

ANDROLOGY

ANATOMY OF MALE REPRODUCTIVE SYSTEM

The male reproductive system consists of the following organs.

I. Testes:

- The testes are situated in the scrotum which has the important function of regulating the internal temperature of the testes.
- Each testis is an ovoid organ, measuring about 4.5 X 3 X 2.5 cm (the average volume is 20 ml).
- It is surrounded by a thick white outer capsule composed of 3 layers: the visceral layer of the tunica vaginalis, tunica albuginea & inner tunica vasculosa.
- It is composed of seminiferous tubules separated by fibrous septa extending from the tunica albuginea into about 250 lobules.
- The seminiferous tubules have a thin basement membrane, a central lumen & 2 types of lining cells:
 - 1-Spermatogenic cells.
 - 2-Sertoli cells.
- The interstitial tissue between the seminiferous tubules is composed of Leydig cells, blood vessels, lymphatics, fibroblasts & histiocytes.

II. Epididymis:

- A sausage-shaped structure, about 5 cm in length, that rests on the posterolateral aspect of the testis along its long axis & consists of 3 distinct anatomical regions; head, body & tail.
- It is formed of a single highly convoluted tubule, measuring 5.5-6 meters in length.

III. Vas deferens:

- Thick walled tube, 35-45 cm long.
- It starts at the epididymal tail & its terminal section enlarges to form an ampullary portion that joins the duct of the seminal vesicle to form the ejaculatory duct which passes through the prostate to open in the prostatic urethra.

IV. Prostate:

- A pyramidal-shaped, firm elastic gland that lies between urogenital diaphragm & bladder neck.
- It surrounds the prostatic urethra, & is transpierced by the ejaculatory duct.
- It has a fibromuscular capsule that extends into the substance of the gland separating the external part into lobules. The inner portion of the gland is made up of periurethral glands & is not lobulated.

V. Seminal Vesicles:

- Paired, 5 cm long, lobulated structures that lie in close apposition to the bladder lateral to the ampulla of the vas deferens.
- Its duct joins the ampulla of vas forming the ejaculatory duct.

VI. Cowper's glands:

- These paired glands lie on both sides of the membranous urethra between the two layers of the triangular ligament.
- Their ducts open into the proximal part of the bulbous urethra.

Functions of Male Reproduction System

I. Testes:

A-Spermatogenesis:

The developing germ cells undergo mitotic & then meiotic division to halve their chromosome content. There is progression from spermatogonia through the stages of primary spermatocytes, secondary spermatocytes, spermatids & spermatozoa.

Spermatogenesis may be subdivided into 3 stages:

- 1-Spermatocytogenesis: transformation of spermatogonia into spermatids.
- 2-Spermiogenesis: morphological changes of spermatids into sperms.
- 3-Spermiation: release of sperms into tubular lumen helped by Sertoli cells.

Spermatozoa provide the male genetic contribution for fertilization of the ovum.

B-Sertoli cells:

- Blood testicular barrier.
- Provide nutrient to other cells.
- Phagocytosis.
- Coordination of spermatogenesis & spermiation.
- Secretion of testicular fluid, androgen binding protein, inhibin & others.
- Mechanical support to the germinal epithelium.

C-Leydig cells:

Luteinising hormone(LH) acts on the Leydig cells to stimulate the production of testosterone.

Testosterone is responsible for :

- Male sexual differentiation & maturation.
- Regulation of sexual behaviour.
- Initiation & maintenance of spermatogenesis.
- Differentiation, maintenance & functional integrity of the accessory sexual glands (seminal vesicles, prostate & bulbourethral glands).
- Potent protein anabolic action (promotion of growth in muscle, bone & somatic tissue).

Control of testicular function: testicular function is dependent primarily on the pituitary gland. Two major hormones (gonadotropins) secreted by the anterior pituitary, the follicle-stimulating hormone (FSH) & luteinising hormone (LH), are responsible for the maintenance & regulation of spermatogenesis & steroidogenesis in the testes. The secretion of gonadotropins is regulated by hypothalamic gonadotropin-releasing hormone (GnRH), but can be modulated by gonadal steroids.

II. Epididymis:

- Secretion of the complex epididymal plasma in which spermatozoa are suspended & undergo maturation.
- Absorption of testicular fluid & degenerated sperms.
- Sperm maturation (development of the capacity for motility & fertilizing ability).
- Sperm transport.
- Sperm storage.

III. Vas deferens:

Sperm transport.

IV. Accessory sexual glands:

The secretions of these glands contribute to the complex content of the seminal fluid, which provide energy sources for ejaculated spermatozoa, buffer them from pH changes & provide a liquid vehicle for the transport of sperms.

MALE INFERTILITY

Definition:

Infertility is generally defined as failure to conceive following one year of unprotected intercourse.

One of five married couples demonstrates primary infertility. A male factor is responsible in approximately one third to one half of these couples.

Sterile male is one who presents with incurable absence of spermatogenesis at any stage.

Causes:

A)Pretesticular causes:

- Hypothalamic causes: e.g., Kallman syndrome (a genetic defect in gonadotropin secretion due to gonadotropin releasing hormone deficiency which is often associated with other congenital anomalies such as anosmia, hare lip & cleft palate).
- Pituitary causes: e.g., isolated LH or FSH deficiency & panhypopituitarism which may be idiopathic prepubertal or secondary to neurohypophyseal lesions resulting from tumours, infarction, iatrogenic damage (by surgery or radiation) & infiltrative or granulomatous processes (such as tuberculosis) involving the hypothalamus or the pituitary gland.
- Adrenal disorders: congenital adrenal hyperplasia, Addison's disease & Cushing's syndrome.
- Thyroid disorders: both hypothyroidism & hyperthyroidism alter spermatogenesis.
- Hyperprolactinaemia (sexual & reproductive dysfunction).
- Androgen or estrogen excess inhibit gonadotropin secretion & depress spermatogenesis.

B) Testicular causes:

- Genetic & chromosomal abnormalities, e.g., myotonia dystrophia, hermaphroditism & Klinefelter's syndrome.
- Developmental abnormalities, e.g., bilateral anorchia, varicocele & Sertoli-cell-only syndrome (germinal cell aplasia).
- Defective androgen synthesis & action.
- Cryptorchidism.
- Testicular atrophy following trauma or infection (e.g., leprosy & mumps orchitis).
- Gonadal toxins such as drugs (e.g., alkylating agents) & chemicals (e.g., pesticides).
- Heat exposure.
- Radiation.
- Hypogonadism associated with systemic diseases (chronic renal failure, liver cirrhosis, diabetes mellitus, sickle cell anaemia).

C) Posttesticular causes:

- Inadequate sexual performance (erectile & ejaculatory disorders).
- Ductal obstruction:
 - Congenital absence of the ductal system, e.g., aplasia of the vasa deferentia.
 - Acquired obstruction following infection (e.g., bilateral gonococcal or tuberculous epididymitis) or vas ligation (voluntary or iatrogenic).
- Semen factors: impaired sperm motility (resulting from faulty maturation in the epididymis or biochemical abnormalities of seminal plasma due to infection or idiopathic).

Evaluation:**A) History:**

- 1-Personal history: name, age, occupation & special habits.
- 2-Infertility history:
 - Primary or secondary.
 - Duration of infertility.
 - Previous investigations &/ or treatments.
- 3-Sexual history:
 - disorders of erection & ejaculation.
 - frequency & timing of intercourse.
- 4-Past history: History of diseases with possible adverse effect on fertility.
- Childhood & development (undescended testicles, testicular torsion, onset of puberty).
 - Surgical operations & testicular trauma.
 - Medical diseases, infections & drugs.
 - Gonadotoxins (chemicals, drugs, radiation & thermal exposure).
- 5-Family history:
 - Androgen receptor deficiency.
 - Cystic fibrosis (recurrent respiratory infections in association with infertility. The vas deferens & epididymis may be absent).

B)Examination:

1-General examination:

- Height, weight & blood pressure.
- General physical examination to detect systemic diseases with influence on fertility.
- Secondary sex characteristics should be evaluated for signs of hypoandrogenism (body habitus, hair distribution, gynecomastia).
- Neurological examination should test the sense of smell, visual fields & reflexes.

2-Genital examination:

- Penis: hypospadias, size, curvature, indurated plaques.
- Testes: site, size, consistency.
- Epididymis: thickened, tender, cystic, non-palpable.
- Vas deferens: absent, thickened, nodules.
- Spermatic cord for varicocele.
- Scrotal swelling: hydrocele, hernia, varicocele.
- Inguinal examination: hernia, surgical or infection scar, lymphadenopathy.

3-Rectal examination:

- Prostate: tenderness,swelling.
- Seminal vesicles: these are normally not felt.

C)Investigations:

1-Semen analysis:

Physical examination of semen:

1-Volume:

Normally 2-6 mL.

- Aspermia: absence of semen (no ejaculate).
- Hypospermia :< 2 mL.
- Hyperspermia: > 6 mL.

2-Colour:

Normally: grayish white colour.

- Greenish colour: genital tract infection.
- Red or brown colour: haemospermia & drugs.
- Yellow colour: e.g., jaundice, drugs.

3-Characteristic odour.

4-Liquefaction time:

- Normally semen liquefies within 10-20 minutes.
- The semen is ejaculated in a liquid form. Seminal vesicle protein is responsible for coagulation & prostatic proteolytic enzymes are responsible for liquefaction.

5-Viscosity:

- High viscosity may cause infertility.

6-pH:

- Normally: 7.2 -7.8.
- pH changes may be caused by acute & chronic inflammation of the prostate, epididymis or seminal vesicles.

Microscopic examination of semen:

1-Sperm Concentration:

- Normal : 20-200 millions/mL.
- Zero: azoospermia.
- < 20 millions/mL: oligozoospermia.
- > 200 millions/mL: polyzoospermia.

2-Motility:

- % of motile spermatozoa: after 1 hour 70%.
- after 2 hours 60%.
- Asthenozoospermia: motility < 60% after 2 hours.

3-Sperm morphology:

- Normally: up to 40% of the total sperms may show abnormalities.
- Teratozoospermia: abnormal forms >40% of the total sperm count.
- Abnormalities may be in the head tail or both.

4-Viability:

- We must differentiate between non-motile, living sperms from dead sperms by:
 - Eosin-Negrosin (vital) stain: stains dead sperms only.
 - In vitro stimulation of motility by adding certain chemicals.
- Necrozoospermia: All spermatozoa are dead by vital stain.

5-Sperm agglutination:

- Types: head to head, head to tail or tail to tail.
- Significant sperm agglutination: is agglutination of > 10% of sperms, and is usually due to infection or immunological factors (autoantibodies).

6-Cellular components other than sperms:

- Leucocytes: normally 2-5/HPF.

Pyospermia is the presence of > 5 leucocytes in the ejaculate.

- RBCs: normally absent.

Haemospermia is the presence of red cells in the ejaculate and can be caused by :

- Prostatovesiculitis.
- Bilharziasis of the genital tract
- Tuberculosis of the genital tract.
- idiopathic.
- Haemorrhagic diathesis
- Congestion.
- Malignancy.

- Germinal cells.
- Epithelial cells.

2-Endocrine evaluation:

- Evaluation of the hypothalamo-pituitary-gonadal axis (FSH, LH & testosterone levels). Serum FSH assesses the state of the seminiferous epithelium, while serum LH reflects the adequacy of Leydig cell function.
- Measurement of serum prolactin should be obtained in all patients with signs or symptoms suggestive of pituitary tumour & in patients with sexual dysfunction.
- Serum estradiol should be measured in patients with gynecomastia.
- Adrenal hormones.
- Thyroid hormones.

3- Genetic & chromosomal evaluation:

- Buccal smear:(to demonstrate the presence or absence of sex chromatin).
- Sex chromatin is absent in normal males.
- Klinefelter's males are sex-chromatin positive.

Karyotyping:

- Karyotyping is indicated in difficult diagnostic problems or when chromosomal mosaicism or structural alterations are suspected.

4-Testicular biopsy:

Indications:

- Azoospermia (to distinguish between reproductive tract obstruction & testicular failure).
- Severe oligozoospermia (sperm density < 5 millions/mL).
- Cryptorchidism & infertility.
- Varicocele with azoospermia or severe oligozoospermia.
- Intersex.

Findings:

- Normal spermatogenesis (may be encountered in obstructive azoospermia).
- Maturation arrest (the spermatogenic process fails to progress beyond one of the early stages,e.g.,at spermatid or primary spermatocyte level).
- Hypospermatogenesis (generalized reduction in the number of germ cells of all stages).
- Sertoli cell-only syndrome (complete loss of germinal cells in the tubules).
- Premature sloughing (immature forms,especially spermatocytes,slough into the lumina of the tubules).
- Peritubular fibrosis & tubular hyalinization.

5-Genital exploration :

- Surgical exploration of scrotal contents.

6-Vasography:

- Absent or obstructed vas & ejaculatory ducts.

7-Ultrasonography:

- Varicocele.
- Evaluation of scrotal masses.
- Searching for undescended testes.
- Ejaculatory duct obstruction.

Treatment:

I. Medical treatment:

A)Hormonal treatment:

- Gonadotropin releasing hormones (GnRH):
 - GnRH Stimulates secretion of LH & FSH.
 - It can be used in hypogonadotropic hypogonadism.
- Gonadotropins:
 - Human Chorionic Gonadotropins (HCG):
 - Mainly LH activity.

b) Human menopausal gonadotropins (HMG):

Both LH & FSH activity, but mainly FSH.

3-Androgens:

a) Parenteral androgens, e.g., testosterone propionate.

b) Oral androgens, e.g., testosterone undecanoate.

4-Antiestrogen therapy

a) Clomiphene citrate.

b) Tamoxifene.

c) Testolactone.

5-Bromocryptine: for treatment of hyperprolactinemia.

B) Non hormonal treatment:

1-Kallikrein: It stimulates sperm motility; enhances sperm transport & activates fructolysis.

2-Nucleotides such as ATP which increases sperm motility.

3-Others: e.g., methylxanthine, arginine & zinc.

II. Surgical treatment:

1-Repair of penile & urethral disorders such as hypospadias, chordee, urethral fistula or stricture.

2-Orchiopexy early in life for correction of cryptorchidism, if trial of gonadotropin fails.

3-Varicocelectomy.

4-Vasovasostomy (correction of vasal occlusion):

- Vasectomy reversal.

- Vasal defects caused by congenital aplasia, inflammation & inadvertent vas excision during herniorrhaphy.

5-Epididymovasostomy for epididymal obstruction.

6-Artificial spermatocele: vasal aplasia, long unbridgeable vasal stenosis, or failure of repeated reconstructive surgery on the seminal pathways.

III. Assisted reproductive techniques:

-Artificial Insemination Husband (AIH).

-Semen processing to improve sperm quality before artificial insemination or in vitro fertilization.

-In Vitro Fertilization (IVF).

-Gamete Intrafallopian Transfer (GIFT).

-Microfertilization or microinsemination for severe male factor infertility, e.g., subzonal insemination (SUZI) & intracytoplasmic sperm injection (ICSI).

SEXOLOGY

Sexology is the science that deals with the scientific study of sex & sexual relations.

Physiology of the sexual act:

Sexual act is a complex physiologic response that is dependent upon the integration of vascular, endocrine, psychological and neurogenic mechanisms. For the successful completion of the sexual act, sexual drive (libido), an attractive partner & a suitable environment that provide freedom from distraction & anxiety are needed.

The physiologic sexual response cycle has been divided into 4 phases:

1-Excitement phase: is marked by penile erection in the male & vaginal lubrication (transudate) in the female.

2-Plateau phase: is the phase of full sexual excitement marked by full erection and appearance of Cowper's gland secretions at the urinary meatus in male. In female, it is marked by ballooning of the inner two thirds & congestion and swelling of the outer third of the vagina.

3-Orgasmic phase: highly pleasurable sensation associated with ejaculation in male and rhythmic contractions of the outer third of the vagina and pelvic floor muscles in female.

4-Resolution phase: during this phase, there is detumescence as well as decongestion of the genital organs together with a sense of relaxation. It is rapid in male & gradual in female.

N.B.: Refractory period occurs only in male, during which further erection and ejaculation are inhibited.

Mechanism of erection (neurovascular events):

Stimuli for erection (sexual arousal):

1-Psychogenic stimuli: act through CNS which sends them to the spinal cord, e.g. thoughts, auditory, visual, olfactory or tactile erotic stimuli.

2-Genital stimuli: from penile skin through dorsal nerve of the penis to the spinal cord erection center (S2-S4).

Center of erection:

Sacral segments (S2-S4) of the spinal cord (parasympathetic system).

Efferent pathway:

Erection center sends impulses along the pelvic nerves to relay in the parasympathetic ganglia within the walls of the pelvic viscera, and reach the corpora cavernosa and cavernosal arteries through the cavernosal nerves to release neurotransmitters which act on penile blood vessels.

Vascular response:

1-Cavernosal artery dilatation leading to increased blood flow.

2-Relaxation of the smooth muscles of the blood sinusoids of corpora cavernosa.

3-Mechanical venous occlusion.

Ejaculation:

Ejaculation is the process of semen expulsion from the sex organs to the outside and this occurs through three rapidly successive phases which are reflex in nature:

1-Emission: expulsion of semen into posterior urethra (sympathetic control from T10 - L2).

2-Bladder neck closure: to avoid retrograde ejaculation with formation of posterior urethral chamber (sympathetic control from T10-L2).

3-Ejaculation proper: propulsion of semen out of the urethra. This involves opening of external urethral sphincter, contraction of bulbourethral muscle and contraction of pelvic floor muscles (somatic control from S2-S4 through pudendal nerve).

Orgasm:

A cortical sensory experience. It is the sum of the reactions & sensations in the body at climax that evokes feelings of release & pleasure.

IMPOTENCE

Definition:

Consistent inability to achieve or sustain an erection of sufficient rigidity for sexual intercourse to the point of satisfaction of both partners.

The term erectile dysfunction is more preferred than the term impotence because the latter is a comprehensive label for disturbances which may occur in libido, erection, ejaculation, or orgasm.

Aetiology:

With the introduction of new diagnostic techniques, the old theory that 90% of impotence cases are due to psychogenic causes has become obsolete. It is now estimated that organic causes are present in approximately 70% of cases of erectile dysfunction. However, in many cases both organic and psychogenic factors are involved.

Psychogenic causes:

These act by inhibiting the reflex mechanism which control the erection and ejaculation.

- 1- Depression.
- 2- Sexual ignorance.
- 3- Fear of failure (performance anxiety), pregnancy or venereal diseases.
- 4- Fixation at an early stage of infantile sexuality e.g. oral erotic stage.
- 5- Sense of guilt as from extramarital relations.
- 6- Unattractive partner.
- 7- Family troubles and poor communication between partners.

Organic causes:

1-Congenital penile deformities:

-Epispadias: urethral meatus opens proximally on the dorsum of the penis.

- Penoscrotal hyposadias (ectopic external urinary meatus at penoscrotal junction), it is usually associated with a fibrous band extending from the meatus to the tip of the penis.
- Congenital chordee without hypospadias (fixed bending of the penis).

2- Mechanical causes:

- Morbid obesity.
- Huge bilateral hydrocele or inguinal hernia.
- Elephantiasis of penis & scrotum.
- Peyrone's disease (fibrotic scar of the tunica albuginea surrounding the corpora cavernosa resulting in curvature of the penis on erection).
- Carcinoma of penis.

3-Endocrinal causes:

- Hypogonadal androgen deficiency,e.g., Klinefelter's syndrome, mumps orchitis, trauma, castration and male climacteric (weak desire and performance due to aging process).
- Abnormalities of hypothalamopituitary function,e.g. panhypopituitarism, isolated gonadotropin deficiency, and hyperprolactinaemia (increased prolactin level has antiandrogenic effects).
- Adrenal cortical dysfunction especially when there is excess secretion of female hormones, e.g. feminizing adrenal tumours.
- Hypo- and hyperthyroidism.

4-Metabolic causes:

- | | |
|---------------------|-----------------------|
| a-Diabetes mellitus | b-Hoemochromatosis |
| c-Alcoholism | d-Sickle cell disease |
| e-Hepatic failure. | f- Renal failure. |

5-Neurogenic causes:

- Cortical lesions as temporal lobe epilepsy, general paresis of insane and cerebral atherosclerosis.
- Spinal cord lesions as tabes dorsalis & syringomyelia.
- Pyramidal tract lesions as hemiplegia and paraplegia.
- Peripheral neuropathies.
- Cauda equina lesions.
- Multiple sclerosis.

6-Vasculogenic causes:

- Any lesion decreasing the arterial inflow or enhancing the venous outflow, e.g.
- Atherosclerosis of hypogastric-cavernous arterial bed.
 - Leriche syndrome (obstruction of the terminal aorta).
 - Pelvic steal syndrome (unilateral obstruction of internal iliac artery).
 - Trauma to blood vessels (blunt perineal trauma, fracture pelvis).
 - Arteriovenous malformations.

7-Iatrogenic causes: iatrogenic influences originate from surgery or from drugs.

a)Surgery: injury of mechanism of erection, e.g., thoracolumbar sympathectomy, radical prostatectomy & abdominoperineal resection of rectum.

b)Drugs:

- Antihypertensives, e.g. clonidine , methyldopa & reserpine.

- Antiandrogens, e.g. cyproterone acetate.
- Major tranquilizers as phenothiazines.
- 8-Exercise intolerance :(general diseases with a bad general condition)
- Pulmonary insufficiency & emphysema.
- Ischaemic heart disease.
- Severe anaemia.
- Myasthenia gravis.

Diagnosis of erectile dysfunction:

I-Thorough sexual, medical & drug history:

- To differentiate organic from psychogenic impotence :
 - Onset, course & duration: organic impotence is of insidious onset & there is progressive loss of erectile capacity in all sexually arousing situations.
 - Presence of morning, nocturnal, psychogenic & reflex erections (defective in organic impotence).
- To determine the etiology: e.g.,
 - History of systemic disease, e.g., diabetes, hypertension, peripheral neuritis, or organ failure.
 - Risk factors for atherosclerosis such as smoking , hypertension & hyperlipidaemia.
 - History of marital troubles, drug intake, trauma, or surgery.

II-Examination:

General examination:

- Male secondary sexual characters (signs of hypoandrogenism, gynaecomastia).
- Pulse, blood pressure, sensation & reflexes.
- Scars from previous surgery or trauma.

Local examination:

- Penis: size, meatus, scars, plaques, pulses.
- Scrotum: testicular size and sensation.
- Rectal examination of prostate and seminal vesicles.

III-Investigations:

1. Complete urine analysis (sugar, pus, parasites).
2. Stool examination (bleeding, parasites).
3. Complete blood picture (anaemia, leukaemias).
4. Serological testing for syphilis.
5. Blood chemistry (fasting & postprandial blood sugar, liver & kidney function tests).
6. Endocrinal evaluation: assay of serum testosterone and prolactin. Other hormones may be assayed if a specific endocrine abnormality is suspected.
7. Specialized methods for investigation:
 - Psychological testing for measurement of psychosexual functioning.
 - Monitoring of nocturnal erections that occur during rapid eye movement sleep to differentiate organic from psychogenic impotence.
 - Penile-brachial pressure ratio.

- Doppler studies: Evaluation of the blood vessels by Doppler ultrasound examination to determine the blood flow, blood pressure and imaging the defects in penile blood vessels.
- Cavernosometry & cavernosography to study the venous drainage system of the penis (the veno-occlusive mechanism of the corpus cavernosum).
- Neurologic evaluation of afferent and efferent pathways of erection: electromyography, nerve conduction studies, thermal or vibratory threshold & bulbocavernosus latency.

Treatment:

- 1-Avoiding risk factors, e.g., drugs, smoking and alcohol.
- 2-Treatment of underlying cause e.g. hypogonadism, surgical correction of correctable causes, control of diabetes, etc.
- 3-Psychogenic impotence:
Psychotherapy, behavior modification therapy, sexual counselling &/or the use of a variety of medications. Such counselling is useful, even if the sexual dysfunction has a strictly organic basis.
- 4-Organic impotence:
 - Hormonal pharmacotherapy.
 1. Androgens: hypogonadism is the principal indication. Most impotent men have normal testosterone levels; therefore, the administration of testosterone to these individuals provides no benefit.
 2. Bromocriptine: erectile impotence secondary to hyperprolactinemia.
 - Non-hormonal pharmacotherapy.
 1. Phosphodiesterase inhibitors e.g., sildenafil, tadalafil & vardenafil they act by allowing more nitric oxide to accumulate causing vasodilatation and good penile erection.
 2. Intracorporal pharmacotherapy: induction of artificial erection can be done, in selected cases, by injection of vasoactive drugs into corpora cavernosa to induce vasodilation & erection. Papaverine, phentolamine & prostaglandin E1 are commonly used for intracorporal injection.
 - Hemodynamic treatment (for treatment of vasculogenic impotence).
 1. Arterial reconstructive surgery.
 2. Venous reconstructive surgery.
 - Penile prosthesis:
Penile implants are reserved for erectile impotence that is not amenable to any other form of therapy. They are divided into inflatable & noninflatable devices. Noninflatable devices include rigid rods & malleable devices.
 - Other treatment options are available, e.g., vacuum-constriction devices & electrostimulation therapy.

DISORDERS OF EJACULATION

Premature ejaculation:

Premature or rapid ejaculation is recurrent ejaculation with minimal stimulation that occurs before, upon, or shortly after penetration (before the affected individual wishes to ejaculate).

Organic causes are rare. Anxiety is the basic problem in premature ejaculation.

Retarded ejaculation:

Persistent or recurrent delay in ejaculation following a period of normal sexual arousal. It may be caused by different forms of phobias (fear of pregnancy or fear of losing control), but it is mostly iatrogenic induced (phenothiazin, ismelin, MAO-inhibitors).

Retrograde ejaculation:

The semen is propelled backward into the bladder rather than antegrade through the urethra during the ejaculatory process.

The sexual act has normal duration ending with orgasm in the absence of antegrade ejaculation, but in the presence of postejaculatory urine containing sperm and fructose.

SEXUALLY TRANSMITTED DISEASES

SEXUALLY-TRANSMITTED DISEASES(STDs)

A group of contagious conditions in which the principal mode of transmission is sexual activity.

Classification :

I. Bacterial :

- 1- Gonorrhoea
- 2- Nongonococcal urethritis
- 3- Syphilis
- 4- Lymphogranuloma venereum
- 5- Chancroid
- 6- Granuloma inguinale
- 7- Bacterial vaginosis
- 8- Salmonellosis
- 9- Shigellosis

II. Viral :

- 1- Genital herpes
- 2- Condyloma accuminatum
- 3- Molluscum contagiosum
- 4- Hepatitis A, B, C and D
- 5- Cytomegalovirus infection
- 6- Acquired immune deficiency syndrome (AIDS)

III. Fungal :

- Candidiasis

IV. Protozoal :

- 1- Trichomoniasis
- 2- Ameobiasis
- 3- Giardiasis
- 4- Cryptosporidiosis

V. Helminths & Ectoparasites :

- 1- Enterobiasis
- 2- Strongyloidiasis
- 3- Pubic louse
- 4- Scabies

ANATOMICAL CONSIDERATIONS

Anatomy of Male Urethra

- The male urethra is a conduit between vesical neck and external urethral meatus.
- Its length is about 20 cm.
- It is formed of two parts: anterior urethra & posterior urethra.

Posterior urethra:

The posterior urethra is subdivided into 2 parts:

- Membranous urethra which lies between the two layers of the triangular ligament & is devoid of any glands. It is 1.2cm long & is lined by transitional epithelium.
- Prostatic urethra which passes through the prostate gland, is about 3cm long & is lined by transitional epithelium. The prostatic ducts open on to both its anterior & posterior walls. The common ejaculatory ducts (2cm in length) open on its posterior wall on either side of a ridge (verumontanum).
- The seminal vesicles are lined by a columnar epithelium containing goblet cells.

Anterior urethra:

Anterior urethra is 15cm in length. It tunnels the corpus spongiosum and consists of 2 parts:

- Bulbous urethra (the proximal dilated fixed part) into which open the ducts of Cowper's glands.
- Penile urethra (the pendulous distal part) into which open the ducts of Littre's glands.

- The bulbous urethra is the widest & the external urinary meatus is the narrowest part of the urethra and opens into the fossa navicularis which is a fusiform dilatation lined by stratified squamous epithelium. The rest of the anterior urethra & the ducts of Littre's & Cowper's glands are lined by columnar epithelium.
- Lacuna of Morgagni: are small mucous plications found in linear midline series forming crypts on the roof of the first few centimeters of the anterior urethra. The fundus of these lacunae is directed backward towards the bladder.
- Littre's glands secrete mucus & their ducts open into the roof & sides of penile urethra.
- Cowper's glands lie on either side of the membranous urethra but their long ducts open into the floor of the bulbous urethra.
- Tyson's glands are two modified sebaceous glands of the corona of the penis which secrete smegma & open on either side of the fraenum. They atrophy following circumcision.
- Paraurethral ducts are small blind channels in the substance of the glans penis that open near or within the lips of the external urinary meatus.

Female Urethra

Female urethra is 4cm long. The part adjacent to the bladder is lined by transitional epithelium & the length is lined by stratified squamous epithelium with islets of columnar epithelium in the proximal part. Many small mucous glands open into the urethra & their ducts are lined by columnar epithelium.

Skene's glands are situated on either side of the lower end of the urethra. Their ducts which open beside or just inside the urethral orifice are lined by columnar epithelium.

Bartholin's glands lie in the posterior third of each labium majus & their ducts open on the inner surface of each labium minus at the junction of the middle & posterior thirds. The ducts are lined by columnar epithelium.

Anal Canal & Rectum

The anal orifice is lined by stratified squamous epithelium. The upper half of the canal & the rectum are lined by columnar epithelium.

Conjunctiva

Palpebral conjunctiva, except the margins, is lined by multiple layers of columnar epithelium. In the bulbar conjunctiva the superficial cells are flattened & the deeper cells are columnar.

Pharynx

The nasal part of the pharynx is lined by ciliated columnar epithelium while the oral & laryngeal parts are lined by stratified squamous epithelium.

GONORRHOEA

Definition:

An acute infectious disease of the genitourinary mucous membrane caused by *Neisseria gonorrhoeae*. It is almost exclusively transmitted by sexual intercourse & may also cause local or metastatic complications.

Neisseriae gonorrhoeae:

Morphology:

- Kidney shaped Gram-negative diplococci.
- Non-motile, non-capsulated & non-sporulated.
- L-form: an alteration in the organism morphology to show many pleomorphic elements.
- The gonococcus cannot survive long outside the body, as it is rapidly killed by drying, heat & weak antiseptics.

Culture:

The organism is aerobic or facultative anaerobe that can be cultivated on enriched media in the presence of moisture and 5% CO₂.

-Culture media: The organism does not grow on ordinary media.

1-Transport media : non-nutritional, semisolid media that maintain a state of reduction during transport, e.g. Stuart's medium.

2-Growth media:

a) Enriched non-selective media, e.g. McLeod's chocolate agar.

b) Selective media that eliminate the growth of common contaminants by addition of antimicrobial agents, e.g. Thayer-Martin medium.

3-Growth-transport media that provide both nutritional and transport requirements, e.g. modified Thayer-Martin medium.

4-Biological environment chamber: selective growth-transport medium.

-Colonial morphology: Examination of the culture after 48 hours revealed 4 colonial types:

- Type 1 & type 2 : virulent & possess pili.
- Type 3 & type 4 : much less virulent & lack pili.

-Confirmation of a presumptively positive culture is only obtained by :

1-Oxidase test: The organism is oxidase positive. The test permits easy identification of *Neisseria* in mixed cultures.

2-Fermentation reactions: The gonococcus ferments glucose only. This permits its differentiation from other *Neisseria*; & this is especially useful in medicolegal cases.

Pathogenesis:

The gonococcus has a predilection for columnar epithelium which is readily available after the gonococcus has gained entrance at any of the body's main orifices such as urethra, rectum, oropharynx & conjunctiva in both sexes; and endocervix & Bartholin's ducts in females. Subsequently the infection can spread to the other structures lined with columnar epithelium such as Littre's glands, Cowper's glands, prostate gland, seminal

vesicles & epididymes in the male; and Skene's glands & fallopian tubes in the female. The infection spreads along the epithelial & subepithelial layers. There is polymorphonuclear response in the submucosa, with patchy destruction of the epithelium. In the untreated cases the inflammatory process may resolve by fibrosis.

GONORRHOEA IN MEN

Gonococcal Urethritis:

Mode of infection: Sexual intercourse is the principal mode of infection in adults.

Incubation period: 2-5 days.

Symptoms and signs:

- Dysuria
- Urethral discharge : profuse, yellowish & usually purulent.
- Constitutional symptoms, e.g. fever, headache, malaise, may occasionally develop.
- The urinary meatus may appear red and oedematous.
- Slight tender enlargement of inguinal lymph nodes occurs in some cases.

Investigations:

1-Smear examination:

Direct microscopic examination of urethral smears stained with Gram-stain : Gram-negative intracellular (within pus cells) and extracellular diplococci. This must be the minimum requirement to diagnose gonorrhoea.

2-Culture:

- The culture is superior to smear in diagnosis. It is the most dependable & hence of legal importance.
- It can differentiate *Neisseria gonorrhoeae* from commensal *Neisseriae*.

3-Two-glass test:

- The urine is micturated in two glasses.
- In anterior urethritis: the first specimen is hazy while the second is clear.
- In posterior urethritis: both glasses of urine are hazy in appearance.

4-Three-glass test:

Anterior urethra is irrigated with saline (glass I). The patient passes few ounces of urine (glass II)& then the remainder is passed (glass III).

- Turbidity only in glass I : anterior urethritis.
- Turbidity in glasses I& II: posterior urethritis
- Turbidity in the three glasses: infection extends to the bladder

5-Serological tests:

These tests depend on detection of antibody against gonococci in the patient serum. However , they do not show a high degree of specificity or sensitivity & will not differentiate between past & present gonococcal infection.

Differential Diagnosis:

1-Non-gonococcal urethritis (NGU):

| | Gonococcal urethritis | NGU |
|-------------------|-----------------------|----------------|
| Symptoms | Severe | mild |
| Incubation period | Short | short or long |
| Discharge | Profuse ,purulent | scanty, mucoid |

2-Intrameatal sores (chancre, chancroid) & tumours (warts).

3-Chemical and traumatic urethritis.

4-Cystitis.

Local Complications of Anterior Urethritis:

Complications tend to occur when symptoms & signs have been ignored & treatment delayed.

Predisposing factors include alcoholism, physical exertion, trauma (instrumentation), vigorous prostatic massage, irrigation & sexual indulgence.

1-Balanoposthitis: inflammation of preputial sac and glans penis may occur in uncircumcised patient, severe phimosis then develops.

2-Tysonitis may occur when the prepuce is long & hygiene is poor. A tender swelling with a bead of pus will be found next to the frenum, abscess may develop.

3-Paraurethritis: paraurethral ducts may present beads of pus at their openings on pressure.

4-Littritis: 'threads' may appear in the first glass in the two-glass urine test.

5-Peri-urethral abscess: spread of the infection into the submucous tissue of the urethra results in a boggy, painful swelling on the undersurface of the penis. The abscess may open into the urethra or the surface of the penile shaft or the scrotum.

6-Urethral stricture: a chronic sequel of peri-urethral inflammation which causes fibrous stricture. The patient may complain of morning gleet, difficulty in passing urine & a narrow stream,subsequently retention of urine may occur.

7-Cowperitis & Cowper's gland abscess: a painful swelling palpable on either side of the median raphe of the perineum,best felt between the thumb on the perineum & a forefinger in the rectum.

8-Posterior urethritis : if the infection is untreated , the posterior urethra may become involved in about 10-14 days. There is increasing dysuria ,urgency ,frequency & terminal haematuria. Both glasses of urine in the two-glass urine test are hazy in appearance.

9-Cystitis(trigonitis): when the bladder is infected,the trigon is most often involved.

10-Prostatitis & prostatic abscess: acute prostatitis causes an exacerbation of the symptoms of urethritis together with perineal pain & suprapubic discomfort. The patient is ill with marked fever & malaise. On rectal examination the gland is found to be swollen & tender.

When prostatic abscess develops,the symptoms of acute prostatitis become even worse.The abscess may rupture into the urethra or rectum; or point to the perineum & a sinus or a fistula may form.

11-Seminal vesiculitis: this is usually associated with prostatitis & is manifested by haemospermia, frequent erections & ejaculations. The inflamed seminal vesicles may be felt per rectum as tender sausage-like structures above the prostate.

12-Epididymitis: the condition is usually unilateral & presents as a painful, hot, red swelling. If both epididymes are involved, sterility will result.

GONORRHOEA IN WOMEN

Urogenital Gonorrhoea:

The incubation period of gonorrhoea in women is usually longer than 2 weeks.

The primary sites of female urogenital gonorrhoea are the endocervical canal and the urethra.

Clinical picture:

-The condition is symptomless in almost 50% of cases. In some, symptoms may be related to the co-existing trichomoniasis or candidiasis.

-The other 50% complains of symptoms of urethritis and/or cervicitis.

1-Acute urethritis:

-Dysuria.

-Frequency will indicate the presence of trigonitis or cystitis.

-In severe cases, there is terminal haematuria. On examination (in lithotomy position) the external urinary meatus may be reddened with oedematous lips. On massaging the urethra with the index finger in the vagina (milking of the urethra), yellow purulent discharge can be expressed from the urethral orifice.

2-Cervicitis:

-The condition is often symptomless.

-The patient may complain of low backache or vaginal discharge.

-On examination: a mucopurulent or purulent discharge is seen coming from the external os which appear congested. There may be signs of acute cervical erosions.

N.B. a normal-looking vagina & cervix does not mean the absence of infection.

Diagnosis:

Gram-stained smears from urethra and/or cervical discharge detects Gram-negative diplococci in about one third of infected cases and, therefore, cultures are mandatory to confirm or exclude gonococcal infection in women.

Local complications:

1-Skenitis: Beads of pus may be seen or expressed from the Skene's ducts.

Paraurethral cyst or abscess of Skene's glands rarely occur as a result of blockage of their ducts.

2-Bartholinitis: Bartholin's glands may be infected unilaterally or bilaterally, causing pain & swelling of the vulva with discomfort & difficulty in sitting & walking. If the

duct is blocked, abscess of the gland develops & eventually this may rupture through the skin or mucous membrane. Chronic Bartholinitis or Bartholin's cyst may occur.

On examination, there will be swelling of the vulva on the affected side. The abscess can be felt between the fingers with the thumb on the outer surface of the labium majus & the index finger in the vagina.

3-Pelvic infection: Extension of gonococci to the pelvis may result in salpingitis, pyosalpinx or parametritis.

-Pelvic inflammatory disease (PID) is a collective term for the involvement of the fallopian tubes, ovaries & adjacent peritonium. It is a serious condition with agonizing sequelae such as chronic pelvic pain, dyspareunia, ectopic pregnancy & sterility. Lower abdominal pain, pyrexia & general malaise are common manifestations that often occur during or within a week after menstruation.

EXTRAGENITAL GONOCOCCAL INFECTIONS IN MEN & WOMEN

1-Gonococcal Proctitis:

The rectal mucosa may be infected by the gonococcus in either sex. In women, the rectum is involved as a result of secondary spread from the primary urogenital site (autoinoculation). It can be a primary site of infection in the case of anal coitus. Anorectal gonorrhoea in men occurs almost always in homosexuals as direct inoculation via rectal intercourse, but it may result from rupture of a gonococcal abscess of the prostate or Cowper's gland into the rectum.

The patient may have no symptoms. When present, they may include a change in bowel habits, tenesmus, anal irritation & mucoid, purulent, or blood-stained anal discharge. On proctoscopy the mucosa looks erythematous, edematous & friable with mucopurulent discharge.

Rectal mucosa smear for Gram's stain & culture may help in diagnosis.

2-Oropharyngeal Gonorrhoea:

Mode of infection is by orogenital contact. The condition may be asymptomatic. Sore throat with pyrexia & cervical lymphadenopathy are the common manifestations.

3-Gonococcal Conjunctivitis:

It is rare in adults & occurs from direct contamination of the eye with infectious discharge by fingers or towels.

The symptoms & signs include sore eyes, discharge, photophobia, redness of the conjunctiva & oedema of the eyelids.

4-Disseminated Gonococcal Infection (DGI):

Blood-borne dissemination of gonococci occurs mainly in women, 7-30 days after mucosal infection.

The manifestations are often mild (benign gonococcaemia) presenting as a triad of fever, arthritis, & dermatitis. The rarer but more serious manifestations include endocarditis, myocarditis, pericarditis, meningitis, osteomyelitis & hepatitis.

Gonococcal dermatitis: skin lesions are generally found on the extremities as small macules, papules, pustules, or vesicles that may be haemorrhagic or necrotic. Spontaneous resolution & relapses may occur. Differential diagnosis is mainly from meningococcal septicemia, pyoderma & drug rash.

Diagnosis of DGI:

1. Blood cultures.
2. Smears & cultures from skin lesions & joint aspirate.
3. Swabs should be taken from all sites likely to be the portals of infection.

5-Gonococcal Perihepatitis (Fitz-Hugh-Curtis Syndrome):

The condition occurs mainly in women & there are usually associated symptoms of salpingitis or the pelvic infection may have been asymptomatic. The infection is believed to reach the subphrenic space by spread from the fallopian tube along the peritoneum & paracolic gutters.

The patient presents with pain in the right hypochondrium referred to the shoulder & aggravated on deep breathing. There may be fever, nausea & vomiting.

Clinical examination reveals tenderness in the right hypochondrium, and, in most cases, signs of pelvic infection.

TREATMENT OF GONORRHOEA

Penicillin is still the drug of choice; however the emergence of penicillinase-producing *N.gonorrhoeae* affected its value in the treatment of gonorrhoea. The susceptibility of *N.gonorrhoeae* to antibiotics is likely to change over time, so, the knowledge of antibiotic sensitivities in a locality is of great importance.

Probenicid raises the level & duration of the serum concentrations of penicillins & certain cephalosporins by competitively inhibiting their renal tubular excretion.

The possibility of associated chlamydial infection should be considered in the management of persons with gonorrhoea. If chlamydial diagnostic testing is not available, treatment for chlamydia should be given.

Patients who are found to have both gonorrhoea & syphilis should first be treated for gonorrhoea & then treatment continued for syphilis. If diagnosis of syphilis is in doubt, then gonorrhoea should be treated with a nontreponemal drug such as cotrimoxazole while further investigations are being carried out to avoid masking the syphilis.

General measures:

- Avoidance of sexual intercourse for at least 2-4 weeks.
- Avoidance of Alcohol, exertion, and self examination.
- The patient is warned of the risks of conjunctivitis & transmission of infection.
- Both partners should be treated simultaneously.

Treatment of uncomplicated genital infections in males & females:

A-Treatment regimens in penicillin sensitive strains:

- Aqueous procaine penicillin G, 4.8 million units IM plus probenecid, 1 gm by mouth. OR
- Amoxicillin, 3 gm plus probenecid, 1 gm by mouth. OR
- Tetracycline hydrochloride, 500mg by mouth 4 times daily for 7 days for those allergic to penicillin (tetracycline is contraindicated in pregnancy).

B-Treatment regimens in penicillin resistant strains:

- Ceftriaxone, 250 mg IM. OR
- Spectinomycin, 2 gm IM. OR
- Erythromycin, 500 mg by mouth 4 times daily for 5 days. OR
- Quinolone derivatives: A single oral dose of ciprofloxacin (250mg), or norfloxacin (800mg). OR
- Cotrimoxazole (trimethoprim, 80mg, plus sulphamthoxazole, 400mg) 2 tablets twice daily for 7 days.

Disseminated gonococcal infection:

The patient should be hospitalized & endocarditis & meningitis ruled out.

A- In penicillin sensitive strains:

- Crystalline penicillin, 2 million units IV 4 hourly for 3 days; followed by amoxicillin, 500mg by mouth 4 times daily for 7 days. OR
- Tetracycline hydrochloride 500mg by mouth 4 times daily for 10 days.

B- In penicillin resistant strains:

- Spectinomycin, 2 gm IM twice daily for 5 days. OR
- Cefotaxime, 500mg IV 4 times daily for 7 days.

Gonococcal endocarditis & meningitis require high-dose penicilline therapy IV 10-14 days for the latter & 1 month for the former.

Gonococcal pelvic inflammatory disease:

- Mild or moderate cases: outpatient treatment is suitable. Ampicillin or amoxicillin 500mg every 6 hours by mouth combined with 1 gm probenecid daily is continued for 10 days. Alternatively, tetracycline hydrochloride 1.5gm by mouth followed by 0.5 gm 4 times daily for 10 days can be given.
- Severe cases: should be hospitalized & aqueous crystalline penicillin G, 20 million units daily by slow infusion is given for the first 2 or 3 days (until improvement is shown) followed by ampicillin 500mg by mouth every 6 hours & continued to complete 10 days of treatment. OR
Tetracycline hydrochloride, 2gm daily IV until significant improvement occurs, followed by 0.5 gm orally 4 times daily for 10 days.

Follow-up:

The patients are asked to return 1 week & 2 weeks after treatment for tests of cure; specimens should be taken from the same sites as before treatment. All patients are then seen at the end of 3 months when final blood tests for syphilis are carried out.

GONORRHOEA IN INFANTS & CHILDREN

Genital gonorrhoea in children is rare, & when it occurs ,sexual assault should be considered. It occurs more often in girls than in boys.

Gonococcal Vulvovaginitis

In prepubertal girls the vaginal mucosa is thin, immature & have alkaline pH. Thus ,it is susceptible to gonococcal infection.

Mode of infection:

- Indirect through contact with infected fomites, towels, rectal thermometers, toilet seats in poor hygienic standard.
- Direct sexual assault.

Clinical picture:

- 1-Dysuria ,vulvovaginal itching or soreness & difficulty in walking.
- 2-The underwear may be stained & the purulent discharge is often obvious.
- 3-The vulva and vagina are swollen, red and discharging mucopurulent discharge.

Diagnosis:

- Swabs for Gram stain and culture.
- Other members of the household should be investigated.

Other causes of vulvovaginitis in children:

- 1-Bacteria as B.coli,staphylococci, streptococci,C. diphtheriae & C.trachomatis.
- 2-Foreign bodies inserted accidentally into the vagina. may facilitate secondary infection.
- 3-Entrobis vermicularis infestation.
- 4-Candidal infection.

Treatment:

- 1-Frequent local wash with antiseptic solution as pottasium permanganate 1/8000.
- 2-Procaine penicillin G, 100.000units/kg IM plus oral probenicid 0.5gm. Those who are allergic to penicillin can receive spectinomycin 75mg/kg IM.

Gonococcal Ophthalmia Neonatorum

Infection of the baby's eyes during parturition through the infected cervix.

Clinical Picture:

- Incubation period: 2-5 days.
- The condition is usually bilateral.
- Purulent discharge is seen oozing from between swollen & erythematous lids.
- Without treatment, conjunctivitis may proceed to involvement of the cornea with ulceration & iridocylitis & eventuel blindness.

- If not treated, the cornea becomes involved with cellular infiltration, oedema and ulceration and the eye may be destroyed.

Prophylaxis:

- Treatment of gonorrhoea in the mother before she goes into labour.
- Treatment of the baby's eyes just after delivery with Crede's method by wiping the eyelids and eyelashes free from pus with application of 1% silver nitrate drops, or crystalline penicillin drops 10,000units/ml, or 1% tetracycline ointment.
- If the risk of the disease is considerable, an IM injection of 50.000units of crystalline penicillin should be given.

Treatment:

- Hospitalization and isolation for 24 hours.
- Systemic crystalline penicillin G, 50,000units/kg IM every 6 hours for 7 days.
- Frequent irrigation of the eyes with sterile normal saline helps to remove the copious purulent exudate.
- If manifestations of corneal ulceration appear, 1% atropine sulphate should be applied twice daily.
- Both parents must be examined & treated.

NONGONOCOCCAL URETHRITIS (NGU)

Definition:

Sexually or nonsexually transmitted urethral inflammation not due to *N. gonorrhoea*.

NGU is the commonest sexually transmitted disease in western countries.

Synonyms:NGU=nonspecific urethritis. Patients with postgonococcal urethritis in which the gonococcus disappears but symptoms of urethritis remain are included in this category (NGU). The syndrome results from a dual infection with *N. gonorrhoea* & other agents that cause NGU & the later are unmasked when the gonorrhoea is treated with drugs that are not effective for NGU.

Aetiology:

1- Sexually transmitted urethritis:

- a-*Chlamydia trachomatis* (serotypes D-K) is implicated in 30 - 50% of cases of NGU.
- b-Other organisms that cause 10-15% of cases include *Ureaplasma urealyticum*, *Trichomonas vaginalis*, Herpes simplex virus, *Candida albicans* and *T. pallidum* (intrameatal chancre & mucous patches during secondary stage of syphilis).
- c-There still remains $\leq 30\%$ of cases of urethritis presenting at STD clinics in whom no cause can be found; these cases should truly be designated as non-specific urethritis.

2-Non-Sexually acquired urethritis:

- a-Bacterial urethritis associated with urinary tract infections.
- b-Schistosomiasis of bladder.
- c-During febrile states e.g., influenza & bacillary dysentery.
- d-Steven-Johnson syndrome.
- e-Secondary to :

- Crystalluria & renal stones.
- Catheterization & other urethral instrumentation.
- Foreign bodies in the urethra.
- Urethral stricture.
- Irritants (local antiseptics & local contraceptives).
- Venerophobia with repeated self-examination.

Clinical Picture:

The incubation period is variable & ranges from 5-30 days or more. Whatever the cause of NGU, the clinical features are indistinguishable & include dysuria & urethral discharge. In contrast to gonorrhoea, the symptoms tend to be milder; there may be no discomfort & the discharge is usually mucoid, white & scanty and may be seen only in the morning. Clinical overlap often exists between NGU & gonorrhoea.

Course & Complications:

- The clinical course is usually mild. The disease runs a variable course with a tendency to cease spontaneously, although recurrences are very common.
- The complications or sequelae of untreated or inadequately treated NGU are essentially similar to those in gonorrhoea. Local complications include Littritis, Tysonitis, Cowperitis, epididymitis, prostatitis & urethral stricture. General complications include conjunctivitis (autoinoculation) & sexually-acquired reactive arthritis (Reiter's syndrome). Infection of female sexual partners may occur which may lead to pelvic inflammatory disease & may even transmit the infectious agent to newborns (neonatal conjunctivitis & pneumonia). Complications are more frequent if NGU is caused by chlamydial infection.

Persistent or Recurrent NGU:

Causes are poorly understood.

- 1-Poor compliance by the patient.
- 2-Reinfection due to failure to treat sex partners.
- 3-Abnormalities in the urethra such as stricture, congenital valves & foreign bodies.
- 4-An unusual cause of NGU, unaffected by the therapy employed such as T. vaginalis.

Diagnosis:

1-Diagnosis of urethritis & exclusion of Gonorrhoea:

- Gram-stained urethral smear: ≥ 5 polymorphnuclear leukocytes per high power field & absence of gonococci.
- Two-glass urine test shows threads or haziness in the first glass & usually clear urine in the second.
- Culture for gonococci is necessary in a negative or doubtful Gram's stain & in all cases with possible forensic impact.

2-Diagnosis of the cause of NGU as far as is possible:

Demonstration of chlamydial inclusions by immunofluorescent or Giemsa stain, combined with efforts to isolate agents of possible aetiologic significance by making wet films, stained smears & cultures.

3-Persistent or recurrent cases:

Urologic evaluation is required so that an accurate diagnosis can be made & obvious organic pathology is not overlooked; for example, urethral stricture, congenital urethral valves, urethral foreign bodies or renal calculi and urogenital tuberculosis.

Treatment:

1-Avoidance of sexual intercourse & alcohol intake for 3 weeks.

2-Concomitant treatment of sexual partners is mandatory.

3-Drug treatment.

- Fortunately, most patients will respond to a standard regimen of either doxycycline 100 mg orally twice daily for 7 days; or erythromycin 500 mg orally 4 times a day for 7 days.
- Trichomonal urethritis: Metronidazole 200 mg t.d.s. for 7 days.
- Herpes simplex urethritis in men with primary genital herpes (if severe): Acyclovir 200 mg five times daily for 5 days.

Follow up:

- The patient should be seen at intervals of 1-2 weeks until two consecutive tests are normal.
- A final check including serology for syphilis should be carried out at the end of 3 months.

SYPHILIS

Definition:

Syphilis is a chronic, contagious infection caused by *Treponema pallidum*. It is transferable to the foetus as a congenitally acquired infection. It responds to penicillin.

Causative organism:

Treponema Pallidum.

It is a thin delicate spirochaete made of many narrow regular coils.

- Length : 5-20 μm .

- Breadth: 0.25 μm .

-Number of coils: 5-20 coils.

-Motility : 2 types of movements :

1. Locomotion: rotation along its long axis like a corkscrew with propulsion of the cell through the medium.
2. Change of shape: flexion movements of the whole body (angulation, buckling, coil compression & expansion, and looping).

-Culture: cannot be cultured on artificial media but can be grown only by animal inoculation.

-It is destroyed by dryness, heat and mild antiseptics (even soap).

Pathogenesis of Syphilis:

-The organisms enter through abraded skin or intact mucous membrane, spread to the lymphatics, blood vessels, spleen & bone marrow.

-The first lesion is due to local inflammatory reaction at the site of entrance.

-The organisms then multiply in blood and lymphatic system and attacks skin, mucous membranes and all organs & this stage represents the stage of secondary syphilis or stage of generalization.

-In untreated patient, the body immunity overcomes the spirochaetes but not all of them are killed & some remain dormant in lymph glands & various organs and the patient enters the stage of latency (3-10 years) during which there is no signs.

-At the end of the latent period & due to unknown cause, the body develops a state of hypersensitivity towards the remaining spirochaetes giving extensive & intense lesions, e.g. gumma, malignant syphilis and tendency to destruction and replacement by noncontractile fibrous tissue.

Histopathology of Syphilis:

The basic changes are essentially the same in all stages of syphilis.

1-Endarteritis obliterans: endothelial proliferation occludes small blood vessels resulting in:

- Loss of epithelium & erosion in the primary lesion of syphilis.

- Mucosal ulceration in secondary syphilis.

- Tissue destruction & ulceration in gumma, cardiovascular & neurosyphilis.

2-Perivascular infiltration: lymphocytes, macrophages & many plasma cells. In late secondary & tertiary syphilis, a granulomatous infiltrate of epithelioid & giant cells is usually found.

3-Fibroblast activity: leads to healing with fibrosis, scarring & deformity which is marked in late syphilis.

In primary & secondary stages, the causative organism (*T.pallidum*) can often be demonstrated by silver staining or fluorescent antibody staining of tissue sections.

Serological Tests of Syphilis:

Syphilitic infection gives rise to a variety of circulating antibodies, including antilipoidal reagin (non-specific) & specific treponemal antibodies. Serological tests are of two types:

1-Non-treponemal (reagin) tests: These tests measure antibodies formed in response to products of tissue destruction. Reagins are non-specific & can appear in the course of certain other diseases giving rise to biological false positive reactions. Reagin tests are of 2 types:

a- Complement fixation tests such as Wasserman reaction.

b- Flocculation or precipitation tests such as Kahn's test & the more reliable Venereal Diseases Research Laboratory (VDRL) test & Rapid Plasma Reagin (RPR) test.

Reagin tests become positive after 5 - 8 weeks following infection, i.e., 2 weeks after the appearance of chancre. They are 100% positive in the second stage & in 70-90% of cases of the tertiary stage.

Reactive reagin tests must always be confirmed by one of the specific tests as few normal persons may give positive reagin tests but their sera will show negative specific tests. A titrated VDRL test should be done for treatment follow-up. Effective therapy in early syphilis can cause seronegativity after six months to one year. In the later stages of syphilis, the reversal of these tests is slow & variable.

2-Treponemal (specific) tests: serologic tests that measure antibodies directed against *T. pallidum* itself. Once positive, they usually remain so for life regardless of treatment or disease activity. They include:

- Treponema Pallidum Immobilization (TPI) test.
- Fluorescent Treponemal Antibody (FTA) test.
- Fluorescent Treponemal Antibody Absorption (FTA-ABS) test.
- Treponema Pallidum Haemagglutination (TPHA) test.

In general, non treponemal tests are suited to the task of screening for the disease & monitoring response to treatment; while treponemal tests are more specific & best suited to the confirmation of the diagnosis. VDRL (or RPR) combined with & TPHA tests have proved to be very satisfactory for routine use.

Biological false positive (BFP) reactions:

A persistent or transient positive reagin test in the absence of reactive specific tests can occur in nonsyphilitic sera. BFP reactions are divided into:

1. Acute BFP reactions: the test becomes negative within 6 months & this is associated with a number of bacterial & viral infections such as mycoplasma pneumonia, glandular fever, measles & viral hepatitis. It may occur in pregnancy & malaria.
2. Chronic BFP reactions: seropositivity lasts for more than 6 months & may be found in:
 - Chronic infections such as tuberculosis & leprosy.
 - Autoimmune diseases such as systemic lupus erythematosus, rheumatoid arthritis, haemolytic anaemia & thyroiditis.
 - Intravenous drug abuse.
 - Malignancy.

Classification of syphilis:

Acquired syphilis:

- * **Early:** Primary
Secondary
Early latent
- * **Late:** Late latent
Tertiary
Cardiovascular

Neurosyphilis

Congenital syphilis:

- * Early
- * Late
- * Stigmata

Acquired Syphilis

Modes of Infection:

A) Venereal route: sexual intercourse (95 % of cases).

B) Non-venereal routes :

- Direct : kissing, bites, breast feeding from infected mother or wet nurse.
- Indirect : contagious secretions transferred by cups, spoons, cigarettes, pipes, medical instruments & moist towels (extremely rare).
- Needle prick inoculation and blood transfusion with infected blood leads to infection with syphilis but without appearance of chancre (syphilis d'emblee).

The organism cannot penetrate intact skin, but can pass the intact mucous membrane.

Incubation Period:

- 9-90 days.
- It depends on virulence of the organism & host resistance.
- The disease is infectious by blood transfusion during the incubation period.

Primary Syphilis

It is the stage of chancre or hard sore.

Characters of chancre :

- It is usually single & painless (when uncomplicated).
- Shape is oval or rounded with an eroded surface.
- Size: 1-3 cm in diameter.
- Edge is well-defined & slopes to the floor giving a saucer-like appearance.
- Floor is clean & fleshy in color.
- Base is indurated like a button.
- It exudes clear serum on manipulation.
- It heals with thin atrophic scar.
- Sites:
 - Genital sites in men: glans penis, frenulum, coronal sulcus, shaft of the penis, scrotum, intrameatal, and anal canal in homosexuals.
 - Genital sites in women: cervix uteri is the commonest site of primary lesions in women. Other sites include labia majora or minora, region of fourchette , clitoris, urethral orifice, vagina, mons pubis and anal canal.
 - Extragenital Chancre (5-10% of the primary lesions):
 1. Lips, tongue & tonsils.
 2. Nipple & breast.
 3. Fingers & hands.

-Regional lymph nodes: unilateral or bilateral adenopathy. The palpable nodes are mobile, discrete, firm, rubbery and not painful nor tender unless secondarily infected.

Special types of Chancre:

- 1-Kissing chancres: on contagious surfaces, e.g. scrotum & thigh.
- 2-Mixed chancre: chancre mixed with chancroid (painful).
- 3-Condom chancre: at the root of the penis of those wearing condoms.
- 4- Concealed chancre: intracervical, intrameatal or intraanal.
- 5-Phagedenic chancre: chancre mixed with fusiform bacilli and anaerobic spirochaetes. It causes destruction of tissue & may affect the whole glans penis or part of the shaft.

Fate of primary syphilis:

- 30% of cases: the disease burns itself out.
- 30% of cases become serologically positive for life.
- 20% of cases pass to benign tertiary syphilis.
- 20% of cases pass to malignant syphilis (cardiovascular & neurosyphilis).

Investigations of primary syphilis:

- 1-Dark ground microscopy:is used to identify T. pallidum, provided that antimicrobial therapy has not already been started.
- 2-Lymph node puncture & dark ground microscopy of the aspirate: in hidden chancre, mouth chancre & in septic, healing or partially treated chancres.
- 3-Tissue biopsy.
- 4-Serological tests in old chancre (they do not become positive until 1-2 weeks following the appearanc of the chancre).

Differential diagnosis of genital chancre:

- 1-Lymphogranuloma venerium.
- 2-Granuloma inguinale.
- 3-Herpes progenitalis.
- 4-Herpes zoster involving the third ssacral segment.
- 5-Scabies.
- 6-Traumatic ulcer (superficial & painful).
- 7-Malignant ulcer (old age, raised everted edge, with stony hard lymph nodes).
- 8-Tuberculosis.
- 9-Fixed drug eruption.
- 10- Lichen planus.
- 11- Behcet's disease (recurrent oral & genital ulcers, & relapsing uveitis).
- 12- Reiter's syndrome (uretheritis, conjunctivitis & arthritis).
- 13- Gummatous ulcer (punched-out edge, wash-leather floor & regional lymph nodes are not enlarged).
- 14- Gonococcal ulcer (superficial ulcer in uncircumcised men).

Differential diagnosis of intrameatal chancre:

It may be misdiagnosed as nonspecific urethritis (it presents with scanty serous discharge).

Differential diagnosis of extragenital chancre:

- Lips & tongue: secondary syphilis, tuberculosis, gumma, herpes simplex, aphthosis, Behcet's syndrome, epithelioma & trauma.
- Tonsils: vincent angina & diphtheria.
- Nipple: simple fissuring & Paget's disease.
- Anus: anal fissure & thrombosed external pile.
- Fingers: whitlow or paronychia due to bacterial or herpetic infection.

History, thorough clinical examination, dark-field microscopy, serology, biopsy and ,if possible,examination of the consort may be necessary before a final diagnosis can be made.The possibility of a coincidental syphilis must be borne in mind in all of the above cases.

Secondary Syphilis

In untreated patients, the clinical manifestations of secondary syphilis usually appear within six months. It is the stage of generalization.

1- Skin rash (syphilides):

- The skin is involved in more than 80% of the cases.
- Characters: the rash is polymorphic, coppery red in color , widely & symmetrically distributed, not itchy, never vesicular & very seldom pustular.
- There may be a single eruption or a series of recurrence of rashes.

-Types of skin rash:

- macular syphilide.
- papular syphilide. The papules may form a line along the hair margin (the corona veneris). They may appear in groups with tendency to annular arrangement; this is more common on the face & in black patients.
- papulosquamous or psoriasiform syphilide.
- Follicular syphilide.
- Pustular syphilide (papules with necrotic tissue in the center).
- Vesicles & bullae are never seen.
- Different types of skin rash may coexist (polymorphism).
- Healing takes place in 4-12 weeks without scarring. Hypopigmentation may sometimes result (leukoderma syphiliticum) & is most commonly located on the neck.

2- Condyloma late (syphilitic moist papules) :

- This morphologic variant of papular syphilide appears at the mucocutaneous junction especially on the perianal region , vulva & scrotum.
- Lesions are moist, flat-topped, hypertrophic, sessile papules & masses with rounded outline & indurated base, that do not bleed easily.
- It is the most infectious syphilitic lesion as it is laden with spirochaetes.

3- Mucous patches:

- Rounded, regular, greyish-white pseudomembrane edged by a dull red areola & is liable to ulcerate.
- They may fuse together to form the so-called 'snail-track' ulcers on the tongue, pillars of the fauces & soft palate.
- They may occur inside the lips & cheeks, on the tongue, tonsils, nose, vulva, vagina, cervix, glans penis, prepuce & inside the anus.
- Mucous patches in the urethra cause urethral discharge.

4- Lymph nodes:

- Generalized lymphadenopathy especially the inguinal, epitrochlear, axillary, anterior & posterior cervical, suboccipital & postauricular groups.
- Enlarged lymph nodes are rubbery, discrete, mobile & painless.

5- Other Features: Any organ of the body may be involved.

- Hair: a non-scarring patchy or "moth-eaten" alopecia with irregular edges (follicular syphilide of the scalp). Eyebrows & the beard may be affected.
- Nails: paronychia or onychia.
- Respiratory system: hoarseness of voice & coarse cough.
- GIT: epigastric pain, nausea & diarrhea.
- Liver: hepatitis with jaundice & hepatomegaly.
- Spleen: may be enlarged.
- Muscles: myopathy.
- Joints: arthralgia, arthritis & painless effusion.
- Bones: periostitis.
- Kidney: syphilitic nephritis.
- CNS: Headache, neck stiffness & cranial nerve palsy (eighth nerve).
- Eyes: iridocyclitis.
- Constitutional symptoms: fever, malaise, anorexia, weight loss & pallor.

Differential diagnosis of secondary syphilis:

- 1-Macular rash: Measles, rubella, pityriasis rosea, leprosy, typhoid fever (the rose spots), drug eruptions & erythema multiforme.
- 2-papular lesions: Lichen planus, psoriasis, scabies, ringworm, drug eruptions, pityriasis rubra pilaris & leprosy.
- 3-Condyloma lata: Condyloma acuminata (The viral wart tends to be pedunculated mass with a rough dry surface & soft base. Lymph nodes are not enlarged).
- 4-Mucous patches: Aphthous ulcers, Behcet's syndrome & moniliasis. Glandular fever with its generalized skin rash, throat lesions & lymphadenopathy may very closely resemble secondary syphilide.
- 5-Syphilitic alopecia: alopecia areata & tinea capitis.

Diagnosis of secondary syphilis:

- History & clinical examination.
- Dark ground examination from skin lesions especially moist ones.

- Serological tests are 100% positive in secondary syphilis.
- CSF examinations are positive in 10-20% of cases.
- Histopathology.

Relapsing Syphilis

- It is the return of the disease after its apparent cessation due to inadequate or no treatment.
- Relapse may occur at any time during the first 2 years of infection.

-Types:

- Mucocutaneous relapse is the commonest type.
- Chancre redux : the recurrence of chancre in its original site.
- Serological relapse the nontreponemal antigen tests become positive after having become negative or show a four-fold rise in titer after a decline. It frequently precedes clinical relapse.
- Ocular relapse.
- Transplacental relapse: the birth of a syphilitic child to an apparently cured mother.
- Relapse of any other cutaneous lesions.
- Hepatic relapse with jaundice.
- Bone relapse.
- Neuro relapse (Symptomatic or asymptomatic).
- Infection of sex contacts.

Latent Syphilis

- After the secondary stage; the untreated patient enters latency. Latency may last a lifetime; it seldom lasts less than 5 years & may be up to 50 years before the patient develops further manifestations of the disease referred to as " late syphilis".
- Latent syphilis is asymptomatic & diagnosed by history & positive serology or discovered by chance, e.g. during antenatal investigations, or if the patient is tested as a blood donor. The diagnosis should be confirmed by specific serological tests.
- Latent syphilis is divided into:
 - Early latent syphilis which is contagious & confined to the first 2 years of infection during which relapses of secondary syphilis may occur.
 - Late latent syphilis which is non-infectious with the exception of the possibility of transplacental infection & transmission of infection by blood transfusion.
- The diagnosis is established if no evidence of active disease is detected in any system. Positive serological tests for syphilis must be confirmed by examination of a second specimen.

Late (Tertiary) Syphilis

Late syphilis includes the following:

- Late latent syphilis (mentioned above).

- Benign tertiary syphilis (late benign syphilis).
- Cardiovascular syphilis.
- Neurosyphilis.

N.B. Quaternary syphilis encompasses cardiovascular syphilis & neurosyphilis.

Benign Tertiary Syphilis

- Benign late syphilis occurs in some 16% of cases of untreated syphilis.
- It starts 5-10 years after infection & the lesions are rarely infectious.
- The characteristic lesion is the granuloma called the gumma.
- Benign tertiary syphilis includes all forms of symptomatic acquired syphilis occurring beyond the secondary or relapsing stages, with the exception of cardiovascular & neurosyphilis. It could cause disfigurement but rarely death.

Classification :

- 1- Gumma of skin & mucous membranes.
- 2- Gumma of internal organs.
- 3- Gumma of supporting structures.

Gumma of the skin :

- 1-Nodular Lesions: painless dull red firm nodules that may be arranged in groups with rounded or polycyclic borders & occasionally ulcerate giving punched-out ulcers. They heal by atrophic non-contractile (tissue-paper) scars & may occur on any part of the skin surface.
- 2-Squamous or psoriasiform lesions: larger nodules or plaques covered with waxy scaling resembling psoriasis with central healing are seen especially on the palms & soles.
- 3-Subcutaneous gumma: starts as rounded painless subcutaneous nodule that ulcerate producing gummatous ulcer which is characterized by punched-out edges with rounded or polycyclic borders, indurated base & the floor is covered by adherent dirty yellow slough (wash-leather). No lymph node enlargement & the lesion heals by thin non-contractile scar. It commonly affects the upper outer part of the legs ,but the buttocks, sternum, face & scalp may be involved.
- 4-Pseudochancres: a solitary gumma which appears at the site of previous chancre.

Gummata of mucus membranes :

Gummatous lesions may originate in the submucosa of the mouth, nose & throat and involve deeper tissues (including bone) as well as the mucous membrane. They begin as painless swellings & may break down to form gummatous ulcers & may lead to:

- 1- Perforation of the nasal septum with nasal deformity.
- 2- Perforation of the hard palate.
- 3- Destruction of the uvula and nasal food regurgitation.
- 4- Stenosis of the pharynx & larynx resulting in chronic hoarseness & dysphagia.
- 5-Late syphilis of the tongue may present with localized or diffuse changes:
 - The solitary gumma present as painless nodule.
 - Diffuse gummatous infiltration may start as a painless, smooth enlargement of the tongue,i.e. macroglossia; passes through a stage of chronic interstitial glossitis with

fissuring; & later leukoplakia. In other cases, changes are more superficial, with red smooth glazed areas and loss of papillae.

All the forms of tongue involvement are precancerous, so that regular observation of the patient is essential & biopsy should be taken from any suspicious areas.

Differential diagnosis of skin & mucosal lesions:

The skin lesions on the face may need to be differentiated from lupus vulgaris, leprosy, epithelioma, lupus erythematosus, pyoderma & fungal skin lesions.

On the trunk & limbs, it can resemble psoriasis.

On the legs gummatous ulceration can look like a venous ulcer.

The changes in the tongue should not be confused with the congenital deformity of scrotal tongue & leukoplakia should be differentiated from moniliasis, lichen planus & malignancy.

Positive serological tests for syphilis, response to penicillin therapy & possibly evidence of syphilis elsewhere should clarify the diagnosis, which can usually be confirmed by biopsy in cases still in doubt.

Gummata of internal organs :

-Liver: gummata may undergo fibrosis & scarring resulting in lobulation of the liver (hepar lobatum). There may be pain in the right hypochondrium, jaundice, ascites, portal hypertension & splenic enlargement.

-Stomach: diffuse gummatous infiltration (leather bottle), chronic indigestion without anorexia or marked cachexia.

-Testicles: diffuse gummatous infiltration & dense fibrosis produce an enlarged & hard testicles (billiard ball testicles) associated with loss of testicular sensation. If the gumma involves the skin, it ulcerates on the anterior wall of the scrotum.

-Paroxysmal cold haemoglobinuria (PCH): syphilis is one of the rare causes of this acquired type of hemolytic anemia. It is due to the presence of a hemolysin present in the blood of a patient with late acquired (or late congenital) syphilis. This hemolysin combines with the red blood cells on exposure to low temperatures. These sensitized red cells are haemolysed by complement when the patient returns to a warm environment. The patient may experience fever, headache, malaise, transient jaundice & the urine becomes dark brown.

The condition is diagnosed by positive serology for syphilis & demonstration of hemolysin in the serum (Donath-Landsteiner reaction).

Gummata of supporting structures:

-Bones : osteoperiostitis of long bones present as a localized or diffuse irregular swelling of the bone. Pain is boring & worse at night. X-ray will show periosteal thickening. The bones commonly involved are tibia, clavicles, sternum & skull. Bone lesions of the skull are osteolytic.

-Lesions of the other supporting structures, such as muscles, joints, tendon sheaths & bursae, are rare.

Diagnosis of syphilitic gumma:

- 1-History & clinical picture.
- 2-Histopathology.
- 3-Positive serology: weakly reactive & negative reagin tests, e.g. VDRL, may occur in late skin syphilis. False positive VDRL results may accompany some non-syphilitic but suspect skin lesions. The specific treponemal antigen tests are more frequently positive & therefore, more reliable as supportive evidence of late syphilis
- 4-CSF examination.

Neurosyphilis

Overall less than 10% of all patients develop late involvement of the central nervous system which may be asymptomatic or symptomatic. A diagnosis of latent syphilis cannot be made unless asymptomatic neurosyphilis is excluded by a negative cerebrospinal fluid examination.

Classification:

Neurosyphilis may be divided into the following categories based on the predominant clinical & pathological involvement:

- 1-Asymptomatic neurosyphilis.
- 2-Meningovascular neurosyphilis.
- 3-Parenchymatous neurosyphilis.

Various combinations of meningeal, vascular & parenchymal involvement is not uncommon.

1-Asymptomatic Neurosyphilis:

- There are abnormalities in cerebrospinal fluid (5 or more cells/cc; protein raised to over 40 mg/dl and usually a reactive FTA test) with no signs or symptoms attributable to syphilis. Signs of syphilis of other organs may or may not be present. The blood tests for syphilis are positive.
- In the absence of adequate treatment, a proportion of these cases will progress to symptomatic neurosyphilis.
- Cerebrospinal fluid should be examined 2 years after treatment of early syphilis to exclude the possibility of asymptomatic neurosyphilis.

2-Meningovascular neurosyphilis:

Lesions are mainly meningeal or vascular. Brain or spinal cord may be involved.

1. Cerebral manifestations:

- Syphilitic meningitis: may be localized or generalized
 - Diffuse involvement: increased intracranial pressure & cranial nerve palsies.
 - Focal (gummatous): increased intracranial pressure & focal cerebral symptoms & signs of slow onset.
- Cerebral vascular manifestations: Focal cerebral symptoms & signs of sudden onset.

Patient may suddenly develop monoplegia, hemiplegia, homonymous hemianopia or other symptoms & signs depending on the site of the vascular accident.

2. Spinal manifestations:

– Syphilitic meningomyelitis

- If the dorsolumbar region is involved, the patient develops spastic weakness of the legs & impairment of bladder sphincter control (Erb's spastic paraplegia).
 - Involvement of cervical region (hypertrophic cervical pachymeningitis) causes root pain, atrophy & finally progressive spastic paraplegia & sensory loss below the level of the lesion.
 - Syphilitic amyotrophy: Lower motor neurone lesions predominate (degeneration of the anterior horn cells); sensation is unaffected.
- Spinal vascular lesion such as thrombosis of the anterior spinal artery may cause acute syphilitic transverse myelitis.

3-Parenchymatous neurosyphilis:

There are two main conditions, general paralysis of the insane & tabes dorsalis, affecting the brain & the cord parenchyma respectively. Both may coexist, i.e. taboparesis.

– General paresis (paralysis) of the insane (GPI):

Progressive mental & physical deterioration & finally dementia, convulsions, spastic weakness & incontinence of urine & faeces may develop.

Tabes Dorsalis:

- Locomotor ataxia ,areflexia ,paraesthesias & lightning pains.
- Impotence, loss of testicular sensation & bladder disturbances may result from involvement of sacral roots.
- Ocular manifestations include failing vision due to optic atrophy;pupillary changes often typical of Argyll-Robertson type ; and ophthalmoplegias due to involvement of third,forth & sixth cranial nerves.
- Trophic changes include Charcot's arthropathy & perforating ulcers.

Prognosis of neurosyphilis:

- The prognosis of asymptomatic neurosyphilis is excellent.
- The prognosis of meningovascular neurosyphilis is very good after early & adequate treatment (apart from structural damage that may have already occurred).
- Tabes dorsalis is fatal due to its complications.
- GPI is fatal within months or years if untreated.

Cardiovascular Syphilis

Incidence:

- 10% of late untreated syphilis develop cardiovascular syphilis after a latent period of 10-20 years.
- It may be associated with neurosyphilis in 40% of cases.

Clinical manifestations: The principal lesion is aortitis, which may be uncomplicated & asymptomatic or may cause aortic regurgitation, aneurysm of the aorta; or coronary ostial stenosis.

1-Uncomplicated aortitis:

It usually involves the ascending aorta.

- There are no symptoms & the condition is often undiagnosable during life.
- Fine linear calcification in the ascending aorta may be seen on radiography & positive serological tests for syphilis is supporting evidence.

2-Coronary ostial stenosis:

- Anginal symptoms occur due to narrowing of the coronary ostia.
- ECG changes occur.

3-Aortic incompetence:

It may remain compensated & asymptomatic for several years. Eventually congestive heart failure develops due to the strain on the left ventricle.

4-Aortic aneurism:

An aneurysm may remain asymptomatic for years until pressure symptoms arise or it ruptures. The symptoms & signs will depend on the site affected.

Aneurysm of the ascending aorta is the most frequent localization, followed by aneurysm of the arch, then aneurysm of the descending aorta.

5-Heart block:

A gummatous lesion may rarely occur in the interventricular septum & cause heart block.

Diagnosis of cardiovascular syphilis:

- Clinical picture.
- X-ray, barium swallow, tomography & angiocardiography.
- Serological tests for syphilis are positive in 80% of cases.
- CSF examination to exclude neurosyphilis is essential.

Prognosis:

Tissue damage is not reversible, & in some cases further deterioration occurs even after adequate treatment. The prognosis became less gloomy with the advent of cardiac surgery.

PRENATAL (CONGENITAL) SYPHILIS

Congenital syphilis is acquired by placental transmission of infection from the mother. This is much more likely to occur when the mother is suffering from early syphilis than when she has late syphilis. The disease may be transmitted to the fetus by the infected mother throughout pregnancy but lesions develop only after the fourth month in utero when the fetus becomes immunocompetent.

Congenital syphilis can be prevented by detection & treatment of infected expectant mothers.

The outcome of pregnancy : depends on how recently a woman has been infected. During the early stages of active syphilitic infection there are large numbers of circulating treponemes & the effect on the fetus may be correspondingly severe. Abortion, stillbirth or early neonatal death is a common outcome. When infections occur late in pregnancy or are milder, the child is born alive but prematurely. Some children are born apparently healthy & signs may be delayed for days, weeks or months. Children without early signs of congenital syphilis or with unrecognized signs, may develop overt symptoms & signs in their teens. The division between early & late congenital syphilis is usually placed at the end of the second year of life.

Placental changes in prenatal syphilis:

- The placenta is bulky, heavy, pale and greasy.
- There is hyperplasia of chorionic villi, increased collagen fibres, diminished vascularity, perivascular infiltration with lymphocytes and plasma cells & endarteritis obliterans of the villous vessels.

Syphilitic stillbirth:

- The skin is macerated, livid red, shows haemorrhagic bullae which contain many spirochaetes.
- The skull is collapsed.
- Abdomen is protuberant with enlarged liver and spleen.
- The lungs are heavy, unexpanded, & pale gray in color (pneumonia alba or white pneumonia).
- Long bones are affected at the zone of provisional calcification showing thickening and gives a zig-zag appearance in x-ray.

Clinical manifestations of prenatal (congenital) syphilis:

There is no primary stage (i.e., no chancre) and clinical manifestations are divided into:

- 1-Early prenatal syphilis.
- 2-Late prenatal syphilis.
- 3-Stigmata.

A)Early prenatal syphilis:

- Manifestations occur during the first two years of life.
- Lesions are infectious & resemble those of secondary acquired syphilis.

1-General features:

- The child is usually born underweight with senile facies.
- Coryzal symptoms with rhinitis & hoarse breathing.
- Cafe au lait (brownish-yellow) wrinkled skin.
- Failure to thrive.
- Alopecia.

2-Mucous membrane lesions:

- Mucous patches in the mouth, pharynx & larynx (aphonic cry).Involvement of the nasal cavity gives rise to nasal obstruction & discharge (syphilitic snuffles).

3-Skin lesions:

-There may be a symmetrical rash like that of secondary stage of acquired syphilis (i.e., macular, papular, or papulosquamous) but there may be a bullous rash which is very infectious & is concentrated on the palms and soles. On the lower half of the face the rash may become prominent producing radiating fissures from the angle of the mouth which leave linear scars on healing (rhagades).

4-Condyloma lata in the napkin area.

5-Bone involvement:

-Osteochondritis: Pain, swelling & tenderness affecting chiefly the distal ends of the radius & ulna, and the upper end of the tibia. the affected limb is held completely immobile & may appear to be paralysed (Parrot's pseudoparalysis).

-Osteoperiostitis of the proximal phalanges (syphilitic dactylitis).

6-Visceral involvement:

-Enlarged liver & spleen.

-Lungs show pneumonia alba in fatal cases.

-Renal complications: nephrotic syndrome or acute glomerulonephritis.

7-Eye affection: Iritis and choroidoretinitis (The residual areas of pigment & atrophy have been called the " salt & pepper fundus").

8-Orchitis is rare.

9-Generalized lymphadenopathy: enlarged lymph nodes are discrete, rubbery and not tender.

10-Meningitis & asymptomatic neurosyphilis with abnormal CSF.

Diagnosis of early prenatal syphilis:

- Dark-field microscopy of serum obtained from open lesions of the skin & mucous membranes.
- Serological tests: a positive blood test for syphilis in the absence of other evidence of syphilis must be evaluated in order to exclude the possibility of passive transfer of maternal antibodies of the IgG class. Test for treponemal-specific IgM(FTA-ABS-IgM), which is a large molecule & cannot pass across the placenta, is of value as evidence of congenital infection. A rising titre in the reagin (VDRL) test &/or failure of the test to become negative within 6 months, in the absence of clinical signs, suggest the diagnosis of early latent congenital syphilis.
- Radiological examination of long bones.
- CSF examination.

B) Late prenatal syphilis:

- Manifestations develop after the second year of life & are unusual before the age of 5 years.

- The lesions are not infectious & resemble tertiary stage of acquired syphilis (gummata).

- Late latent congenital syphilis: the only abnormal finding is a persistent positive antitreponemal test for syphilis.

- Late symptomatic congenital syphilis:

1-Interstitial keratitis:

The commonest late lesion & may begin at any age between 5 & 30 years. It is an immunological reaction rather than due to the direct effect of infection. It responds to topical corticosteroids which may prevent corneal scarring.

2-Neurosyphilis:

It may be asymptomatic (discovered by CSF examination) or symptomatic. The lesions may be meningeal resulting in meningitis & cranial nerve palsies; vascular resulting in monoplegia, hemiplegia or sensory loss; or parenchymatous resulting in juvenile tabes dorsalis or GPI, appearing about the age of 10 years.

3-Ear affection and eighth nerve deafness.

4-Skin and mucous membrane involvement:

In general, the changes are similar to those seen in acquired tertiary syphilis. Gummata are particularly common in the nasal septum & palate. The former may result in perforation of the nasal septum while the latter may cause destruction of the palate, resulting in nasal voice & regurgitation of food.

5-Bilateral hydroarthrosis (Clutton's joints):

- It is chronic painless synovitis usually of the knees.
- It is a manifestation of an immune reaction rather than due to direct involvement of *T.pallidum*. It responds to corticosteroids but not to penicillin or salicylate.

6-Bone involvement:

- Osteoperiostitis of the tibia is common & thickening of the middle third gives rise to a characteristic shape called 'sabre tibia'.
- Localized osteoperiostitis with thickening may involve the vault of the skull (Parrot's nodes).

7-Paroxysmal cold haemoglobinuria.

8-Visceral and cardiovascular involvement are rare.

Diagnosis of late prenatal syphilis is usually difficult & depends on a thorough history & clinical examination. The results of serological testing, both reagin & specific, are of marginal help. The examination of the mother & siblings may be helpful.

C) Stigmata of prenatal syphilis

Scars & deformities which are the consequences of early & late congenital syphilis. They persist as characteristic features of the disease & have diagnostic importance in distinguishing it from acquired syphilis.

A-Stigmata of early lesions:

1-Saddle nose (depression of the nasal bridge).

2-Short maxilla.

3-High arched palate.

4-Hutchinson's teeth: deformity of the permanent central incisors with central notching in the cutting edge which is narrower & smaller than the gingival edge (screwdriver teeth).

5-Moon's molars: the first lower permanent molars have a flat occlusive surface with underdeveloped cusps & poor enamel.

- 6-Rhagades at the corner of the mouth.
- 7-Salt & pepper fundus.

B-Stigmata of late lesions:

- 1-Corneal opacities & ghost vessels (following interstitial keratitis).
- 2-Sabre tibia.
- 3- Parrot’s nodes: frontal & parietal bossing (the result of local periostitis).
- 4-Optic atrophy.
- 5-Eighth nerve deafness.
- 6-Gummatous scars.
- 7-Perforation of the hard palate or of the nasal septum.

Interstitial keratitis, Hutchinson's teeth & eighth nerve deafness form Hutchinson's triad which is pathognomonic of late prenatal syphilis.

MANAGEMENT OF SYPHILIS

Sexual contact should be forbidden until treatment has been completed. Penicillin is the drug of choice in all stages of the disease because it is the cheapest , most effective & least toxic.

Unlike in the case of gonorrhoea, serum levels of penicillin required in the treatment of syphilis are relatively low but need to be maintained for a much longer period. Hence, long-acting penicillins are used & the ones available are: aqueous suspension of procaine penicillin , of which a single dose (600.000 units) provides effective blood level for 24 hours ; and benzathine penicillin G of which a single dose (2.4 million units) can provide effective blood level for over 2 weeks. However, benzathine penicillin G is not suitable for the treatment of neurosyphilis because of its inability to penetrate into the CSF.

Penicillin treatment regimens for acquired syphilis:

| Stage of syphilis | Treatment Regimens | |
|---|---|------------------------------------|
| | Benzathine penicillin G | Aqueous procaine penicillin G |
| Early syphilis (primary, secondary, early latent) | 2.4 million units IM | 600,000 units IM daily for 15 days |
| Late latent & late benign syphilis | 2.4 million units IM. once a week for 3 weeks | 600,000 units IM daily for 15 days |
| Cardiovascular syphilis | — | 600,000 units IM daily for 20 days |
| Neurosyphilis | — | 600,000 units IM daily for 20 days |

Alternative regimen for penicillin-allergic patients :-

- 1-Tetracycline hydrochloride:500 mg four times daily by mouth for 15 days in early syphilis & for 30 days in late syphilis. It is contraindicated during pregnancy.
- 2-Erythromycin:500mg four times daily by mouth for 15 days in early syphilis & for 30 days in late syphilis. It is especially indicated in pregnancy.

Follow-up of early syphilis :

Patient should be followed up for 1-2 years. Quantitative blood tests such as VDRL should be done at the end of 3 months , 6 months , 12 months , 18 months and 2 years. In a successfully treated case, the titres of the non-treponemal tests begin to fall , becoming negative within 6 months in most cases. If the non-treponemal tests are negative at the end of one year , the patient may be discharged. CSF examination should be done before final discharge.

Follow-up of late syphilis :

Quantitative non-treponemal tests should be performed at 3 months , 6 months & 12 months after treatment & then yearly for as long as necessary. In those with CSF abnormalities , examination of CSF should be repeated after 6 months & then once yearly until normal.

Treatment of prenatal syphilis :

- Necessary precautions should be taken against the transfer of infection from skin & mucous membrane lesions.
- Infants with prenatal syphilis should have CSF examination before treatment:
 - a) **Infants with normal CSF:** benzathine penicillin G 50,000 units/kg IM in a single dose.
 - b) **Infants with abnormal CSF:** aqueous crystalline penicillin G 50,000 units/kg IM or IV daily in two divided doses for 15 days, or aqueous procaine penicillin G 50,000 units/kg IM daily for 15 days.
- Adult regimens should be used for children over the age of 15.
- Those allergic to penicillin should receive erythromycin or tetracycline. however , tetracycline should not be given to children below the age of 12 years.

Treatment Of Reactions:

1- The jarisch herxheimer reaction:

An acute febrile reaction characterized by local & systemic manifestations that may commence within a few hours after the first administration of penicillin or any other antisyphilitic drug at any dose; it lasts for a few hours & usually resolves within 24 hours. It is not seen with subsequent treatment.

The mechanism is unknown. It is not a drug reaction. An immunologically based phenomenon which result from the rapid release of treponemal antigens leading to an allergic reaction is postulated.

The reaction can occur in all stages of syphilis but more frequently in early syphilis. Generalized manifestations comprise flu-like symptoms which include fever , headache & general malaise. The localized component consists of worsening of pre-existing skin & mucosal lesions. In neurosyphilis focal reactions may occur & in cardiovascular syphilis there is risk of coronary ostial occlusion or ruptured aneurysm. Pregnant patients should be warned that early labour may occur.

Bed rest & antipyretics are recommended, but no proven methods exist for preventing this reaction. Some physicians recommend short courses of steroids prior to antibiotic treatment in cases of cardiovascular & neurosyphilis.

2- Therapeutic paradox :

A worsening of the disease after antisyphilitic therapy resulting from excessive scarring produced by too rapid destruction of treponemes.

It is most notable in patients with aortic & liver disease.

3- Penicillin reactions :

a) Immediate reactions (develop within seconds or minutes): These include urticaria, angioedema, generalized pruritus & anaphylactic shock.

b) Delayed reactions (manifest after 5 - 14 days or longer): Serum sickness-like symptoms.

4- Procaine reaction :

Acute psychotic symptoms due to accidental intravenous injection of procaine penicillin. The procaine fraction is responsible for this toxic reaction. The reaction subsides within few minutes & treatment is bed rest & maintenance of patent airway.

5- Vasovagal attack (faint) :

This may occur following an injection. Recovery is rapid once the patient is laid flat.

Chancroid (Soft Sore)

Definition:

A sexually transmitted infection characterized by necrotizing ulceration, usually of the genital region, and often followed by painful bubo formation.

Causative Organism:

Haemophilus ducreyi: a small, non-motile, non-spore-forming gram-negative bacillus.

Incubation Period:

7 days (ranges from 3 days to 3 weeks).

Clinical Manifestations:

- Symptoms: they are the most painful of all genital lesions.
- The lesions start at the site of inoculation as tender papules that soon become pustules, & finally break down to form multiple, small, shallow, circular or oval, nonindurated ulcers with ragged undermined edges and red margins.
- The labia majora are the usual sites among women, while the prepuce, the frenum and the coronal sulcus are the common sites in men.
- The regional inguinal lymph nodes become enlarged, painful and tender within 1 week of ulceration in 50% of cases. If untreated, the lymphadenopathy progresses within 3 to 14 days to suppurative bubos.

Diagnosis:

- 1-Direct smear stained with Gram's stain (the material is obtained from beneath the undermined edge of the soft sore or from bubo aspirates).

2-Culture on specific media.

Differential Diagnosis:

- The most important consideration should be the exclusion of syphilis & herpes simplex.
- All patients with genital ulcer disease should routinely have darkfield examination & serial serology to exclude T.pallidum infection, regardless of the presence of other etiologic agents of genital ulcer disease.

Treatment:

- 1-Cotrimoxazole(trimethoprim,80mg, plus sulphamethoxazole,400 mg) 2 tablets. twice daily for 7 days. OR
- 2-Erythromycin, 500 mg orally 4 times daily for 7-10 days. OR
- 3-Amoxicillin, 500 mg plus clavulanic acid, 250 mg orally every 8 hours for 3 days.

N.B. The erythromycin and amoxicillin regimens may mask syphilis and hence should be reserved as alternatives and for pregnant women.

Granuloma Inguinale (Donovanosis)

Definition:

A chronic, mildly contagious, sexually transmitted disease characterized by granulomatous ulceration of the genitalia & neighbouring sites.

Causative organism:

Calymmatobacterium granulomatis:

A Gram-negative encapsulated bacterium.

- The organism is difficult to grow on artificial media.
- In smears of lesions, it is seen in intracytoplasmic vacuoles within histiocytes or polymorphonuclear leucocytes as deeply stained bodies showing a closed safety-pin appearance due to its characteristic bipolar staining.

Incubation period:

9 - 90 days.

Clinical picture:

- Onset of the disease is marked by formation of a firm painless papule which erodes to form a beefy granulomatous ulcer with rolled edges.
- The lymph nodes are not enlarged unless secondary infection sets in.
- Untreated, the lesion may remain dormant or progress slowly involving the whole of the external genitalia, anus and inguinal region.
- Healing takes place by intense fibrosis with tissue destruction.

Diagnosis:

- 1-History of sexual contact.
- 2-Clinical appearance of the lesion.
- 3-Smears from scrapings obtained from the margin of the lesion are stained by Wright's, Giemsa's or Gram's stain.

Treatment:

- Cotrimoxazole(trimethoprim,80 mg, plus sulphamethoxazole,400 mg), 2 tablets by mouth twice daily for 14 days is the treatment of choice.
- Other alternative regimens include:
 - 1-Oral tetracycline, 500 mg 4 times daily for 14 days. OR
 - 2-Oral chloramphenicol, 500 mg 4 times daily for 21 days. OR
 - 3-IM Gentamycin, 1 mg/kg 3 times daily for 21 days.

LYMPHOGRANULOMA VENERIUM

Definition:

- Lymphogranuloma venerium (LGV) is a chronic systemic sexually transmitted infection caused by one of the three specific immunotypes of Chlamydia trachomatis.

Causative organism:

Chlamydia trachomatis serotypes L1, L2, or L3 (a bacteria belonging to the Rickettsiae family).

Incubation period:

1- 6 weeks.

Clinical picture:**1-Primary stage:**

-This usually manifests as transient, painless, papule, ulcer, or herpetiform vesicular lesions at the site of inoculation (external genitalia, anus or rectum). These heal within a week & are usually overlooked by the patients. Women & homosexual men may present with haemorrhagic proctitis, accompanied by rectal bleeding & purulent discharge.

2-Secondary stage:

The secondary stage consists of either inguinal lymphadenitis with bubo formation (inguinal syndrome), which is found especially in heterosexual men; or acute proctocolitis (the anogenitoretal syndrome) which is seen in homosexual men & in women.

-Inguinal syndrome: regional suppurative lymphadenitis & constitutional manifestations begin 1-4 weeks after the disappearance of the primary lesions. Lymph nodes above & below the inguinal ligament are involved with the inguinal ligament appearing as a groove between the two lymph node masses (groove sign). The adenitis (bubo) is tender & may be uni- or bilateral. The overlying skin is usually normal unless suppuration occurs, in which case multiple discharging sinuses are formed.

-The anorectal syndrome is characterized by acute proctocolitis & extension of inflammation to the perirectal lymphatics. There are signs & symptoms of proctitis, with anal pruritis, rectal pain & tenesmus. Perirectal abscesses & anal fissure may be the presenting feature.

3-Late manifestations:

a)Anogenital & rectal syndrome:

-This complication can develop in both sexes & is a consequence of an infection that starts in the rectal mucosa. The rectal mucosa is gradually invaded by a chronic, inflammatory granuloma, which manifests itself by anal itching & a mucopurulent discharge. The chronic inflammatory process progresses to fibrosis resulting in a stricture that causes chronic constipation & ribbon-like feces to be passed. The perianal skin & the rectal mucosa below the stricture are frequently the sites of perirectal or rectovaginal fistulae & anal fissuring. Bowel perforation followed by acute peritonitis is the most common direct cause of death in LGV patients.

b)Genital elephantiasis:

- Lymphatic obstruction may lead to elephantiasis of the external genitalia (vulva, penis & scrotum).

c)Malignant transformation:

Development of cancer following rectal strictures &/or genital elephantiasis may occur in these patients.

Diagnosis:

- Direct demonstration of *C. trachomatis* in smears or tissues using monoclonal antibodies (the use of lugol solution or Giemsa's stain is unreliable).
- Culture by inoculation of pathologic material in mouse brain, yolk sac, or tissue culture.
- Serologic tests:
 - Complement fixation test is unreliable due to the frequent existence of other *C. trachomatis* infections in the general population.
 - Microimmunofluorescence test is sensitive, specific & can identify individual strains.

Differential diagnosis :

LGV should be considered in every case of enlarged, tender, matted inguinal lymph nodes; active proctitis; draining inguinal or perianal fistulas & rectal strictures. It must be distinguished from inguinal adenopathy of any cause (e.g. pyogenic infection of lower limbs, chancroid & syphilis).

Treatment of LGV:

A) Medical treatment:

- Tetracycline, 500 mg 4 times daily for 3 weeks. OR
- Sulfamethoxazole, 1 gm 2 times daily for 3 weeks.

B)Surgical treatment:

- Aspiration of fluctuant bubo.
- Rectal stricture & fistulae are corrected surgically.

GENITAL HERPES

Aetiology:

Herpes simplex virus (HSV):

Most cases are due to HSV type 2; the proportion of cases due to type 1 is rising as a result of increased practice of orogenital contact.

Transmission:

- Sexual contact or contact with genital secretions.
- Contaminated fomites, towels & underclothing.

Incubation period:

2-7 days.

Clinical features:

The genital infection may be asymptomatic or present with varying degrees of severity.

1-Primary attack:

- Constitutional symptoms including fever, headache, malaise & muscle pains are associated with primary disease in some cases.
- It presents as grouped vesicles on an erythematous base. The vesicles rupture in a day or two to form superficial, tender non-indurated polycyclic erosions on the genitalia that heal within 2-3 weeks. Inguinal lymph nodes are enlarged & tender.
- The rectum may be infected by anal intercourse resulting in rectal pain, rectal ulcerations & blood in stools.
- Involvement of the urethra may result in dysuria & minimal clear mucoid urethral discharge.

2-Recurrent attacks:

- Recurrent lesions are the hallmark of herpes simplex infections, both the frequency & severity of the attacks diminish with time.
- These recurrences are due to reactivation of latent HSV present in the sacral ganglia & triggered off by emotional stress, menses, trauma, surgery or fever.

Diagnosis of genital herpes:

- 1-Tzanck smear: Examination of Giemsa's stained slide prepared from scrapings of the floor of early lesions to demonstrate multinucleated giant cells &/or intranuclear inclusion bodies. A newer technique uses fluorescent monoclonal antibody staining.
- 2-Electron microscopic examination to demonstrate HSV particles.
- 3-Cell cultures (e.g. chorioallantoic membrane) show characteristic cytopathic effects.
- 4- Complement fixation test.

Differential Diagnosis:

Syphilis, chancroid, folliculitis, lichen planus, Behcet's disease & pemphigus. Mixed infections may occur.

Treatment:

- Symptomatic treatment, in the form of local antiseptics, analgesics & good local hygiene, is usually sufficient in the majority of cases.
- Specific treatment: Acyclovir, 5mg/kg IV 8 hourly by slow infusion (for patients with normal renal function), or 1 tablet (200mg) 5 times daily for 5 days, or 5% acyclovir cream applied 5 times daily for 5-10 days.

- Therapy in both primary & recurrent herpes does not prevent further recurrences as it dose not eradicate the virus from the ganglia. It should be reserved for patients with impaired immune responses & those with severe initial episodes of genital herpes.
- Sexual intercourse should be forbidden until the lesions heal.

CONDYLOMA ACCUMINATUM

Definition:

Papillomatous growth found in the urogenital, perineal & perianal regions caused by infection with the human papillomavirus (HPV).

Clinical findings:

Genital lesions are skin colored to slightly pink or white verrucous papules that may be solitary or confluent, taking a cauliflower appearance. Anal, urethral, vaginal & cervical papillomas may be seen. The eruption may be mild & asymptomatic or large & extensive with a tendency to irritation, traumatic ulceration & secondary infection.

Malignancy is the most significant complication of HPV infection.

Management:

- All women with external lesions need to be evaluated for cervical & vaginal involvement. Anoscopy is indicated for patients with perianal disease & urethroscopy may be indicated when meatal condylomata are present.
- Modes of treatment include podophyllin 25% in tincture of benzoin, cryotherapy, electrodesiccation or laser therapy.

ACQUIRED IMMUNE DEFICIENCY SYNDROME (AIDS)

Definition

HIV-positive status and infection with one of the opportunistic infections, cancer, or other conditions associated with AIDS that are indicative of underlying cellular immune deficiency.

Causative Organism:

- Human Immunodeficiency Virus (HIV) which is a retrovirus that selectively infects T4 (helper) cells.
- The virus is susceptible to soap,detergents & 1% solution of hypochlorite (household bleach).

Modes of Transmission:

1. Close sexual contact both heterosexual & homosexual.
2. Injection of infected blood or blood products.
3. Usage of contaminated needles (among IV drug users), or sharp objects (such as tattooing).
4. Intrauterine (transplacental), perinatal (contact with infected blood at the time of delivery) and postnatal (possibly via breast milk) infection.

There is no evidence of HIV transmission by casual social contact or by non-sexual household contact, communal eating or by cough, sneezing or by blood-sucking insects.

Pathogenesis:

HIV has a particular tropism to T-helper lymphocytes & their depletion leads to profound immune deficiency. This is manifested by a wide spectrum of opportunistic infections & unusual malignancies.

Incubation period:

3-10 years.

Clinical Presentations:

HIV infection can have myriad manifestations ranging from subclinical laboratory abnormalities to the opportunistic infections & malignancies that define the acquired immunodeficiency syndrome (AIDS).

The term AIDS has been used to describe the more severe manifestations of this disorder, particularly opportunistic infections & unusual tumours associated with immunodeficiency. The other major clinical presentations of HIV infection include PGL (persistent generalized lymphadenopathy) and ARC (AIDS-related complex).

It is not known which patients will progress from the asymptomatic seropositive state to the symptomatic phase of ARC or AIDS.

The clinical presentations of HIV infection include:

1- Asymptomatic carrier state.

2- Persistent generalized lymphadenopathy (PGL):

PGL is defined as lymphadenopathy of more than 3 months' duration affecting two or more extralingual sites and for which no other cause may be found. The lymph nodes are firm, non-tender, mobile & symmetrical. The histology shows a nonspecific reactive hyperplasia.

They may disappear spontaneously & in some cases their resolution may be associated with the onset of opportunistic infection.

3- AIDS-related complex (ARC):

Criteria for diagnosis of ARC : patient should have at least two of the following clinical features for at least 3 months:

-Unexplained fever >38.5°C.

-Weight loss >10% of body weight.

-Unexplained diarrhea.

-Extreme fatigue.

-Night sweats.

In addition to two or more of the following laboratory abnormalities:

-Low number of T helper cells (< 400 / mm³).

-Helper:suppressor T cell ratio <1.0 .

-Cytopenia (anaemia, leukopenia, thrombocytopenia).

-Cutaneous anergy.

-Elevated serum immunoglobulin level.

In some cases these features may disappear spontaneously. In others ARC may be an intermediate stage between the initial infection & AIDS, or a chronic manifestation of HIV infection.

4- Acquired immunodeficiency syndrome (AIDS):

Severe opportunistic infections & uncommon malignancies occur on a background of profound immunosuppression & the mortality is high. The patients present in many ways.

Cutaneous manifestations of AIDS:

The cutaneous manifestations may be divided into 3 large categories: infections , neoplastic & others. Some conditions, such as molluscum contagiosum & psoriasis, are not specific to AIDS but may present in atypical or exaggerated forms because of the underlying immunosuppression.

1-Neoplastic diseases:

- Kaposi's sarcoma : a multicentric tumour arising from local hyperplasia of vascular endothelium which occurs as deep red to blue macular, plaque & nodular lesions on the skin , oral mucosa & internal organs.
- Lymphomas.
- Squamous cell carcinoma (oral & anorectal).
- Basal cell carcinoma.
- Melanoma.

2-Infectious diseases:

- Bacterial infections: Impetigo, ecthyma, cellulitis, folliculitis , actinomycosis, mycobacterial infection, atypical syphilis.
- Viral infections: herpes simplex , herpes zoster, molluscum contagiosum, condyloma acuminata.
- Fungal & yeast infections: candidosis, dermatophytosis, cryptococcosis.
- Protozoal infections: amoebiasis cutis.
- Arthropod infestations: scabies, crusted (Norwegian) scabies.

3-Other manifestations:

- Vascular lesions: vasculitis, thrombocytopenic purpura.
- Papulosquamous disorders: seborrheic dermatitis, psoriasis, pityriasis rosea.
- Miscellaneous: ichthyosis, nutritional deficiencies, exanthemata, erythroderma, atopic dermatitis, bullous pemphigoid, drug reactions, urticaria, pruritus.
- Hair changes: telogen effluvium, alopecia areata.
- Nail changes: nail deformities, nail color changes.
- Oral disorders: Aphthosis, gingivitis & angular cheilitis(perleche).

Biopsy, acid-fast and fungal staining, and appropriate culture of all skin lesions in AIDS patients are mandatory even if the clinical diagnosis seems certain.

Major noncutaneous clinical manifestations of AIDS:

The clinical manifestations of AIDS are protean & affect virtually every organ in the body. The clinical manifestations depend upon the particular secondary disease.

A. Protozoal & helminthic infections:

- 1- Intestinal cryptosporidiosis causing diarrhoea for over 1 month.
- 2- Pneumocystis carinii pneumonia.
- 3- Strongyloidiasis, causing pneumonia,, CNS infection or disseminated infection.
- 4- Toxoplasmosis. of the CNS or pneumonia.

B- Fungal infections:

- 1-Candidiasis,causing oesophagitis, bronchopulmonary candidiasis.
- 2-Cryptococcosis of CNS or disseminated infection.
- 3-Histoplasmosis, disseminated.
- 4-Aspergillosis, disseminated.

C- Bacterial infections:

Mycobacterium avium intracellulare, or Mycobacterium kansasii, causing widely disseminated disease.

D- Viral infections:

- 1-Cytomegalovirus causing infection of internal organs other than liver, spleen, or lymph nodes.
- 2-Herpes simplex virus, causing chronic mucocutaneous infection with ulcers persisting longer than 1 month ; or pulmonary, gastrointestinal tract (beyond mouth, throat or rectum), or disseminated infection.
- 3-Progressive multifocal leukoencephalopathy, presumed to be caused by papova virus.

E- Cancer:

- 1-Kaposi's sarcoma.
- 2-Lymphoma limited to the brain.
- 3-Non-Hodgkin's lymphoma with positive test for HIV.

Testing for HIV infections:

1. HIV culture is the most accurate but difficult.
2. Detection of HIV antibodies by enzyme-linked immunosorbent assay (ELISA) & Western blot test.
3. Detection of HIV antigen by ELISA & polymerase chain reaction (PCR).

The condition should be sought in all persons presenting with a disease that is predictive of a defect in cell mediated immunity in the absence of any other known cause for diminished resistance to that disease. Serologic testing for HIV currently involves a screening test (ELISA) followed by a confirmatory test (Western blot) for all positives. Patients are excluded if they are HIV antibody negative & have normal T helper lymphocyte counts & normal T helper : T suppressor ratios.

Treatment of AIDs:

There is no specific treatment.

- 1-Each infection & neoplasm should be treated appropriately.
- 2-Antiviral agents, e.g. Azidothymidine (AZT).
- 3-Immunomodulators aimed at restoring T cells or their normal products such as interferon, interleukin-2,and isoprinosine.

GENITAL CANDIDOSIS (MONILIASIS)

Definition:

- Candidosis is the various clinical conditions caused by candida, mostly *Candida albicans*.
- It is the most common cause of abnormal vaginal discharge.

Predisposing factors in females:

- 1-Excessive humidity (wearing of nylon tights).
- 2-Glycosuria (diabetes mellitus and pregnancy).
- 3-Use of antibiotics and chemotherapeutics or immunosuppressive drugs.
- 4-Influence of hormones (steroids, contraceptive pills and pregnancy).
- 5-Severe anaemia or other debilitating illnesses.
- 6-Reinfection from an infected male.

Clinical Picture:

Females:

- Candidosis may be asymptomatic
- Common symptoms are vulval irritation &/or soreness and white curd-like vaginal discharge.
- Clinical examination may reveal:
 - Dry congestion of the vulva, vulvar erosions or excoriation of perineal skin and thighs.
 - There may be white curd-like deposits of yeast at the introitus and covering the walls of the vagina as a pseudomembrane which leaves reddened haemorrhagic areas when removed.

Males:

- Balanitis, mainly in the uncircumcised, or balanoposthitis
- Monilial urethritis is rare & may be asymptomatic.

Diagnosis:

- Gram-stained smear may show large Gram-positive, oval budding yeast-like cells with elongated pseudo-hyphae in vaginal secretions.
- Culture on Sabouraud's medium or Fienberg-Whittington medium (the later will detect both *Candida* & *Trichomonas*).
- Serological diagnosis by agglutinating or immunofluorescent antibody or precipitation tests.

Treatment:

- 1-Removal of predisposing factors and treatment of the second partner.
- 2-Antifungal treatment: several antifungal preparations are available:
 - Clotrimazole: 100 mg vaginal tablet 1-2/ day for six applications.
 - Miconazole nitrate: 2% cream or 100 mg pessaries once/ day for 2 weeks.
 - Nystatin: 100,000 U pessaries or cream.
 - Fluconazole: 150 mg one single capsule orally.
 - Amphotericin B: 50 mg pessaries or 4 gm vaginal cream.

TRICHOMONIASIS

Trichomoniasis is a common infection of the female genitourinary tract. It is less often diagnosed in males & is rare in children & after menopause.

Aetiology:

Trichomonas vaginalis (a flagellated protozoan).

Mode of infection:

Mode of infection in the adults is usually sexual contact. Accidental infection from improperly sterilized instruments, gloves, moist towels, toilet seats & baths is possible.

Trichomoniasis in the female:

- Some cases are asymptomatic. Many cases present with vaginal discharge and vaginal & vulvar irritation.
- Clinical examination may show a frothy, malodorous, grayish-green watery vaginal discharge & a bright red or petechiae-studded vaginal mucosa.

Trichomoniasis in the male:

- Males are often asymptomatic, but can transmit the infection. They may develop balanitis or balanoposthitis.
- Trichomonal urethritis: symptoms & signs are indistinguishable from other causes of NGU.

Diagnosis:

- Wet smear: The trichomonads are recognised by their shape, size & jerky rotatory movements.
- Culture: Fienberg-Whittington medium.

Treatment:

- Metronidazole: 200 mg 3 times a day for one week.
- Sex partners should be treated at the same time.