Tamimi	Senior Specialist - Family Medicine & Public Health Directorate General for Health Services - Muscat
Dr. Dalal Al Ghafri	Consultant - Family Medicine & Public Health Director of ibri hospital - Al Dhahirah governorate
Dr. Khawla Al Musalhi	Senior Specialist – Biochemistry - Royal Hospital
Edited by	Juanita Singh Roshmi Albert, Public Health Specialist, DWCH

TABLE OF CONTENTS

List of Figures:

List of Tables:

List of Algorithms

List of Annexures

ACRONYMS

AFS	American Fertility Society
AMH	Anti Müllerian Hormone
ART	Assisted Reproductive Technology
BMD	Bone mineral density
BMI	Body mass index
CAH	Congenital adrenal hyperplasia
CBC	Complete blood count
CT	Computerized tomography
D	Day
DFCH	Department of family & community health
DMPA	Depot medroxyprogesterone acetate
DWCH	Department of woman & child health
ESR	Erythrocyte sedimentation rate
FSH	Follicular stimulating hormone
GIFT	Gamete Intra Fallopian Transfer
HCG	Human chorionic Gonadotropins
HIV	Human immunodeficiency virus
HMG	Human menopausal Gonadotropins
HSG	Hysterosalpingography
HVS	High vaginal swab
ICSI	Intra cytoplasmic sperm injection
IM	Intramuscular
IU	International unit
IUCD	Intra uterine contraceptive device
IUI	Intra uterine insemination
IVF	In vitro fertilization
IVF-ET	In vitro fertilization and embryo transfer
LFT	Liver function test
LH	Luteinizing hormone
LHRH	Luteinizing hormone releasing hormone

MESA	Microsurgical epididymal sperm aspiration
MOH	Ministry of health
MPA	Medroxyprogesterone acetate
MRI	Magnetic resonance image
OHSS	Ovarian Hyper Stimulation Syndrome
PCOS	Polycystic ovarian syndrome
PESA	Percutaneous epididymal sperm aspiration
PHC	Primary Health Care
PID	Pelvic inflammatory disease
PRL	Prolactin hormone
PZD	Partial Zona Dissection
RFT	Renal function test
RPR	rapid plasma reagin test
SC	Subcutaneous
STI	Sexually transmitted infections
SUZI	Sub zonal insemination
T	Testosterone
T4	Thyroid hormone
TESA	Testicular sperm aspiration
TESE	Testicular sperm extraction
TID	Three times a day
TSH	Thyroid stimulating hormone
TURED	Transurethral resection of the ejaculatory ducts
U/S	Ultrasound
VAS	Vas deference
VIT	Vitamins
WHO	World health organization

DEFINITIONS

- **Infertility** is defined as "inability of a couple to achieve conception after a year of regular unprotected intercourse". It is classified into primary and secondary infertility.

- **Primary Infertility**

"A couple has never conceived despite unprotected regular intercourse for at least 12 months".

- **Secondary Infertility**

A couple has previously conceived but has subsequently been unable to conceive within 12 months after delivery or abortion, despite exposure to regular unprotected intercourse.

- **Pregnancy Wastage**

The woman is able to conceive but unable to produce a live birth

- **Sub Fertility**

Any form of reduced fertility with prolonged time of unwanted non-conception.

- **WHO Classification of Ovulatory Dysfunctions**

Group I	Hypogonadotropic hypogonadism
Group II	Hypothalamic-pituitary dysfunction
Group III	Ovarian failure
Group IV	Congenital or acquired genital tract disorders
Group V	Hyperprolactinemia with detectable pituitary tumor
Group VI	Hyperprolactinemia without pituitary tumor
Group VII	Amenorrhoea with pituitary tumor

CHAPTER 1: INTRODUCTION, PURPOSE, SCOPE AND STRUCTURE

1.1 Introduction

Infertility is a critical component of reproductive health. Worldwide, the inability to have children affects men and women as Infertility can lead to distress and depression, as well as discrimination. Global infertility prevalence rates are difficult to determine because infertility can be due to male and female factors, which complicate any estimate that may only address the woman and an outcome of a pregnancy diagnosis or live birth. It was estimated that one in every four couples suffer from infertility[1].

Despite management of infertility being considered an essential component of reproductive health, it has always been neglected especially in developing countries. In Oman, the main goal of reproductive health is stated as "*All married couples have optimal reproductive health and a satisfying and fulfilling family life*". Thus, diagnosis and management of infertility was integrated into the Maternal and Child health program.

In Oman, services for diagnosing and management of infertility started gradually. Until 1974, only the patient's history and physical examinations were carried out in the hospitals. In 1975 at Khawlah hospital, semen analysis, hystrosalpingography for tubal potency, dilatation and curettage for studying the secretory endometrium to confirm the ovulation, were started followed by introducing laparoscopic examination in 1980. In 1984, an infertility clinic was started at Khoula Hospital and a basic Performa for the infertile couple was introduced. With the opening of Royal Hospital in 1987, a separate infertility clinic for both female and male patients was established. Investigations such as hormonal assay and ultrasound for follicular studies were started. Intrauterine insemination (IUI) was initiated in 1996.

Data on cohorts of the cases registered from 2002-2005 in infertility clinic showed that around 73% of female infertile clients were in the age group of 20-29 while around 60% of infertile males were within ages of 25-34. Most of the clients in this survey (53%) were in non-

[1] *World Health Organization (2022) Global prevalence of infertility, infecundity and childlessness available at https://www.who.int/reproductivehealth/topics/infertility/burden/en/ Accessed on 30/3/2022*

consanguineous marriages. Primary infertility accounted for 53% of all cases registered during that period. The most common cause of infertility in male and female clients was of gonadal counting of approximately 25%. By gender, female clients alone were found to be the cause of infertility in 51% of the cases. In 10% of the cases, the cause remained unknown. Based on Annual Health Report (2020), data from MOH healthcare institutions showed that female infertility was 48 per 10,000 women aged 15-49 years and male infertility was 8 per 10,000 males.

1.2 Purpose

The development of the 3rd Edition of this guideline is an effort by the Ministry of Health in Oman to keep providers' knowledge updated with evidence based practices and to ensure the best possible standards of health care delivery.

The interventions described in this guideline are based on the latest available scientific evidence & best practices as per the common consensus of an expert group in the country.

As the provision of infertility services has to be different at different levels of health care systems, this **2rd Edition** of the guideline deals with the standard operating procedures to be followed by all health care workers either working in infertility clinics or in any other clinics in management and treatment of infertile couples.

1.3 Scope

This guideline is targeted for all healthcare facilities levels (primary, secondary and tertiary) that provide services for infertile couples.

1.3.1 Services Target:

Married couples that are:

- Unable to achieve conception **after 12 months** of regular unprotected intercourse.
- Unable to achieve conception **after 6 months** of regular unprotected intercourse when the woman **aged is 36- 40years.**
- Unable to achieve conception **after 3 months** of regular unprotected intercourse when the woman **aged is 40 years or more**.
- Married couple who has previously conceived but subsequently unable to conceive, despite exposure to regular unprotected intercourse. (For Married couple who has previously conceived and have **≥ 5 live children** should be counseled extensively and discouraged because of the high risk associated with pregnancy).
- Have known clinical cause of infertility or a history of predisposing factors for infertility (immediately)
- When a treatment is planned that may result in infertility (such as treatment for cancer), early fertility specialist referral should be offered.
- Couples aged less than 20 years, should be counseled about risk of adolescent pregnancy on mother and newborn. They can be physically examined, reassured and explained about the fertile period of menstrual cycle and the most non-invasive tests like semen analysis and hormonal profile may be carried out.

  Note: Child Law defined a "child" in Oman as every human being below the age of eighteen years as per the Gregorian calendar and by law, the age of marriage is 18 years.

1.3.2 Service Provision:

1. Standardized infertility services should be provided by the parent health care institution for all couples wherever trained health care providers are available.
2. Infertility care should be readily and easily accessible to all couples and should be sensitive to the needs of all couples and the local community.
3. Registration of the couple should be carried out in the parent primary health care facility whenever the couple fulfills the criteria of infertility even if they started already the treatment in private or secondary care level.
4. Infertility Health Record **(HP- 217)** should be issued to infertility couple at the time of registration to document the client's history, clinical examination and investigations. It is to be given to couple to carry it with them for all infertility clinic visit.
5. The couple should be advised to present their Issued Infertility Health Record (White Book) to the treating doctors at a different level of care (secondary and tertiary).
6. Clear management including counseling should be provided by trained service providers at all health care levels.
7. Specific day(s) will be fixed in all health institutions to provide infertility services.
8. At secondary health care facilities, a combined male/female infertility clinic is advised to run at the same time and place when possible.
9. Referral to tertiary health care facility is allowed when investigations and/or management are not available at secondary health care facilities.
10. Couples should receive information on Intra-Uterine Insemination IUI and other assisted reproductive technology (ART) method.
11. At tertiary health care level, if no cause of infertility is found or if the cause is not treatable, the couple should be briefed on the outcome of fertility assessment.

1.4 Guidelines Structure

This guideline is structured in the following manner: -

Chapter 1:

Consists of the introduction, purpose, scope and structure of the document. It provides an overview of the journey of infertility services in Oman.

Chapter 2:

Covers the basics for infertility care management, factors affecting fertility and conditions contributing to infertility. It is divided into the evaluation of infertile couple at PHC and at the secondary / tertiary care level. The management of female infertility and male infertility is also dealt with in this chapter. It gives a brief view of the assisted reproductive technologies available and concludes with the prevention of infertility in males and females.

Chapter 3:

Requirement and Responsibilities.

Chapter 4:

Annexes and references

CHAPTER 2: METHODS AND PROCEDURES USED

2.1 Basics for Infertility Care Management

A. Record of Personal Information

At registration all the personal information should be documented as per the infertility health record.

B. History Taking

History as per the infertility health record parameters which includes marital history, infertility history and clinical history should be documented (see the infertility health record for details).

C. Physical Examination

Include general examination, systemic examination, pelvic examination (female), urogenital examination (male) (See the infertility health record for details).

D. Investigations

For male:

- Semen analysis
- General investigations, if indicated (see the infertility health record for details).

For female:

- General investigations
- Ovulation & endocrine profile.

E. Counselling

Counseling should be provided at any step of evaluation and management

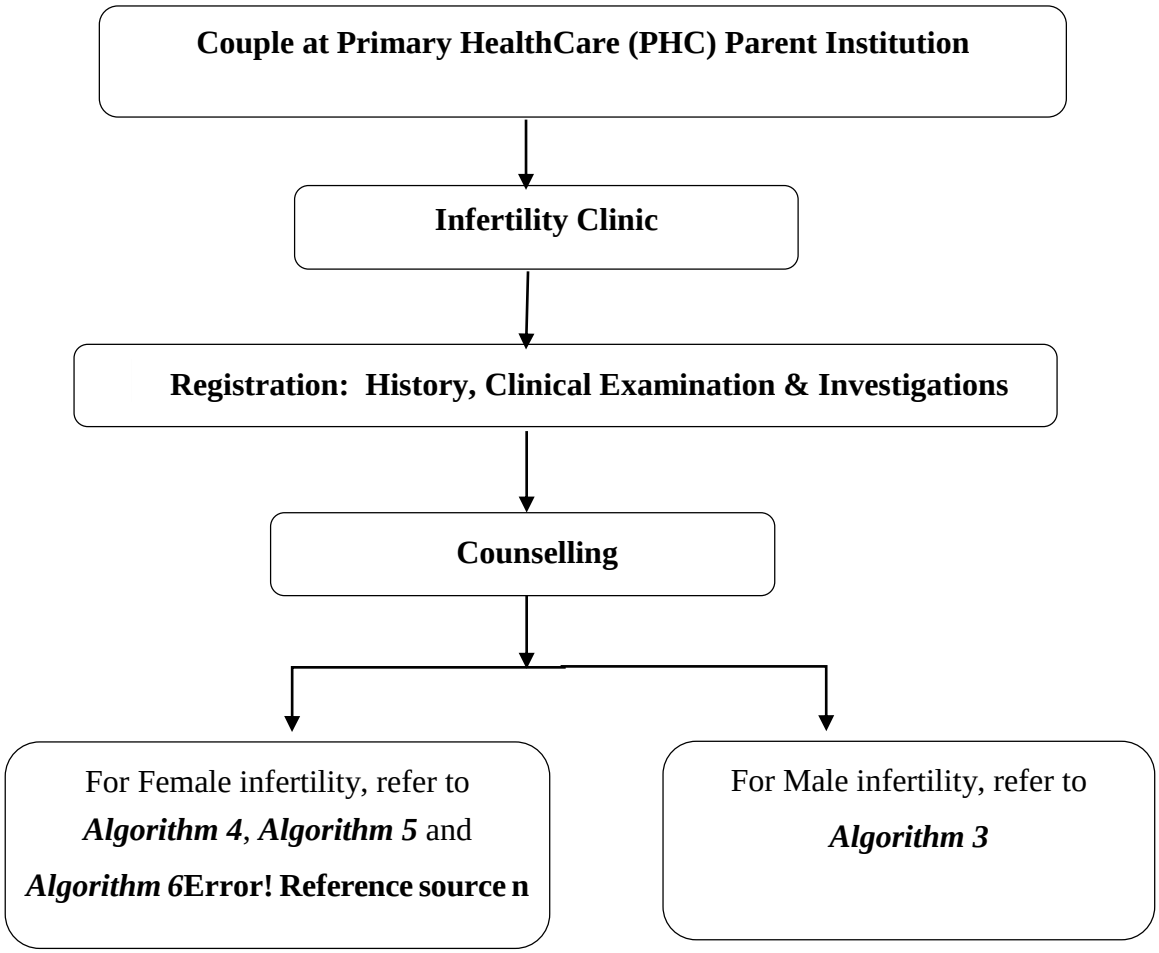
F. Management

Management will be according to the cause of infertility

G. Referral to Higher Health Care Facilities

Referral from primary health care to secondary and tertiary health care facility for further evaluation and management

Algorithm 1: Client Flow in the Health Facility

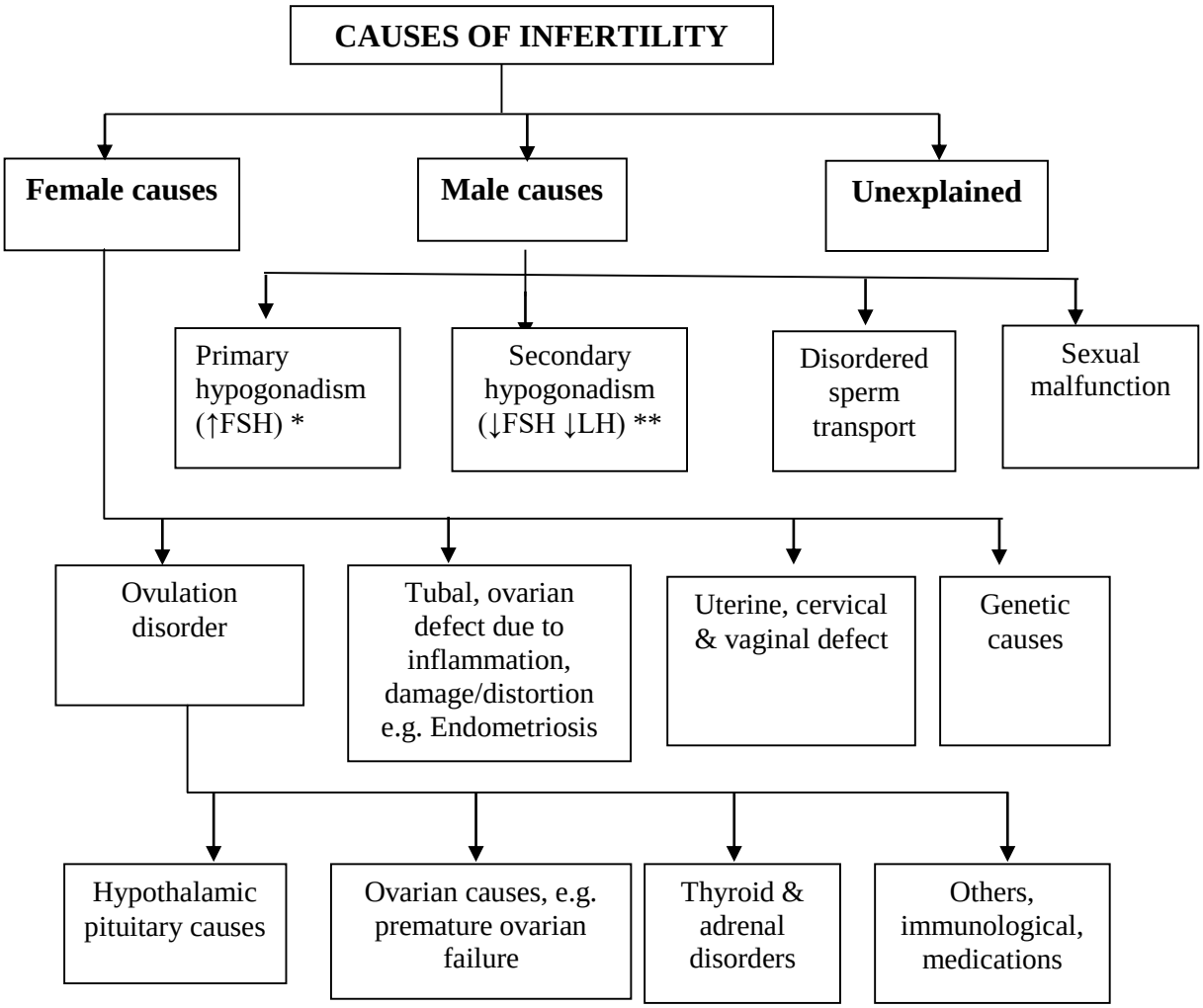


2.2 Causes of Infertility

1. **Infertility due to female factors**
    - Anovulatory factors
    - Cervical, Tubal or Uterine factors
    - Endometriosis
2. **Infertility due to male factor**
3. **Unexplained infertility**
4. **Infertility due to Combined (Male & Female) factors**

Only 5% of couples suffer from infertility due to anatomical, genetic, endocrinological and immunological causes. In 10-30% infertile couples, even with thorough evaluation will not find any cause for their infertility (unexplained infertility). All that remains are largely because of preventable conditions (Table 1 & Table 2).

Algorithm 2 : Causes of infertility



**FSH: Follicular Stimulating Hormone.*
***LH: Luteinizing Hormone.*

2.3 Factors Affecting Fertility

A. Age of Woman

After 30's there is slight decline in fertility and some women may take longer to conceive.

B. Age of Man

Although age does not affect sperm capabilities, it does affect the sexual functions and coital frequency thus, indirectly affecting the reproductive performances.

C. Obesity/ underweight

D. Frequency of sexual intercourse

People who are concerned about their fertility should be informed that vaginal sexual intercourse every 2 to 3 days optimizes the chance of pregnancy. Sperm survives for 48 - 72 hours in genital tract, whereas ovum survives only for 12 - 24 hours and the window time for fertilization is only few hours, so for fertilization to occur, the sperm should be available in genital tract shortly after ovulation.

E. Douching

Douching of vagina soon after intercourse can destroy sperms.

F. Chronic diseases

Examples: Hypothyroidism and diabetes

G. Previous or Current Drug Use

- Many drugs like narcotics, anti-cancer, phenothiazines, monoamine oxidase inhibitors, methyldopa, Cimetidine, Sulfasalazine and toxins such as arsenic and lead can interfere with ovulation, change semen quality and reduce sperm count.
- Anxiolytics drugs like haloperidol might cause hyperprolactinemia and diabetes associated with impotence.
- Contraceptives like depot medroxy progesterone acetate or Norplant can temporarily delay the return of fertility in female clients for few months.
- Some drugs, alcohol, tobacco and exposure to radiation can cause pregnancy wastage.
- Drugs like Guanethidine, Methyldopa may affect ejaculation.

Table 1: Diagnostic Approach to Causes of Female Infertility

Problem	Condition	Diseases & Contributory factors
Inability to conceive	**Ovarian, tubal & uterine inflammation damage/distortion**	• **Pelvic inflammatory disease (PID)** STIs: (Gonorrhea, Chlamydia & Mycoplasma) Non STIs: Postpartum or post abortion infections, Tuberculosis • **Endometriosis** • **Extensive surgery on reproductive tract** • **Congenital anomalies**
	Ovulation disorders	• **Hypothalamic:** Anorexia Nervosa, Kallmann Syndrome, psychological disturbances, Obesity • **Pituitary:** Tumours- Prolactinoma, Sheehan's Syndrome, damage due to surgery/radio therapy • **Ovarian:** Poly cystic ovarian disease, Premature ovarian failure, Resistant ovary syndrome, damage due to surgery/radio therapy, Stress/Physical exertion/heat, menopause • **Thyroid and adrenal disorders** • **Psychosomatic** • **Immunological** • **Drugs:** Narcotics, Anticancer, Phenothiazines, Monoamine oxidase inhibitors, Methyldopa, Cimetidine, Sulfasalazine. • **Toxins:** lead • **Radiation**
	Cervical & Vaginal causes	• **Congenital anomalies:** Cervical stenosis, Transverse vaginal septum, Müllerian agenesis, Hostile Cervical Mucus • **Infections:** leading to chronic cervicitis • **Previous surgery on:** Cervix cryotherapy, cone biopsy, cervical polyps

Problem	Condition	Diseases & Contributory factors
		• **Immunological:** Female sperm antibodies • **Dyspareunia:** Vulvovaginitis, PID, Endometriosis, Psychosomatic
Genetic causes		• Androgen insensitivity syndrome, • Turners syndrome, • Rokinstansky-Kuster-Hauser syndrome • late onset congenital adrenal hyperplasia
Pregnancy wastage		• Infections: STI, Syphilis, Mycoplasma, Tuberculosis, Malaria, Toxoplasmosis, Schistosomiasis, Filariasis, Leprosy. • Systemic diseases: Sickle cell disease, Hormonal disorders, diabetes mellitus • Environmental: Toxins e.g. lead, Radiation • Alcohol, tobacco & drugs • Uterine defects; Benign & malignant tumours, Cervical incompetence • Psychosomatic • Immunological

Table 2: Diagnostic Approach to Causes of Male Infertility

Problem	Contributory Factors / Diseases
I. Blocking of Sperm Duct	**Epididymitis:** Secondary to infections **STIs:** Gonorrhea, Chlamydia & Mycoplasma **Non STIs:** Tuberculosis, Schistosomiasis, Toxoplasmosis, Filariasis, Leprosy **Congenital:** Obstruction to duct, absence of (Vas deference)
II. Poor semen quality/poor sperm production **III. Oligospermia (sperm count < 15 million/ml)**	**Hormonal imbalance** **Infections:** Mumps, STIs **Systemic illness** **Malnutrition** **Bilateral hydrocele, varicocele in 30 –50%** **Unilateral cryptorchidism** **Partial retrograde ejaculation** **Partial obstruction of duct** **Environmental:** Radiation, heat exposure **Toxins:** Arsenic, Aflatoxin, fungal metabolites, **Pesticides & other chemicals** **Drugs:** Phenothiazines, Monoamine oxidase inhibitors, Nitrofurantoin, Cimetidine, Sulfasalazine **Genetic:** Klinefelter's syndrome, mild hypogonadism **Immunological:** Anti-sperm antibodies
IV. Azoospermia (no sperm in the semen)	**Hormonal imbalance.** **Environmental & occupational** **Radiation** **Drugs:** Androgens, Clomiphene Citrate. **Addiction:** Alcohol and Tobacco. **Genetic:** Klinefelter's syndrome, Kallmann syndrome, Congenital bilateral absence of cord, Bilateral Cryptorchidism, Bilateral anorchia, severe hypogonadism, Serotoli cell syndrome. **Post inflammatory :** bilateral cord obstruction

V. Sexual malfunction ejaculatory failure	**Psychosocial/psychosomatic** **Systemic diseases:** Sickle cell disease, DM, CVD **Impotence** **Congenital anomalies:** Hypospadias **Drugs:** Guanethidine, Methyldopa.

2.4 Evaluation of Infertile Couple at PHC

Evaluation should begin with asking full medical history, doing physical examination and investigations as per the availability of healthcare personnel expertise and laboratory facilities

2.4.1 History

General Information

- Age of client
- Occupation
- Duration of current marriage

Infertility History

- Duration of infertility
- Whether infertility is primary or secondary
- H/O previous attempts of infertility management

Marital History

- Number of marriages
- Number of wives for male partner
- Number of pregnancies that she/he had previously from other husband/wives
- Number of living & dead children
- Consanguineous marriage

Sexual History

- Desire problems
- Frequency of coitus (coital frequency 2-3 times a week is considered to be within normal range), or if couples are away from each other for long time
- Coital difficulties and potency
- Dyspareunia
- Pelvic inflammatory diseases (PID) for female
- H/O Sexual Transmitted Infections(STIs), or extramarital relationships
- Use of lubricants during intercourse

Menstrual History

- Age of menarche, late menarche is associated with ovulatory disorders
- Oligomenorrhoea (cycle > 35 days) with scanty menses may indicate, high prolactenima, PCOD, ovarian tumors, etc.
- Polymenorrhea and menorrhagia may indicate anovulation, fibroids, plops etc.
- Secondary dysmenorrhoea may indicate endometriosis, PID or fibroid uterus.
- Post coital bleeding, intermenstrual bleeding
- Abnormal vaginal discharge

Obstetrical History

- Parity, live born, abortions, miscarriages (first or second trimester), ectopic pregnancy& molar pregnancy.
- Uneventful pregnancies, any complications in pregnancies
- History of post abortion complications (sepsis) or puerperal sepsis
- Amenorrhea following postpartum hemorrhage (PPH) (Sheehan's syndrome).
- Amenorrhea following medical procedures (such as D&C) or cancer treatment, a condition called Asherman's syndrome.

Medical History

- Present or past history of: systemic diseases like diabetes mellitus, Hypertension, thyroid disease, autoimmune disease, cardiac disease, cystic fibrosis, and neurological disorders.
- Inquire about symptoms of hyperprolactinemia (Galactorrhea)
- Weight loss or gain

Surgical History

For Female:

- History of any pelvic surgery, laparotomy, laparoscopy, hysteroscopy, D&C, evacuation, or any major gynecology surgery.
- H/o any general surgery e.g. Thyroid surgeries

For male:

- Surgery for varicocele, hydrocele, undescended tests, inguinal hernia repair

- Surgery on urethral valve, bladder neck operations, repair of urethral stricture, reconstructive surgery, etc.
- Surgery for scrotal trauma or swelling,

Drug History

- Present or past use of drugs - cytotoxic agents, phenothiazines, haloperidol and tricyclic antidepressants - monoamine oxidase inhibitors, antihypertensive drugs (e.g. methyldopa, amlodipine), metoclopramide, Cimetidine, steroids, ovulation induction drugs.
- Use of contraceptives in immediate or past & type of it.
- H/O allergies

Family History

- Endocrine disease e.g. (PCOS, Thyroid) is often familial
- Genetic and hereditary disease
- Congenital abnormalities
- H/o infertility on the family either male or female

Social History

- Smoking, alcohol intake or addiction of drugs likes heroin,
- Stresses in living /work circumstances

Environmental and Occupational History

- Intense physical activity for the female
- Exposure to petroleum & heavy metal like lead, cadmium, mercury etc.
- Exposure to X- Rays, radiation & high temperature for males

2.4.2 Physical Examination for infertile couple

Table 3: Physical Examination for Male

Examination	Male
Weight	Gross over weight/obesity
Height	Span (Long limbs length) has been associated with Klinefelter's syndrome
Vitals	**Blood pressure , heart rate**
Fat and hair distribution	Feminine fat distribution and sparse or absent pubic, axillary and chest hair, poor beard growth suggests hypogonadism.
Breast examination	Gynaecomastia
Systemic examination	**Thyroid examination** **Chest examination** **Cardiovascular examination** **Abdominal examination** for organomegaly and any pelvic mass.
Genital Examination: (Annexure 1)	▪ **Penis:** Size, deformities, phimosis, ulceration or urethral discharge, surgical or traumatic scar (may indicate urethral stricture). ▪ **Scrotum:** presence of any swelling, hydrocoele, and varicocele, calcified nodules of vas deferens (VAS) or absence of VAS. ▪ **Testes** **Size:** Normal volume (15-25 ml). **Consistency:** Normally it is rubbery to firm. If hard & small Klinefelter's syndrome. If soft & small hypogonadotropic hypogonadism **Site**: Normally it is in the scrotum. Abnormal locations - in scrotal neck, inguinal, ectopic, impalpable, incomplete descent ▪ **Inguinal examination** Look for hernia, scar of healed tuberculosis or lymphogranuloma venereum, or lymphadenopathy. ▪ **Prostate:** per rectum examination: Normal prostate is rubbery regular and non-tender. It is tender in infections and hard in malignancy.

Table 4: Physical Examination for Female:

Examination	Female
Weight	▪ Overweight or underweight may have ovulatory disorders, Sudden gain or decrease of 10% in weight within past one year may be associated with oligomenorrhoea or amenorrhoea and anovulation. ▪ Very thin give a clue – anorexia nervosa WHO Group I ▪ Obese and short give a clue (PCOS), WHO group ∏
Height	Short stature, primary amenorrhoea, webbed neck suggests Turner's syndrome
Vitals	Blood pressure, pulse
Fat and hair distribution	Presence of abnormal distribution of hair may suggest hyperandrogenism, adrenal hyperplasia, hypothyroidism and ovarian dysfunction (PCOS).
Breast examination	▪ Breast abnormalities (masses, nipple retractions, abnormal discharges, etc.) ▪ Breast developmental deficiencies: hypogonadism ▪ Hyperprolactinemia, press nipple to confirm galactorrhea
Systemic examination	▪ Cardio-vascular, Respiratory, Thyroid ▪ Abdominal examination to look for organomegaly or pelvic masses, which could indicate systemic diseases.
Genital Examination (Annexure 3)	Speculum examination ▪ Inspect external genitalia, clitoris greater than 2cm and gland more than 1cm indicates virilism ▪ Look for imperforate hymen and vaginismus. ▪ Inspect vagina and cervix for any lesions and discharge. ▪ Collect cervical smear and vagina swab for microbiological examination wherever indicated. ▪ Palpation to look for any vaginal or cervical tenderness, or nodules indicating endometriosis, PID or any cervical lesions.

2.4.3 Investigations:

Male Investigations

First line: Semen analysis

- Semen analysis is the principal test for the evaluation of the male.
- If abnormal semen analysis, refer the male for repeat test after 7 days in another lab (e.g. polyclinic). If persistent abnormalities, to be referred to fertility male clinic
- If gross spermatozoa deficiency (azoospermia or severe oligozoospermia) has been detected the repeat test should be undertaken as soon as possible.
- Criteria for semen analysis (See below)

Table 5: WHO Criteria for Semen Analysis

Parameter	**Lower reference limits (WHO 2021)**
Semen volume	1.4 ml
Sperm concentration	16 million sperm /ml
Progressive motility	30%
Total motility	42%
Vitality	54% live
Morphology (strict criteria)	4% normal forms

Instructions for collection of semen sample refer to (Annexure 4)

1. Abstain from intercourse (no ejaculation) for at least 2days.
2. Do not drink alcohol or take a hot shower or hot bath immediately prior to producing specimen.
3. Produce a semen specimen by masturbation into a small, sterile, dry, wide mouth glass jar. Be sure, the entire specimen is captured in the container.
4. Lubricant jellies or soaps are not to be used for masturbation and if required glycerin is permitted. Ordinary condoms contain spermicidal and hence should not be used.
5. Take the specimen to the laboratory as soon as possible (The specimen should arrive in the laboratory within 1 hour of collection at room temperature).
6. Label the jar with the client's name, hospital number, date and time of collection.

Second line investigation: If abnormal result of semen analysis to do:

- CBC, Blood sugar, sickling test, Urine microscopy, Rapid Plasma Reagin (RPR) test
- RFT, LFT, ESR Hepatitis B, urine culture if indicated

- Infertility Hormone profile (for abnormal semen/azoospermia): FSH, LH, TSH, Prolactin and Testosterone
- Scrotum ultrasound if indicated

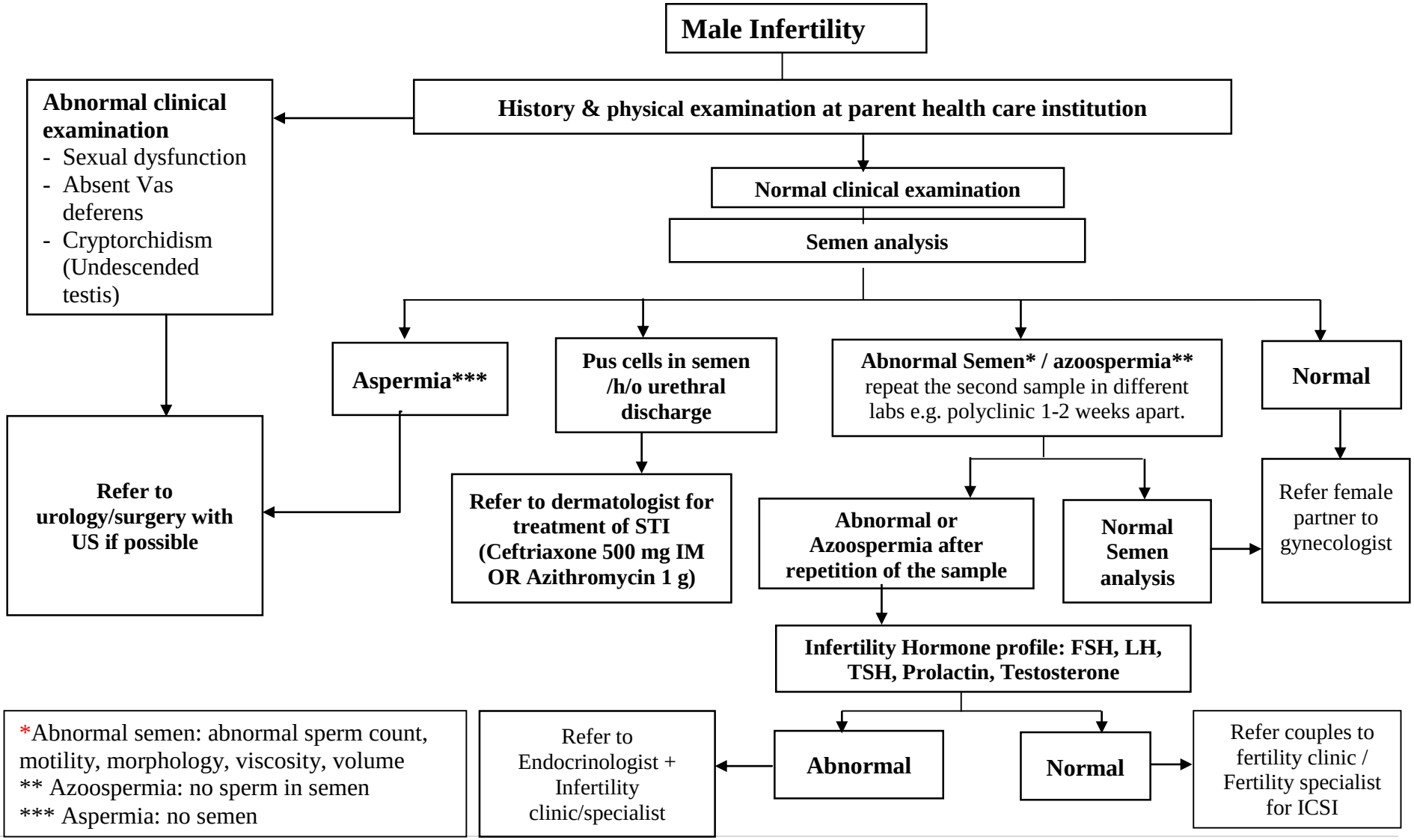
Female investigations

- **CBC, blood sugar, Rapid Plasma Regain (RPR) test, Sickling, blood group, urine microscopy**
- **ESR, RFT, LFT, Urine culture, hepatitis profile, HIV, Chlamydia, Rubella** if indicated
- **Hormonal assays (**At day 2 - 4 of menstruation), according to menstrual history (check algorithm 5)
    1. **FSH, LH, TSH, Prolactin**
        - **High levels of FSH and LH, basal FSH levels** > 25 mIU/mL (depending on the laboratory used) indicates **Premature ovarian insufficiency (POI).** POI is diagnosed based on the following criteria: (oligo/amenorrhea for at least 4 months and an elevated FSH level >25 IU/L on two occasions >4weeks apart)
        - **TSH** < 3.5 mmol/l (even within normal range but needs to make it less (≤ 2.5mlU/L) for patients going for IVF)
        - **Prolactin** levels ≥ 1000 mIU/ litre to rule out **pituitary tumors** by pituitary MRI (**Note:** Prolactin test should not be done after pelvic or breast examination or early in the morning as that may give high false positive results and repeated test for prolactin is advised.
    2. **Testosterone and 17-hydroxyprogesterone (17-OHP)** test if any androgenic clinical features e.g. hirsutism, acne, coarse facial features, voice. or for any irregular cycles
        - **High Testosterone** level **> 0.5-2.4 nmol/l indicate e.g. PCOS.** In some cases of PCOS will have normal testosterone levels but with high DHEAS
    3. **Mid luteal serum progesterone:** Day 21(28-day cycle) or one week before menses. The test should not be done in patient with irregular cycle

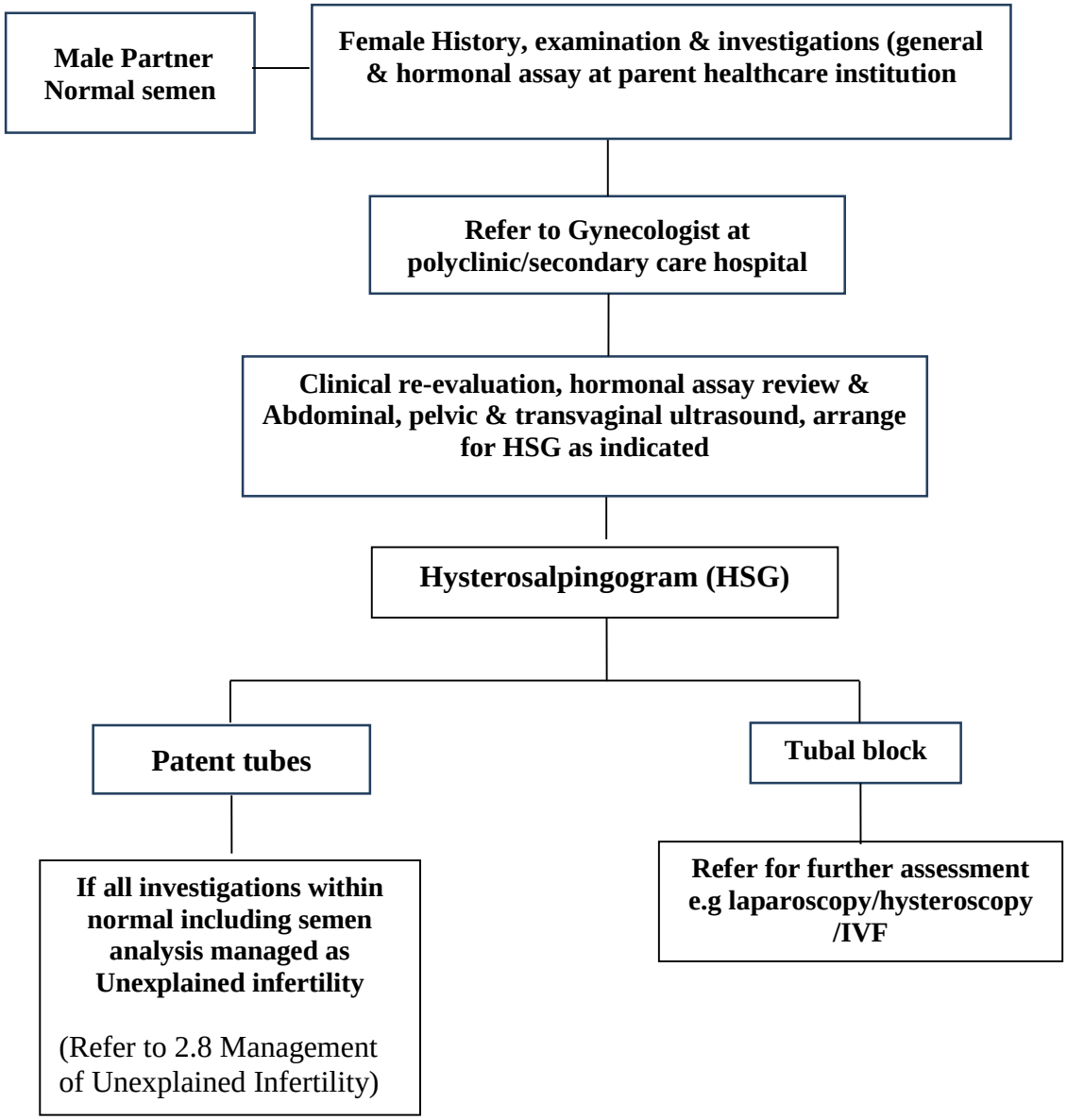
2.4.4 Diagnosis and management

- Review investigations and refer to the algorithms for management of the couple

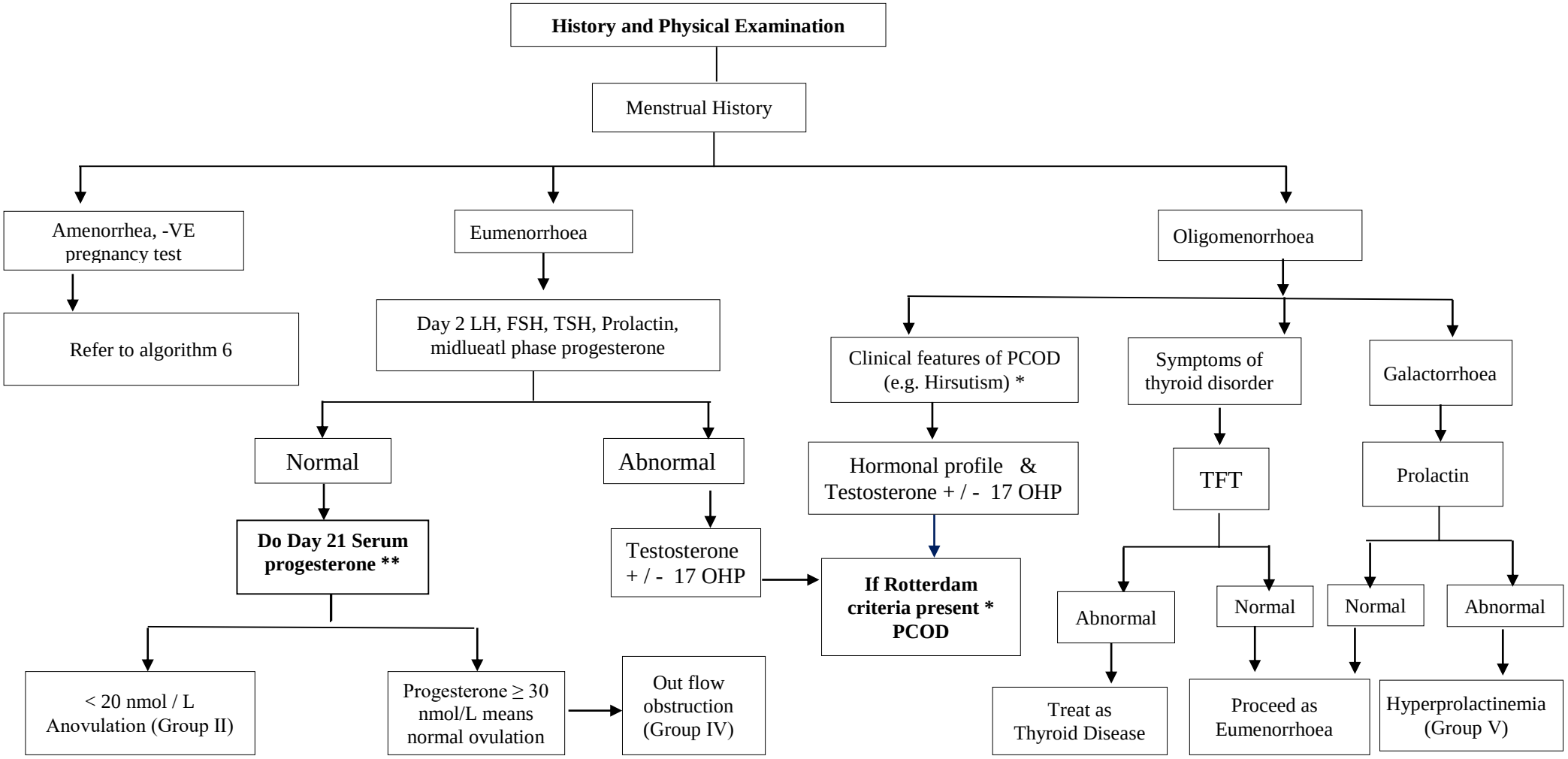
Algorithm 3: Male infertility evaluation (A)



Algorithm 4: Diagnosis of Female Infertility

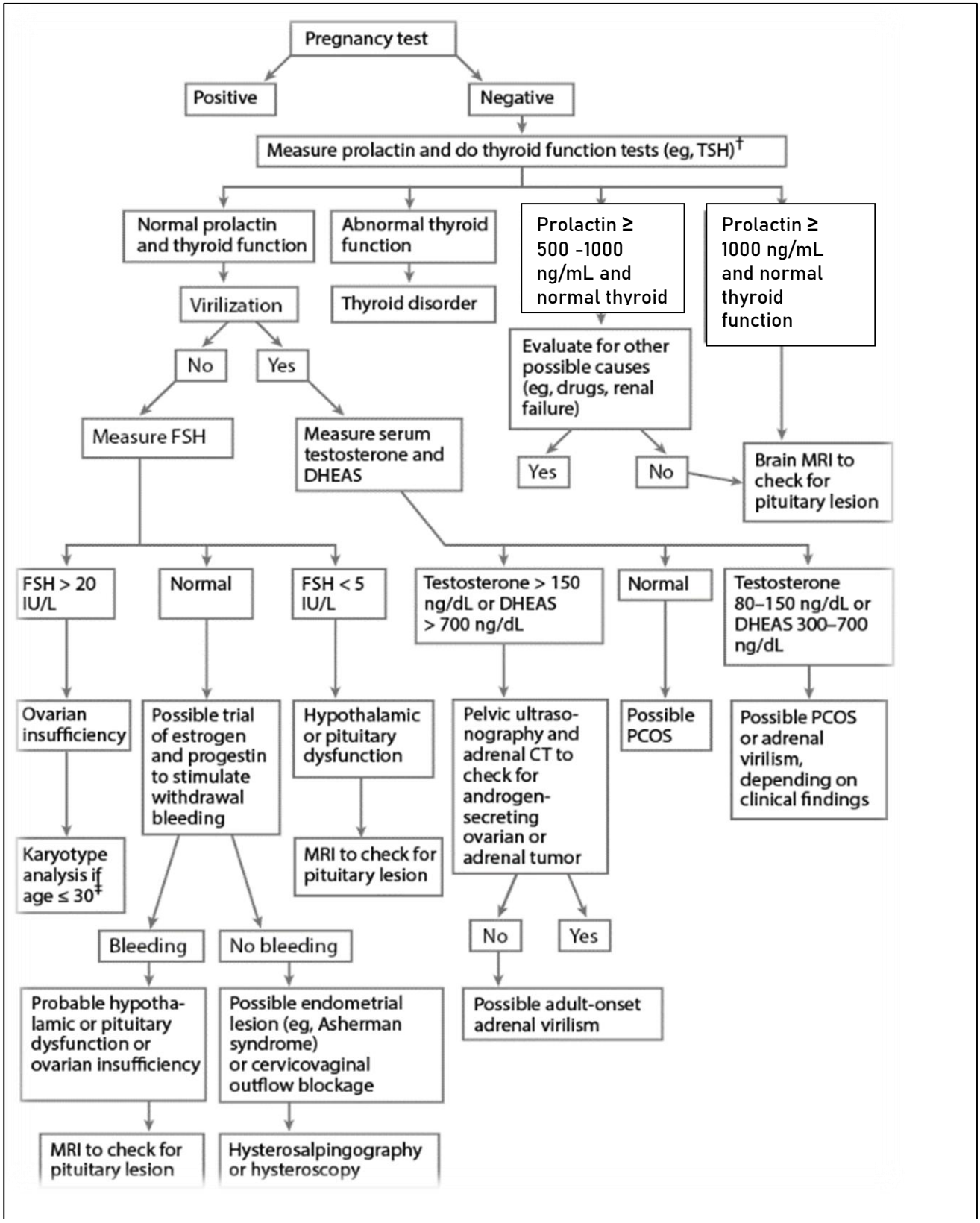


Algorithm 5: Evaluation of Ovulatory Dysfunction



* **Rotterdam criteria:** the presence of two of three of the following criteria: **oligo-anovulation, hyperandrogenism and polycystic ovaries** (≥ 12 follicles measuring 2-9 mm in diameter and/or an ovarian volume > 10 mL in at least one ovary).
** Day 21 serum progesterone in 28 days cycle or one week before the next menses.

Algorithm 6: Evaluation of Secondary Amenorrhea



Source: https://www.msdmanuals.com/professional/multimedia/table/evaluation-of-secondary-amenorrhea

2.4.5 Counselling of Infertile Couple

Understanding the individual /couple's situation is vital to help them obtain the best form of infertility counseling possible. Counseling should be provided at each step of evaluation and management at primary, secondary & tertiary health care level.

Each couple should receive counseling that:

- Infertility is a shared concern and evaluating both partners is mandatory. Explain to the couple that infertility can be contributed by either of them, or by both of them.
- Fertility declines with age
- Couple who are concerned about their fertility should be informed that over 80% of couples in the general population will conceive within 1 year if:
  - The woman is aged under 40 years
  - They do not use contraception and have regular sexual intercourse
- Of those who do not conceive in the first year, about half will do so in the second year (cumulative pregnancy rate over 90%).
- Frequency of coitus is positively related with the frequency of pregnancy
- Explain how to calculate fertility period
- Healthy Lifestyle e.g. maintain normal body weight, quit smoking and alcohol consuming, reduce caffeine intake as all these can affect the fertility.
- Avoid things that lead to prolonged heat for the testicles.
- Reduce stress.
- Avoid exposure to pesticides, heavy metals and other toxins.
- Early detection and management of male genitalia abnormalities e.g., Undescended testis, hypospadias, varicocele etc
- Frequent genital tract infections can lead to infertility hence should be treated properly.
- Adequate hygiene should be practiced during delivery and post-partum to reduce the incidence of postpartum infections.
- Inform the couple that the process of investigations and treatment (including surgical intervention or assisted reproductive technology (ART)) may take a considerable amount of time.
- Involvement of mental health professionals will help to alleviate stress and improve patient care.

- Being knowledgeable about the impact of infertility on sexual relationship, is essential in order to improve quality of life within the couple's relationship.

2.5 Evaluation of Infertile Couple at Secondary / Tertiary Care Level

2.5.1 Evaluation of male client:

To be seen by urologist /endocrinologist according to probable diagnosis from primary health care doctor (see & Algorithm 4)

- Review client's records.
- Take history and conduct physical examination.
- **Repeat semen analysis, if indicated.**
- **Assess hormonal profile:** FSH, LH, testosterone, Prolactin and TSH
- **Ultrasonography:** To detect sub clinical varicocele or search for the varicocele on the other side when present on one of the inguinal regions
- **Doppler ultrasound examination:** To detect sub clinical varicocele
- **The following tests to be done if indicated:**
  - **Anti-sperm antibodies** (Immunobead test or mixed antiglobulin reaction)
  - **Immunoglobulin G & M** (for Chlamydia Trachomatis)
  - **Testicular biopsy**

  To be done in case of severe oligozoospermia or Azoospermia with normal testicular volume and normal serum follicular stimulating hormone values.

  (It is advised to be done in center where IVF services are available in order to freeze any retrieved sperms and use them in fertilization instead of waste sperms just to confirm the diagnosis).

2.5.2 Evaluation of female client:

To be seen by gynecologist

- Review client's records.
- History & physical examination.
- Repeat investigations if needed
- **Ultrasound (Abdominal, trans-vaginal) and hystrosonography** to detect any abdominal organomegaly, and uterine, ovarian and tubal pathology.
- **If patient presenting with amenorrhea with negative pregnancy test and normal TSH and prolactin levels progesterone challenges test need to be done (**see algorithm 7)

- If the initial blood analyses including hormonal assay and semen analysis are normal, then the patient can be evaluated for the need of **diagnostic laparoscopy** or **hysterosalpingography (HSG)** for tubal patency testing.

- **Hysterosalpingography (HSG):** Can be done as preliminary procedure for tubal testing.
  HSG is typically performed on Day 7 to Day 10 of a 28-day cycle
  It is important to counsel patients who are found to have patent tubes to try spontaneously for 3-6 months after the intervention, as a good proportion of them will become pregnant without further help.
- **Laparoscopy:** Preferred compared to hysterosalpingography as it has the advantage of direct visualization of the pelvis.
  It should be done during proliferate phase on Day 7 to Day 10 of a 28-day cycle.
  Is indicated in female client with history suggestive of PID, history of longstanding infertility and if client's age is above 30 years and she is just beginning her fertility evaluation work up.
  Endometrial biopsy to be taken in suspected cases of genital tuberculosis.
- **Hysteroscopy** if indicated can be combined with laparoscopy.
- **Anti-Mullerian Hormone (AMH), AFC; To be done, if indicated** as per the cause diagnosed by laparoscopy / hysteroscopy

2.5.3 Evaluation outcome

Once the above work up is complete, couple's cause of infertility will be categorized

1. Infertility due to female factors:
   - Anovulatory factors
   - Cervical, tubal or uterine factors
   - Endometriosis
2. Infertility due to male factor
3. Unexplained infertility
4. Infertility due to Combined factors

2.6 Management of Female Infertility

2.6.1 Infertility Due to Anovulation

- Incidence: 30 - 40 % infertile females have ovarian dysfunction. If appropriately diagnosed and managed, the success rate is as high 98%
- Regular ovulation occurs when the hypothalamic-pituitary ovarian axis is intact. Any disorder occurring at one or more levels of hypothalamic-pituitary ovarian axis may lead to anovulation.
- Treatment of anovulation depends on the site of involvement, which is assessed by specific hormonal assays.
- WHO classification (based on the hormonal assay results) for ovulatory disturbances, is as follows:

Table 6 : WHO Classification for Ovulatory Disturbances

Group I	Hypogonadotropic hypogonadism
Group II	Hypothalamic-pituitary dysfunction
Group III	Ovarian failure
Group IV	Congenital or acquired genital tract disorders
Group V	Hyperprolactinemia with detectable pituitary tumor
Group VI	Hyperprolactinemia without pituitary tumor
Group VII	Amenorrhoea with pituitary tumor

Clinical presentation:

- Regular or irregular cycle
- Oligomenorrhoea
- Amenorrhoea
- Galactorrhea
- Obesity
- Abnormal development of secondary sexual characters
- Hirsutism, and virilism
- Anosmia
- Manifestation of other endocrine abnormalities e.g. thyroid dysfunction

Management of WHO Group I &Group II

Hypogonadotropic hypogonadism& Hypothalamic-pituitary dysfunction

- Advise woman with WHO group I or Group II anovulatory infertility that they can improve their chance of regular ovulation, conception and an uncomplicated pregnancy by adjustment to their **normal body weight (normal body mass index).**
- Advice woman with WHO group I or Group II anovulatory infertility to moderate their exercise levels if they undertake high levels of exercise.

The commonly used drugs for ovulation induction are:

- Clomiphene citrate (alone) OR
- Clomiphene citrate & Human Menopausal Gonadotropins (HMG) +Follicular stimulating gonadotrophin(FSH)
- Human Chorionic Gonadotropins (HCG)

1. Clomiphene citrate (selective estrogen receptor modulators):

- In management of anovulation (Group I)
- Start with Clomiphene 100 mg from Day 2-6 of menstrual cycle for three cycles
- If no ovarian response is seen, increase the dose by 50 mg every cycle until maximum dose i.e. 250 mg is reached and the ovarian response is seen (serum progesterone ≥ 30 nmol /litre on Day 21 –23 of menstrual cycle).

  Note: For woman with irregular menses, at any day the progesterone level ≥ 30 nmol /litre means she is ovulating.
- The dose at which ovulation occurs, should be continued for a period of **6-9 months**.
- If there is failure of ovulation with maximum dose of Clomiphene citrate (250 mg), administration of **Human Chronic Gonadotropins (HCG)** can be initiated or laparoscopy plus ovarian drilling can be done.

2. Gonadotropins; (Human Menopausal Gonadotropins (HMG) & Human Chorionic Gonadotropins (HCG)

- To be used if the patient fails to ovulate with maximum dose of Clomiphene citrate
- Start with Human Menopausal Gonadotropins (HMG) one ampoule intra muscular daily for 5 days from **Day 2 / 3 of menstrual cycle** (One ampoule of HMG = 75 IU of follicular stimulating hormone + 75 IU of luteinizing hormone).
- Do follicular study by trans-vaginal ultrasound on **Day 7/8 of menstrual cycle**.

- Continue with same dose of HMG & follicular study every 2 – 3 day interval until follicles reach to 18 mm size.
- Give Human Chronic Gonadotropins (HCG) 5,000- units (when follicle is ≥ 18mm).
- Advise intercourse between 24 –36 hours following HCG administration.
- If on Day 8 of stimulation no follicular response is seen, increase HMG by one ampoule followed by follicular study every 2 – 3 days for 5 – 6 days.

Note: If on day 8 of menstrual cycle multiple follicles 8 or more of ≥ 10 mm in number are seen, it indicates **ovarian hyper-stimulation syndrome** due to gonadotropins therapy.

Ovarian Hyper Stimulation Syndrome (OHSS):

It is a known **life threatening complication** of gonadotropins therapy and needs early recognition and management.

Symptoms and Signs are:

- Abdominal pain and Abdominal bloating,
- Nausea, vomiting
- Breathlessness, inability to lie flat or talk in full sentences
- Signs of hydrothorax
- Reduced urine output
- Leg swelling
- Vulval swelling
- Associated comorbidities such as thrombosis

Management:

Patient should be stabilized and referred immediately to hospital for management whenever OHSS is suspected.

Ovarian Hyper Stimulation Syndrome is life-threatening complication of Gonadotropins therapy. Gonadotropins should not be used for more than 6 cycles

Management of WHO Group IV: Congenital or acquired genital tract disorders

May need surgical intervention depending on the cause.

Management of WHO group V & VI:

Hyperprolactinemia with detectable pituitary tumor & Hyperprolactinemia without pituitary tumor, treatment:

Cabergoline

- More specific D2 agonist
- 0.5 mg once weekly OR 0.25 mg twice weekly
- Adjust by 0.25 mg twice weekly up to 1 mg 2 times weekly.
- Check prolactin level every 3-4 months to adjust the dose.
- Mild side effect compares to Bromocriptine
- Not yet indicated for use during pregnancy.
- Cardiac valvular regurgitation seen with very high doses =3mg =10-20 times higher than the maximum dose use for prolactinomas.
- Discontinue if at least 2 years of normalization of prolactin level, tapering decrease by 0.25 mg of the weekly dose in 3 months' interval.

Bromocriptine:

- Dopamine receptor agonist is indicated in anovulatory cycle associated with hyperprolactinemia.
- Start with dose 1.25 mg a day for 7 days, then increase gradually to 5 mg twice a day over next 2-3 months,
- Followed by doubling of dose every 4-6 weeks until maximum daily dose of 20 mg is reached i.e. 10 mg three times a day and beyond which the dose should not exceed.
- Alternate route 2.5 mg per vagina daily with fewer side effects.
- Monitor Serum prolactin level on monthly basis and adjust Bromocriptine dose accordingly as per the response (i.e. decrease in serum prolactin level and reduction in Galactorrhea)
- Once prolactin levels are normal, maintain same dose for 4 – 6 months.
- If still not ovulatory in spite of normal prolactin levels add Clomiphene citrate as mention before (page 432)
- If prolactin levels are still high in spite of maximum dose of Bromocriptine, refer patient to **Endocrinologist**.

2.6.2 Infertility Due to Tubal and Uterine Factors

Tubal factors should be assessed after initial work up of ovulation and semen analysis are completed.

Evaluation for tubal factors:

Hyesterosalpingogram (HSG):

- Also known as uterosalpingography is a radiographic procedure to investigate the shape of the uterine cavity and the shape and patency of the fallopian tubes. It injects a radio-opaque material into the cervical anal and usually fluoroscopy with image intensification.
- HSG gets priority when the couple is very young with past history of P.I.D.
- HSG should be performed during proliferative phase (day 7 to day 10) of the cycle.
- Explain to the patient regarding the procedure.
- Carry out a detailed physical examination and if indicated high vaginal swab (HVS) to rule out acute infection.
- Give non-steroidal anti-inflammatory drug/antispasmodic 30-60 min before procedure to lessen the pain and tubal spasm.
- In clients with history of PID give antibiotic cover with Doxycycline 100 mg twice for a week to both partners.
- Carry out the procedure under aseptic precautions.
- Inject 20 ml of water soluble dye slowly through the cervical canal into the uterine cavity.
- Avoid leakage by steady traction on the vulsellum accompanied by gentle push on the cannula. Partial or complete withdrawal of the bivalve speculum will allow an adequate view of the cervix.
- A late film would help in visualizing peritubal adhesions and delayed spill.
- The use of the contrast should be considered to improve subsequent spontaneous pregnancy rates.
- It is just as important to counsel patients who are found to have patent tubes to try spontaneously for 3-6 months after the intervention, as a good proportion of them will become pregnant without further help.

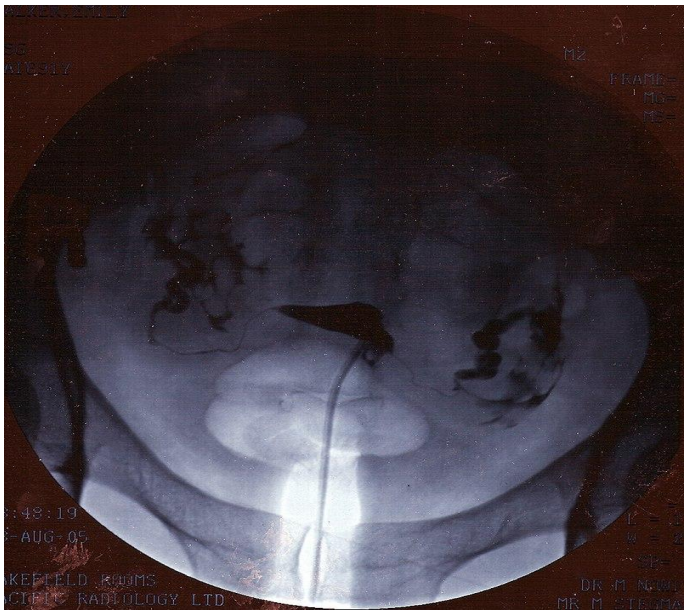


Figure 1: Hysterosalpingogram (HSG):

Laparoscopy :

- Laparoscopy is the gold standard investigation for tube testing. But HSG should be first line to avoid anesthesia complications & surgical complications.
- It should be done during proliferate phase on day 7 to day 10.
- Visualization of the pelvic organs should be systematic and thorough describing each organ in detail including its dimensions, thickness, appearance, relation to adjacent structures, mobility etc.

2.6.3 Infertility Due to Endometriosis

Endometriosis is an inflammatory disease associated with pelvic pain and infertility that is characterized by lesions of endometrial-like tissue outside of the uterus. 25-50% of infertile women have endometriosis**.** Prevalence of Endometriosis among women: 6–8%

Clinical Presentation:

- 20–25% of the patients are asymptomatic
- Dysmenorrhea affecting daily activities and quality of life
- Chronic pelvic pain
- Deep Dyspareunia
- Infertility
- Period-related or cyclical gastrointestinal symptoms, in particular, painful bowel movements
- Period-related or cyclical urinary symptoms, in particular, dysuria & hematuria

Clinical Examination:

In mild cases no abnormality may be found clinically despite severe symptoms.

In pelvic endometriosis discomfort and tenderness on bimanual examination along with/ without palpable adenexal masses and indurations of utero-sacral ligaments may be found.

Diagnosis:

Do not exclude the possibility of endometriosis if the abdominal or pelvic examination, ultrasound or MRI is normal. If clinical suspicion remains or symptoms persist, consider referral for further assessment and investigation.

Diagnostic procedures:

1. **Ultrasonography:** Consider transvaginal ultrasound

- To investigate suspected endometriosis even if the pelvic and/or abdominal examination is normal
- To identify endometriomas and deep endometriosis involving the bowel, bladder or ureter.
- If a transvaginal scan is not appropriate, consider a transabdominal ultrasound scan.

2. **MRI**

- MRI should not be done as primary investigation to diagnose endometriosis in women with symptoms or signs suggestive of endometriosis.
- Consider pelvic MRI to assess the extent of deep endometriosis involving the bowel, bladder or ureter.

3. **Laparoscopy:**

- To diagnose endometriosis in women with suspected endometriosis, even if the ultrasound was normal.
- Consider **pelvic ultrasound or MRI** before an operative laparoscopy
- Consider taking a biopsy of suspected endometriosis to confirm the diagnosis of endometriosis (be aware that a negative histological result does not exclude endometriosis)
- If a full, systematic laparoscopy is performed and is normal, explain to the woman that she does not have endometriosis, and offer alternative management.
- Laparoscopy facilitates a good diagnosis and staging as per the **American Fertility society (A.F.S) revised classification**.

The 4 Stages of Endometriosis ((A.F.S) revised classification) are dictated by the location, the number, and the size of endometrial implants; specifically:

- The extent to which the implants have spread
- Other pelvic structures involved
- The extent of pelvic adhesions
- The blockage of the fallopian tubes

Breaking endometriosis up into stages can be beneficial both for the patient and the doctor. It ensures that the doctor accurately expresses the severity of the woman's condition. Determination of the stage or degree of endometrial involvement is based on a weighted point system (See annexure 2)

Most cases of endometriosis are mild to moderate. Infertility could be encountered primarily even in mild cases. The severity of symptoms does not correlate with any given stage. It is possible for a woman with stage 3 endometriosis to have symptoms similar to a woman with stage one.

Management:

- Depend on client age, stages and previous treatment trial
- The treatment is essentially chosen by each individual woman, depending on symptoms, age, and fertility.
- The treatment includes medical, surgical, or a combination of these approaches.

A. <u>Pain management:</u>

- Start with short trial (for example, 3 months) of Paracetamol or an NSAID (alone or in combination).

- If a trial of Paracetamol or an NSAID (alone or in combination) does not provide adequate pain relief, consider other forms of pain management (hormonal &surgical) management

Hormonal:

- Explain to women with suspected or confirmed endometriosis that early hormonal treatment for endometriosis can reduce pain and has no permanent negative effect on subsequent fertility.
- This treatment to be decided in secondary and tertiary center, prescribrtion of hormonal treatment depends on her wishing for conception single or married, all endometriosis cases to be referred to specialist in endometriosis
- For women with suspected, confirmed or recurrent endometriosis offer hormonal treatment for example:
  - Combined oral contraceptive pill OR
  - Medroxy Progesterone acetate injection 150mg (Depo-Provera) OR
  - Dehydrogesterone Duphaston OR
  - Gonadotropin-releasing hormone analogues (GnRH) & Luteinizing Hormone-Releasing Hormone (LHRH) Analog

Table 7: Medical Management of Endometriosis-Associated Pain:

Agent	Dose	Route	Dosing frequency	Common side effects
Combined oral contraceptives	30–35 µg ethinyl estradiol, plus progestin	Oral	Daily (cyclic or continuous)	Irregular bleeding, weight gain, bloating, breast tension and headache
GnRH& LHRH				
GnRH agonists			6-month duration	Vasomotor symptoms and accelerated bone loss If given for more than 6 months give back therapy
(Lhrh)Triptorelin√	3.7 mg	IM injection	Monthly for 6 months	She should be apprised of the potential hazard to the fetus if she got pregnant
(Lhrh)Triptorelin depot	11.25 mg	IM injection	Every 3 months	
Goserelin	3.6 mg	SC implant	Monthly for 6 months	
Progestin				
progestogen-only hormone Dienogest (Vissane)	2 mg	Oral	Daily	
Megestrol acetate	40 mg	Oral	Daily up 2 years	Irregular bleeding, weight gain, bloating and edema
Norethindrone acetate	10-15 mg	Oral	Daily starting on day 5 of cycle	spotting : increase the dose to 20-25 mg daily and reduce when bleeding stop
Medroxyprogesterone acetate (MPA)	30 mg/ day	Oral	8-10 mg bid daily	
depot medroxyprogesterone	150 mg	IM injection	Every 3 months	Also with transient BMD decline

Agent	Dose	Route	Dosing frequency	Common side effects
acetate (DMPA-IM 150) Depo-Provera				

B. Surgical Management:

Laparoscopic treatment

- To be done by skilled person in endometriosis surgery
- Perform surgery for endometriosis laparoscopically unless there are contraindications.
- During a laparoscopy to diagnose endometriosis, consider laparoscopic treatment of the following, if present:
  - Peritoneal endometriosis not involving the bowel, bladder or ureter
  - Uncomplicated ovarian endometriomas.
- As an adjunct to surgery for deep endometriosis involving the bowel, bladder or ureter, consider **excision** rather than ablation to treat endometriomas, taking into account the woman's desire for fertility and her ovarian reserve
- Offer laparoscopic **ovarian cystectomy** with excision of the cyst wall to women with ovarian endometriomas, because this improves the chance of spontaneous pregnancy and reduces recurrence. Take into account the woman's ovarian reserve, size of endometrioma, patient symptoms.

C. Fertility Management:

- Clomiphene & Intra-Uterine Insemination (IUI) treatment. If treatment is not successful after three or more months, the next step is
- The use of **injected gonadotropins medications with IUI**, if not successful go to
- **In vitro fertilization (IVF)**

2.7 Management of Male Infertility

A. Treatment of infections

Infections e.g. STIs &Non STIs infections (Table 2) should be treated with appropriate antimicrobial therapy

B. Lifestyle changes

- Patients should be encouraged to stop smoking cigarettes and to limit environmental exposures to harmful substances and/or conditions.
- Stress-relief therapy and consultation of other appropriate psychological and social professionals may be advised.

C. Hormonal / Medial Management (for oligospermia or oligoasthenospermia)

1. **Androgens:**
   - **Testosterone undecanoate capsules:** 40mg orally 3–4 capsules daily during the first 2–3 weeks, followed by a gradual decrease to 1–3 capsules daily for 3 months.
   - **Synthetic androgens Mesterolone (Proviron):** 25 mg T.I.D for 3 months
   - **Testosterone esters oily preparation:** 250mg I.M injection twice a month for life long to improve the potency.

   Clinical application of androgens:

   - Hypergonadotropic Hypogonadism i.e. testicular failure or complete atrophy
   - Idiopathic delayed puberty.
   - Asthenozoospermia, only in case of hypogonadism
   - Andropause and male aging syndrome.

   Note: Androgens use is for health wellbeing benefit not for infertility treatment.

   Patient who has congenital adrenal hyperplasia (CAH) with isolated testosterone deficiency may respond to testosterone replacement.

- **Gonadotropins:**

To improve spermatogenesis

- **Luteinizing Hormone LH i.e**. **Human Chorionic Gonadotropins (HCG) (Pregnyl)** 1500 I.U. Twice /week for three months
- **Human Menopausal Gonadotropins (HMG)** Intramuscular Injection one ampoule twice/week for three months

Clinical application of HMG & HCG

- Hypogonadotrophic hypogonadism.
- Idiopathic oligozoospermia
- Maturation arrest (doubtful)

- **Clomiphene citrate (Clomid)**

To improve spermatogenesis

- 25mg once daily for 3-6 months
- It is closely related to estrogens that compete with oestrogen for steroid receptor in the hypothalamus inhibiting negative feedback mechanism exerted by oestrogens leading to increase of Luteinising Releasing Hormone and Follicular Stimulating Hormone. Increase in FSH & LH improves spermatogenesis.
- Need to repeat semen analysis for response.

- **Cyclic Steroids**

For Patients with antisperm antibody levels greater than 1:32

It may respond to immunosuppressant using cyclic steroids for 3-6 months. However, patient needs to be aware of the potential side effects of steroids, including avascular necrosis of the hip, weight gain, and iatrogenic Cushing syndrome.

- **Imipramine or alpha-sympathomimetics such as pseudoephedrine**

Use in management of retrograde ejaculation.

- However, these medicines are of limited efficacy, especially in patients with a fixed abnormality such as a bladder neck abnormality occurring after a surgical procedure.
- More recently, the injection of collagen to the bladder neck has allowed antegrade ejaculation in a patient who had previously undergone a V-Y plasty of the bladder neck and for whom pseudoephedrine and intrauterine insemination had failed.

- **Bromocriptine (Parlodel)**

For patients with hyperprolactinemia

Start with low dose **2.5mg daily** and increase gradually weekly until desired dose is reached. The dose has to be adjusted according to the rise in the value of prolactin.

- **Vitamins A and E (Retinol)**

A combination of Vitamin A 200,000 I.U with Vitamin E 40 I.U is given once daily for 3 months.

D. Surgical Management:

1. Management of Varicocele

- Various techniques for varicocelectomy have been proposed and used, each with advantages and disadvantages.
- The retroperitoneal approach may be performed as an open procedure or laparoscopically.
- Successful varicocelectomy results in improvement in semen parameters in 60-70% of patients.

2. Management of Obstructive Azoospermia:

- Confirm the obstructive level and rule out cystic fibrosis
- Obstructive azoospermia managed in one of two ways:
  - Surgical correction of the **obstruction**, which may allow the couple to conceive naturally, or
  - Retrieval of sperm directly from the epididymis or testis, followed by in vitro fertilization (IVF)

Surgical correction of the obstruction:

- **Vasovasostomy or vasoepididymostomy**
  - These microsurgical techniques are performed in patients with known e pididymal or vasal obstruction, both congenital and acquired (e.g., due to surgery, trauma, infection).
  - Improved surgical techniques and the use of the operating microscope have improved the outcomes in patients requiring vasectomy reversal or those with primary vas obstruction.
- **Transurethral Resection of the Ejaculatory Ducts (TURED)**
  - For patients with a known or suspected obstruction of the ejaculatory ducts to improve semen quality.
  - Risks with this procedure include watery (urine) ejaculate, chemical or bacterial epididymitis due to reflux, bleeding, and retrograde ejaculation.
- **Sperm retrieval techniques**
  - Testicular sperm extraction (TESE) is performed at the time of testicular biopsy or as a separate procedure using the same technique.

- Common methods for sperm retrieval techniques:
    1. Microsurgical epididymal sperm aspiration (MESA)
    2. Percutaneous epididymal sperm aspiration (PESA)
    3. Testicular sperm aspiration (TESA)
    4. Percutaneous testicular sperm aspiration

E. Management of Congenital Deformities

1. Management of Hypospadias

- Hypospadias is a congenital anomaly of the urogenital tract characterized by abnormal location of the external urethral meatus over ventral aspect of penis. Can Cause male factor infertility since the urethra carries semen out of the body.
- The ideal time to correct primary hypospadias is when aged 6-12 months. However, patients operated in either childhood or in adulthood, there was no significant difference in fertility potential noted.

The goals of surgical treatment of hypospadias are as follows:

- To create a straight penis by repairing any curvature (orthoplasty)
- To create a urethra with its meatus at the tip of the penis (urethroplasty)
- To re-form the glans into a more natural conical configuration (glansplasty)

2. Management of Cryptorchidism

- Cryptorchidism or undescended testicle is usually diagnosed during the newborn examination. cryptorchidism the leading cause of azoospermia
- **Orchiopexy** is the surgery done for treatment for cryptorchidism
- The ideal time to correct undescended testicle is when early childhood (1-2 year)
- Recognition of the condition, identification of associated syndromes, proper diagnostic evaluation and timely referral for urologic surgical therapy are important to prevent adverse consequences (malignancy & infertility).

F. Management of Ejaculatory Failure

Treatment of ejaculatory failure can restore fertility without the need for invasive methods of sperm retrieval or the use of assisted reproduction procedures. However, further evaluation of different treatment options is needed.

2.8 Management of Unexplained Infertility:

It is a type of infertility diagnosis when there is no determinable cause for the source of infertility, even after standard infertility tests.

The optimal treatment strategy needs to be based on individual patient characteristics such as age, treatment efficacy, side-effect profile such as multiple pregnancy, and cost considerations. The principal treatments for unexplained infertility include expectant observation with timed intercourse and lifestyle changes. Couples who are having regular unprotected sexual intercourse to be advised to try to conceive for a total of 2 years (this can include up to 1 year before their fertility investigations) before IVF is considered .

2.9 Assisted Reproductive Technologies (ART)

Indications for ART:

- Tubal disease with tubal block or absent tubes
- Severe Endometriosis after sufficient treatment without success.
- Unexplained infertility
- Poly cystic ovarian disease with failed ovulation induction
- Oligoasthenozoospermia

Preliminary Requirement:

- Age < 40 years preferable
- Psychological evaluation- mentally sound and stable marriage
- Semen analysis- count >5-20 million (for IVF), motility - 30%
- Laparoscopy and if possible, Hysteroscopy
- Cervical patency - depth and direction of cervical and uterine cavity, to ensure atraumatic transfer of embryo.
- Patient to be fully informed about the procedure, the cost involved and the success rate (Individualized success rate variable depend on many factors).

2.9.1 Intra-Uterine Insemination (IUI)

It is a fertility treatment that involves placing sperm inside a woman's uterus to facilitate fertilization. The goal of IUI is to increase the number of sperm that reach the fallopian tubes and subsequently increase the chance of fertilization.

Intra-uterine insemination is the only ART procedure provided by MOH at the time of publishing the guidelines.

Indications for IUI

The main indication for IUI is a low sperm count or decreased sperm mobility.

However, IUI may be selected as a fertility treatment for any of the following conditions as well:

- unexplained infertility
- Mild endometriosis
- Mild male factor infertility ≥ 5 million motile sperms

- Disability (physical or psychological) preventing vaginal sexual intercourse
- Conditions that require specific consideration in relation to methods of conception (such as after sperm washing in a couple where the male is HIV positive)

IUI is not recommended for the following patients:

- Women who have severe disease of the fallopian tubes
- Women with a history of pelvic infections
- Women with moderate to severe endometriosis

Procedure:

- Before intrauterine insemination, ovulation stimulating medications may be used, in which case careful monitoring will be necessary to determine when the oocytes are mature.
- The IUI procedure will then be performed around the time of ovulation, typically about 24-36 hours after HCG triggering done.
- A semen sample will be washed to separate the semen from the seminal fluid.
- A catheter will then be used to insert the sperm directly into the uterus.
- This process maximizes the number of sperm cells that are placed in the uterus, thus increasing the possibility of conception.

The risks of IUI:

- The chance of multiple pregnancies is increased if patient had fertility medication when having IUI.
- There is also a small risk of infection after IUI.
- Success rate is high depending on variables such as female age, the reason for infertility, and whether fertility drugs were used, among other variables.

A woman of reproductive age who is using artificial insemination to conceive should be offered further clinical assessment and investigation if she has not conceived after 6 cycles of treatment, in the absence of any known cause of infertility. The referral for clinical assessment and investigation should include her partner.

While IUI is a less invasive and less expensive option, pregnancy rate from IUI is lower than from IVF.

2.9.2 In Vitro Fertilization and Embryo Transfer (IVF-ET)

In vitro fertilization (IVF) is a complex series of procedures used to treat fertility or genetic problems. It is the most effective form of assisted reproductive technology.

Procedure:

1. Super ovulation induction.
2. Oocytes retrieval
3. Sperm retrieval
4. Fertilization of ova and growth of embryo is done in vitro. Fertilization can be attempted using two common methods:
    - Conventional IVF: Insemination of healthy sperm and mature oocytes are mixed and incubated overnight which is called or
    - Intracytoplasmic sperm injection ICSI: a single healthy sperm is injected directly into each mature oocyte.
5. Embryo transfer: (1-2) embryos replaced back into the uterus at blastocyst stage (Day 5) trans- vaginally.

Indications for IVF:

1. Fallopian tube damage or blockage
2. Ovulation disorders.
3. low ovarian reserve despite age less than 40 (Alone not indication for IVF)
4. Endometriosis.
5. Previous tubal sterilization or removal.
6. Impaired sperm production or function.
7. Unexplained infertility.
8. Sometimes, IVF is offered as a primary treatment for infertility in women over 40.

Risk of IVF

- **Multiple pregnancies:** if more than one embryo is implanted in the uterus.
- **Premature delivery and low birth weight:** Research suggests that use of IVF slightly increases the risk that a baby will be born early or with a low birth weight.
- **Miscarriage:** The rate of miscarriage for women who conceive using IVF is similar to that of women who conceive naturally — about 10% — but the rate increases with maternal age.
- **Complications due to Oocytes-retrieval procedure:** aspirating needle used to collect oocytes could possibly cause bleeding, infection or bowel, bladder or blood vessel injuries. Risks are also associated with general anesthesia, if used.
- **Ectopic pregnancy:** About 2 to 5 percent of women who use IVF will have an ectopic pregnancy.
- **Stress:** IVF can be financially, physically and emotionally draining. Support from counselors, family and friends can help.

Intracytoplasmic Sperm Injection (ICSI):

ICSI is often used when semen quality or number is a problem or if fertilization attempts during prior IVF cycles failed.

The recognized indications for treatment by ICSI include:

- Few eggs have been collected
- Severe deficits in semen quality
- Surgical refined sperms (frozen sperm in case of azoospermia)
- Obstructive azoospermia
- Non-obstructive azoospermia.
- In addition, treatment by ICSI should be considered for couples in whom a previous IVF treatment cycle has resulted in failed or very poor fertilization.
- ICSI improves fertilization rates compared to IVF alone.
- Preimplantation genetic diagnosis (PGD)

Criteria of patient accepted in the IVF center in Khoula Hospital:

- Less than 42 yrs. old.
- No healthy living child
- Controlled medical disorders if any (e.g DM, HTN)
- No contraindications for management of infertility and pregnancy (some cardiac disorders)
- Patients of 42-44 yrs. only if normal ovarian reserve (AMH, FSH, AFC)
- Patient above age of 44 years old will not be accepted for any fertility treatments.
- BMI less than 35 yrs.
- Patients for fertility preservation for married and unmarried females /males (oocytes, sperms and embryos preservation) should be referred to fertility preservation clinic in Wattaya poly clinic in order to decide on feasibility for same taking in consideration same above criteria.

CHAPTER THREE: REQUIREMENTS

3.1 Responsibilities

A. Document writer (individual, committee or task force)

- This document is a guideline on Infertility Management
- Document request form was filled and approval to submit the document was received from the quality department.
- Task force was established including different members from primary, secondary and tertiary health institutions
- The document is evidenced based and it is produced in accordance with the quality document guideline.
- The document is produced after a thorough review of different updated international guidelines.
- New sections, algorithms, tables, summaries were added to this guideline to make it friendly and easy to use.
- The draft was sent to reviewer's taskforce from the governorates and from the secondary and tertiary health care institutions for review and give comments.
- Draft was reviewed and input was provided by members of the guideline taskforce.

B. Department of Women and Child Health, Ministry of Health

- Ensure that the guideline is disseminated to the governorates
- Conduct training on infertility guideline
- Ensure that guideline is implemented by the governorate

C. Women and Child Health Sections in the governorates

- Ensure that the guideline is disseminated to all health institutions in the governorate
- Cascade training on the infertility guidelines to other health institutions in the governorate.
- Ensure that guideline is implemented in the infertility clinics.

D. Hospital Directors

- Support staff training and ensure implementation of the guideline and integrate it in practice

E. Directorate General of Information Technology

- Ensure that approved guideline is uploaded on the MOH website/hospital local site and Al Shifa system.
- Ensure that all cancelled guidelines are removed from the MOH website/hospital local site and Al Shifa system.

F. **Roles in infertility clinic in Primary Health Care institutions**

1. Trained Nurses/ Midwife: -

- Register the women and her husband at infertility clinic and issue Fertility Assessment Booklet (white booklet)
- Fulfil all personal information of the couple as per the Fertility Assessment Booklet.
- For women, take detailed marital, infertility and clinical history (medical, surgical, menstrual, coital, environmental /occupational history affecting fertility.
- Review also the previous green cards, birth spacing cards, or any other document of fertility assessment or investigations done in private or abroad if available for further information.
- Perform general physical examination including: Height, Weight, BMI, Blood pressure
- Document all details of history and examination in the Fertility Assessment Booklet, infertility register and in Al Shifa system in infertility page.
- Collect investigations mentioned in the booklet (shared task with doctors)
- Arrange and direct the man to be seen and examined by a male GP in the HC for general assessment.
- Trace investigations and document in the booklet.
- Send the couples to be seen and examined by the doctors in the clinic.

2. Trained doctors

- Review the detailed history of the couples
- For women, take and complete marital history, infertility and clinical history (medical, surgical, menstrual, coital, environmental /occupational history affecting fertility.
- For men, take the detailed marital history, previous marriages, infertility history, clinical history (medical, surgical, personal, sexual functions, environmental/occupational history affecting fertility).
- Review also any previous investigations, fertility assessment for the couples including

any previous green cards, birth spacing cards, or any other document of fertility assessment or investigations done in private or abroad if available.

- Perform a clinical physical examination for clients at registration including: - systemic examination, breast, cardiovascular, chest, abdominal and pelvic examination (urogenital examination for men by a male doctor)
- Ensure that semen analysis for the husband is done and documented in the booklet.
- Give comprehensive counselling
- Collect and trace blood investigations (shared work with nurses
- Refer the couple to secondary care for review and further assessment.
- Provide health education and support to all couples

3. Gynecologist at polyclinic /secondary care hospitals

- Review the client records
- Review the clinical history /examination and investigations done in primary health care.
- Repeat investigations if needed
- Do PAP smear, HVS swab/culture (if indicated and not done in PHC).
- Conduct Ultrasound (Abdominal, trans-vaginal) and hydrosonography to detect any abdominal organomegaly, and uterine, ovarian and tubal pathology
- Perform Hysterosalpingography (HSG) as preliminary procedure for tubal testing.
- Laparoscopy / Hysteroscopy if indicated can be combined with laparoscopy.
- Anti-Mullerian Hormone (AMH), AFC; To be done if indicated
- Treatment based on the cause and follow up of the clients
- Give comprehensive counselling to the clients
- Send feedback to the referred health institutions.

4. Endocrinologist /Internist in secondary /tertiary care institutions

- Review the referred cases in regards of abnormal hormonal profile and do the further management
- Repeat semen analysis if indicated.
- Assess hormonal profile: FSH, LH, testosterone, Prolactin & TSH
- Give comprehensive counselling
- Treatment as per causes
- Send feedback to the referred health institutions

5. Urologist

- Received referred cases of Sexual dysfunction, Absent Vas deferens, Cryptorchidism (Undescended testis), Palpable varicocel, Testicular masses
- Do Ultrasonography: To detect sub clinical varicocele or search for the varicocele on the other side when present on one of the inguinal regions and Doppler ultrasound if needed for varices.
- Give comprehensive counselling.
- Treatment as per cause.
- Send feedback to the referred health institutions.

CHAPTER 4: DOCUMENT HISTORY, ANNEXURES AND REFERENCES

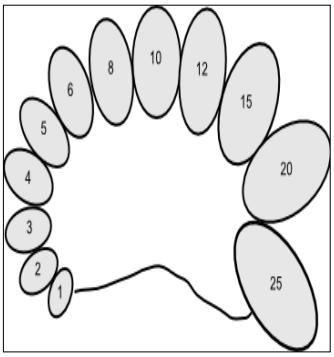
4.1 Document History and Version Control

Version	Description	Review Date
01	Initial Release – 1st Edition	2001
02	2nd Edition	2022
03	3rd Edition	2023

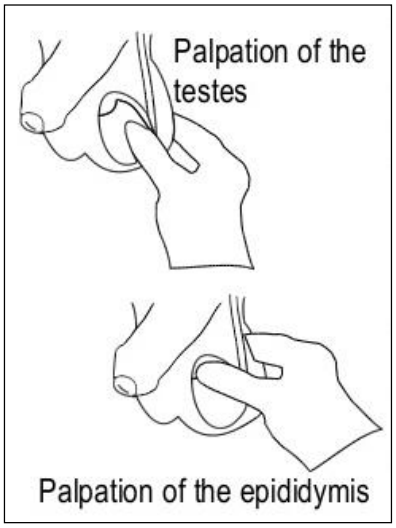
4.2 Annexures

Annexure 1: Male Genital Examination

- Wash your hands
- Use disposable gloves
- Expose as little of the patient as possible
- Cover upper abdomen and thighs where possible

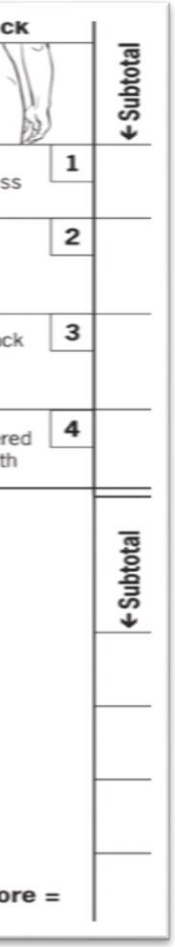


- **Examine the penis** with the patient in supine position, look for size, deformities, phimosis, ulceration or urethral discharge, surgical or traumatic scar (may indicate urethral stricture) & indurations.
- **Inspect the scrotal** skin which is pigmented compare to the rest of the body
- The left testis lies lower than the right but both be visible
- True scrotal swelling: swelling originating in the scrotum e.g. torsion of testies, epididmytis, lump on the testis



- False scrotal swelling: (may not palpable when the patient is supine) swelling originate outside the scrotum e.g. hernia, hydrococle, varicocele,
- **Examine the testes** by using gentle pressure on both testis (on at a time), using the thumb and two fingers.
- Note the size and consistency of the testes, you may use an **orchidometer** (is a chart or a set of beads indicating the size/ volume of the testicle in milliliters
- Palpate the epididymis: situated along the posterolateral surface, it should feel smooth and broadest superiorly at it is head.
- Roll with thumb and fingers to palpate for **vasdeference**, normally on palpation it feels like a cord (Check if it they are normal or thickened or not palpable).
- Examination of scrotum and testis should be performed with the patient in supine and standing position
- Examine for presence of hernia, scar of healed tuberculosis or lymphogranuloma venereum, or lymphadenopathy in the inguinal region.
- **Palpate the prostate** by per rectum examination: normally it is soft regular and non-tender. If it is tender, it indicates infections and if hard do further evaluation to exclude malignancy.

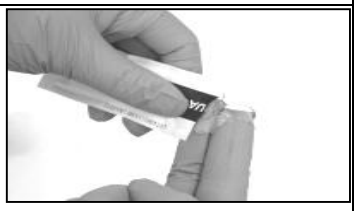
Annexure 2: Ferriman-Gallwey Hirsutes score – clinical assessment of body hair growth in women



Score of 8 or more indicates hirsutism

Annexure 3: Bimanual vaginal (PV) examination

1. Introduce yourself to the patient and clarify her identity. Explain what you would like to do and obtain verbal consent.
2. Explain she should feel little, if any, discomfort and that the examination should be over quickly.
3. The patient should be exposed from the waist down. Ask her to lie on her back, ankles together and to let her knees apart.



4. Wash your hands, put on gloves and inspect the outside of the vagina. Check the labia and the clitoris looking for any obvious abnormalities such as erosions.
5. Lubricate the index and middle finger of your right hand (**Error! Reference source not found.**).
6. Explain to the patient that you are about to start the procedure.

1. Use the thumb and index finger of your left hand to separate the labia majora and first insert your index finger, then insert your middle finger (**Error! Reference source not found.**).
2. Palpate the entire vaginal wall as you advance your fingers feeling for any obvious abnormality.

3. Using your fingertips palpate for the cervix, feel for its size, shape and mobility – check with the patient if it is tender.
4. At this point palpate the uterus (**Error! Reference source not found.**) by pressing it between your right middle and index fingers and your left hand placed on the lower abdomen. Feel for any masses.

5. You should also try to palpate each of the ovaries (**Error! Reference source not found.** & **Error! Reference source not found.**). This is done by placing your internal fingers in the right fornix and trying to press the ovary between them and your left hand in the right iliac

fossa. Do the same for the left ovary. Note any tenderness or masses, which may you feel.

6. Once you complete, remove your fingers, check your glove for any discharge or blood ( ) and then discard your gloves in the clinical waste bin.
7. Offer the patient a tissue, cover her up, you should now report your finding in the patient record.

Annexure 4: Instruction for collection of semen sample for evaluation:

- Abstain from intercourse (no ejaculation) for at least 2days.
- Do not drink alcohol or take a hot shower or hot bath immediately prior to producing specimen.
- Produce a semen specimen by masturbation into a small, sterile, dry, wide mouth glass jar. Be sure, the entire specimen is captured in the container.
- Lubricant jellies or soaps are not to be used for masturbation and if required glycerin is permitted. Ordinary condoms contain spermicidal and hence should not be used.
- Take the specimen to the laboratory as soon as possible (The specimen should arrive in the laboratory within 1 hour of collection at room temperature).
- Label the jar with the client's name, hospital number, date and time of collection.
- If abnormal result of semen analysis to do general investigations (CBC, ESR, sickling test, Blood sugar, RFT, LFT, Hepatitis B, VDRL, Urine microscopy).

Annexure 5: The Four Stages of Endometriosis (American Fertility Society Revised Classification)

STAGE I (MINIMAL)

PERITONEUM		
Superficial endo	1–3cm	–2
R OVARY		
Superficial endo	< 1cm	–1
Filmy adhesions	< $\frac{1}{3}$	–1
TOTAL POINTS		4

STAGE II (MILD)

PERITONEUM		
Deep endo	> 3cm	–6
R OVARY		
Superficial endo	< 1cm	–1
Filmy adhesions	< $\frac{1}{3}$	–1
L OVARY		
Superficial endo	< 1cm	–1
TOTAL POINTS		9

STAGE III (MODERATE)

PERITONEUM		
Deep endo	> 3cm	–6
CULDESAC		
Partial obliteration		–4
L OVARY		
Deep endo	1–3cm	–16
TOTAL POINTS		26

STAGE III (MODERATE)

PERITONEUM		
Superficial endo	>3cm	–4
R TUBE		
Filmy adhesions	< $\frac{1}{3}$	–1
R OVARY		
Filmy adhesions	< $\frac{1}{3}$	–1
L TUBE		
Dense adhesions	< $\frac{1}{3}$	–16*
L OVARY		
Deep endo	< 1cm	–4
Dense adhesions	< $\frac{1}{3}$	–4
TOTAL POINTS		30

STAGE IV (SEVERE)

PERITONEUM		
superficial endo	> 3cm	–4
L OVARY		
Deep endo	1–3cm	–32**
Dense adhesions	< $\frac{1}{3}$	–8**
L TUBE		
Dense adhesions	< $\frac{1}{3}$	–8**
TOTAL POINTS		52

*Point assignment changed to 16
**Point assignment doubled

STAGE IV (SEVERE)

PERITONEUM		
Deep endo	>3cm	–6
CULDESAC		
Complete obliteration		–40
R OVARY		
Deep endo	1–3cm	–16
Dense adhesions	< $\frac{1}{3}$	–4
L TUBE		
Dense adhesions	> $\frac{2}{3}$	–16
L OVARY		
Deep endo	1–3cm	–16
Dense adhesions	> $\frac{2}{3}$	–16
TOTAL POINTS		114

Determination of the stage or degree of endometrial involvement is based on a weighted point system. Distribution of points has been arbitrarily determined and may require further revision or refinement as knowledge of the disease increases.

To ensure complete evaluation, inspection of the pelvis in a clockwise or counter clockwise fashion is encouraged. Number size and location of endometrial implant, plaques, endometriomas and/or adhesions are noted. For example, five separate 0.5cm superficial implants on the peritoneum (2.5 cm total) would be assigned 2 points. (The surface of the uterus should be considered peritoneum). The severity of the endometriosis or adhesions should be assigned the highest score only for peritoneum, ovary, tube or cal-de-sac. For example, a 4 cm superficial and a 2 cm deep implant of the peritoneum should be given a score of 6 (not 7). A 4 cm deep endometrioma of the ovary associated with more than 3 cm of superficial disease should be scored 20 (not 24).

In those patients with only one adenexa, points applied to disease of the remaining tube and ovary should be multiplied by two. ** Points assigned may circled and totaled. Aggregation of points indicates stage of disease (minimal, mild, moderate or severe).

The presence of endometriosis of the bowel, urinary tract, fallopian tube, vagina, cervix, skin, etc. Should be documented under “additional endometriosis. “Other pathology such as tubal occlusion, leiomyomata, uterine anomaly etc. should be documented under “associated pathology”. All pathology should be depicted as specifically as possible on the sketch of pelvic organs, and means of observation (laparoscopy or laparotomy) should be noted.

4.3 References

- *American Society for Reproductive Medicine, Endometriosis: advances and controversies in classification, pathogenesis, diagnosis, and treatment - Scientific Figure on ResearchGate. Available from: [https://www.researchgate.net/figure/American-Society-for-Reproductive-Medicine-revised-classification_fig2_332592830]*

- *Ministry of Health, Sultanate of Oman, Infertility standard operating procedure (2001).*

- *MSD Manual Professional Version. Evaluation of Secondary Amenorrhea. Available online: [msdmanuals.com]*

- *Nice, (2017). Fertility Problems Assessment and Treatment available online [nice.org.uk]*

- *Shannon Harrison and Najwa Somani and Wilma Bergfeld (2010) Update on the management of hirsutism, published in Cleveland Clinic Journal of Medicine, volume 77,Pages 388 - 398,Available online [https://api.semanticscholar.org/CorpusID:44999159]*

- *WHO, (2021) laboratory manual for the examination and processing of human semen. 6th edition, Available online [WHO.int).*

- *WHO, manual for the* **standardized investigation and diagnosis** *of the* **infertile couple**. *World Health Organization. Issue Date: 1993. Publisher: Cambridge, Mass.: Cambridge University Press.*