BIOS222
Pathology and Clinical Science 2 & 3

Session 18
Female Reproductive Disorders 1
Bioscience Department
Session Learning Outcomes

At the end of the session, you should be able to:

- Review the normal structure and functioning of female reproductive system.
- Describe and discuss the common clinical presentation in female reproductive system.
- Discuss the aetiology, pathophysiology, clinical features and management of dysmenorrhoea.
- Discuss the aetiology, clinical features and management of various urogenital disorders including Cystitis, Vaginal prolapse, Urinary incontinence.
Session Plan

- Overview of the female reproductive system
- Presenting problems in female reproductive diseases
  - Delayed puberty
  - Turner's syndrome
  - Menstrual Disorders:
    - Amenorrhoea
    - Menorrhagia
    - Dysmenorrhoea
    - Pre-Menstrual Syndrome
    - Menopause
  - Hirsutism
Session Plan

- Urogenital Disorders:
  - Cystitis
  - Vaginal prolapse
  - Urinary incontinence
Overview of the Female Reproductive System
Female Reproductive System

Tortora, GJ & Derrickson, B 2014, Principles of anatomy and physiology, 14th edn, John Wiley & Sons, Hoboken, NJ.
Follicular development in ovaries

Tortora, GJ & Derrickson, B 2014, Principles of anatomy and physiology, 14th edn, John Wiley & Sons, Hoboken, NJ.
Female hormones

- **Oestrogen**
  - Secondary Sexual Characteristics
  - Protein anabolism, ↓ blood cholesterol
  - Moderate levels modulate GnRH

- **Progesterone**
  - Proliferation of the endometrium, Modulation of GnRH

- **Relaxin**
  - Inhibits uterine contraction which may be detrimental to fertilisation
  - During pregnancy it increases flexibility of pubic symphysis, may help dilate cervix

- **Inhibin**
  - Inhibits FSH & LH
Menstrual cycle and its hormonal control

Tortora, GJ & Derrickson, B 2014, Principles of anatomy and physiology, 14th edn, John Wiley & Sons, Hoboken, NJ.
Presenting Problems in Female Reproductive Diseases
Delayed Puberty

- Definition: Puberty is considered to be delayed if the onset of the physical features of sexual maturation has not occurred by a chronological age that is 2.5 standard deviations (SD) above the national average.

- Aetiology:
  - Constitutional delay
  - Hypogonadotrophic hypogonadism
  - Hypergonadotrophic hypogonadism

- Diagnosis:
  - Random LH and FSH, Oestradiol
  - Karyotype

- Management:
  - Low doses of oral oestrogen
20.22 Causes of delayed puberty and hypogonadism

Constitutional delay

Hypogonadotrophic hypogonadism
- Structural hypothalamic/pituitary disease (see Box 20.59, p. 787)
- Functional gonadotrophin deficiency
  Chronic systemic illness (e.g. asthma, malabsorption, coeliac disease, cystic fibrosis, renal failure)
  Psychological stress
  Anorexia nervosa
  Excessive physical exercise
  Hyperprolactinaemia
  Other endocrine disease (e.g. Cushing’s syndrome, primary hypothyroidism)
- Isolated gonadotrophin deficiency (Kallmann’s syndrome)

Hypermotrophic hypogonadism
- Acquired gonadal damage
  Chemotherapy/radiotherapy to gonads
  Trauma/surgery to gonads
  Autoimmune gonadal failure
  Mumps orchitis
  Tuberculosis
  Haemochromatosis
- Developmental/congenital gonadal disorders
  Steroid biosynthetic defects
  Anorchidism/cryptorchidism in males
  Klinefelter’s syndrome (47XXY, male phenotype)
  Turner’s syndrome (45XO, female phenotype)
Turner’s Syndrome

- **Definition:** It is a genetic abnormality with mainly 45XO karyotype, characterised by the loss of the majority of oocytes by the age of 2 years leading to primary amenorrhoea and no development of secondary sex characteristics.

- **Clinical features:**
  - Short stature
  - Fail to enter puberty
  - Cardiac abnormalities
  - Hearing and vision difficulties
  - A small size mandible
  - A small webbed neck
  - Difficulty in driving mathematics, and psychomotor skills
  - Attention deficit disorders
Turner’s Syndrome

- Diagnosis:
  - Clinical presentation
  - Karyotype analysis

- Management:
  - Growth hormone therapy
  - Oestrogen therapy
  - Prophylactic gonadectomy
## Menstrual Disorders

<table>
<thead>
<tr>
<th>Terminology</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oligomenorrhoea</strong></td>
<td>Infrequent menstruation, periods more than 35 days apart</td>
</tr>
<tr>
<td><strong>Amenorrhoea</strong></td>
<td>Absence of periods</td>
</tr>
<tr>
<td><strong>Dysmenorrhoea</strong></td>
<td>Pain or discomfort with menstruation</td>
</tr>
<tr>
<td><strong>Menarche</strong></td>
<td>Commencement of periods</td>
</tr>
<tr>
<td><strong>Polymenorrhoea</strong></td>
<td>Frequent menstruation, periods less than 21 days apart</td>
</tr>
<tr>
<td><strong>Menorrhagia</strong></td>
<td>Heavier/excessive menstruation</td>
</tr>
<tr>
<td><strong>Metrorrhagia</strong></td>
<td>Bleeding between periods</td>
</tr>
<tr>
<td><strong>Postmenopausal bleeding</strong></td>
<td>Bleeding that occurs &gt;12 months after last menstrual cycle</td>
</tr>
</tbody>
</table>
Primary Amenorrhoea

- Definition: It is the condition of a female patient who has never menstruated.

- Aetiology:
  - Delayed Puberty
  - Anatomical defects of the female reproductive system
    - Imperforated hymen, endometrial hypoplasia or vaginal agenesis.
  - Resistant ovary
  - Genetic disorders
  - Chronic illness
  - Anorexia nervosa and weight loss
Primary Amenorrhoea

Diagnosis:
- Clinical history and physical examination
- Serum LH, FSH, oestradiol, prolactin, testosterone, T4 and TSH
- Imaging of pelvic organs, brain
- Karyotype analysis

Management:
- Treatment of the underlying cause
  - Anorexia nervosa and weight loss: Reduce exercise, correct diet, and regain some weight
  - Treat structural pituitary and hypothalamic disease
Secondary Amenorrhoea

- **Definition:** Cessation of menstruation.

- **Aetiology:**
  - Physiological
    - Pregnancy
    - Menopause
  - Hypogonadotrophic hypogonadism
  - Ovarian dysfunction
    - Hypergonadotrophic hypogonadism
    - Polycystic ovarian syndrome
    - Androgen-secreting tumours
  - Uterine dysfunction
Secondary Amenorrhoea

○ Clinical features:
  • Hot flushes (Menopause)
  • Weight loss (Anorexia, TB, malignancy, hyperthyroidism)
  • Weight gain (hypothyroidism, Cushing’s syndrome)
  • Hirsutism, obesity and menstrual irregularity (Polycystic ovarian syndrome)
  • Galactorrhea (Hyperprolactinaemia)
  • Presence of autoimmune disease (ovarian failure)
  • Symptoms of oestrogen deficiency (Hypothalamic/pituitary disease and premature ovarian failure)
Secondary Amenorrhoea

- **Diagnosis:**
  - Clinical history
  - Body weight, and BMI
  - Serum hCG, LH, FSH, oestradiol, prolactin, testosterone,
  - Liver, renal, thyroid function tests
  - Imaging of pelvic organs, brain

- **Management:**
  - Treatment of the underlying cause
  - Hormone replacement therapy
  - Treatment for infertility
Menorrhagia

○ Definition: It is defined as menstruation at regular cycle intervals but with excessive flow and long duration

○ Aetiology:
  • Uterine disorders:
    – Uterine Fibroids, Endometriosis, Endometrial polyps, PID, Endometrial hyperplasia
  • Iatrogenic:
    – Progesterone only contraceptives, IUCD, Anticoagulants
  • Systemic/ Endocrine diseases:
    – PCOS, thyroid and adrenal gland dysfunction, pituitary tumours, obesity
  • Nutrient imbalances:
    – Vit A or K deficiency, Imbalance in Omega FA ratio, Prostaglandin irregularities
Menorrhagia

Clinical features:
- Heavy menstrual blood loss & clots
- Flooding, Frank haemorrhage
- Anaemia
- Dysmenorrhoea

Diagnosis:
- Hormone levels
- Pelvic examination and pap smear
- Endometrial biopsy
- Blood test for nutrient analysis

Management:
- Treatment of the underlying cause
- Iron replacement, Hormonal treatments, NSAIDS, Surgery
Dysmenorrhoea

○ Definition: It is painful menstruation which could be primary or secondary.

○ Aetiology:
  • Primary dysmenorrhoea
    – Idiopathic
  • Secondary dysmenorrhoea
    – Endometriosis
    – Fibroids
    – Chronic PID
    – Adenomyosis
    – Post severe physical trauma
    – Smoking
Dysmenorrhoea

- Pathophysiology:
  
  - **Primary dysmenorrhoea**
    
    - Unknown cause → Increased uterine resting tone, increased active pressure, increased number of contractions, and dysrhythmic uterine activity → Diminished blood flow → ischemia and hypoxia of uterine of tissues → Pain
    
    - Distorted Prostaglandin and Leukotriene levels and Increase vasopressin levels → Pain
  
  - **Secondary dysmenorrhoea**
    
    - Uterine disorder/trauma → induce inflammation → Increase vasopressin levels as well as significantly elevated Prostaglandin and Leukotriene levels → Pain
Dysmenorrhoea

- Clinical features:
  - Painful periods
    - Cramping, shooting, sharp, dull pains, heavy, bearing down pains, spasmodic pains)
    - Pain concentrated in the lower abdomen, in the umbilical region or the suprapubic region of the abdomen
    - May radiate to the thighs and lower back.
    - Pain on urination, defecation, passing blood or clots
  - Heavy periods -> flooding
  - Associated symptoms:
    - Nausea and vomiting, diarrhea or constipation, headache, dizziness, disorientation, hypersensitivity to sound, light, smell and touch, fainting, and fatigue
Dysmenorrhoea

Management:

- **Primary Dysmenorrhoea:**
  - Aimed at Symptomatic control
    - Prostaglandin synthetase inhibitors
    - Oral contraceptives
- **Secondary dysmenorrhoea**
  - Treatment of underlying cause
    - Medical intervention
    - Surgical intervention
    - Smoking cessation
Pre-Menstrual Syndrome

- Definition: It is characterized by mild to moderate physical and psychological symptoms limited to 3 to 14 days preceding menstruation and relieved by onset of the menses.

- Aetiology: Unknown

- Various hypotheses:
  - Endocrine imbalances: hyperprolactinemia, oestrogen excess, alteration in the oestrogen–progesterone ratio and increased aldosterone
  - Pyridoxine (vitamin B6) deficiency
  - Decreased prostaglandin E1
  - Learned beliefs about menstruation
# Pre-Menstrual Syndrome

## Table 54.1 Symptoms of Premenstrual Syndrome by System

<table>
<thead>
<tr>
<th>Body System</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral</td>
<td>Irritability, anxiety, nervousness, fatigue, exhaustion, increased physical and mental activity, lability, crying spells, depression, inability to concentrate</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Craving for sweets or salt, lower abdominal pain, bloating, nausea, vomiting, diarrhea, constipation</td>
</tr>
<tr>
<td>Vascular</td>
<td>Headache, edema, weakness, fainting</td>
</tr>
<tr>
<td>Reproductive</td>
<td>Swelling and tenderness of the breasts, pelvic congestion, ovarian pain, altered libido</td>
</tr>
<tr>
<td>Neuromuscular</td>
<td>Trembling of the extremities, changes in coordination, clumsiness, backache, leg aches</td>
</tr>
<tr>
<td>General</td>
<td>Weight gain, insomnia, dizziness, acne</td>
</tr>
</tbody>
</table>
Pre-Menstrual Syndrome

Diagnosis:
- A complete clinical history and physical examination
- Blood studies, including thyroid hormones, glucose, and prolactin assays
- Psychosocial evaluation

Management:
- Education and support
- Diuretics
- Anxiolytic drugs
- Diet and life style
- Therapeutic regimens
- The SSRI antidepressants
Menopause

Definition: Permanent Cessation of menstrual cycles.

Clinical features:
- Vascular instability: Hot flashes, night sweats, palpitations, dizziness, and headaches
- Urogenital atrophy: vaginal dryness, urinary stress incontinence, urgency, nocturia, vaginitis, and UTI
- Skin, soft tissue: decrease in body hair, skin elasticity, and subcutaneous fat, breast atrophy
- Psychological: Irritability, depression, anxiety, fatigue, insomnia
- Sexual: Dyspareunia, decreased libido
- Increased risk for osteoporosis and cardiovascular disease
Menopause

- **Diagnosis:**
  - Day 3 FSH levels >30 IU/L
  - US examination of numbers of follicles
  - Blood oestrogen & progesterone levels

- **Management:**
  - Hormone replacement
  - Antidepressants
  - Counseling
  - Lifestyle changes
Hormone replacement therapy (HRT)

- Definition: Replacement of hormones that decline from perimenopause onwards.

- Various combinations:
  - Oestrogen and progesterone (EPT),
  - Oestrogen (ET) only

- Delivery systems:
  - Patches/creams
  - Tablets
  - IUDs
Hormone replacement therapy (HRT)

- **Contraindications**
  - Undiagnosed vaginal bleeding
  - Liver disease
  - Coronary artery disease and thrombosis
  - Hormone dependent neoplasms

- **Benefits**:
  - Relief of symptoms associated with menopause
    - Hot flashes, Loss of libido, Vaginal dryness
    - Insomnia
    - Protection against osteoporosis
    - Protection against colorectal cancer
HRT- WHI Study

- Women’s Health Initiative (WHI) study: The first large, double-blind, placebo-controlled clinical trials of HRT
- The study was stopped prematurely as the risks of HRT outweighed its benefits.
- Results:
  - Continuous cyclic estrogen–progesterone therapy [CEPT]:
    - Increased the risk of breast cancer and incidences of CHD, stroke, and venous thromboembolic disease
    - Reduction in colorectal cancer and hip fractures
  - The Oestogen only therapy:
    - No increased risk of breast cancer or heart disease,
    - Similar increased risk of stroke and venous thromboembolic disease.
Hirsutism

- Definition: Excessive growth of hair in an androgen-dependent distribution in women

- Aetiology:
  - Idiopathic
  - Polycystic ovarian syndrome
  - Congenital adrenal hyperplasia
  - Exogenous androgen administration
  - Androgen secreting tumour
  - Cushing’s syndrome
Hirsutism

- **Diagnosis:**
  - Hormone levels - testosterone, prolactin, LH and FSH
  - ACTH stimulation test
  - Imaging studies

- **Management:**
  - Cosmetic therapy
  - Surgery
  - Hormone therapy

Urogenital Disorders
Incontinence

- **Definition:** Involuntary loss of urine that can be demonstrated objectively and is a social or hygienic problem.

- **Aetiology:**
  - Stress incontinence: poor pelvic floor support or a weak urethral sphincter
  - Urge incontinence: Overactivity of bladder/detrusor
  - Overflow Incontinence: bladder distension in the absence of detrusor activity
  - Functional Incontinence: inability to locate, reach or receive assistance in reaching an appropriate place to void
## Incontinence

<table>
<thead>
<tr>
<th>TYPE</th>
<th>CHARACTERISTICS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress</td>
<td>Involuntary loss of urine associated with activities, such as coughing, that increase intra-abdominal pressure</td>
</tr>
<tr>
<td>Overactive bladder/urgine incontinence</td>
<td>Urgency and frequency associated with hyperactivity of the detrusor muscle; may or may not involve involuntary loss of urine</td>
</tr>
<tr>
<td>Overflow</td>
<td>Involuntary loss of urine when intravesicular pressure exceeds maximal urethral pressure in the absence of detrusor activity</td>
</tr>
<tr>
<td>Functional</td>
<td>Lack of cognitive function to go to the bathroom, commode, or urinal/bedpan resulting in spontaneous urination</td>
</tr>
</tbody>
</table>
Incontinence

- **Diagnosis:**
  - Physical and neurological examination,
  - Urodynamics testing
  - Microbial culture
  - Pelvic ultrasound

- **Management:**
  - Kegel Exercise
  - Medications
  - Surgical treatments
Vaginal Prolapse

- **Definition:** Herniation of pelvic viscera through the pelvic floor.

- **Aetiology:**
  - Overstretching of the perineal supporting tissues during pregnancy and childbirth.
  - Relaxation of the pelvic support structures due to aging and postmenopausal changes

- **Conditions include:**
  - Cystocele
  - Rectocele
  - Urethrocele
  - Enterocele
  - Uterine prolapse
Rectocele

Cystocele

Urethrocele

Enterocele

Vaginal Prolapse

- Management:
  - Kegel Exercise
  - Surgical treatments:
    - Vaginal hysterectomy
    - abdominal hysterectomy
    - Colporrhaphy (appropriate repair of the vaginal wall)
    - A vesicourethral suspension
Cystitis

- **Definition:** Infection or inflammation (interstitial) of the urinary bladder

- **Aetiology:**
  - Bacterial infections: E. coli, Proteus, Pseudomonas, Streptococci and Staphylococci

- **Clinical features:**
  - Dysuria
  - Haematuria
  - Frequency and pain

- **Diagnosis:**
  - Microbial examination of the urine

- **Management:**
  - Antibiotics
Reading and Resources

- Crowley LV, 2012, *An Introduction to Human Diseases – Pathology and Pathophysiology Correlations*, 9th edn, Jones and Bartlett Learning
Reading and Resources

- Mosby’s dictionary of medicine, nursing and health professions 2013, 9th edn, Elsevier, St. Louis, MO.
- VanMeter, KC & Hubert, RJ 2014, *Gould's pathophysiology for the health professions*, 5th edn, Elsevier, St Louis, MO.
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