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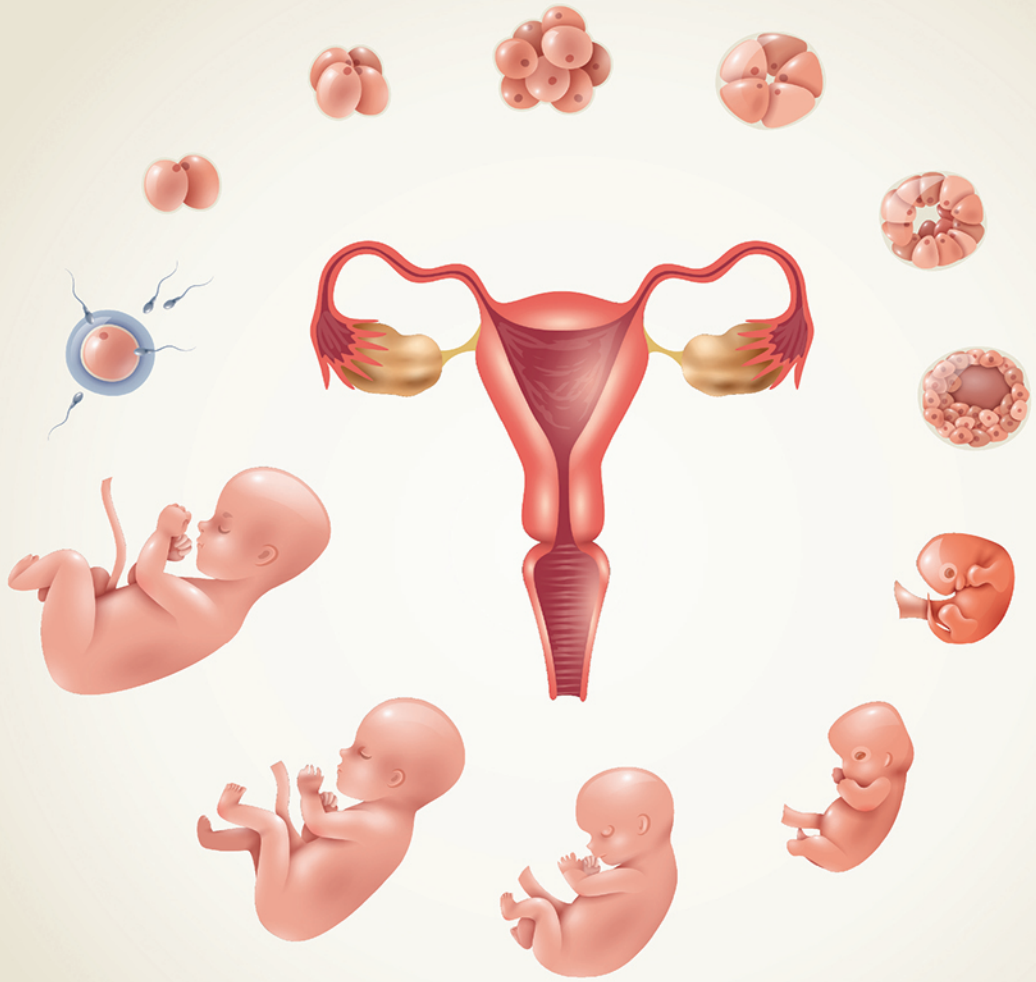

A Synopsis of Obstetrics & Gynecology

Justin C Konje
Badreldeen I Ahmed

JAYPEE

Contents

PART 1: Gynecology

SECTION 1: Anatomy, Physiology, History and Physical Examination

1. Basic Embryology of the Genital Tract 3
2. Basic Anatomy of the Genitourinary System 7
3. Puberty and Pubertal Disorders 17
4. Physiology of Menstruation 21
5. Gynecology—History Taking and Physical Examination: *Proforma to Adapt* 24
6. Principles of Surgery in Gynecology 30

SECTION 2: Early Pregnancy

7. Miscarriage 41
8. Recurrent Miscarriage 45
9. Ectopic Pregnancy 46
10. Gestational Trophoblastic Disease 49
11. Nausea and Vomiting in Pregnancy 52

SECTION 3: Benign Conditions of the Genital Tract

12. Disorders of Menstruation or Abnormal Uterine Bleeding 55
13. Endometriosis and Chronic Pelvic Pain 65
14. Benign Conditions of the Vulva and Vagina 70
15. Benign Conditions of the Uterus 76
16. Benign Conditions of the Ovary 82
17. Subfertility 87
18. Genital Prolapse and Urogynecology (Urinary Incontinence) 95

SECTION 4: Gynecological Oncology

19. Premalignant Disorders of the Genital Tract 107
20. Cancer of the Vulva 114
21. Cancer of the Vagina 118
22. Cancer of the Cervix 120
23. Cancer of the Endometrium 123
24. Cancer of the Ovary and Fallopian Tube 129

SECTION 5: Women's Health

25. Contraception 137
26. Menopause and Menopause Therapy (Hormone Replacement Therapy) 151
27. Sexually Transmitted Infections and Pelvic Inflammatory Disease 154
28. Psychosexual Medicine 161
29. Domestic Violence and Sexual Assault 165
30. Termination of Pregnancy—Induced Abortion 167

PART 2: Obstetrics

SECTION 6: Basics of Obstetrics

31. Normal Physiology of Pregnancy and Embryology 171
32. Obstetric History and Examination 176
33. Antenatal Care 186
34. Prenatal Diagnosis and Management 190
35. Fetal Growth and Monitoring 204

SECTION 7: Multiple Pregnancy and Complications in Pregnancy

36. Multiple Pregnancy 217
37. Bleeding in Pregnancy: Antepartum Hemorrhage 225

38. Abdominal Pain in Pregnancy 229
39. Musculoskeletal Disorders of Pregnancy 233
40. Infections in Pregnancy....234

SECTION 8: Medical Disorders of Pregnancy

41. Hypertensive Disorders of Pregnancy 249
42. Diabetes in Pregnancy....257
43. Other Endocrine Disorders of Pregnancy 260
44. Dermatological Disorders in Pregnancy....262
45. Respiratory Disorders in Pregnancy....266
46. Connective Tissue Disorders 269
47. Cardiac Disorders in Pregnancy....272
48. Renal Tract Disorders in Pregnancy Including Transplant....278
49. Hematological Disorders....280
50. Psychiatric Disorders in Pregnancy 289
51. Gastrointestinal and Hepatobiliary Disorders in Pregnancy 292

SECTION 9: Labor and Delivery

52. Labor: Normal 299
53. Episiotomy and Perineal Tears....318
54. Labor: Abnormal....321
55. Operative Vaginal Delivery 328
56. Postpartum Hemorrhage 339
57. Induction of Labor 345
58. Preterm Labor and Preterm Prelabor Rupture of Membranes....348
59. Abnormal Presentation 352

SECTION 10: Fetal Death, the Puerperium and Maternal Collapse

60. Intrauterine Fetal Death: Late 359

61. Maternal Collapse in Pregnancy 362

62. The Puerperium and Puerperal Disorders 364

63. Lactation and Breast Disorders 369

SECTION 11: Miscellaneous

64. Perinatal and Maternal Mortality 375

65. Female Genital Mutilation 378

66. Fasting in Pregnancy 381

67. Applied Genetics in Obstetrics and Gynecology 383

Index 387

SECTION

3

Benign Conditions of the Genital Tract

12. Disorders of Menstruation or Abnormal Uterine Bleeding
13. Endometriosis and Chronic Pelvic Pain
14. Benign Conditions of the Vulva and Vagina
15. Benign Conditions of the Uterus
16. Benign Conditions of the Ovary
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CHAPTER 12

Disorders of Menstruation or Abnormal Uterine Bleeding

AMENORRHEA—*ABSENCE OF MENSTRUATION*

- Two types—(1) primary and (2) secondary
  1. Primary amenorrhea—failure to start menstruating by the age of 16 years (remember that delayed puberty is defined as failure to develop secondary sexual characteristics by the age of 14 years)
  2. Secondary amenorrhea—absence of periods for at least 6 months in a woman who has previously been menstruating.
- *Causes*: The endocrine causes are shown in **Figure 1**.
  - These will include hypothalamic, pituitary, ovarian, and end-organ (uterine, vagina) disorders.
  - **Figure 1** shows the various causes.
  - Hypothalamic—causes hypogonadotropic hypogonadism:
    - Stress
    - Weight loss (e.g., from excessive exercises as in athletes, eating disorders)

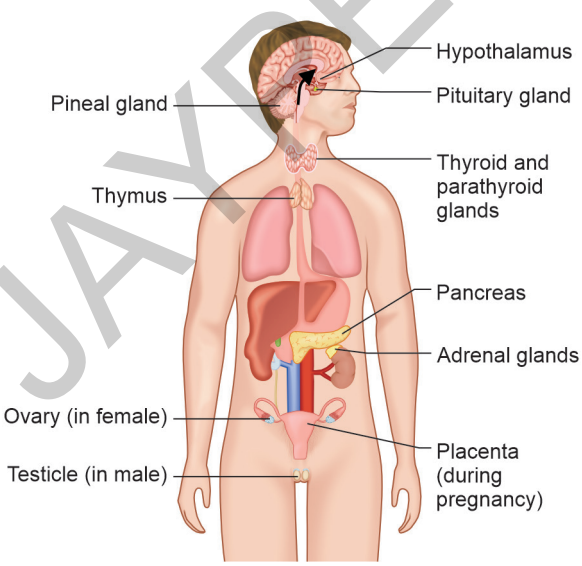

Fig. 1: Endocrine causes of amenorrhea.

    - Pathologies of the hypothalamus—tumors such as craniopharyngiomas and gliomas
    - Head injuries
    - Kallman's syndrome [an X-linked recessive disorder resulting from mutations in genes associated with disruption of the migration of olfactory nerve cells and gonadotropin-releasing hormone (GnRH)-producing neurons in the developing brain resulting in deficiency of smell and GnRH, associated with the underdevelopment of the genitalia and presenting with absent or delayed puberty]
    - Systemic disorders that affect the hypothalamus (e.g., tuberculosis and sarcoidosis).
    - Drugs [steroids such as progestogens, hormone replacement therapy (HRT), and dopamine antagonists]
    - Infections—meningitis, etc.
  - *Pituitary disorders:*
    - Adenomas of the anterior pituitary
    - Pituitary necrosis (e.g., Sheehan syndrome) resulting from prolonged hypotension typically from severe obstetrics hemorrhage
    - Infections—meningitis
    - Surgery
    - Radiotherapy
    - Congenital failure of development of the pituitary
  - *Ovarian disorders:*
    - Ovarian dysgenesis (as seen in those with Turner syndrome, gonadal dysgenesis). Patients with Turner syndrome have characteristic phenotypes as shown in the **Figure 2**.
    - Premature ovarian insufficiency or failure (POI/POF)
    - Polycystic ovary syndrome (PCOS)
  - *Others:*
    - Thyroid disorders (hypothyroidism)

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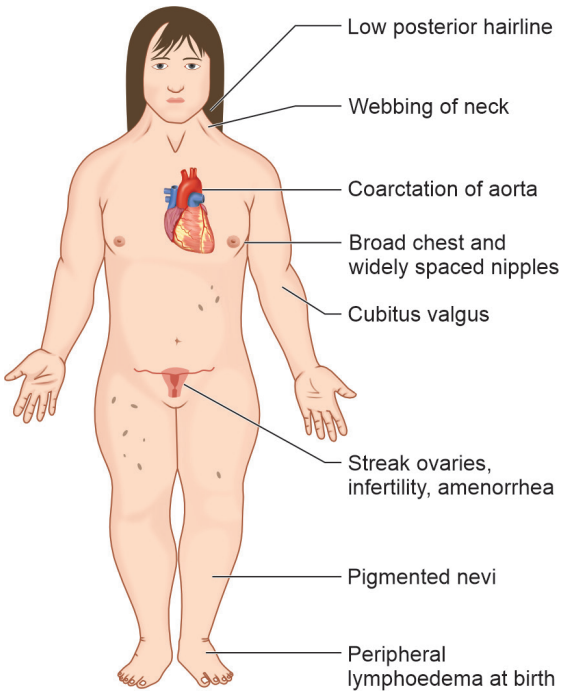

Fig. 2: Phenotype of Turner syndrome which typically presents with primary amenorrhea/infertility.

- Adrenal disorders (Cushing syndrome)
- Other systemic disorders
- *End organ (uterus, vaginal):*
  - Hypoplasia of the uterus (congenital)
  - Asherman's syndrome (intrauterine synechiae or adhesions)
  - Radiotherapy
  - Agenesis of the vagina/cervix (Müllerian abnormalities)

OLIGOMENORRHEA

- Defined as irregular periods occurring at intervals that are >35 days and <6 months (or having only 4–9 periods per year)
- *Causes*:
  - Hormonal—PCOS
  - Endocrine

History

What to ask for when a patient presents with amenorrhea:

- This will depend on the type of amenorrhea (primary or secondary)
- If primary—developmental milestones (timing of breast development, growth of pubic hair), family history (any siblings and when menstruation started), and drugs (exogenous)
- Changes in weight, lifestyle, stressors, and exercises
- Menstrual history—onset of menstruation, cycle (duration and frequency), and flow; cyclical symptoms such as pain (in cases of outflow obstruction)
- Reproductive history—pregnancies including infertility (investigations and treatment), complications of pregnancy (miscarriages and treatment, postpartum hemorrhage, and blood transfusion)
- Past and current medical history—systemic disorders
- Past surgery—evacuation, myomectomy, and polypectomy—all these may cause Asherman's syndrome
- Drug history
- *Symptoms suggestive of causes:*
  - Headaches and vomiting, visual disturbances, and features of a space occupying lesion in the head
  - Discharge from the breast (inappropriate galactorrhea as a sign of hyperprolactinemia)
  - Hirsutism
  - Excessive weight gain

Examination and Investigations

- *Examination*:
  - Weight and height and calculate body mass index (BMI)
  - Any masculinizing features (features of androgenism)—excessive hair (quantify using Ferriman–Gallwey score)
  - General—BP, breast for galactorrhea
  - Abdomen—hair distribution and abdominal masses
  - Pelvis—vulva and vagina—hymen, bulge, etc.
  - Bilateral pelvic examination if sexually active—uterine size and adnexal masses
- *Investigations*:
  - Ultrasound scan—transabdominal or transvaginal
  - Hormone profile—these will depend on the suspected cause.
    - Follicle-stimulating hormone (FSH)/luteinizing hormone (LH), prolactin, testosterone, sex hormone-binding globulin (SHBG), and thyroid function test
    - Hysteroscopy if intrauterine adhesions (Asherman's syndrome suspected)

Management

This will depend on the cause identified:

- *Primary amenorrhea:*
  - If disorder of sexual differentiation (see chapter 3 for appropriate management)

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- Lower genital tract obstruction (outflow obstruction)—treat accordingly—imperforate hymen—hymenectomy; vaginal agenesis—refer to appropriate center for neovaginoplasty
- Other causes—systems/endocrine—treat accordingly (i.e., treat the primary causes)

■ *Secondary*
- *Polycystic ovary syndrome* (historically known as Stein–Leventhal syndrome—after the two gynecologists who described it in 1957)
- Most common endocrine pathology in the reproductive age group—affecting 5–10% of women
- Characterized by amenorrhea/oligomenorrhea, features of androgen excess (hirsutism/excessive hair, acne, and acanthosis nigricans—velvety dark skin at the nape of the neck), obesity, raised insulin resistance, and predisposition to type II diabetes
- Clinically present with menstrual abnormalities (oligomenorrhea/amenorrhea in 75% of cases), hirsutism and subfertility (also in up to 75% of cases)
- Obesity (present in up to 40% of cases)
- Acanthosis nigricans (at the nape of the neck, axilla, and flexor aspect of the upper limbs)
- Diagnosed based on Rotterdam criteria—presence of two of the following three:
  1. Menstrual abnormality (amenorrhea/oligomenorrhea)
  2. Clinical/biochemical [raised testosterone or SHBG and free androgen index (FAI)] hyperandrogenism
  3. Polycystic ovaries on ultrasound scan (8–12 or more cysts <10 mm) or volume >10 mL **(Figs. 3A and B)**

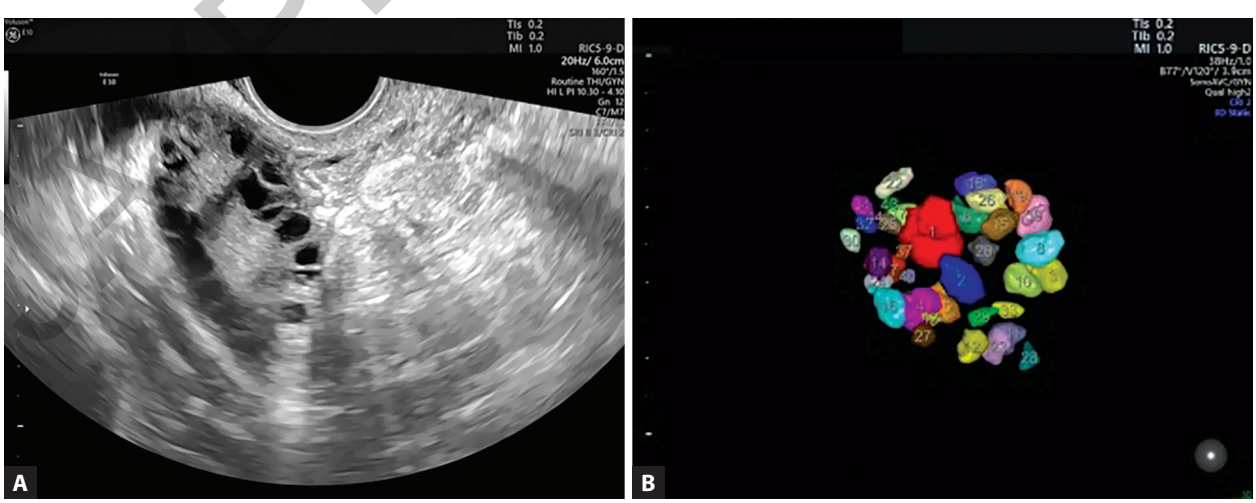
Management of PCOS depends on the presenting symptoms:

■ *Hirsutism (**Figs. 4A and B**):*
- Mechanical treatment (shaving, depilating, electrolysis, and laser)
- Medical treatment—counsel that it will take at least 4–6 months for effects to manifest.
  - Hormonal—antiandrogen (cyproterone acetate or finasteride); eflornithine cream (Vaniqua™)—topical application; contraceptive pill containing cyproterone acetate (e.g., Dianette™)

■ *Menstrual irregularities:*
- Cyclical progestogens
- Combined hormonal contraception (these increase SHBG and therefore reduce free androgen and androgenic effects)—useful to treat hirsutism

■ *Weight:*
- Lifestyle modifications—weight reduction (diet, exercises, etc.)
- Bariatric surgery if BMI >45 kg with associated comorbidities or fails to respond to lifestyle modifications
- Metformin

■ *Subfertility/infertility*: Induction of ovulation with:
- Weight loss
- Clomifene citrate
- Aromatase inhibitors (e.g., letrozole/anastrozole)
- Ovarian drilling
- GnRH/gonadotropins



Figs. 3A and B: Ultrasound scan (USS) images of polycystic ovary syndrome (PCOS)—(A) Typical neck-lace appearance of peripheral cysts; (B) 3D color spatial distribution of the cysts.

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Figs. 4A and B: Hirsutism—note the terminal hair on (A) the face and neck and (B) the legs.

- *Longterm health implications*
  - Endometrial hyperplasia and cancer
  - Hypertension and cardiovascular disorders from hyperlipidemia
  - Type 2 diabetes

DYSMENORRHEA

- Painful menstruation affects 50–90% of women in the reproductive age group and causes absence from work in up to 5–15% of women.
- Two types—(1) primary or (2) secondary. **Table 1** shows differences in the two including investigations and management.

PREMENSTRUAL SYNDROME

- Defined as the occurrence of cyclical emotional, psychological and somatic symptoms in the period before menstruation (the luteal phase) and is significantly improved with the onset of menstruation and tends to be resolved by the end of menstruation if not before.
- Experienced by most women in the reproductive age group but severe enough for clinical consultation in 5–60% of women
- Symptoms are very severe in 5% of women. About 15% of sufferers take time off work each year.
- Symptoms may be severe enough to disrupt everyday life and interpersonal relationships—causing breakdown and divorce, loss of jobs, and in very severe cases suicide.
- A symptom diary is essential for making a diagnosis and qualifying the severity of the premenstrual syndrome (PMS). An example is shown in **Figure 5**.
- *Etiology:*
  - Unknown but related to ovarian cycle
  - Cyclicity in estrogens and progesterone and other neurotransmitters (e.g., serotonin) are thought to be involved.
- *Clinical features:* **Flowchart 1** shows the relationship of symptoms to menstrual cycle:
  - *Psychological:*
    - Mood swings
    - Depression
    - Irritability
    - Anxiety
    - Loss of libido
    - Loss of sleep and interest in environment
  - *Physical:*
    - Bloating
    - Headaches
    - Abdominal cramps
    - Cyclical weight gain (fluid retention)
    - Mastalgia (painful breast)
  - *Behavioral:*
    - Poor concentration
    - Unprovoked aggression
  - *Treatment:* **Flowchart 2** shows an example of a treatment pathway:
    - Diagnosis is based on history and a symptom diary—best kept for at least 3 months.
    - Various treatments have been tried—high placebo effect.
      - Stress management, psychotherapy, and family support
      - Complementary therapy (red clove, isoflavones, vitamin B_6, and magnesium)
      - Selective serotonin reuptake inhibitor (e.g., fluoxetine, citalopram escitalopram)
      - Cognitive behavior therapy (CBT)
      - Cycle suppression—combined hormonal contraception, transdermal estradiol, or progestogens
      - GnRH agonist and add-back therapy
      - Bilateral salpingo-oophorectomy with or without hysterectomy and HRT

ABNORMAL UTERINE BLEEDING

- Defined as any bleeding from the genital tract that is considered abnormal by the woman.
- FIGO in 2011 recommended the acronym *PALM COEIN* for AUB rather than using terms such as menorrhagia,

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TABLE 1: Difference between primary and secondary dysmenorrhea.

Distinctive feature	*Primary*	*Secondary*
Definition	Painful menstruation that typically starts with menarche or shortly after	Painful menstruation that starts after several years of painless menstruation
Relation to periods	• Typically starts before onset of menstruation and improves by the 3rd day of menstruation • Spasmodic in nature	No particular characteristic as nature depends on the cause
Associated symptoms	These tend to be nonspecific and related to the pain: • Nausea • Vomiting • Bloatedness • Migraine • Emotional symptoms	*These tend to be specific depending in the cause of the painful periods:* • Urinary symptoms (hematuria) • Bowel symptoms (constipation or tenesmus—feeling of incompletely emptying the bowel), bleeding per rectum with periods • Painful sexual intercourse (dyspareunia) • Heavy periods • Vaginal discharge • Abdominal swelling/mass • Bloatedness • Intermenstrual bleeding
Physical features	Tend to be none—normal findings on examination	*Depending on the pathology:* Tenderness, induration of the uterosacral ligaments, adnexal masses, enlarged uterus, uterine masses (as in the case of fibroids)
Investigations	None if periods not heavy but if heavy—complete blood count (CBC)	*Depend on suspected cause:* • CBC if heavy periods • Ultrasound scan • Diagnostic laparoscopy • Microbiology
Treatment	• Support, lifestyle changes (e.g., low-fat diet, vegetarian diet, and exercise) and reassurance • Pain killers (such as NSAIDs) during menstruation • Combined hormonal contraception (CHC) or the Levonorgestrel intrauterine system (Mirena)	*Depends on the cause:* • Pain killers such as NSAIDs • Specific treatment for cause of dysmenorrhea • Levonorgestrel intrauterine system (Mirena) depending on cause • Combined hormonal contraception (CHC)
Common causes	Idiopathic and related to prostaglandin-prostacyclin production and ratio	*Commonly secondary to pelvic pathology:* • Clot dysmenorrhea (in women with heavy periods and the passage of clots) • Endometriosis • Adenomyosis • Fibroids • Pelvic inflammatory disease • Pelvic congestion syndrome • Foreign body, e.g., intrauterine contraceptive device (IUD) • Cervical stenosis (especially following surgery on the cervix)

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metrorrhagia, polymenorrhagia, hypermenorrhagia, and dysfunctional uterine bleeding.

- PALM COEIN refers to the pathology responsible for the bleeding:
  - P—*P*olyps
  - A—*A*denomyosis
  - L—*L*eiomyoma (fibroids)
  - M—*M*alignancy
  - C—*C*oagulation
  - O—*O*vulatory disorders
  - E—*E*ndometrial pathology
  - I—*I*atrogenic
  - N—*N*onclassified

DAILY RECORD OF SEVERITY OF PROBLEMS

Please print and use as many sheets as you need for at least two FULL months of ratings.

Name or Initials _____

Month/Year _____

Each evening note the degree to which you experienced each of the problems listed below. Put an "x" in the box which corresponds to the severity: 1 - not at all, 2 - minimal, 3 - mild, 4 - moderate, 5 - severe, 6 - extreme.

		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
	Enter day (Monday="M", Thursday="R", etc) >																															
	Note spotting by entering "S" >																															
	Note menses by entering "M" >																															
	Begin rating on correct calendar day >																															
1	Felt depressed, sad, "down,", or "blue" or felt hopeless; or felt worthless or guilty	6 5 4 3 2 1																														
2	Felt anxious, tense, "keyed up" or "on edge"	6 5 4 3 2 1																														
3	Had mood swings (i.e., suddenly feeling sad or tearful) or was sensitive to rejection or feelings were easily hurt	6 5 4 3 2 1																														
4	Felt angry, or irritable	6 5 4 3 2 1																														
5	Had less interest in usual activities (work, school, friends, hobbies)	6 5 4 3 2 1																														
6	Had difficulty concentrating	6 5 4 3 2 1																														
7	Felt lethargic, tired, or fatigued; or had lack of energy	6 5 4 3 2 1																														
8	Had increased appetite or overate; or had cravings for specific foods	6 5 4 3 2 1																														
9	Slept more, took naps, found it hard to get up when intended; or had trouble getting to sleep or staying asleep	6 5 4 3 2 1																														
10	Felt overwhelmed or unable to cope; or felt out of control	6 5 4 3 2 1																														
11	Had breast tenderness, breast swelling, bloated sensation, weight gain, headache, joint or muscle pain, or other physical symptoms	6 5 4 3 2 1																														
	At work, school, home, or in daily routine, at least one of the problems noted above caused reduction of productivity or inefficiency	6 5 4 3 2 1																														
	At least one of the problems noted above caused avoidance of or less participation in hobbies or social activities	6 5 4 3 2 1																														
	At least one of the problems noted above interfered with relationships with others	6 5 4 3 2 1																														

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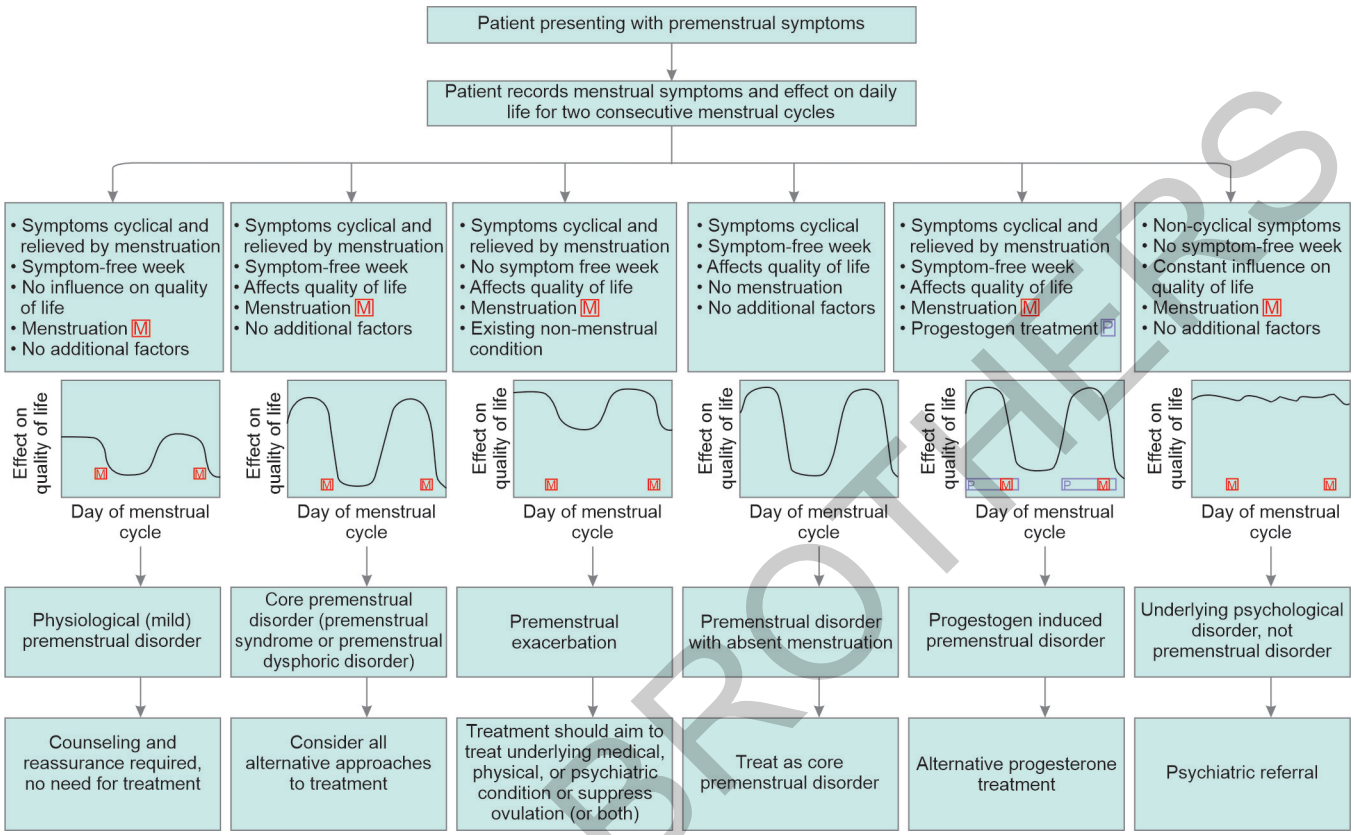
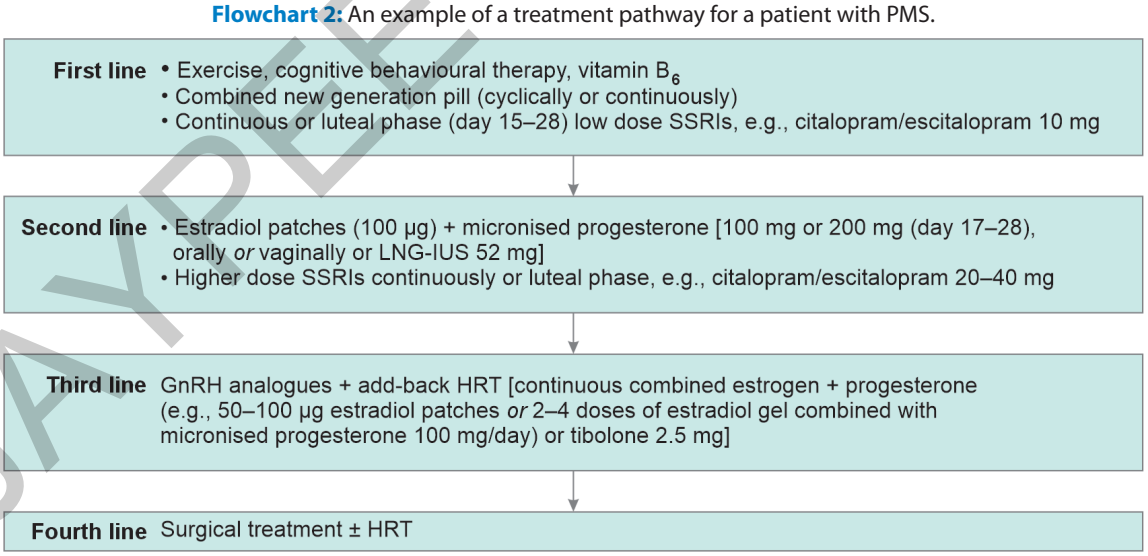
Fig. 5: An example of a chart to record symptoms to aid the diagnosis of premenstrual syndrome (PMS) *(Courtesy:* of RCOG Green-top Guideline)

Flowchart 1: Cyclicity of symptoms in relation to menstrual cycle.



Flowchart 2: An example of a treatment pathway for a patient with PMS.



(GnRH: gonadotropin-releasing hormone; HRT: hormone replacement therapy; IUS: intrauterine system; LNG: levonorgestrel; PMS: premenstrual syndrome; SSRI: selective serotonin reuptake inhibitor)

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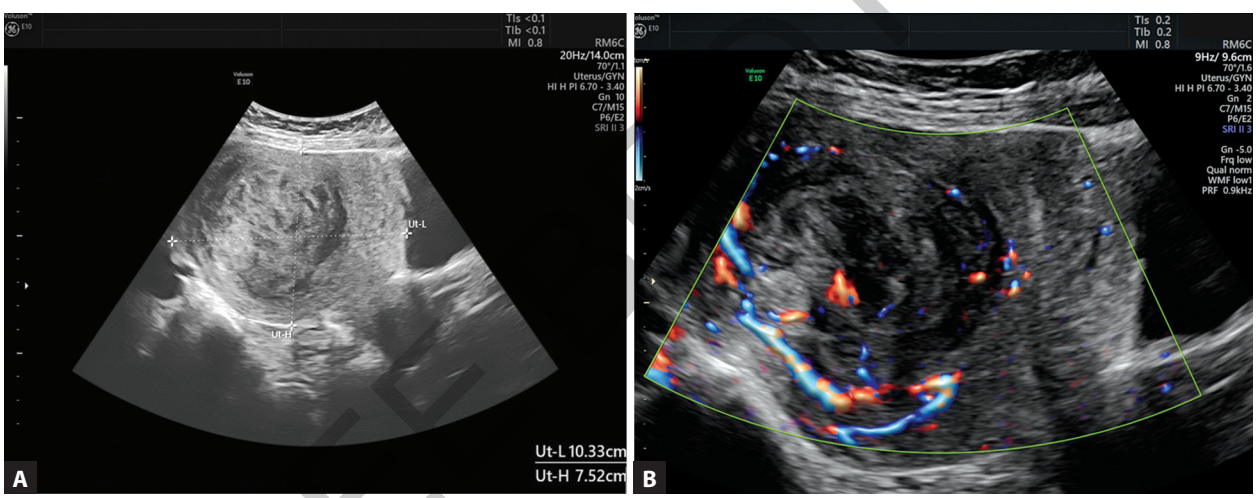
- Other descriptive terms for AUB include heavy menstrual bleeding (HMB), intermenstrual bleeding (IMB), postmenopausal bleeding (PMB), postcoital bleeding (PCB) and bleeding of endometrial origin (BEO)
- Ultrasound images of some of the causes [polyps **(Figs. 6A and B)**, fibroids **(Figs. 7A and B)**, and adenomyosis **(Fig. 8)**] of AUB

Heavy Menstrual Bleeding

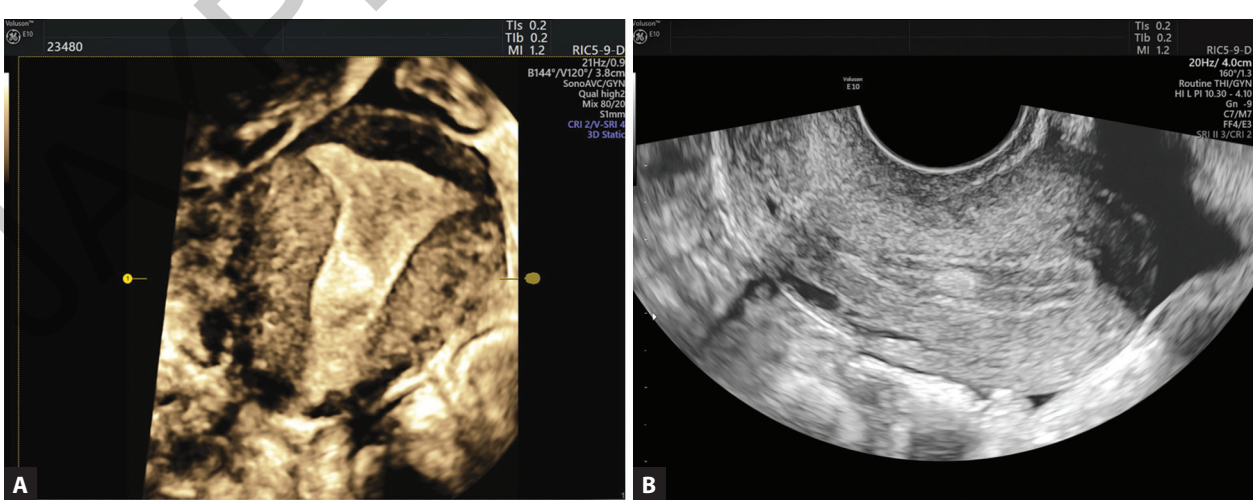
- Normal menstrual loss should not be >80 mL/cycle
- Loss of >80 mL/cycle is defined as HMB
- Patients presenting with HMB do not quantify their menstrual loss hence it is a clinical perception at presentation. Pictorial charts can be used to quantify loss (if objectivity required)
- Affects 20–30% pf women in the reproductive age group
- General practitioner (GP) consultations with this complaint vary depending on the ethnicity and country—5% of UK women aged 30–49 consult with this complaint.

Symptoms at Presentation

- HMB—could be of regular or irregular periods
- Symptoms of anemia—weakness and lethargy
- Symptoms of causes—see below
- Clinical examination—features of anemia (usually iron deficiency) and those of causes (see below)
- Some women especially in the early reproductive years may present with very HMB as an emergency (passage of clots, etc.)



Figs. 6A and B: Uterine fibroids (left—causing an enlarged uterus and right—vascularity coming from the periphery).



Figs. 7A and B: Endometrial fibroid polyp—(A) 3D and (B) 2D.

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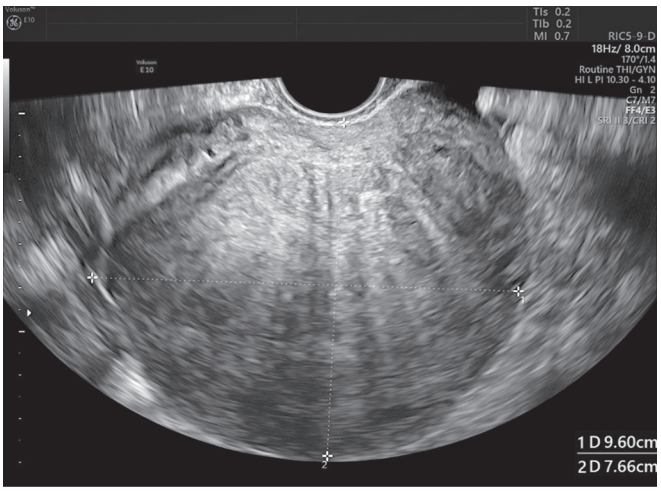

Fig. 8: Adenomyosis (note uniform enlargement of the uterus with no discernible separate myometrium).

Etiology

- Idiopathic in a large number of cases
- Fibroids (leiomyomas)—30% of women with HMB have fibroids
- Adenomyosis—70% of women with adenomyosis present with HMB
- Endometrial polyps
- Pelvic inflammatory disease (PID)
- Thyroid dysfunction (hypo- and hyperthyroidism)
- Hematological (coagulation disorders—hemophilia, factor X deficiency, von Willebrand disease, etc.)
- Foreign body—intrauterine contraceptive device
- Malignancy—endometrial and cervical
- Drugs—especially anticoagulants (e.g., warfarin)

Investigations

- Full blood count (to rule out anemia)
- Coagulation screen (if family history of coagulation disorder or HMB since menarche)
- Pelvic ultrasound—indicated for suspected pelvic pathology such as fibroids, adenomyosis, or foreign body
- Hormonal investigations—for thyroid disorders if clinically suspected
- Swabs—from the cervix and vagina if PID suspected (it is rare for these to be positive though)
- Endometrial biopsy with Pipelle (for irregular bleeding in women >40 years, PMB If endometrial thickness is >4 mm on ultrasound scan), in those <40 years who fail to respond to hormonal treatment or prior to ablation (treatment option).
- Hysteroscopy—if initial biopsy fails, insufficient sample obtained by Pipelle or bleeding is persisting, transvaginal sonography (TVS) shows abnormality that can be removed at hysteroscopy or is inconclusive and hysteroscopy required to confirm pathology.
  - Outpatient if possible or under anesthesia if cervix is stenosed/narrow or polyps/submucous fibroids need resecting.

Management

- Determined by patient's reproductive plans including contraceptive needs (current and future), cause of the HMB, drug and surgical history (**Flowchart 3** is an algorithm for management of a woman presenting with AUB and **Flowchart 4** for a woman presenting with life threatening bleeding)
- *Medical—hormonal or nonhormonal:*
  - *Hormonal:*
    - Levonorgestrel intrauterine system (Mirena)—first choice especially in women who have had children
    - Combined hormonal contraception
    - Progestogens taken cyclically (e.g., norethisterone 10–15 mg daily from days 5 to 25). Luteal phase progestogens not very effective.
    - GnRH agonist—induce hypogonadotropic hypogonadism and also reduce size of fibroids.
  - *Nonhormonal:*
    - Tranexamic acid—taken during menstruation (1 g four times/day)—reduces blood loss by 50%
    - Mefenamic acid—during menstruation (also reduces pain)—reduces blood loss by 30%.
  - *Surgical—depending on the cause:*
    - Myomectomy—removal of fibroids (laparoscopic, hysteroscopic resection, robotic, or open surgery)
    - Endometrial ablation—in cases where no cause is found (prior to this a hysteroscopic biopsy is recommended to exclude pathology). Suitable for those who have completed their family and have a uterus that is <10 weeks size. Approaches to ablation include—microwave (Microsulis™), thermal and impedance controlled (Novosure™)
    - Uterine artery embolization
    - Hysterectomy

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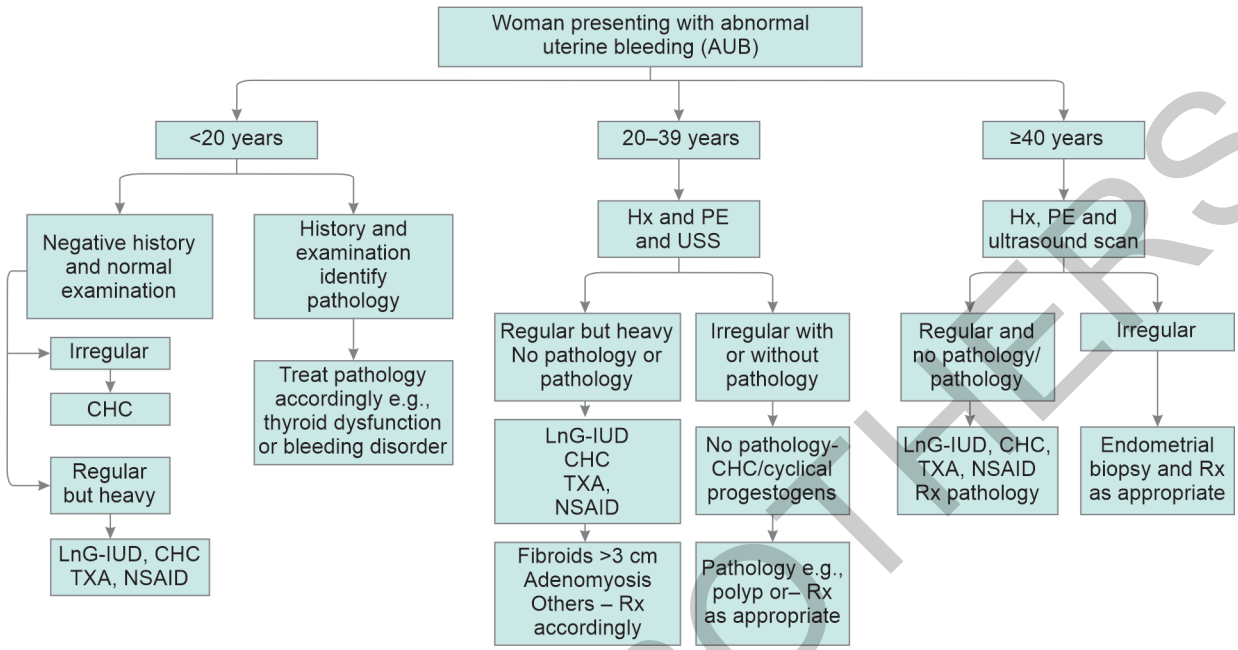
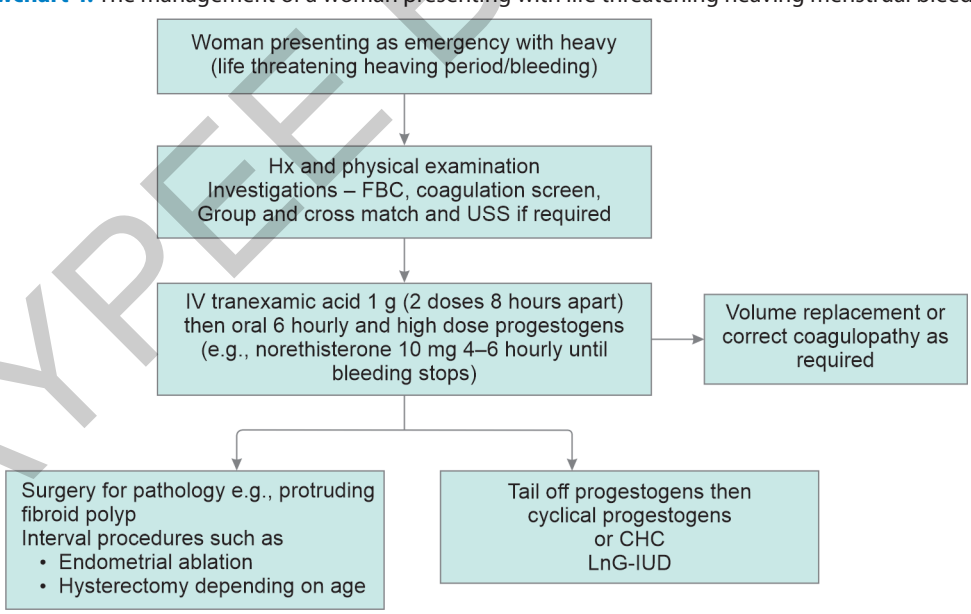
Flowchart 3: The management of a woman presenting with heaving menstrual bleeding.



[CHC: combined hormonal contraception; Hx: history; LnG-IUD: The levonorgestrel intrauterine system; NSAID: nonsteroidal anti-inflammatory drug; PE: physical examination including pelvic examination; TXA: tranexamic acid; USS: ultrasound scan (transabdominal/transvaginal)]

Flowchart 4: The management of a woman presenting with life threatening heaving menstrual bleeding.



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