

Week 5: Genitourethral Pathophysiology

Learning Objectives:

- Name, understand, describe and explain the pathophysiology of disorders associated with the male and female genito-urinary system, incl. the underlying cause(s) and presenting symptoms, methods of diagnosis and treatment

Neoplasia

- Neoplasia → uncontrolled tissue growth, cancer
 - o Adj: neoplastic, n: neoplasm
 - o Means “new growth”
 - o Hyperplasia, dysplasia, then neoplasia
 - o Benign, carcinoma in situ, malignant or metastatic
 - o Caused by mutations → usually 2 bc mutations on both chromosomes
 - o Original tissue type matters
 - o Initiation and progression of neoplasia
 - Dysplasia = different growth
 - Invasive = cancer forming

Female Cancers

- Can affect almost any part of the reproductive system
 - o Vulva, vagina, cervix, uterus, ovaries
- Breast cancer growth is often affected by exposure to female sex hormones
 - o Similarly to some of the cancers listed above
 - o ∴ reduce oestrogen to slow cancer growth

Cervical Cancer

- HPV most important factor for neoplasia
 - o However, not alone sufficient
 - Co-carcinogens → inflammation = genetic disruption, spermicides = extra inflammation
 - o HPV proteins disrupt tumour suppressor proteins
- Transformation zone = where the squamous cells and glandular cells meet
 - o Vulnerable, 70% of cervical cancers begin in this area
 - Maybe bc ↑ cell proliferation + changes in DNA
- Precancerous lesions = areas of abnormal tissue that are not cancer, but may lead to cancer
 - o Some disappear without treatment, while others progress
- Squamous intraepithelial lesion grading
 - o LSIL = low grade squamous intraepithelial lesion
 - o HSIL = high grade squamous intraepithelial lesion

Lesion	Regress	Persist	Progress
LSIL	60%	30%	10% to HSIL
HSIL	30%	60%	10% to carcinoma

- Early stage cancer is sub-clinical
 - o Subclinical = not severe enough to present definite/observable symptoms
 - o Once symptoms begin = bad sign

- Invasive cancer = spread beyond layer of tissue it started in, growing into surrounding tissue
 - o Generally in those non-participating in screening
 - o Micro-invasive = 100% 5-year survival
 - o Invaded beyond pelvis < 50% 5-year survival
- Early stage = surgical
- Advanced = chemo +/- radiotherapy

Male Cancers → male genital cancers can also affect nearly any part of the system

Benign Prostatic Hyperplasia (BPH)

- Benign = opposed to malignant, harmless
- Enlarged prostate gland
 - o Not cancerous, does not ↑ cancer risk, but is still problematic
- Problematic growth of the transitional zone → bet. Inner prostate + urethra
 - o Increased local mitogenic DHT signalling
 - Mitogenic = creative using mitosis
 - DHT = dihydrotestosterone → more active version of testosterone
 - o Treatment = drugs, lifestyle, surgery, heat to cause cell death
 - Alpha blockers = relax smooth muscle in bladder neck = relieves urine flow
 - DHT inhibitors = inhibit their production
 - Surgery = gold standard when medications don't work = remove tissue through urethra
 - o Diagnosis by digital rectal examination
 - o Pain, storage and voiding symptoms
 - Urgency, frequency, incontinence (not being able to hold urine), interruption (trouble starting flow, trouble mid flow, discontinuous)
 - Bc surrounds urethra
 - o Result of hormonal changes, common in aging
 - o Rate of cell proliferation exceeds the rate of programmed cell death → apoptosis

Prostate Cancer

- Main risk factor is age, but also Western diet
 - o Low fat, plant based diet
- Most commonly occurs in the peripheral zone → area closest to the rectum
 - o ∴ can easily be felt by doctors in digital rectal examination
- Early cancer is asymptomatic
 - o Lower urinary tract symptoms suggest advanced disease
 - o Hesitancy, urgency, frequency, incontinence, urinary retention, nocturia
- Prostate serum antigen (PSA) is useful marker, diagnosis by biopsy
 - o Protein produced by prostate, elevated in prostate cancer
 - o Nodules are indicative and helpful but sometimes difficult to tell the difference bc non-specific
 - o Better way of diagnosing
- Surveillance, minimisation, early intervention
- Can have non-symptomatic cancer without blocking the urethra

Inflammation

- Inflammation is host-mediated

- Calor, dolor, rubor, tumor = heat, pain, redness, swelling
- Often in response to environmental insults
 - Irritants
 - Pathogens
 - Trauma → can be co-carcinogens if already have mutation on chromosome
- Treatment by resolving cause

Inflammatory Disorders (F)

- Pelvic inflammatory disease
 - Complication of chlamydia or gonorrhoea
 - Sometimes polymicrobial after childbirth
 - Infection ascends along mucosal surfaces
 - Acute complications:
 - Peritonitis = inflammation of the peritoneum
 - Bacteraemia = bacteria in the blood (should be sterile)
 - May spread to heart/brain
 - Chronic complications: adhesions
 - Fibrosis to repair internal organs, scars these leave aren't as good as original tissue
 - Can cause nearby organs to stick together = pelvic pain, infertility, intestinal obstruction

Inflammatory Disorders (M)

- Balanitis + Balanoposthitis
 - Inflammation of glans penis + balanoposthitis if it involves foreskin as well
- Urethritis (also in females) → inflammation of the urethra
- Epididymitis → inflammation of the epididymis
- Orchitis → inflammation of the testes
- Peyronie's Disease → fibrotic tissue/plaque as a result of inflammation

Non-Infectious Disorders

- What can go wrong without infection or inflammation?
 - Genetic, congenital, hormonal, psychological, certain trauma

Non-Infectious (F)

- Menstrual disorders
 - Amenorrhea = absence of menstruation
 - Primary → hypothalamus > pituitary > gonad > end organ
 - Secondary → generally pregnancy or PCOS
 - Dysmenorrhea = painful menstruation
 - Prostaglandins (cytokine) → myometrial and vascular contraction
 - ↑ synthesis = primary dysmenorrhea, no pelvic pathology
- Endometriosis
 - Cause unknown, treatment for pain or adhesions
- Polycystic Ovary Syndrome (PCOS)
 - Complex endocrine disorder, metabolic assocns
 - Obesity, type-2 diabetes, premature atherosclerosis
 - Excess androgens, typify symptoms: acne, hirsutism
 - Androgens = male sex hormones
 - Oligomenorrhea (infrequent menstruation)/amenorrhea, pelvic pain
 - Characterised by numerous follicle cysts