CASE FOUR

Short case number: 3_24_4
Category: Endocrine & Reproductive Symptoms
Discipline: Obstetrics & Gynaecology
Setting: General Practice
Topic: Infertility

Case
John and Anthea Ingles, are both 28 years old, they have been married for 4 years. They are concerned that they will are unable to have children as they have 'been trying' for 10 months without success. **Anthea has never been pregnant before and John does not have any children.** **They ask you if they are infertile.**

Questions
1. Based on the definition of primary infertility what would you explain to John & Anthea? 2. What are the key features of history and examination in your assessment of John & Anthea? 3. In a flow diagram summarise the investigations that you would undertake in your assessment of John & Anthea. 4. There are many possible causes of infertility, summarise the diagnostic categories in infertility under the following headings; ovulatory disorders, male factor infertility, tubal factor infertility, endometriosis and unexplained infertility. 5. In considering the diagnostic categories outlined above, briefly describe the possible treatments under each category.

Suggested reading:

1. Abbott, J., Bowyer, L., & Finn, M. (2014). *Obstetrics and Gynaecology: an evidence-based guide (2nd ed).* Australia, Elsevier.
2. Edmonds, K. (ed). (2007) *Dewhurst's Textbook of Obstetrics & Gynaecology.* Blackwell Publishing. Chapter 45

Define Primary Infertility?

Failure to conceive after 12 months of exposure to the possibility of pregnancy

What are the key features of history and examination in your assessment of John & Anthea?

FHx
Prev Preg
STI, Sexual, OBGYN

Age of each partner

In a flow diagram summarise the investigations that you would undertake in your assessment of John & Anthea.

Ix for Male
Semen Analysis (Vol, count, motility, morphology)

Hormone Analysis: Serum FSH, LH, test,

Karyotype

Imaging - Scrotal Ultrasound (varicocele, obstructions, masses)

STI Screen

Ix for Female
Mid-Luteal serum progesterone (confirm ovulation)

Hormones: FSH, LH, PRolactin, Estrogens, Anti-Mullerian Hormone

Karyotype

Imaging - Pelvic US (Structuer & no. antral follicles)

STI Screen

List FIVE diagnostic categories of Infertility.
For each one give some examples/causes & treatment options.

OVULATORY DISORDERS
PCOS
Ovarian Dysfunction
Primary / Secondary Oligo/Amenorrhoea

Treatment
Treat underlying disorder to encourage ovulation.

TUBAL FACTOR INFERTILITY
Damaged fallopian tubes (e.g. as a complication of PID, endometriosis or tubal surgery) can cause ectopics and infertility.

Treatment
- Surgical tuboplasty
- IVF to bypass tubes

ENDOMETRIOSIS
Structural damage and adhesions about the reproductive organs

Treatment:
- Endometrial Ablation surgery
- IVF if other treatments don't result in pregnancy

UNEXPLAINED INFERTILITY

No idendifiable cause after Hx, Ex & Ix

Treatment
Expectanat management (if young and good prognosis), ovulation induction with timed intercourse, IVF.

MALE FACTOR INFERTILITY
- Low Sperm Count
- Reduced Motility
- Abnormal Morphology
- Ejaculatory Disorders
- Obstruction (eg. Cystic Fibrosis)
- Varicocele (raises temp due to inflammation and sperm dont develop properly)

Treatment
- Treat underlying cause (e.g. varicocele repair)
- Assisted Reproductive Technology
  - Intrauterine Insemination (Turkey baste loads of sperm into uterus)
  - Intracytoplasmic Sperm Injection (put one sperm cell directly into the oocyte)

ANSWERS

1. **Based on the definition of primary infertility what would you explain to John & Anthea?**

   Infertility is defined as the failure to conceive after 12 months of exposure to the possibility of pregnancy.
   84-90% of women should achieve pregnancy at 12 months
   92-95% of women should achieve pregnancy at 24 months

2. **What are the key features of history and examination in your assessment of John & Anthea?**
   HISTORY
   Menstrual History
   - Regularity: A woman whose cycle is between 28-32 days on a regular basis is highly likely to be ovulatory.
   - Ovulation pain: mid-cycle unilateral abdominal pain is related to rupture of the follicle at ovulation
   - Vaginal secretions: Pre-ovulatory rise in oestradiol stimulates the mucus to be thinner, more alkaline and more copious. Progesterone, secreted following ovulation, results in thickening of the mucus, which becomes tenacious and cellular
   - Premenstrual symptoms: Including bloating, breast tenderness and irritability – indicating ovulation has occurred
   - Painful periods: starting on commencement of bleeding and worse in the first 24h (primary spasmodic dysmenorrhoea) is a further hint ovulation has occurred.
   - Intermenstrual or post-coital bleeding
   - Acne, unwanted hair (hirsutism), galactorrhoea, vasomotor symptoms
   -

   Age of Partners
   - The age of the woman is a vital factor
   - More recently the age of the male has been suggested as a factor

   Previous Pregnancy
   - Recurrent abortions – after 3 consecutive 1st trimester losses, there is a need to further evaluate potential causes
   - mid-trimester abortion warrants investigation? cervical incompetence
     Frequency of intercourse and technique
   - Normal rates of fertility occur with coitus every other day around mid-cycle when ovulation should be occurring. Normal sperm are capable of fertilising the oocyte for 48-72h after ejaculation. The oocyte is fertilisable between 12-24h after ovulation. More frequent ejaculation may result in reduced sperm counts (only an issue if sperm quality is suboptimal)
   - It is normal for large parts of the ejaculate to escape from the vagina. Positioning of the female subsequent to intercourse in an attempt to improve the chances of pregnancy are a myth
   - Need to establish that penetration and ejaculation occur.
     Timing
   - Assess knowledge: Ovulation occurs 14 days prior to menstruation

Contraceptive History

- Hormonal birth control methods have not been implicated in subsequent infertility
- PID and IUD

Medications

- Drugs that may be harmful in early pregnancy
- Drugs that may impair fertility e.g. (chemotherapy for childhood cancers, phenothiazines)

Drug abuse

- Alcohol, marijuana and cigarette use are assoc with impaired semen quality and reduced female fertility

Past medical history

- Previous surgery in lower abdomen and pelvis, pelvic or abdominal infection, Chlamydia/ gonorrhoea (adhesions impairing tubal patency and function)
- Pelvic pain- ? endometriosis ?PID
- Medical diseases assoc with infertility: liver disease, heart disease, renal disease, hypothyroidism
- Polycystic Ovary disease (PCO) – results in annovulation

Family History

- Premature menopause

EXAMINATION

General

- Hair distribution (excessive hair in male pattern suggesting PCO)
- Breasts: galactorrhoea
- Adipose tissue: Cushings syndrome, PCO, diabetes
- Thyroid: enlargement

Vagina

- Structural abnormality
- Muscle spasm

Pelvis

- Fibroids (can inhibit implantation, cause early miscarriage)
- Ovarian cysts
- Endometriosis (tenderness, nodular area of scarring post uterus)
- Tenderness (?PID ?endometriosis)

3. **In a flow diagram summarise the investigations that you would undertake in your assessment of John & Anthea.**

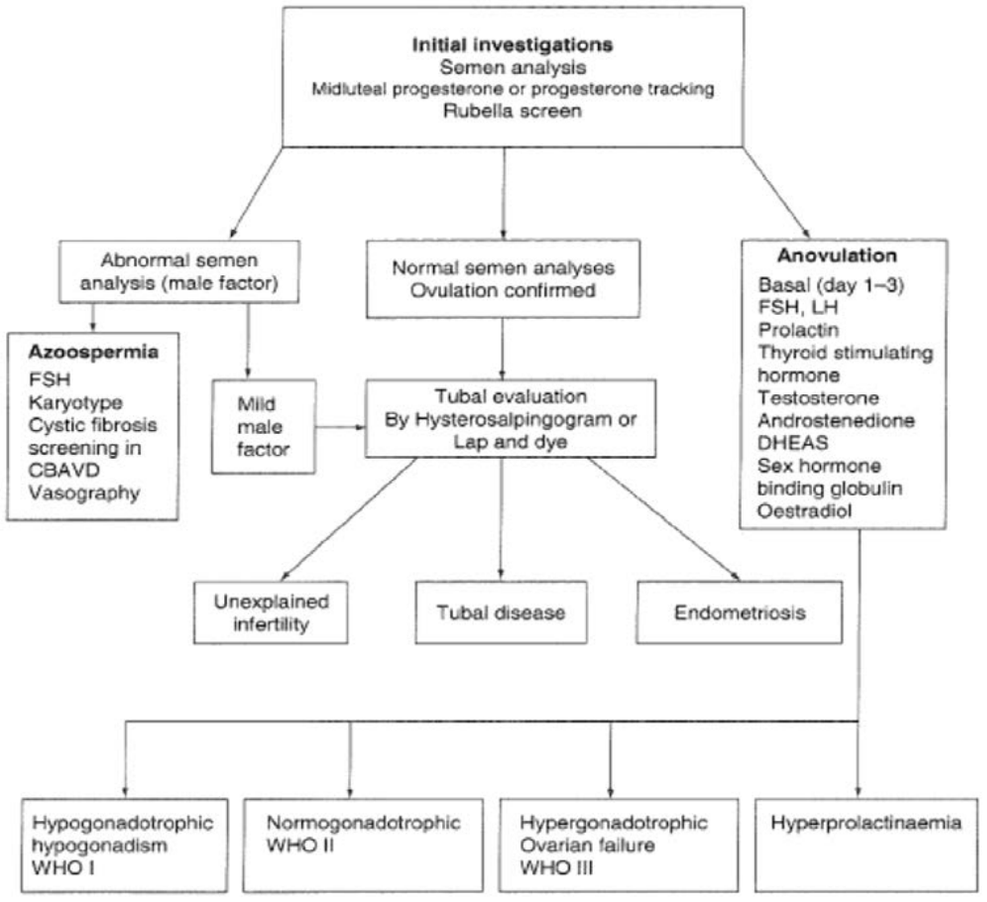

Fig. 45.1 Investigation of infertility.

4. **There are many possible causes of infertility, summarise the diagnostic categories in infertility under the following headings; ovulatory disorders, male factor infertility, tubal factor infertility, endometriosis and unexplained infertility.**

Causes of Infertility

Although single aetiologies can occur, some categories may co-exist

Ovulatory disorders

Anovulation or infrequent ovulation is seen in 1/5 of all women presenting with infertility.

	Site of lesion	Hormone profile
Hypogonadotophic hypogonadism	Central eg. Pituitary tumours, pituitary necrosis, stress, excessive weight loss	Low FSH Normal prolactin Low oestradiol
Normogonadotrophic hypogonadism	Hypothalamic – pituitary eg. PCOS, congenital adrenal hyperplasia	Normal FSH
Hypergonadotrophic hypogonadism	Ovarian Failure eg. Turners syndrome (XO), autoimmune disorders, irradiation	High FSH Low Oestradiol Normal prolactin
Hyperprolactinaemia	Central eg. Pituitary adenoma, primary hypothyroidism, chronic renal failure	Low FSH Low oestradiol High prolactin

Male factor infertility

A lack of sufficient numbers of competent sperm to fertilize the ovum.

Common causes:

- IDIOPATHIC IMPAIRMENT OF SEMEN QUALITY

Azoospermia (absence of sperm)
Oligozoospermia (sperm concentration <20 million per ml)
Asthenozoospermia (impaired motility)
Teratozoospermia (abnormal sperm morphology)

- VARICOCELE

A group of dilated veins in the pampiniform plexus of the spermatic cord. Spermatogeneis is believed to be prejudiced by impaired vascular drainage from the testis due to increased scrotal temperature, hypoxia, raised testicular pressure and reflux of renal metabolites. However, the presence of varicoceles in fertile men, with normal sperm counts questions causal association.

- GENETIC CAUSES

Azoospermia associated with karyotype abnormalities eg. 47XXY, structural abnormalities of Y chromosome

- CRYPTORCHIDISM

Undescended testes which remain untreated at 2yr are likely to be histologically abnormal

- ORCHITIS

Bilateral orchitis can cause atrophy of the seminiferous tubules. Fertility is affected if bilateral orchitis occurs after puberty.

- OCCUPATIONAL AND ENVIRONMENTAL FACTORS

Toxic effects of radiation, drugs and chemicals can affect rapidly dividing germ cells eg, heavy metals, pesticides, tobacco, cannabis, alcohol

- IATROGENIC

Therapeutic drugs interfering with male fertility eg. Chemotherapy, hormone treatment, cimetadine, sulphasalazine, spironolactone, colchicine

- GENITAL TRACT OBSTRUCTION

Previous vasectomy and congenital abnormalities (eg. congenital bilateral absence of the vas deferens associated with cystic fibrosis) are the principle causes, although infections such as TB and gonorrhoea predominate in some parts of the world.

- MALE ACCESSORY GLAND INFECTION

Infections with gram negative enterococci (Chlamydia, gonorrhoea) spreading via urethra, prostate gland, seminal vesicles, vas deferens, epididymis and testis.

- HYPOGONADOTROPHIC HYPOGONADISM

Congenital or aquired hypothalamic and pituitary failure eg. Kallmans syndrome, trauma, tumours, chronic inflammation.

- COITAL DYSFUNCTION

Ejaculatory failure eg. spinal cord injury, diabetes, MS, chronic renal failure
Erectile or ejaculatory problems eg. depression, alcohol abuse, medications (anti-hypertensives)
Loss of libido e.g. hyperprolactinaemia
Retrograde ejaculation e.g. secondary to transurethral prostatectomy, neuropathy

- IMMUNOLOGICAL

Antisperm antibodies. Risk factors include – reversal of vasectomy, prior infection

Tubal factor infertility

Tubal disease accounts for 15-20% of primary infertility and 40% of secondary. It represents the aftermath of pelvic infection or surgery resulting in tissue damage, scarring and adhesion formation. May be partial or total tube occlusion.

Endometriosis

The link between endometriosis and infertility has been demonstrated in some, but not all studies on this subject.

? diminished ovarian reserve

? poor oocyte and embryo quality

? impaired implantation

? high levels of cytokines, growth factors and activated macrophages in peritoneal fluid are toxic to sperm function and embryo survival

Unexplained infertility

Diagnosed where routine investigations are normal, including semen analysis, tubal evaluation and tests of ovulation. Reported incidence 20-30%

In considering the diagnostic categories outlined above, briefly describe the possible treatments under each category.

General advice:

Smoking cessation

Optimise BMI

Start folate (in case do conceive)

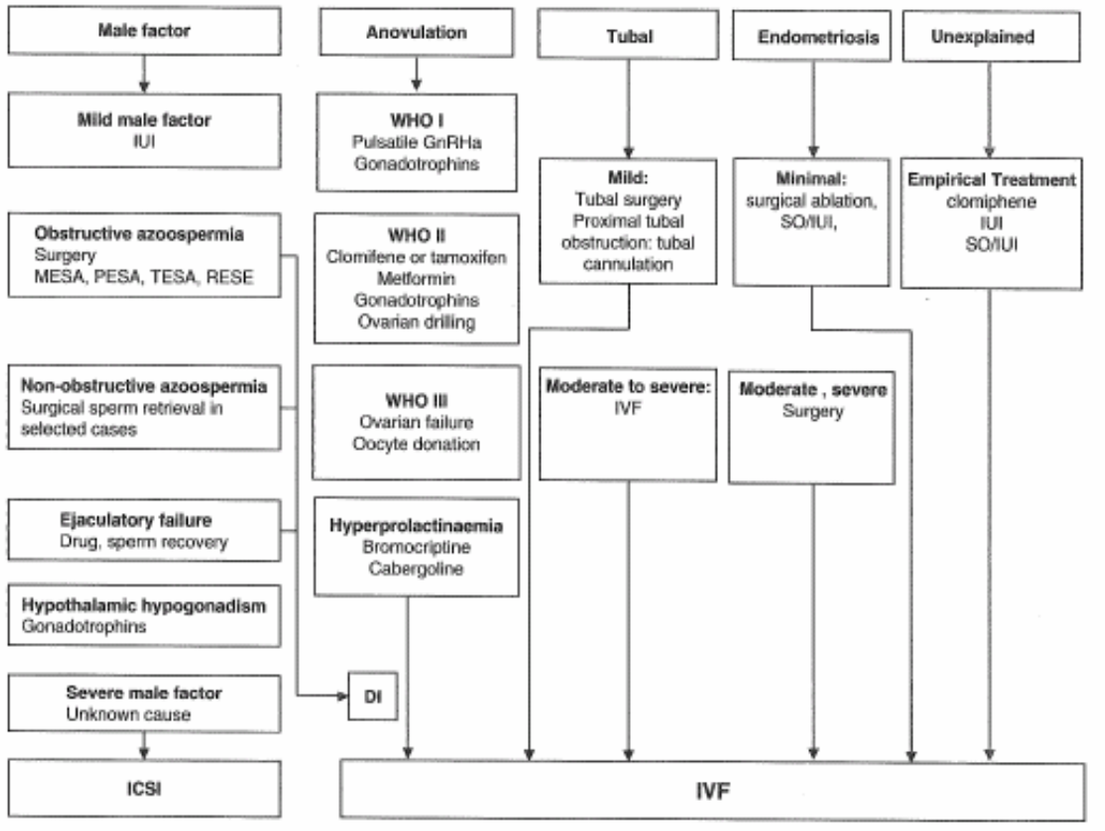

Fig. 45.3 Treatment of infertility.