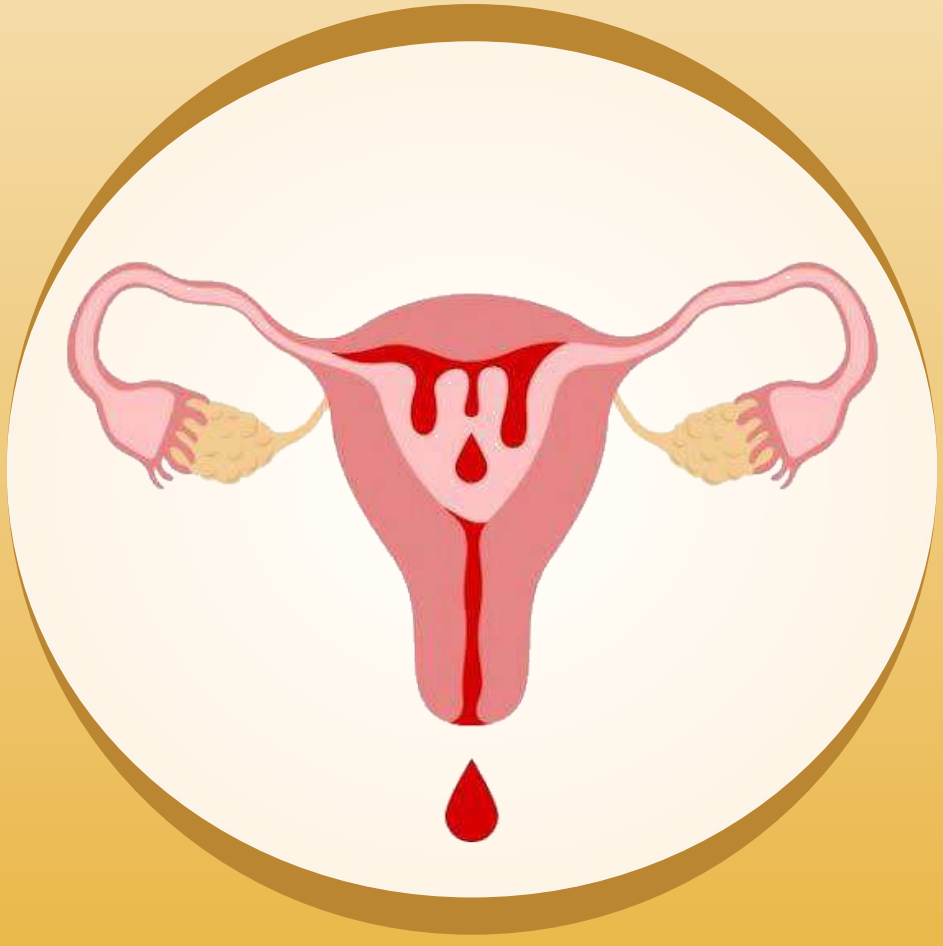
ABNORMAL UTERINE BLEEDING



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UTTAR PRADESH

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MESSAGE

Shri Brajesh Pathak
Hon'ble Deputy Chief Minister
Minister of Medical Health and Family Welfare
Department Government of Uttar Pradesh

Continuing Medical Education (CME) enables medical professionals to enhance their knowledge base and provides an opportunity for knowledge creators to share their expertise with the broader medical community. CMEs facilitate collaboration among medical professionals, fostering valuable networking opportunities.

Primary Health Centers (PHCs) and Community Health Centers (CHCs) serve as the initial point of contact with qualified doctors in the public health sector. By implementing systematic CME programs, these initiatives aim to update the proficiency of medical officers by imparting current knowledge and skills. This will significantly enhance patient care, instill patient confidence, and improve patient satisfaction.

Menstruation has a significant impact on a woman's physical, mental and social well-being. Menstrual health is defined as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity in relation to the menstrual cycle". The current situation requires action to accommodate the needs of female patients and bridge the social gap regarding menstrual health. An inclusive, medical consultant environment requires proactive measures by medical authorities and stakeholders that will reduce gender discrepancy in female patient satisfaction and professional life.

In line with this objective, the State Institute of Health & Family Welfare, Uttar Pradesh (SIHFW), is actively developing CME modules that are crucial for our healthcare personnel. I anticipate that the Abnormal Menstruation, Etiology and Diagnosis, Treatment and Management focusing on recent advancements, will greatly contribute to the knowledge enhancement of medical officers in the Provincial Health & Medical Services in Uttar Pradesh. This will ultimately benefit both the medical officers and their female patients.

I extend my commendations to the State Institute of Health and Family Welfare, Uttar Pradesh and all those involved in the assiduous development of this CME module. I urge medical officials to leverage this scholarly resource to augment their capabilities and actively contribute to our collective endeavor to safeguarding the health of female patients.

(Brajesh Pathak)

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MESSAGE

Shri Mayankeshwar Sharan Singh
Hon'ble State Minister
Medical Health and Family Welfare
Department Government of Uttar Pradesh

It is with great pleasure that I extend my sincere greetings to all recipients of CME module tailored for medical officers, focusing on the women's health. In our ongoing commitment to the health and well-being of our nation, the State Institute of Health and Family Welfare, Uttar Pradesh, is proud to present this comprehensive resource.

The stressful life schedule of women is a clear challenge to their daily lifestyle. Psychosomatic discomfort poses a significant risk due to incorrect self-medication to improve menstrual complications and feel better, thus directly affecting personal and professional well-being.

By collecting relevant information in the field of abnormal menstruation of women, covering all domains such as screening, identification, referral and treatment of female patients, the module aims to be a working document that can be periodically reviewed and updated based on experience.

In lieu of the above the State Institute of Health & Family Welfare (SIHFW), has developed module on Continuing Medical Education (CME) on abnormal mensuration treatment and management for Medical Officers in Provincial Health & Medical Services in Uttar Pradesh. I hope that this module on CME is the first of many to come, that will aid our Medical Officers in knowledge up gradation on concurrent intervention practices.

I wish the director and the team at State Institute of Health and Family Welfare (SIHFW), Uttar Pradesh success in their endeavors of aiding an improved women's health service delivery system through such Continuing Medical Education on Abnormal Menstruation, Etiology and Diagnosis, Treatment and Management.

Shri Mayankeshwar Sharan Singh

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FOREWARD

Shri Partha Sarthi Sen Sharma, IAS
Principal Secretary
Department of Medical, Health and Family Welfare
Government of Uttar Pradesh

Continuing Medical Education (CME) module serves as a mechanism through which medical professionals can remain updated on the rapidly evolving practices in the field of medicine. Given the current COVID era, it has become increasingly important for medical officers to keep pace with the emerging modes of treatment and management, which are developed in response to feedback from the medical community.

Medical officers at the primary level encounter numerous challenges in managing conditions such as Gynecological problem, and other emergencies. Continuous knowledge and skill enhancement are required to effectively address these challenges. However, due to their responsibilities in managing healthcare centers and implementing government policies, medical officers have limited time to dedicate to learning.

To address and rectify this situation, the State Institute of Health & Family Welfare (SIHFW) in Uttar Pradesh has developed a CME module specifically focused on Abnormal Menstruation, Etiology and Diagnosis, Treatment and Management for Medical Officers in the Provincial Health & Medical Services. This module has been created in collaboration with subject matter experts.

The module provides a comprehensive overview of recent developments in screening, prevention, and advanced treatment for gynecologist problem, abnormal uterine bleeding and related emergencies. Its primary goal is to enhance the skills and knowledge of Medical Officers, ultimately leading to improved healthcare services for the general population.

I would like to extend my congratulations to State Institute of Health and Family Welfare, Uttar Pradesh and the other subject matter experts involved in the development of this comprehensive module. I hope that this CME module will shed light on the diagnosis, treatment and management of Abnormal Mensuration and contribute to better women's healthcare outcomes.

(Partha Sarthi Sen Sharma)

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MESSAGE

Dr. Brijesh Rathor

Director General
Medical Health and Family Welfare
Uttar Pradesh

Continuing Medical Education (CME) modules provide a means for healthcare professionals to stay abreast of the swiftly evolving practices in the field of Gynaecology. Particularly in the realm of the Abnormal Menstruation, Etiology and Diagnosis, Treatment and Management module, it has become increasingly essential for medical officers to stay updated on treatment methods and management approaches.

Medical officers operating at the primary healthcare level encounter numerous challenges in effectively handling cases involving mensural disorder. Ongoing acquisition of knowledge and skills is imperative to tackle these challenges. However, due to their responsibilities in managing healthcare facilities and implementing government policies, medical officers have limited time for further education and skill development.

To address and rectify this situation, the State Institute of Health & Family Welfare (SIHFW) in Uttar Pradesh has formulated a specialized CME module centred on the treatment of Abnormal Menstruation, Etiology and Diagnosis, Treatment and Management for Medical Officers in the Provincial Health & Medical Services in Uttar Pradesh. This CME module incorporates the latest advancements in the field and provides detailed guidance on essential management strategies for these conditions at the primary level. The aim is to facilitate early screening, detection, referrals, and treatment of women's patients.

I want to extend my congratulations to SIHFW team and the subject matter experts who played a role in creating this comprehensive module. I am hopeful that this CME module will shed light on the effective diagnosis and management of abnormal mensuration.

(Dr. Brijesh Rathor)

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MESSAGE

Dr. Shailesh Kumar Srivastava

Director General (Family Welfare)
Medical Health and Family Welfare
Uttar Pradesh

Abnormal Menstruation, Etiology and Diagnosis, Treatment and Management is very important in saving women's lives and mensural disorder. The reaching of an effected female patient to a center which has facilities for treatment of abnormal mensural disorder.

To meet the specific needs of Medical Officers in the Provincial Health & Medical Services of Uttar Pradesh, the State Institute of Health & Family Welfare (SIHFW) has designed an extensive Continuing Medical Education (CME) program centered on abnormal mensuration disorders and their management. This program encompasses the latest advancements in the field and offers detailed guidance on essential management approaches for these conditions at the primary level. The objective is to facilitate early screening, detection, referrals, and treatment of female patients.

Upon completion of this CME program, it is anticipated that Medical Officers in Uttar Pradesh will be able to elevate their service delivery through proficient screening, effective case management, appropriate referrals, and provision of treatment within their healthcare facilities. Consequently, communities will enjoy enhanced access to healthcare services, heightened female patient satisfaction, and improved overall population health. This CME program not only enriches clinical and technical proficiency but also reinforces the delivery of healthcare services, bridging the gap between theoretical knowledge and practical application in healthcare management.

We extend our warmest wishes to the SIHFW team and look forward to the release of many more customized CME modules in the times ahead.

(Dr. Shailesh Kumar Srivastava)

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MESSAGE

Dr. Narendra Agrawal

Director General-Training
Medical, Health and Family Welfare
Uttar Pradesh

The effective management of Abnormal Menstruation disorder treatment and management is pivotal in preserving lives and preventing serious women's health complications.

This module on Continuing Medical Education (CME) on abnormal mensuration disorders and their treatment for Medical Officers in Provincial Health & Medical Services in Uttar Pradesh provides a coherent and research-based insight to gynaecology management. It has been designed and written for Medical Officers and healthcare professionals and takes government perspective in consideration, drawing upon and comparing ideas and developments from national and international health care practices.

Medical Officers in Uttar Pradesh will be able to scale up the services delivery in provide screening, management, referral and treatment in gynocology care after this CME, thus benefitting communities. In addition to improving clinical and technical area of expertise, this CME will lead to providing improved access to abnormal mensuration disorder services and enhancing women's patient satisfaction and population health.

The director and the team at State Institute of Health & Family Welfare, Uttar Pradesh and the team of experts of the field has done a commendable job by publishing this CME module on abnormal mensuration disorders, diagnosis and management for Medical Officers in Provincial Health & Medical Services in Uttar Pradesh. I hope the participants coming to attend their upcoming CME will take advantage of this initiative and make the most in their field with this handy module.

(Dr. Narendra Agrawal)

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ACKNOWLEGMENT

Dr. Rajaganapathy R.
I.A.S
Director
State Institute of Health and Family Welfare
Uttar Pradesh

The primary objective of Continuing Medical Education (CME) is to ensure the perpetual learning and advancement of Medical Officers in order to deliver optimal medical care to their patients. The purpose of CME is to aid Medical Officers in augmenting their performance in terms of women's patient care and satisfaction.

In the realm of women's healthcare, there has been a notable effort to underscore the importance of effectively managing and treatment of abnormal mensuration among Medical Officers in Provincial Health & Medical Services. It has been observed that a lack of systematic management has led to numerous unfortunate outcomes. Therefore, there is a need for a customized CME program tailored to equip Medical Officers in Uttar Pradesh with exposure to the Abnormal Menstruation, Etiology and Diagnosis, Treatment and Management.

I hope that after this CME, Medical Officers in Uttar Pradesh will be able to scale up the services delivery in provide screening, management, referral and treatment in abnormal mensuration diagnosis, thereby benefitting the women's communities. In addition to improving clinical and technical area of expertise, this CME will lead to providing improved access to abnormal mensuration diagnosis and management services and enhance female patient satisfaction and population health.

To achieve this objective and enhance knowledge, the research and training faculty at the State Institute of Health and Family Welfare (SIHFW), Uttar Pradesh, in collaboration with the assistance of Professor and Head Dr. Smriti Agrawal, and their team, Department of Obstetrics & Gynecology, Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow, has contributed to the development of this CME module. It is expected that this module will be widely distributed, and feedback on its effectiveness will be gathered in the coming months.

(Dr. Rajaganapathy R.)

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CHAPTER 1

PHYSIOLOGY OF NORMAL MENSTRUATION

INTRODUCTION

Menstruation is normal discharge of blood and tissue from the uterine lining through the vagina that occurs as part of a woman‘s monthly menstrual cycle (NICHD).

The Menstrual cycle is the monthly process of changes that occur to prepare the body for possible pregnancy. A menstrual cycle is considered as the first day of menstrual bleeding of one cycle to the first day of menstrual bleeding of the next cycle (ACOG).

There is an orderly cyclic hormone production and parallel changes in the uterine lining preparing for implantation of the embryo. The finely tuned process is easily disturbed, leading to reproductive failure. It poses a significant clinical challenge for gynaecologists, underscoring the importance of comprehending the normal physiology of the menstrual cycle.

THE MENSTRUAL CYCLE

The normal menstrual cycle can be described from 2 aspects based on the organ under examination

A. Ovarian cycle- **1.** Follicular phase
2. Luteal phase
B. Uterine cycle- **1.** Proliferative
2. Secretory phase

OVARIAN CYLCLE

- By 20 weeks of gestation the number of follicles in the ovary of the fetus peaks at 6 to 7 million but simultaneously the follicular atresia also begins
- Only 1 to 2 million oocytes remain at birth
- By puberty only 300,000 oocytes are available for ovulation during the reproductive life
- Out of this a mere 300 to 400 oocytes are finally released during ovulation.
- Central dogma of reproductive biology- there is no potential for oocyte production in mammalian females after their birth.

DEVELOPMENT OF OOCYTE

- In the fetus the oogonia enter the prophase I of meiosis I and is arrested at the diplotene stage of prophase I to form the primary oocyte and remain so till ovulation begins after menarche.
- Mechanism of meiotic arrest- ovulation maturation inhibitor (OMI) produced by the granulosa cells
- LH surge disrupts the action of OMI and meiosis resumes at ovulation resulting in formation of the secondary oocyte

Note: oogonia and spermatogonia differ in the only a single final daughter cell is produced from each precursor cell in oogonia.

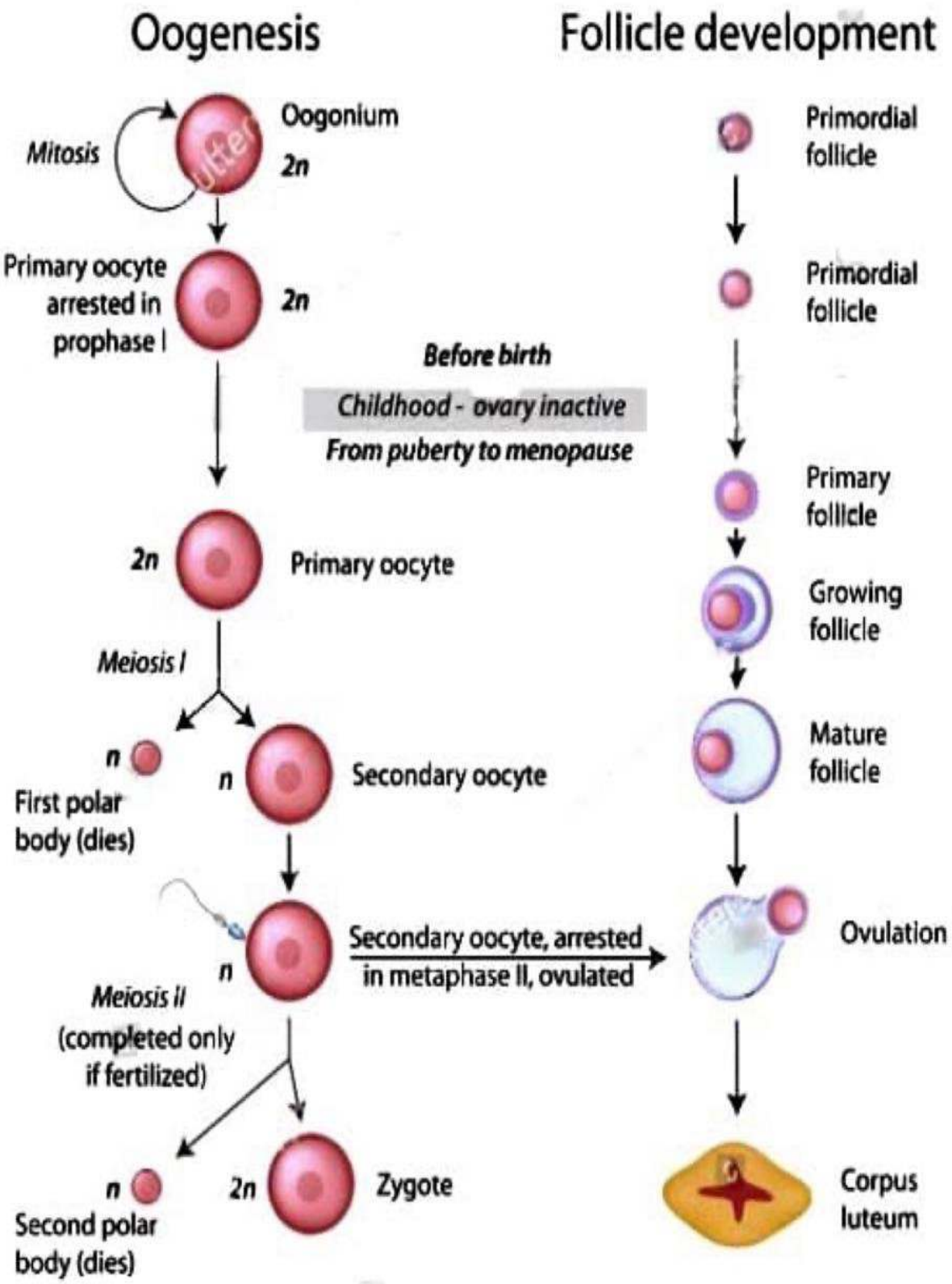

Fig: Development of oocyte and ovarian follicle

FOLLICULAR PHASE

- Follicular development begins at menarche and ceases at menopause.
- It allows for recruitment of a cohort of follicles out of which a single mature dominant follicle emerges and release the secondary oocyte during ovulation.

PRIMORDIAL FOLLICLE

- The primordial follicle contains the primary oocyte with a single layer of the follicular granulosa cells which later becomes multilayered
- The initial recruitment and development is gonadotropin independent.
- Further follicular development and maturation is controlled by increasing levels of FSH

PREANTRAL FOLLICLE

- A glycoprotein -rich layer, the zona pellucida is secreted by the enlarging oocyte which separates it from the surrounding granulosa cells
- The adjacent stroma give rise to the theca cells surrounding the granulosa cells

PREOVULATORY FOLLICLE

- It contains a fluid filled antrum
- The oocyte is connected to the rest of the follicle by cumulus oophorus -stalk made of specialised granulosa cells
- The rising levels of estrogen produced by the granulosa cells has negative feedback on FSH - fall in FSH levels
- Estrogen has a biphasic action on LH production
    - Lower levels lead to inhibition of LH secretion
    - Sustained high levels(200pg/ml) for more than 48 hours enhance production and LH surge

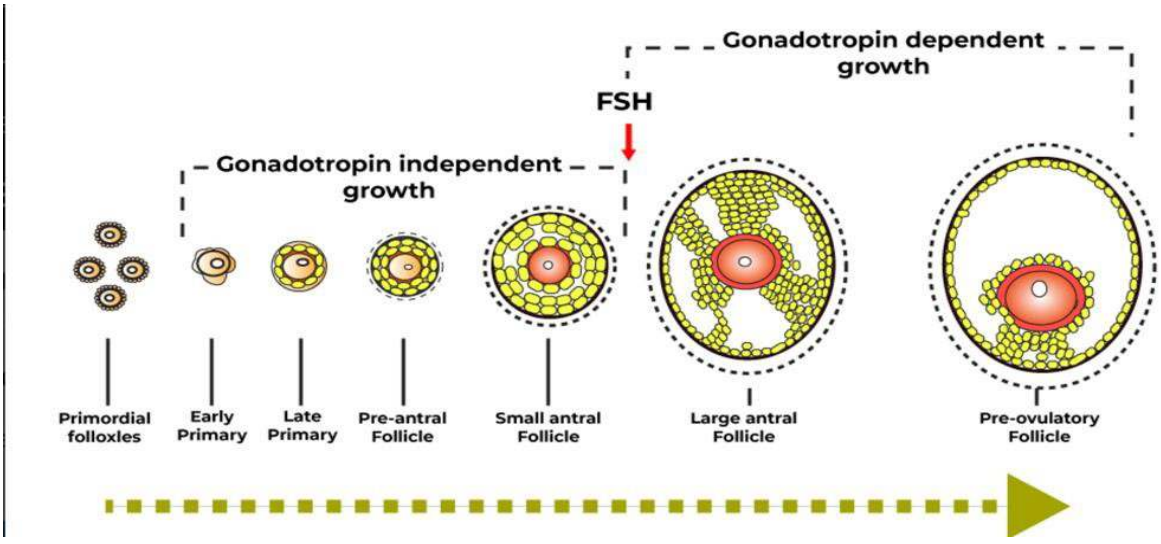

Fig: Hormonal control of development of oocyte

OVULATION

During LH surge there is dramatic increase in local concentrations of prostaglandin and proteolytic enzymes in the follicular wall weakens and there is subsequent perforation and slow release of oocyte.

It occurs in the single mature / Graafian follicle 10 to 12 hours after peak of LH surge or 24 to 36 hours of initial midcycle rise of LH.

LUTEAL PHASE

- Begins from the time of ovulation till onset of menses.

Structure of corpus luteum

- The follicular shell left after ovulation transforms into corpus luteum-the primary regulator of luteal phase
- The granulosa cells take up lipids and lutein pigment which gives the characteristic yellow colour
- In addition to progesterone production, corpus luteum produces significant quantities of estrogen and inhibin A
- The sustenance of corpus luteum requires continued LH production
- In the absence of which it invariably regresses within 12 to16 days and form corpora albicans (scar like)
- The corpus luteum regresses in the absence of pregnancy and estrogen and progesterone levels falls resulting in lifting the central inhibition on gonadotropins and allows the rise in levels of FSH and LH to recruits a new cohort of follicles.

Luteal-placental shift

- In case pregnancy occurs the placental human chorionic gonadotropin (hCG) mimics LH action and continue to stimulate the corpus luteum
- Luteal function is essential up to 5 weeks gestation for maintenance of pregnancy, when sufficient progesterone is produced by the placenta and it takes over.

UTERINE CYCLE

- The endometrium undergoes specific anatomic and functional changes within glandular, vascular, and stromal components in association with the ovulatory cycle.

MORPHOLOGY OF ENDOMETRIUM

―Functionalis‖ layer/ Decidua functionalis - superficial two-third -composed of the deeper intermediate zone (stratum spongiosum) and superficial compact zone (stratum compactum)

- Prepare for implantation of the blastocyst
- Site of proliferation, secretion, and degeneration
- Ultimately shed during menses

Basalis layer/decidua basalis –deepest one-third

- Site of endometrial regeneration after each menses

Endometrial stem cells

Endometrial epithelial stem cells are found in glands within the basalis layer

Endometrial mesenchymal stem cells/are found around the blood vessels in the basalis layer

They are thought to be responsible for reepithelization and subsequent glandular proliferation to regenerate the functionalis layer under the influence of estrogen

UTERINE VASCULATURE

The two uterine arteries branch off from the anterior division of the internal iliac arteries.

Uterine arteries divide in arcuate arteries which run parallel to the uterine cavity and anastomose with each other.

Radial arteries branch off from the arcuate arteries and run perpendicular to the cavity to supply the myometrium.

At the endometrium the radial arteries branch off laterally into small basal arteries supplying the basalis layer.

The radial arteries continue towards the endometrium forming corkscrew appearing vessel called spiral arteries supplying the functionalis layer.

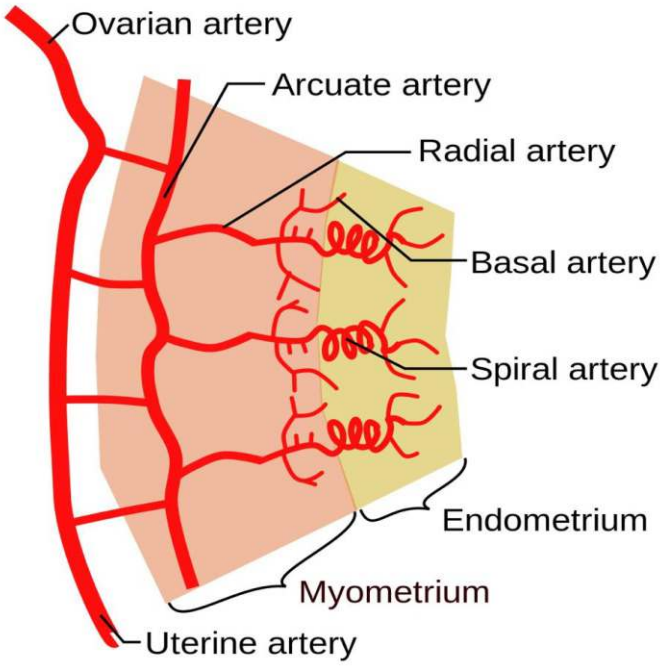

Fig.: Uterine vasculature

- Basal arteries are not responsive to hormonal changes
- Spiral arteries (end arteries) are highly sensitive to the hormonal changes and ischaemia

The uterine cycle maybe be divided into 5 phases:

1. Menstrual endometrium
2. Proliferative phase
3. Secretory phase
4. Preparation for implantation
5. Phase of endometrial breakdown

However, the cycle is an integrated process of growth and regression that occurs approximately 400 times during the reproductive life of the human female.

MENSTRUAL ENDOMETRIUM

- The day 1 of the menstrual cycle correspond to the first day of vaginal bleeding by convention.
- It is composed of thin layer of decidua basalis with primordial glands and dense scant stroma of the residual stratum spongiosum
- It is the transitional state between the proliferative and the exfoliative phases of the cycle
- The entire uterine cavity is re-epithelised by days 5-6 and then the stromal growth begins

PROLIFERATIVE PHASE

- There is progressive mitotic growth of the decidua functionalis
- It is associated with ovarian follicular growth and increased estrogen production
- It peaks on days 8-10 of the cycle
- The glands, stroma and the endothelial cells demonstrate proliferation
- The endometrium grows from 0.5mm to 3.5 to 6mm in height
- Trilaminar appearance

SECRETORY PHASE

- It is the postovulatory phase where the endometrium shows a combined reaction to estrogen and progesterone
- It begins 48 to 72 hours after ovulation where there is progesterone induced histologic changes
- The term secretory comes from the presence of eosinophilic protein-rich secretions in the glandular lumen
- Progesterone receptor expression is upregulated by the rising estrogen levels during the proliferative phase (ER-a), whereas the estrogen receptor expression is inhibited by progesterone resulting in reduced DNA synthesis and cellular growth.

Table: Proliferative and secretory phase of menstrual cycle

Components	Proliferative phase	Secretory phase
Glands	Initially straight, narrow, and short evolve into longer tortuous structures Histology-glands have multiple mitotic cells and change from low columnar in the early period to pseudostratified before ovulation.	Glands form the characteristic PAS-positive glycogen containing vacuoles which are finally secreted into glandular lumen On Postovulatory day 6 or 7 there is maximum secretory activity and receptivity for implantation
Stroma	Dense and compact	There is progressive increase in stromal oedema around postovulatory day 7 Histology -eosinophilic staining pattern in the perivascular stroma know as Cuffing There is a dramatic leucocytic infiltration approximately 2 days before menses heralding the collapse of the endometrial stroma and the onset of menstrual flow
Vascular structures	Infrequently seen	Spiral arteries progressively lengthen and coil and become prominent
Predominant hormone	Estrogen	Progesterone

PHASE OF IMPLANTATION

- Postovulatory days 7 to 13(day 21-27 of cycle)
- Endometrium differentiated into three distinct zones-basalis layer (lower 25%), stratum spongiosum (middle 50%) and superficial stratum compactum (upper 25 %)
- Histologic feature-endometrial stromal oedema-known as pseudo decidual -mimics decidua of pregnancy

PHASE OF ENDOMETRIAL BREAKDOWN

In the absence of fertilisation and implantation (no hCG production by trophoblast) corpus luteum regresses and estrogen and progesterone levels fall resulting in menstruation.

The withdrawal of estrogen and progesterone initiates-

- vasomotor reactions-profound spiral artery vascular spam -endometrial ischaemia
- the process of apoptosis and tissue loss- breakdown of lysosome and release of proteolytic enzymes

Prostaglandins are produced during the entire menstrual cycle reach their peak levels during menses and cause

- Arterial vasospasm and ischaemia
- Myometrial contractions that reduce local uterine wall blood flow and help to physically expel the sloughing endometrium from the uterus

HORMONAL VARIATION DURING MENSTRUAL CYCLE

- Beginning of the menstrual cycle there is low levels of gonadal steroids
- FSH begins to rise with the cohort of growing follicles recruited
- Follicles secrete estrogen which stimulates endometrial proliferation
- Mid-point of the follicular phase, the rising estrogen and inhibin B (produced by the proliferating granulosa cells) inhibit pituitary FSH production.
- Late in follicular phase, high estrogen levels stimulate LH secretion (biphasic response)
- Before ovulation, FSH-induced LH receptors are present on granulosa cells. Estrogenic stimulation triggers pituitary LH surge causes ovulation 24 to 36 hours later.
- Ovulation heralds the transition to the luteal-secretory phase
- In the early luteal phase, estrogen levels decrease whereas in the mid luteal phase Estrogen and inhibin A increases (produced by corpus luteum).
- Progesterone levels rise precipitously after ovulation: presumptive sign of ovulation
- Progesterone, estrogen, and inhibin A
    - Act centrally to supress the gonadotropin secretion and new follicular growth
    - Remain elevated through the lifespan of the corpus luteum and wane with its demise

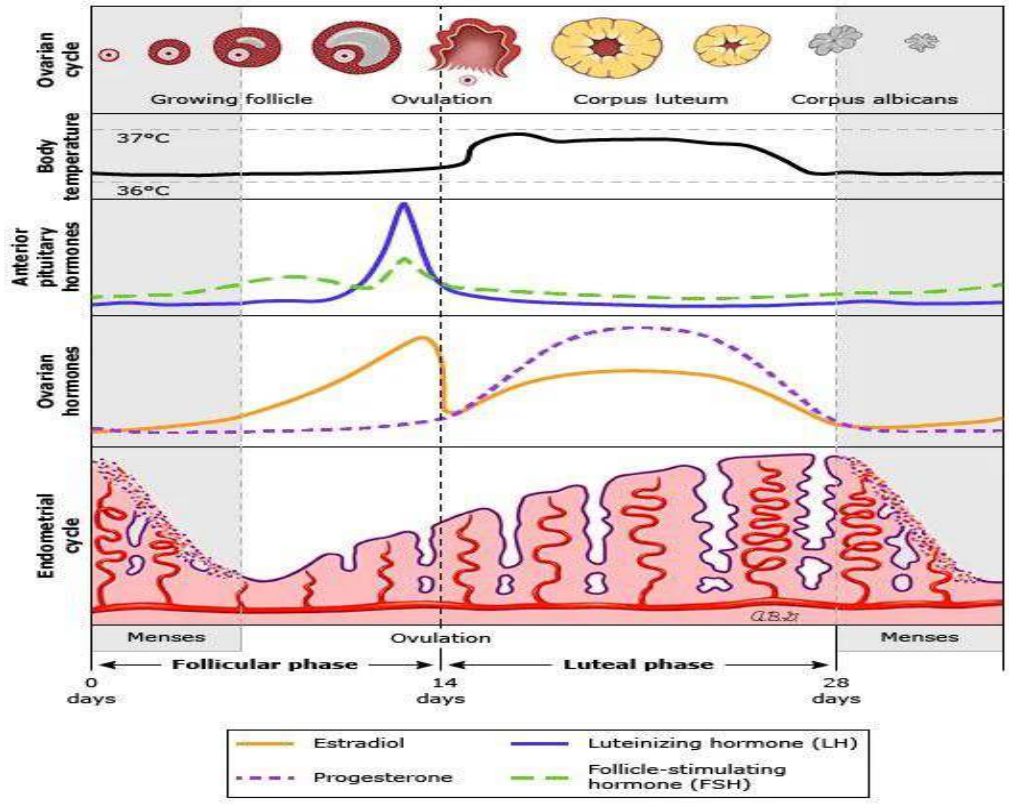

Fig: *Phase of Menstrual Cycle*

NORMAL MENSES

In the first 24 hours of menstrual flow, 50% of the menstrual debris is expelled.
Menstrual fluid composition-
Autolysed functionalis, inflammatory exudate, RBCs, and proteolytic enzymes
(One such enzyme -plasmin lyses the fibrin clots-prevents menstrual blood from clotting.)

PARAMETER	NORMAL	ABNORMAL
Frequency	Absent (no bleeding) =amenorrhea	
	Infrequent (>38 days)	
	Normal (>/= 24 to</=38 days)	
	Frequent (<24 days)	
Duration	Normal</=8 days	
	Prolonged (>8 days)	
Regularity	Normal or ―regular‖ (shortest to longest cycle variation:</= 7-9 days*)	
	Irregular (shortest to longest cycle variation: >/=8 -10 days)	
Flow volume (patient determined)	Light	
	Normal	
	Heavy	
Intermenstrual bleeding (IMB) Bleeding between cyclically regular onset of menses	None	
	Random	
	Cyclic(predictable)	Early cycle
		Mid cycle
		Late cycle
Unscheduled bleeding on Progestin+- estrogen gonadal steroids (birth control pills, rings, patches, or injections)	Not applicable (not on gonadal steroid medication)	
	None (on gonadal steroid medication)	
	Present	

Fig: FIGO AUB system 1

*Normal range (shortest to longest) varies with age: 18 -25 y of age, </=9 days; 26-41y of age, </=7 days; 42-45y, </=9 days.

PBAC

It is also desirable to use objective method of assessing blood loss (Fig. 1).

PADS	DAY							
	1	2	3	4	5	6	7	8
								
								
								
TAMPONS	**DAY**							
	1	2	3	4	5	6	7	8
								
								
								

Figure: PBAC, Pictorial Blood Loss Assessment Chart (Woman fills on the Chart how many Pads/tampons she uses each day and to which degree they are soiled. A score is calculated by multiplying by factor of 1 for lightly soiled, 5 for medium soiled and 10 for totally soiled items)

PBAC score is calculated by adding all the score, PBAC score>100 is considered as menorrhagia.

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CHAPTER 2

CAUSES AND DIFFERENTIAL DIAGNOSIS OF AUB

Abnormal uterine bleeding has varied etiology which differs with the age of the patient. It is usually common at the extremes of age, the time of menarche and attainment of menopause, though the reproductive age group may also be affected by AUB.

PALM-COEIN is an acronym provided by the International Federation of Obstetrics and Gynaecology (FIGO) to classify the etiologies of AUB. PALM describes structural causes while COEIN is for non-structural issues.

P – Polyp

A – Adenomyosis

L – Leiomyoma

M – Malignancy and hyperplasia

C – Coagulopathy

O – Ovulatory dysfunction

E – Endometrial disorders

I – Iatrogenic

N – Not otherwise classified

One or more of the above may co-exist and contribute to AUB.

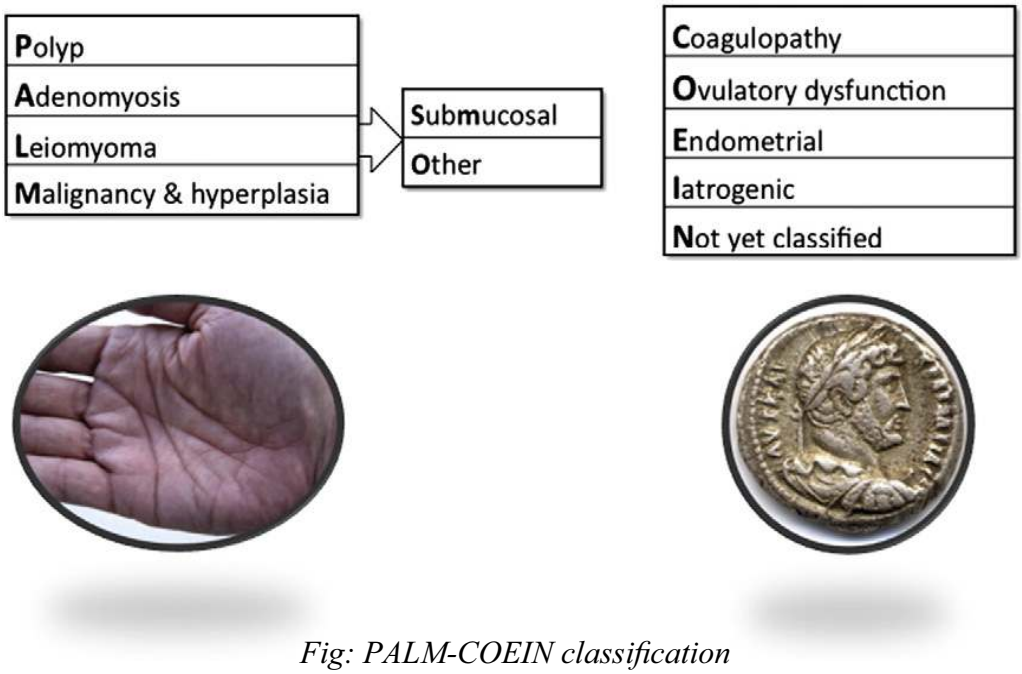

Fig: PALM-COEIN classification

In the years following attainment of menarche, AUB may occur for a few months or years due to anovulatory cycles. Same is the case at the time of menopause when ovulation becomes infrequent or ceases. These cycles tend to be prolonged and heavy following varied periods of amenorrhoea. Coagulopathies like Idiopathic Thrombocytopenic Purpura and deficiency of von Willebrand factor and others may also present as AUB at menarche.

Iatrogenic factors tend to be more common in the **perimenopausal group** due to use of intrauterine devices, exogenous hormone use for various reasons or endogenous production from ovarian/ adrenal tumors resulting in endometrial hyperplasia. Anticoagulants used for medical reasons may affecting coagulation profile. Vulvovaginal causes and cervical factors (polyp, ectropion, dysplasia and malignancy) are also common in perimenopausal AUB.

In the **reproductive age group**, the causes of AUB are more well defined. Pregnancy should be ruled out at first in any female of reproductive years presenting with heavy or irregular bleeding. The structural causes implicated in AUB are polyps which may be cervical or uterine arising from the endometrium; adenomyosis, which is diagnosed by characteristic symptoms of heavy painful bleeding with tender and enlarged uterus and confirmed on imaging; fibroids, more commonly submucosal or large fibroids presenting at the cervical os, intramural fibroids abutting the endometrium or causing distortion of the cavity and rarely also large sub-serosal fibroids due to various mechanisms; endometrial hyperplasia which may occur due to estrogen excess in the body or from an exogenous source and may progress to endometrial carcinoma. All these are structural causes resulting in abnormal uterine bleeding which can be diagnosed either by imaging and/or histopathological examination of tissue.

The other causes of AUB in reproductive age group are the non-structural including coagulopathies (inherited/ acquired); ovulatory dysfunction which heralds irregular bleeding following amenorrhoea; endometrial causes, and iatrogenic factors including use of hormones and intrauterine devices. Iatrogenic causes also include use of anticoagulants and medicines altering dopamine metabolism like antidepressants which cause AUB. Pelvic inflammatory disease, cervicitis and chronic liver conditions, arterio-venous malformations, myometrial hyperplasia, endometritis and lower segment cervical niche ―isthmocele‖ associated with previous cesarean section are included in ―not otherwise classified‖ causes of AUB.

Differential diagnosis of AUB

Complications of pregnancy	Abortions, ectopic pregnancy, placenta previa
Pelvic causes	Pelvic inflammatory disease, Tubo-ovarian mass, malignancy, hematosalpinx, endometriosis, Ovarian tumours
Genital tract causes	Benign growths, sexually transmitted infections, vaginitis, malignancy, trauma, foreign bodies
Urinary tract causes	Infections, malignancy, hematuria
Gastrointestinal tract causes	Inflammatory bowel disease, Behçet syndrome

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CHAPTER 3

POLYP

Polyps are polypoidal outgrowths of endometrium comprising of mucosal layer of endometrium with fibrovascular core.

- May be solitary or multiple, varying in size from a few millimeters to centimeters and may be sessile or pedunculated.
- Common in reproductive age group (estrogen dependent), incidence of polyps ranges from 7.8 to 34.9% of women and increases with age.
- Also occur with Tamoxifen use and cases of Infertility or recurrent pregnancy loss.
- Most polyps are asymptomatic and may be incidentally diagnosed on imaging done for other problems.
- Present as AUB in the form of heavy menstrual bleeding or irregular intermenstrual bleeding in up to 67% of premenopausal women with endometrial polyps.
- Usually restricted to endometrial cavity but sometimes may be large enough to protrude through cervical os.

CLINICAL FEATURES

- Young women of reproductive age group
- Heavy bleeding during menses
- Intermenstrual bleeding at irregular intervals
- Previous unsuccessful AUB treatment
- Large polyps may be visible at the os during speculum examination

DIAGNOSIS

- In all women presenting with AUB, during internal examination, evaluation for structural abnormalities like polyps affecting the endometrial cavity is performed to identify pathology.
- Transvaginal ultrasonography (TVUS) is an appropriate and important screening tool and, in most instances, should be performed early in course of the investigation.
- TVUS is not 100% sensitive even in ideal circumstances because polyps and other small lesions may elude detection, even in the context of a normal study.
- If there are imaging features that indicate the presence of endometrial polyp(s), if there are leiomyomas that may encroach on the endometrial cavity, or if the examination is suboptimal, imaging with more sensitive techniques is recommended
- Doppler may be useful in identifying feeding vessel.
- Hysteroscopy and/or transvaginal ultrasonography with intrauterine contrast, either gel or saline ―sonohysterography‖ is helpful.
- When office hysteroscopy is available particularly when polyps are suspected, hysteroscopy directed polypectomy will be feasible in the same setting: see and treat approach.

MANAGEMENT

- Gonadotropin-releasing hormone agonists, progestins can be prescribed to relieve symptoms of polyp. These drugs are useful for short period.
- Hysteroscopic polypectomy, which can be done at the same setting with office hysteroscopy.
- Histopathological examination of endometrial tissue to establish the diagnosis of endometrial polyp and rule out hyperplasia and malignancy specially in elderly females.

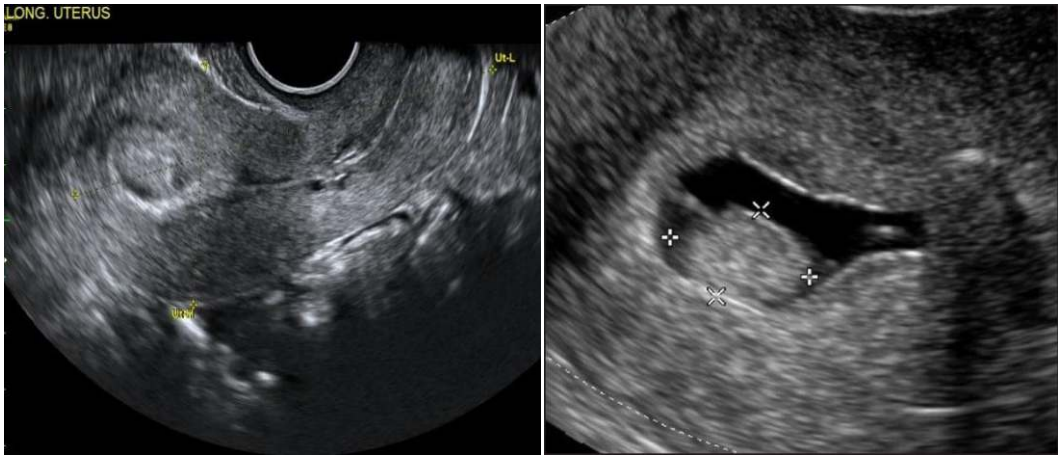

Fig: ultrasound image of endometrial polyp

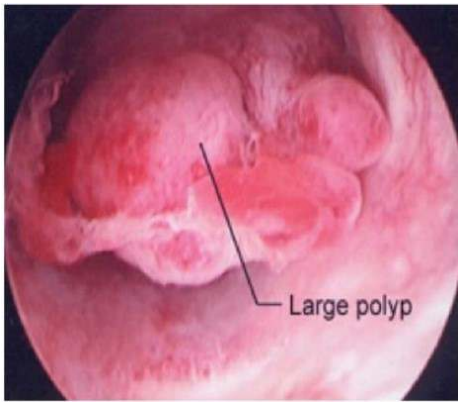

Fig:Hysterscopic image of endometrial polyp

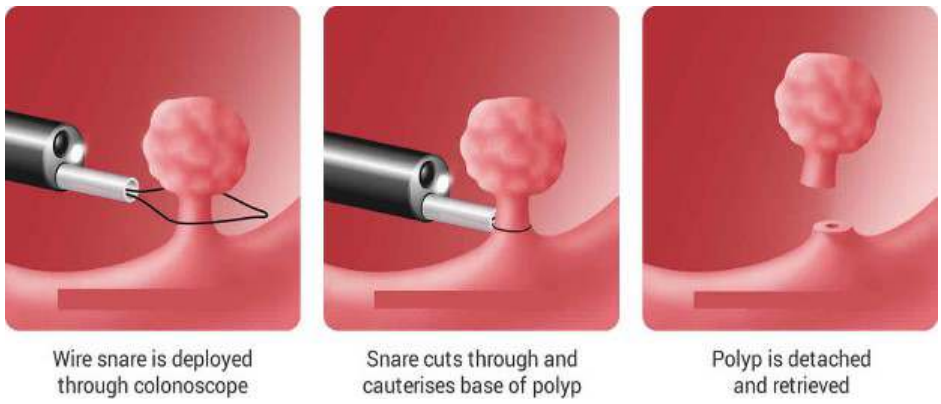

Fig: Hysteroscopic polypectomy

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CHAPTER 4

LEIOMYOMA

- Leiomyoma/ fibroid is the most common tumour of the female pelvis.
- An estimated 70% of women up to menopause develop fibroids and 25% of them are symptomatic requiring treatment.
- Leiomyoma is the leading gynaecological cause for hysterectomy and healthcare expenditure.
- These are estrogen dependent and occur in the reproductive age group.
- The common age of presentation is 35 to 45 years.
- Leiomyoma is a frequent cause of AUB especially when submucous in location.
- Though usually benign, rarely, sarcomatous changes may occur.

ETIOLOGY

- Exact etiology for leiomyomas is not known.
- Genetic basis is defined for these monoclonal tumours.
- Familial occurrence common.

RISK FACTORS

- High incidence in nullipara or women with low parity.
- The incidence is higher in women with a family history (leiomyoma history in mother or sister)
- Early menarche
- Obesity
- Presence of diabetes and hypertension.

FACTORS WHICH REDUCE THE RISK OF LEIOMYOMAS

- High parity
- Exercise
- Use of progesterone only contraceptives
- Intake of green vegetables.

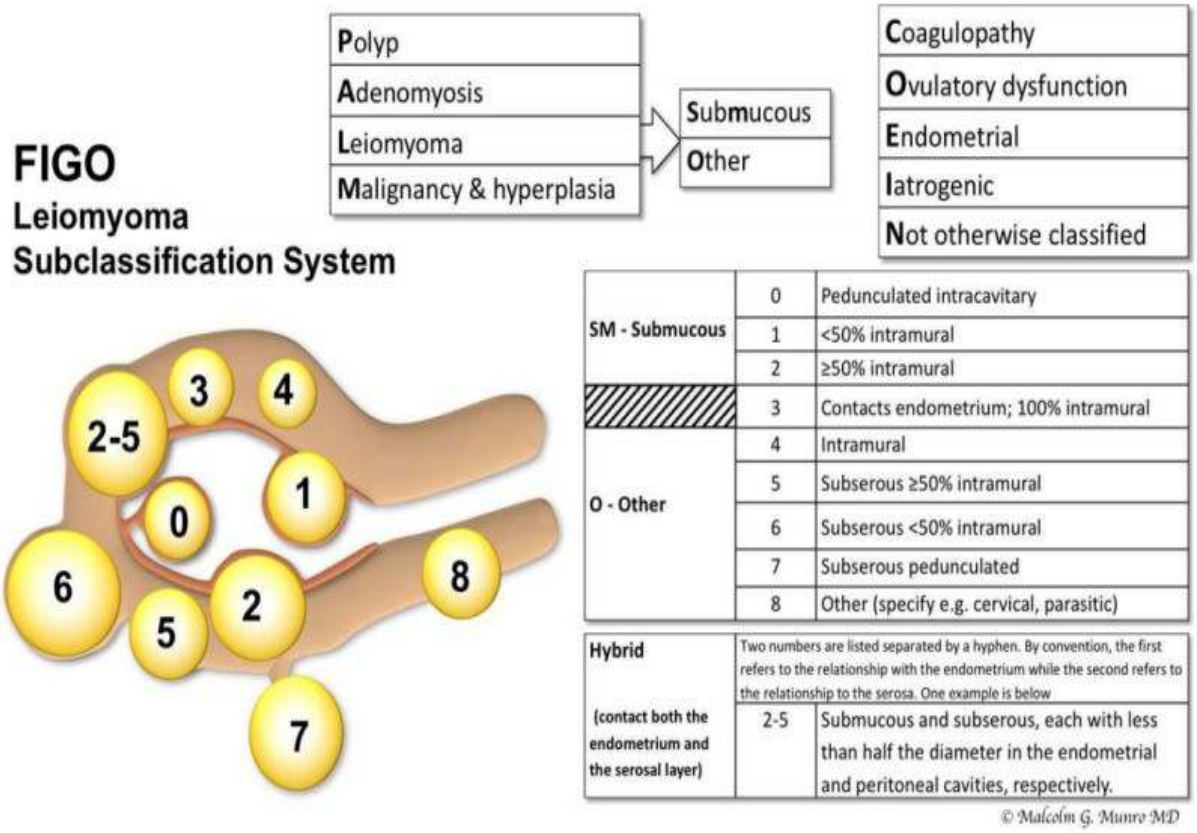

Figure: FIGO Leiomyoma Subclassification System

TYPES

- All leiomyomas are interstitial to begin with and then enlarge to remain intramural or become subserosal or submucosal in location.
- Located mostly in uterine corpus, less common in cervix, rarely in broad ligament and round ligament.
- Submucous fibroid may become pedunculated and present in the vagina through the cervix.
- Large submucous fibroid may pull down the cervix resulting in chronic inversion.
- Subserosal Leiomyomas may become pedunculated and occasionally parasitic receiving blood from other organs usually omentum.

For the primary leiomyoma categorization, the myometrium is assessed primarily with a combination of TVUS and transabdominal ultrasonography to identify leiomyomas, with any such identified lesion leading to an ―L‖ assignment.

For the secondary subclassification, it is necessary to determine the relationship (contact or not) of the endometrium with the leiomyoma by performing some combination of TVUS, contrast sonohysterography, hysteroscopy, and MRI. Should one or more submucous leiomyomas be found (Types 0, 1, 2, or 3) then the woman is stated to have LSM, if only Type 4, 5, 6, 7, and/or 8 are identified, the categorization is Lo.

Tertiary subclassification of leiomyoma type requires that the relationship of the leiomyomas with the endometrium, endometrial cavity, myometrium, and uterine serosa is clarified. At least for those leiomyomas that do not distort the endometrial cavity (Types 3 and above), this distinction requires the use of imaging, either ultrasonography, or, more accurately MRI.

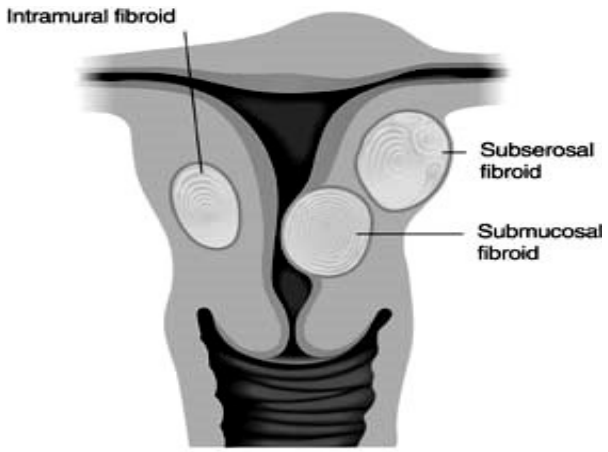

Fig: Types of Fibroid

CLINICAL FEATURES

Most leiomyomas are asymptomatic. Around 20-50% women experience symptoms attributable to leiomyomas. These may affect overall wellbeing and quality of life. Leiomyomas may be diagnosed during evaluation for symptoms or work-up for infertility, or these may be incidental finding in women presenting with other / non-specific complaints.

On examination, leiomyomas distort and enlarge the uterus, uterus may be enlarged enough to be palpable per abdominally.

ABNORMAL UTERINE BLEEDING

- Patients with large leiomyomas may have history of normal bleeding.
- AUB is more common with submucosal leiomyomas. May occur with intramural and subserosal leiomyomas also.
- Intramural leiomyomas near serosal surface or pedunculated subserous tumours when associated with AUB should be investigated for other underlying causes.
- Postmenopausal bleeding with leiomyoma needs to be investigated for cervical, vaginal or endometrial causes of bleeding.
- Anaemia is common in women with heavy menstrual bleeding.
- A rare but serious presentation is acute, life threatening haemorrhage requiring urgent hospitalization and management along with blood transfusion.

ETIOLOGY OF AUB IN LEIOMYOMA

- It is due to increased surface area, increase in vascularity, thinning and ulceration of overlying endometrium and venous obstruction.

- Associated local hyperestrogenism may causes endometrial hyperplasia and polyps.
- Leiomyomas interfere with myometrial contractility and contraction of spiral arterioles in basal portion of endometrium.
- Associated anovulation may co-exist and contribute to abnormal bleeding.
- Postmenopausal leiomyomas may cause bleeding if it shrinks less compared with surrounding myometrium.

PAIN

- Abdominal or pelvic, pain or discomfort
- Dyspareunia may be present in 1/3rd cases
- Acute abdomen – twisting of pedunculated subserous leiomyoma (more during pregnancy and after menopause)
- Acute pain due to torsion, infection, expulsion, red degeneration, vascular complication
- Acute carneous/ red degeneration – more common during pregnancy
- Dysmenorrhoea – Spasmodic and congestive in nature.
- Concomitant pelvic disease may cause pain in 1/3rd patients
- Lower backache may be present.

PRESSURE

- Symptoms due to pressure on nearby viscera
- Urinary bladder – urgency, frequency, incontinence
- Compression of urethra and bladder neck against pubic bone – difficulty in emptyi ng bladder, rarely acute retention of urine or overflow incontinence
- Size of uterus >12 weeks gravid uterus, large pedunculated submucous tumours becomes incarcerated in POD and causes wedging of cervix against urethra obstructing flow of urine
- Silent ureteral obstruction due to pressure by enlarged uterus against the pelvic brim leading to hydronephrosis and chronic kidney disease followed by uremia in prolonged neglected cases.
- Chronic bladder neck obstruction causes increase in bladder wall thickness
- Bowel effects – Constipation due to pressure against the rectum
- Rarely, intermittent intestinal obstruction due to subserous pedunculated fibroid becoming entwined with small bowel
- Rapid growth with pregnancy and malignancy

INFERTILITY

- 2 to 10 % incidence with leiomyomas
- Submucosal and intracavitary leiomyomas associated with decreased implantation and clinical pregnancy rates, improves with removal of these leiomyomas.
- Anovulatory, irregular cavity interfering with sperm transport, endometrial changes are common causes
- Proximity of fibroid to the endometrial cavity affects pregnancy rates though more research required to establish association.

PREGNANCY COMPLICATIONS

- Recurrent pregnancy loss with submucous fibroids and those which distort cavity
- Foetal growth restriction
- Malpresentations
- Abruption
- Still births
- Prelabour rupture of membranes
- Labour dystocia and uterine inertia
- Red degeneration in 2nd trimester – due to rapid growth there is central necrosis with interstitial haemorrhage and venous thrombosis
- Increased operative interference
- Entrapment of placenta with increases chances of manual removal
- Postpartum haemorrhage due to interference with uterine contraction
- Puerperium – Uterine subinvolution, Secondary Postpartum haemorrhage, Puerperal sepsis, Inversion

RARE

- Rupture of subserous vein may lead to internal haemorrhage
- Ascites
- Uterine inversion
- Polycythaemia

DIAGNOSIS

- Suspicion on clinical history or physical examination.
- Ultrasonography, transabdominal and transvaginal is most commonly used for evaluation due to low cost and availability to confirm presence, location, number and size of leiomyoma (mapping).
- Transvaginal ultrasonography has detection rate of 65 to 99%.
- On ultrasonography – Well defined hypoechoic lesions with peripheral calcification and distal shadowing in old fibroids is seen.
- Sonohysterography has advantages of delineating and differentiating submucosal and intramural fibroids from polyps.
- MRI is better for leiomyoma mapping specially in large uterus with small, multiple lesions, help in differentiating leiomyomas from adenomyosis, leiomyosarcomas and adnexal pathology, also useful in identifying degenerative changes.
- Also diagnosed on hysterosalpingography, hysteroscopy and laparoscopy.

MANAGEMENT

Expectant management is advocated in asymptomatic incidental leiomyomas satisfying the following criteria:

- Size of the uterus is < 12 weeks
- Women nearing menopause

- Agree to regular follow up every 6 months with pelvic examination
- Baseline imaging to compare regression is available

MEDICAL MANAGEMENT

- Not a definitive treatment
- Treatment will depend on nature and severity of symptoms, the size, location, and multiplicity of myomas and desire for fertility.
- Also useful to decrease menstrual blood loss
- May be used preoperatively to decrease the size as adjuvant therapy
- For symptomatic relief from pain and bleeding – Nonsteroidal anti-inflammatory drugs and tranexamic acid. Nonsteroidal anti-inflammatory drugs (NSAIDs): Mefenamic acid 150–600 mg taken daily started with onset of bleeding and given for 3–5 days. Tranexamic acid tab 500 mg 3 times a day for 4–7 days during menses. It is contraindicated in patients with history of thromboembolism.
- Danazol administered daily in divided doses ranging from 200 to 400 mg for 3 months minimizes blood loss or even produce amenorrhea by its antigonadotropin and androgen agonist actions. It reduces the size of the tumour by 60%.
- Progestogens, antiprogestogens (Mifepristone) and GnRH analogues are used.

GnRH ANALOGUES

- Approved for management of leiomyomas
- Cause decrease in size of myoma by 20 to 50 %
- Help in reducing bleeding preoperatively with increases in Haemoglobin levels and reduced requirement for blood transfusions
- Decreases blood loss during surgery
- Hysterectomy may be avoided and myomectomy may be possible with conservation of uterus.
- Hysteroscopic resection may be possible with shrinking in size of fibroid on use.
- Disadvantages are high cost, hypoestrogenic side effects leading to medical menopause which is reversible on discontinuation.
- Rarely there is increase in bleeding due to degeneration and enucleation of leiomyoma may be difficult due to loss of tissue plane.
- GnRH agonists (leuprolide, buserelin, narfereline) can be used as injections, nasal spray, or implants. Injection leuprolide 3.75 mg monthly IM/SC for a period of three or six months.
- Buserelin injection SC/nasal spray 200–300 µg daily. They shrink the volume and vascularity by 50 to 80%. There is increase in size of the fibroid after stoppage of the drug. Narfereline 200 µg intranasally daily for 6 months.
- GnRH antagonists (degarelix, ganirelix, cetrorelix)— depot cetrorelix shows quick response.

SELECTIVE ESTROGEN RECEPTOR MODULATORS

- Raloxifene 60 mg /day is tried for 6 to 12 months.
- Higher doses (180 mg) are required for effective decrease in size.

SELECTIVE PROGESTERONE RECEPTOR MODULATORS

- Mifepristone 5 – 25 mg is used continuously for 3 months
- Decrease in myoma volume by 26-74 %.
- No effect on bone density
- With long-term therapy it causes endometrial hyperplasia so it is to be avoided.
- Asoprisnil: It is selective progesterone receptor modulator. There is no endometrial hyperplasia with this treatment

AROMATASE INHIBITORS

- Directly inhibit estrogen synthesis and rapidly produce hypoestrogenic state.
- Fadrozole/ Letrozole is tried in couple of studies
- 71 % reduction occurred in 8 weeks
- Appears to be promising therapy.

PROGESTERONE RELEASING INTRAUTERINE DEVICE

- Progesterone releasing IUD – Levonorgestrel Intrauterine System
- Used in leiomyoma with uterus <12 weeks size with menorrhagia
- However, expulsion rates higher in presence of leiomyomas especially submucosal.
- Contains Progesterone Levonorgestrel 52 mg releasing 20 ug /day
- Leiomyoma decreases in size over 6 – 12 months of use.
- May have variable effects on uterine myomas depending upon balance of growth factors
- Suitable for those who also desire contraception

SURGICAL MANAGEMENT

MYOMECTOMY

- Performed during hysteroscopy, abdominally or vaginally
- Myomectomy is done in leiomyomas with heavy abnormal uterine bleeding, leiomyoma with pain or pressure symptoms, Infertility, Recurrent pregnancy loss with no other identifiable cause in young patients where preservation of uterus is desirable
- Hysteroscopic myomectomy - < 5 cm in size, < 50 % intramural component, < 12 cm uterine size
- Suspicion of malignancy, infection and excessive mural component contraindicates surgery
- Advantages are short procedure, rapid recovery & all disadvantages of laparotomy avoided
- Large fibroids can be morcellated prior to removal

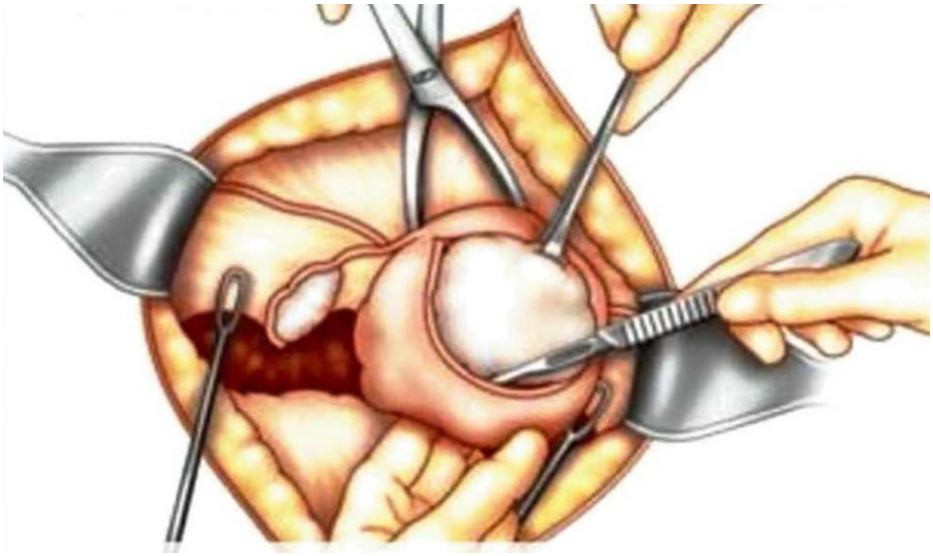

Fig: Myomectomy

LAPAROSCOPIC MYOMECTOMY

- Suitable for subserous and intramural leiomyoma up to 10 cm size
- Fibroid excised are removed by electronic morcellators or through posterior colpotomy incision vaginally.

ABDOMINAL / OPEN MYOMECTOMY

- Using minimum uterine incisions preferably single midline vertical, lower Segment, anterior wall removal of as many fibroids as possible through one incision and secondary tunnelling incisions
- Meticulous closure of all dead space
- Proper haemostasis
- Multiple small fibroids can be removed enbloc by wedge resection
- Measures for adhesion prevention should be taken
- Medical or mechanical means to control blood loss → Bonney‘s myomectomy clamp, rubber tourniquet, manual pressure at isthmic region or use of vasopressin 10 – 20 units diluted in 100ml saline infiltrated before the incision.
- Bonney‘s hood – for posterior large fundal fibroid transverse fundal incision posterior to tubal insertion and after enucleation uterine wall is sutured anteriorly covering the fundus as a hood.
- Complications of myomectomy: haemorrhage and infection.

VAGINAL MYOMECTOMY

- Submucous pedunculated or small sessile cervical fibroids are removed vaginally.
- Ligation of pedicle is done if accessible
- Twisting off the fibroids if pedicle not accessible in case of small & me dium size fibroids
- To gain access to pedicle of large leiomyomas high up in uterine cavity, incision on the cervix facilitates procedure.

LAPAROSCOPIC MYOLYSIS

- Using ND-YAG laser or long bipolar needle electrode through laparoscopic approach, blood supply of myoma is coagulated.
- Leiomyoma atrophies following the procedure.
- Applicable to small leiomyomas, 3 -10 cm size < 4 in number.

UTERINE ARTERY EMBOLIZATION

Uterine artery embolization (UAE) involves embolization of uterine artery through the femoral artery. Success of bilateral UAE is about 95%. It is used in managing heavy menstrual bleeding or dysmenorrhea associated with intramural fibroids in women not desirous of future child bearing.

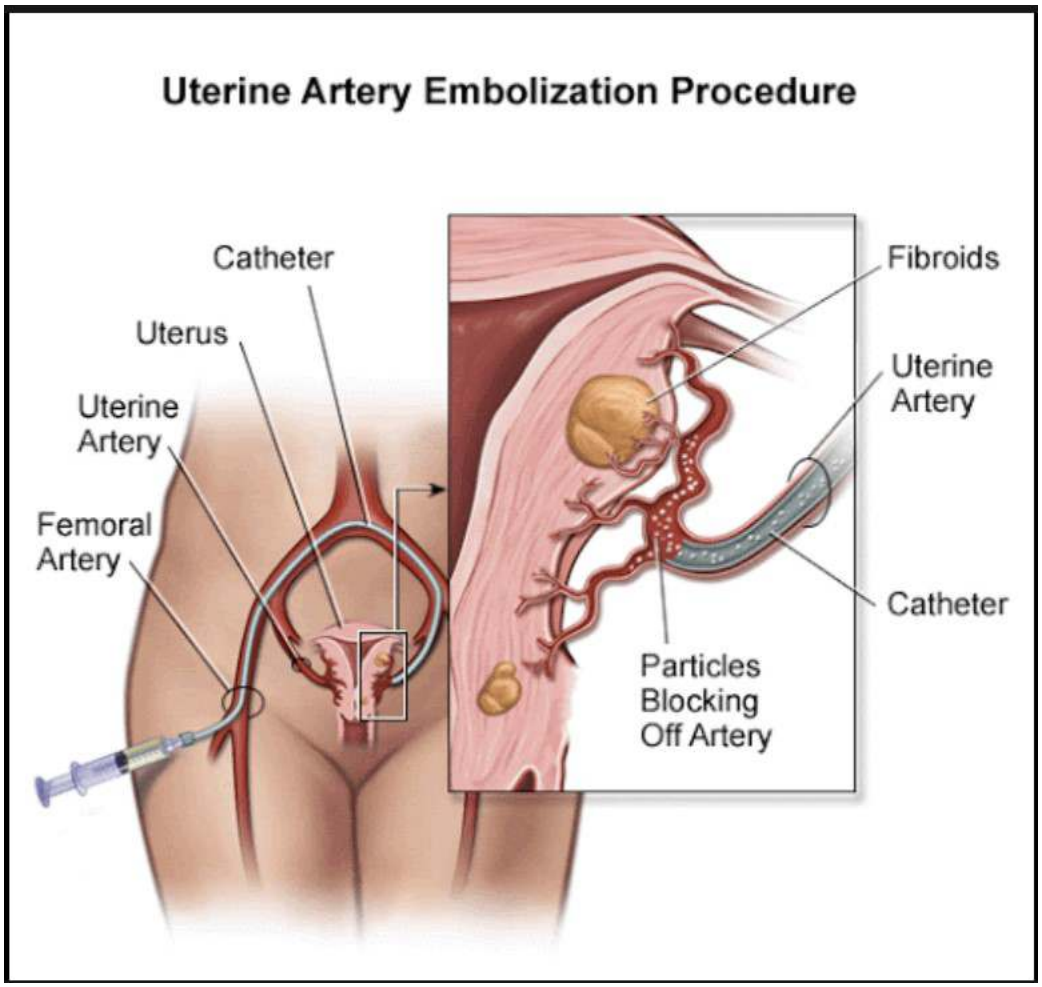

Fig: Technique of uterine artery embolisation

INDICATIONS

- Adenomyosis
- Postpartum haemorrhage
- Prophylaxis of Intra-Operative or Post-Operative Bleeding in malignant tumours/ Placenta Accrete Spectrum (PAS)

- Failed Medical Therapy or Poor Candidate for Other Therapies for Fibroids

CONTRAINDICATIONS

- Viable active pregnancy
- Active endometritis
- Malignancy of the uterus/cervix without concurrent surgical treatment planned
- Postmenopausal patient with bleeding of undiagnosed etiology
- Fibroid that is already infarcted (based on MRI)
- Fibroid smaller than 1 cm in size
- Fibroid with pedunculated morphology (such as stalk width less than 50% of the maximum width; some people use different percentage cutoffs)
- Fibroid located in the cervix
- Concurrent use of a GnRH agonist
- Prior pelvic radiation therapy
- Immunocompromised state
- Fibroid growth resulting in overall uterus size equivalent or greater than the expected size at 24 weeks gestation (uterus reaching up to the umbilicus)
- Severe contrast allergy
- Severe renal insufficiency not receiving dialysis therapy
- Uncorrectable coagulopathy
- Patient desire for future pregnancy
- Adenomyosis

TECHNIQUE

Performed by interventional radiologist under C-arm fluoroscopic guidance. The right femoral artery is accessed and a 5 or 6 French sheath is inserted. An arteriogram to demonstrate the arterial anatomy and find the uterine artery origins. This is manipulated into the uterine artery via anterior division of internal iliac. Once a stable position is obtained, the embolic agent is injected under fluoroscopic guidance to avoid reflux and non-target embolization. Tumors are embolized with particles 500 to 700 micron size, including tris-acryl gelatin (TAG) spheres, non-spherical polyvinyl alcohol (PVA), and spherical PVA. The procedure is then repeated on the contralateral side. Final images showing the state of intra-arterial contrast flow to the uterus are obtained. The catheter is then removed and haemostasis obtained.

COMPLICATIONS

MAJOR COMPLICATIONS

- Death (less than 1/1000)
- Need for surgery due to a complication of the procedure, such as arterial perforation (2 to 3 in 100)
- Abscess/other serious intrauterine infection (1 in 100)
- Pulmonary embolism
- Subsequent pregnancy-related complications, such as spontaneous uterine rupture at the mid-posterior wall during subsequent pregnancy or placenta accreta
- Premature ovarian failure

- Buttock/leg ischemia
- Expulsion of Fibroids
- Angiography Complications - hematoma, dissection, pseudoaneurysm, and contrast-induced nephropathy.
- Persistent pain
- Rarely petechial rash on the torso and limbs.

MAGNETIC RESONANCE GUIDED FOCUSED ULTRASOUND MRgFUS

Magnetic Resonance-guided focused Ultrasound Surgery (MRgFUS) is an alternative to medical and surgical interventions in the management of symptomatic uterine fibroids. it is an effective non-invasive treatment with minimal associated risks as compared to myomectomy and hysterectomy and can be offered to majority of patients suffering from symptomatic uterine fibroids. MRgFUS is a safe and effective treatment for symptomatic uterine fibroids with significant improvement in clin ical symptoms in 70% to 80% of women with myomas.

TECHNIQUE

MRgFUS procedures are performed using the ExAblate 2000 (InSightec, Haifa, Israel), which is fully integrated with a 1.5 Tesla MR scanner (GE Medical Systems, Milwaukee, WI). ExAblate uses a _sonication' process wherein focused ultrasound (FUS) destroys tissues by concentrating a high-energy beam on a specific point and raising its temperature to 60°-85°C. Multiple sonications (focal delivery of energy) are required to ablate a specific tissue. The MRI system provides critical data such as high-resolution 3D imaging of the location of the tumour and internal organs as well as real-time temperature feedback that indicates the degree of tissue heating and coagulation. Thus, this integration of FUS with MRI provides a —closed loop therapy and feedback system‖ that enables the physician to adjust treatment parameters and control the treatment, helping to ensure a high level of safety and efficacy. Pre-treatment of large fibroids with a gonadotropin-releasing hormone (GnRH) agonist helps to reduce fibroid volume and increase fibroid tissue susceptibility to the treatment, which may improve MRgFUS outcomes.

INDICATIONS

- Symptomatic Uterine myomas
- Fibroid accessible by the system
- Volume of fibroid is not to o large
- Myoma mass should be no more than 12 cm depth away from the skin line (which is the maximum depth of penetration of the sound).

CONTRAINDICATIONS

- Anaemia
- Cardiac conditions
- Hypertension
- Cerebrovascular disease
- Currently using anticoagulants
- Uterine pathology other than leiomyoma
- Undiagnosed pelvic mass outside uterus

- Active pelvic infection
- Morbid obesity
- Using standard MRI incompatible devices (cardiac pace makers, metallic implants)
- Patient with extensive longitudinal abdominal scarring in an area of the abdomen directly anterior to the treatment area
- Individuals who are not able or willing to tolerate the required prolonged stationary prone position during treatment
- Patients with more than six uterine fibroids of more than 4 cm in size each should also possibly be excluded.

HYSTERECTOMY

Women with large leiomyomas, age>40 years, symptoms not controlled by medical management, heavy acute bleeding requiring blood transfusion, completed family, co-existent pathology, suspicion of malignancy should be offered hysterectomy.

- Abdominal or vaginal route depends on size of uterus.
- Complications related to surgery and anaesthesia.
- Rarely, myomectomy may end up as hysterectomy as a lifesaving procedure.

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CHAPTER 5

ADENOMYOSIS

Adenomyosis is a gynecological condition where there is ectopic endometrium in uterine myometrium. Though with the advent of modern diagnostic methods, diagnosis is reasonably certain, the etiology is still very perplexing. It is thought that there is a disrupted boundary between the deepest layer of endometrium and uterine myometrium. This leads to inappropriate endometrial proliferation in myometrium in response to estrogen due to which subsequent small vessel proliferation and smooth muscle hypertrophy and hyperplasia also takes place. Due to endometrial tissue proliferation, there is increased prostaglandin production which leads to contractions of myometrium.

Risk factors

Increased parity,
Early menarche,
Short menstrual cycles,
Increased BMI,
Cesarean section,
Dilatation and curettage.

DIAGNOSIS

CINICAL

The clinical diagnosis of adenomyosis is difficult as a lot of symptoms are common and they overlap with other gynaecological conditions. The commonest symptoms are heavy menstrual bleeding, dysmenorrhea. Sometimes women may also complain of chronic pelvic pain, dyspareunia, and infertility. The clinical diagnostic accuracy is nether very sensitive or specific. The physical examination reveals a soft boggy uterus which is tender on examination.

LABORATORY EVA LUATION

Apart from anaemia which may be due to presence of heavy menstrual bleeding, there are no other associated haematological or biochemical abnormalities.

RADIOLOGICAL EVALUATION

Imaging is the primary modality for confirming the diagnosis. MRI was considered as the imaging modality of choice for many years. However recently transvaginal ultrasound has found to have similar sensitivity and specificity. In view of increased availability and ultrasound and increased cost of MRI, ultrasound is the preferred modality of choice.

The characteristic diagnostic features on ultrasound are

a. Presence of myometrial cysts,
b. Focal or diffuse myometrial thickening
c. Poorly defined endo-myometrial junction

d. Unequal myometrial thickness
e. Venetian blinding pattern
f. Increased vascularity in myometrium

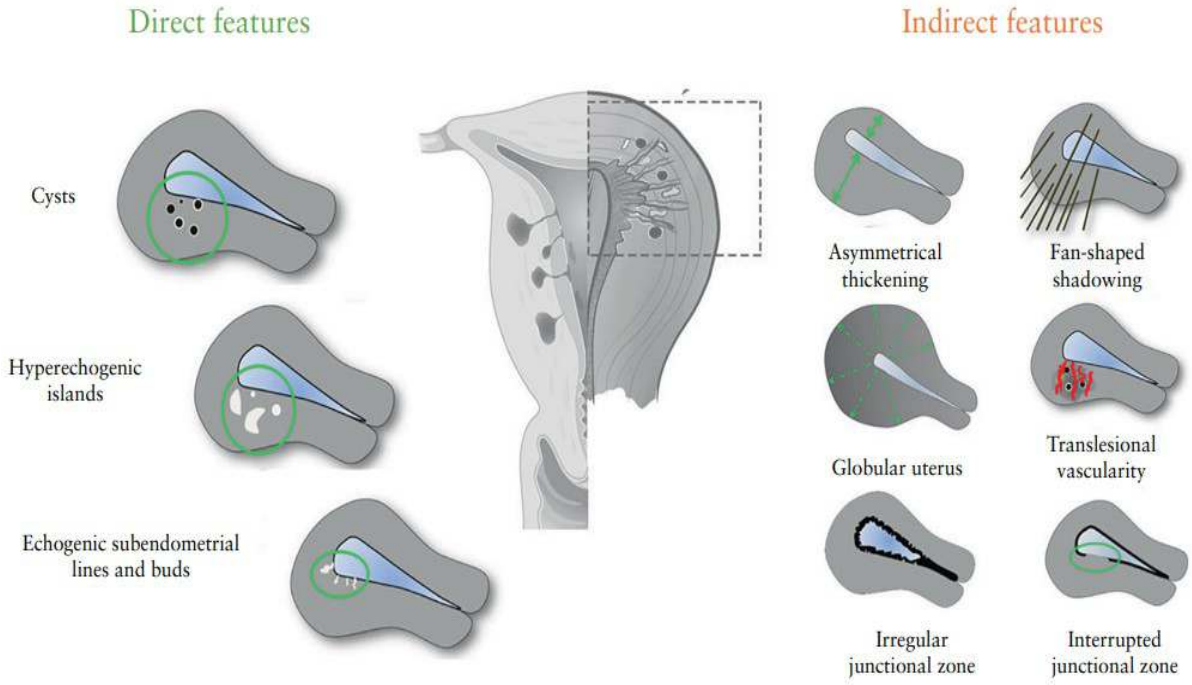

Figure 5 Schematic representation of direct and indirect Morphological Uterus Sonographic Assessment (MUSA) features of uterine adenomyosis (not endometriosis), according to modified Delphi procedure. Adapted from Van den Bosch *et al.*[6].

Distinction between direct and indirect features Ultrasound features that are typical of adenomyosis are direct features, while ultrasound features that are a consequence of ectopic endometrium in the myometrium are indirect features.

In the absence of intramyometrial abnormalities (myometrial cysts, hyperechogenic islands or subendometrial lines or buds), indirect features are not conclusive for the presence of adenomyosis.

Currently, the importance of each individual ultrasound feature of adenomyosis is unknown.

Prospective studies are needed to elucidate the clinical relevance of each individual feature.

Direct features: cysts in the myometrium; hyperechogenic islands; echogenic sub endometrial lines or buds.

Indirect features: globular uterus; asymmetrical myometrial thickening; fan-shaped shadowing; translesional vascularity; irregular JZ; interrupted JZ.

Clinical relevance of endometrial–myometrial JZ Although multiplanar assessment of the JZ in a 3D ultrasound volume is difficult technically, an abnormal JZ in 3D ultrasound images indicates possible adenomyosis.

Referral to a specialized gynaecological practice for 3D ultrasound might be useful if there is uncertainty about the diagnosis.

A regular, uninterrupted JZ is an indicator of absence of adenomyosis.

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CHAPTER 6

MALIGNANCY AND HYPERPLASIA

AUB-M

Women with AUB and associated malignant or premalignant lesions (e.g. Endometrial cancer, leiomyosarcoma and atypical endometrial hyperplasia) are categorised here.

Endometrial hyperplasia

Endometrial hyperplasia (EH) is defined as irregular proliferation of endometrial glands with an increase in the gland to stroma ratio

WHO classification of endometrial hyperplasia 2014

Terminology	Histopathological features	Coexistent invasive cancer	Relative risk of progression to invasive cancer
EH without atypia	Glands to stroma ratio >2:1 Glands - mildly crowded but do not show nuclear atypia	<1%	1.01 - 1.03
Atypical hyperplasia	Further increase in glands to stroma ratio Disorganization of glands with nuclear atypia	25 - 33%	14 - 45

RISK FACTORS

Unopposed estrogen therapy, Tamoxifen therapy, Early menarche and late menopause (after age 55 years), Nulliparity, COS (Chronic anovulation),Diabetes mellitus, Hypertension, Granulosa cell tumors ,Lynch syndrome (HNPCC),Cowden syndrome, Family history of endometrial, ovarian, breast or colon cancer, Increasing age (older than 35 years),Obesity

Clinical presentation

- UB (Most common)
- Postmenopausal bleeding (5% -10%)
- Abnormal cytologic findings on cervical cancer screening (e.g., Atypical glandular cells)
- Postmenopausal patient with a thickened endometrial stripe on imaging
- Incidental finding after hysterectomy

Diagnosis-ultrasound and endometrial sampling

Management-the goal is to prevent progression to endometrial cancer

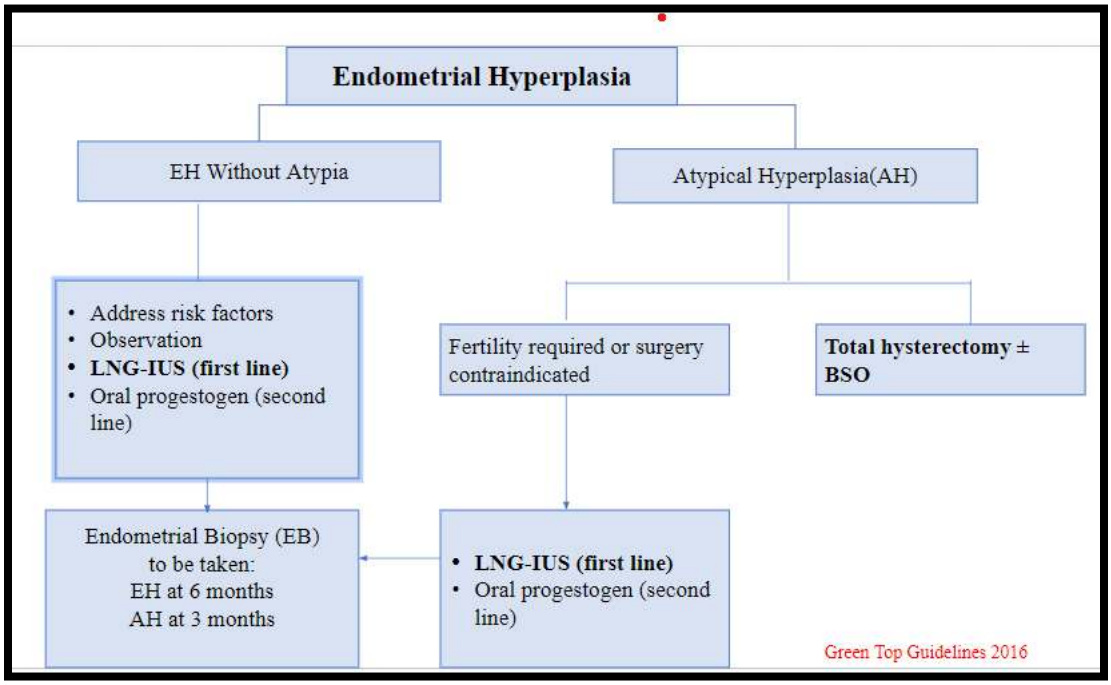

Fig: Management of endometrial hyperplasia

ENDOMETRIAL CANCER

- Affects women in the 6th and 7th decades of life (average age 60 years)
- It is the 3rd most common gynecological malignancy in India and 2nd most common worldwide. (GLOBOCAN 2018)
- There is no routine screening of general population for endometrial cancers.

Risk factors for Endometrial cancer

(Consensus document for management of uterine cancer ICMR 2019)

Table 1: Relative risk of developing carcinoma endometrium with some epidemiological risk factors (3,4,5):	
RISK FACTOR	**RELATIVE RISK**
Prolonged estrogen exposure	
Estrogen-only hormonal therapy	2-10
Early menarche	1.5-2
Late menopause	2-3
Nulliparity	2.0
Anovulation (Polycystic Ovarian Syndrome)	3.0
Demographic Characteristics	
increasing age (> 55 years)	1.4
High socioeconomic status	1.3
Family history of uterine malignancy (Lynch syndrome)	22-50% life time risk

Associated Medical Illness	
Diabetes mellitus	2.0
Obesity **For type I endometrial cancer:** • BMI 25.0 to <30 kg/m^2 • BMI 30.0 to 39.9 kg/m^2 • BMI 40.0 kg/m^2	2-4 OR 1.5 OR 2.5-4.5 OR 7.1
For type II endometrial cancer: • BMI 25.0 to <30 kg/m^2 • BMI 30.0 to <39.9 kg/m^2 • BMI 40.0 kg/m^2	 OR 1.2 OR 1.7-2.2 OR 3
Hypertension	1.5
Prior pelvic RT	8
Tamoxifen	2

- Vaginal bleeding or discharge will be the only presenting symptoms in 90% of women with endometrial cancer
- Any instances of unusual bleeding during the perimenopausal and postmenopausal period should be treated seriously and thoroughly investigated regardless of their minimal and non-persistent nature.
- Endometrial sampling and transvaginal ultrasound is the accepted first step in management (TVS+EA- Negative predictive value- 96%)
- CE-MRI is the modality of choice to detect myometrial invasion.
- The staging for endometrial carcinoma is surgical. It was updated in 2023 to include various histopathological types, tumor patters and molecular classification to better indicate appropriate surgical radiation and systemic therapies.

Indications for endometrial sampling

a) women with age >45 years with AUB- whether prolonged, heavy, irregular or intermenstrual bleeding pattern.

b) women with age <45 years but who are obese, have prolonged intervals between cycles, intermenstrual bleeding or at high risk for endometrial cancer. Women who are obese have high conversion of androstenedione to estrone and aromatisation of androgens to estradiol in adipose tissue thus increasing the exposure of unopposed estrogen and risk of endometrial cancer.

Methods of endometrial sampling are

- Office biopsy
- Dilatation and curettage
- Hysteroscopy directed biopsy

Imaging modalities in women with AUB to rule out structural causes

1. **Pelvic ultrasound-** it is the fist imaging modality of choice in women with AUB. Transvaginal ultrasound should be preferred as it helps in ruling out any structural causes in myometrium or endometrium.
2. **Saline infusion sonography-** it is a technique in whivh steril saline is instilled into endometrial cavity and a transvaginal sonography performed. This technique helps to evaluate endometrial cavity to detect lesions tlike small polyps or submucosal fibroids that may appear as thickened endometrium on transvaginal sonography
3. **Hysteroscopy-** this allows direct visualisation of endometrial cavity. It allows diagnosing lesions and also rargeted biopsy

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CHAPTER 7

OTHER CAUSES OF AUB

The COEIN group has been described as follows:

1. **Coagulopathy (AUB-C) -**

AUB-C includes the spectrum of systemic disorders of haemostasis that lead

to heavy menstrual bleeding.

- It accounts for approximately 13% of women presenting with AUB, von Willibrand disease being the commonest. It usually presents in peripubertal age group.
- Suspected if the patient has coagulopathy screen positive on the basis of history, bruises and petechiae on examination and deranged coagulation profile
- Desmopressin can be used to control acute episode of bleeding. Recombinant Factor VIII or von Willebrand factor are also available and may be required to control severe bleeding.
- Further cause specific management should be done by a haematologist.

2. Ovulatory dysfunction (AUB-O) –

Most common cause of AUB, usually seen in adolescent and perimenopausal women.

- Presentation ranges for infrequent scanty periods to prolonged and heavy bleeding.
- There is anovulation or oligo-ovulation. In anovulatory cycles, there is no mid-cycle LH surge, no ovulation and no progesterone production. Unopposed estrogen action leads to prolonged and heavy bleeding.
- In some cases, insufficient follicular development leads to low estrogen levels that cannot sustain the endometrium or trigger LH surge. There is no ovulation or progesterone production, cycles short and bleeding is profuse due to lack of PGF2α.
- Medical treatment is the first line of management. It includes progestin therapy, OCPs, LNG-IUS. Surgical treatment is resorted only when hormonal therapy fails.

3. Endometrial causes (AUB-E) –

In AUB-E, the primary disorder is at the level of the endometrium. These women have regular ovulatory cycles with heavy menstrual bleeding and no structural abnormality.

- There might be alteration in the ratio of prostaglandins and thromboxane production. There might be increase in the fibrinolytic activity.
- Chronic inflammation of the endometrium with or without associated PID may lead to HMB.
- This type of AUB responds well to NSAIDS and antifibrinolytics.

4. Iatrogenic causes (AUB-I) –

Hormonal contraceptives like OCPs, injectables and implants are an important cause of AUB. Intrauterine contraceptive devices are also associated with heavy menstrual bleeding, intermenstrual and irregular bleeding, especially during initial few months of insertion.

Other drugs like steroid hormones, thyroid hormone, anticoagulant drugs may also lead to AUB.

5. Not classified (AUB-N) –

Some rare causes like congenital and acquired arteriovenous malformations in the uterus can present as heavy menstrual bleeding. Chronic medical disorders like renal failure may be included in this type of abnormal uterine bleeding.

Causes of Postmenopausal bleeding

Cause of bleeding	**Percentage(%)**
Atrophy	60-80
Exogenous estrogen	15-25
Polyps(Endometrial/cervical)	2-12
Endometrial hyperplasia	5-10
Endomertial cancer	10
Cervical cancer	<1

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CHAPTER 8

ACUTE AUB

ACUTE AUB

AUB can be acute or chronic and is defined as bleeding from the uterus that is outside the normal regularity, frequency, volume and duration and occurs in the absence of pregnancy.

Acute AUB refers to an episode of heavy bleeding that, in the opinion of the clinician, is of sufficient quantity to require immediate intervention to prevent further blood loss.

Approach to a patient of acute AUB can be done in following stages:

1. Rapid initial assessment and resuscitation
2. Determine the most probable diagnosis
3. Choose the most appropriate treatment for the patient

DIAGNOSIS OF ACUTE AUB

Rapid initial assessment and resuscitation:

- Prompt assessment of vitals and signs of hypovolemia
- If patient is hemodynamically unstable or is in shock, establish intravenous access with two large bore IV cannulas (18G). Resuscitation with crystalloids should be started immediately.
- Prepare for blood transfusion and clotting factor replacements
- After initial shock management and stabilization, evaluate the most likely aetiology of acute AUB

Determine the most probable diagnosis:

History: Guided by PALM-COEIN system

- Rule out pregnancy
- Medical history focussed on the current episode of bleeding, age of menarche, LMP
- detailed past menstrual history, its regularity, frequency, duration and volume, no. of pads used per day, passage of clots, intermenstrual bleed
- obstetric history, details of past pregnancy events
- associated dysmenorrhoea, pressure symptoms

Screening for coagulopathy – History of PPH, frequent gum bleed, surgical haemorrhage, bruising one or two times per month, frequent epistaxis or family history of coagulopathy.

Past and treatment history for any medical disorders, hormonal therapy, steroids, contraceptives

Physical examination: General-

- Weight, height, BMI
- Pallor, gum bleed, edema, icterus
- Gum bleed, bruises, petechiae,

- Thyroid enlargement, lymphadenopathy
- any signs of endocrine disorders

Systemic examination-

- Respiratory system (chest auscultation –signs of pulmonary edema)
- Cardiovascular system (signs of cardiac failure, cardiomegaly, murmur)
- Abdominal examination- hepatosplenomegaly, any palpable lump

Pelvic examination-

- Per speculum: condition of the cervix, any visible polyps, abnormal discharge or growth.
- Bimanual palpation: uterine size, position, asymmetrical enlargement, any adnexal mass, any tenderness

INVESTIGATIONS:

Laboratory investigations- Urine pregnancy test, complete blood counts, iron profile, coagulation profile, peripheral blood smear, thyroid profile, hepatic and renal function tests, hormone profile.

Imaging studies: Transabdominal ultrasonography and transvaginal sonography to show the size and shape of uterus, endometrial thickness and rule out structural causes of AUB. Saline infusion sonography can be done to delineate the endometrial cavity and show submucosal fibroids and polyps. MRI can be done for surgical planning, but is costly and not the first line modality for AUB.

Treatment:

Choice of treatment of AUB depends on the hemodynamic stability of the patient, suspected cause of bleeding, desire for future fertility and underlying medical disorders.

Aims of management of acute AUB-

1. To control the current episode of heavy bleeding
2. To reduce menstrual blood loss in the subsequent cycles

Hormonal therapy is the first line treatment for acute abnormal uterine bleeding, without known or suspected bleeding disorders, as described below-

- Intravenous conjugated Equine Estrogen 20-40mg, 6-8 hourly till the bleeding is controlled
- Intravenous tranexamic acid (500mg -1g) 12hourly to prevent fibrin degradation
- Tamponade of uterus with Foley‘s catheter used as a mechanical option to control the acute episode of AUB
- Bleeding due to coagulopathies can be managed by intranasal, subcutaneous or intravenous Desmopressin. Recombinant factor VIII and von Willibrand factor are also available and may be required to control severe bleeding.
- if not controlled, Dilatation and curettage is done as an emergency management in patients with acute AUB. The procedure is diagnostic as well as therapeutic therapeutic.

Once the bleeding is controlled, patient is put on high dose monophasic combined oral contraceptive pills. Other options like LNG-IUS or Progestin therapy can also be given to reduce menstrual bleeding in subsequent cycles. Based upon the PALM-COEIN classification of AUB, the cause is determined and specific treatment is given accordingly.

Surgical management: Need for surgical management depends on patient‘s hemodynamic stability, severity of bleeding, contraindications to medical management, failure of response to medical therapy, desire for fertility and underlying medical condition.

Surgical options for management of acute AUB include-

- Dilatation and curettage (D&C)
- Endometrial ablation
- Transcervical endometrial resection
- Uterine artery embolization
- Hysterectomy

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CHAPTER 9

CHRONIC AUB

Chronic AUB is defined as bleeding from the uterine corpus which is abnormal in duration, volume, frequency and or regularity and has been present for the majority of the preceding 6 months.

MANAGEMENT OF CHRONIC AUB

The treatment options for AUB are guided by several factors

a) Etiology of AUB
b) Severity of bleeding
c) Associated symptoms and fertility issues
d) Contraceptive needs
e) Medical comorbidities
f) Patients'preferences regarding medical versus surgical treatment
g) Time to menopause

The various options of medical management of chronic AUB are-

1. **Estrogen -progestin contraceptives-** For many patients with AUB, combined estrogen progesterone containing contraceptives are a good option. They act by making the cycles more regular, reduce the amount of bleeding, reduce dysmenorrhoea and also provide contraception.

2. **Selective estrogen receptor modulator-** Also a Non-hormonal non-steroidal contraceptive like ormeloxifene is also widely used in AUB. Ormeloxifene is given in the dosage of 60 mg tablet twice a week for 3 months followed by once a week for another 3 months. It helps in thinning of endometrium. Women using this drug often experience amenorrhoea in 3-4 months. The safety profile of ormeloxifene is excellent with few side effect like nausea, headache, weight gain delayed or prolonged mensuration.

3. **Levonorgestrel containing intrauterine device-** for women in whom estrogen is contraindicated or desire long contraception, the intra uterine device containing 52 mg of progesterone is an ideal choice. It leads to scant bleeding, or amenorrhoea.

4. **Oral progestins-** Oral progestin formulations like norethisterone acetate, Medroxyprogesterone acetate are used in women in whom estrogen is contraindicated and are not willing to use progesterone containing IUD. The dose of oral progesterone is tab norethisterone 5 mg two to three times daily or tab medroxyprogesterone acetate 5-10 mg once or twice daily. These medicines are given either continuously for entire cycle starting from day 5 of cycle or from day 14 in only secretory phase. Continuous therapy is more effective in controlling bleeding than cyclic therapy. DMPA can also be used in AUB especially in those women who also need contraception.

5. **Tranexamic acid-** It acts by blocking the conversion of plasminogen to plasmin thereby reducing fibrinolysis. It is given in a dose of 500-1000mg three times daily. During menstruation. In women who have compromised kidney function, the dose needs to be reduced.

6. **NSAID-** they act by reducing the prostaglandin production in the endometrium leading to vasoconstriction and a decrease in bleeding. Common NSAID used are ibuprofen, mefenamic acid and naproxen. They reduce the bleeding and also relieve dysmenorrhoea. The dose of ibuprofen is 600 mg 2-3 times daily, mefenamic acid is 500 mg three times daily, naproxen 250-500 mg two- three times daily.

7. Aromatase inhibitor, GnRH analogues, Mifepristone have also been used in AUB though for in selected cases.

Non-Medical Management Options of Chronic AUB are

1. TRANSCERVICAL RESECTION OF ENDOMETRIUM

Transcervical resection of endometrium (T.C.R.E.) is a first generation hysteroscopic endometrial ablation technique that is an alternative to hysterectomy for patients presenting with abnormal uterine bleeding. It is effective in producing hypomenorrhea in 80% to 90% and amenorrhoea in 25% to 50%.

INDICATIONS

- Failed medical management
- Medical management was contraindicated or had adverse effects (previous history of deep venous thrombosis, thromboembolism, liver disease)
- Cases who are unfit for hysterectomy / unwilling

CONTRAINDICATIONS

- Women who want to retain fertility
- Acute genital tract infections
- Adenomyosis
- Uterine size greater than 12 weeks/ cavity greater than 12 cm
- Abnormal endometrial and cervical cytology.

TECHNIQUE

Cervix is dilated up to Hegar 10 and then the resectoscope is introduced. The uterus is distended with the help of 1.5% glycine to maintain a steady intrauterine pressure. A pure cutting current (100 watts) is used to resect the endometrium using a cutting loop electrode. The procedure is started at the fundus and then the endometrium from anterior, posterior and lateral walls is systematically shaved up to basal layer. Special care is taken near lateral walls especially near the isthmus where injury to the branches of uterine vessels should be avoided. Endometrial removed at the end of surgery is sent for histopathological examination.

ADVANTAGES OF TCRE OVER OTHER SECOND -GENERATION ABLATION TECHNIQUES

- Tissue can be obtained for histopathological diagnosis
- Direct visualization of uterine cavity is possible
- Equipment failure, nausea, vomiting and uterine cramping less common than with second generation devices

- Microwave and thermal ablation are contraindicated in previous classical scar or previous surgery or trauma leading to uterine wall thickness of less than 8 mm.

COMPLICATIONS

- Fluid overload
- Uterine perforation
- Bowel injury
- Haemorrhage
- Delayed – secondary haemorrhage, pyrexia, hematometra, pelvic infection

2. ENDOMETRIAL ABLATION

The various endometrial ablation techniques destroy the endometrial lining, removing both the functional and basal layers. Endometrial ablation is performed as an outpatient procedure, generally under anaesthesia. By destroying these layers, the endometrium is no longer able to regenerate, thereby causing menstruation suppression. After endometrial ablation, necrosis, fibrosis, and inflammation are common histology findings of the uterine cavity. A preoperative endometrial biopsy must be done.

INDICATIONS

- Women of reproductive age who have completed family with heavy menstrual bleeding due to a benign cause that significantly impacts their quality of life.
- AUB that is not related to a structural cause, hyperplasia or malignancy.
- Failure or intolerance of medical management.
- Uterine cavity no larger than 12 weeks gravid uterus size with a normal contour.

ABSOLUTE CONTRAINDICATIONS TO ENDOME TRIAL ABLATION ARE:

- Currently pregnant / fertility preservation required
- Endometrial hyperplasia or uterine malignancy
- Active pelvic infection
- Intrauterine device
- History of transmyometrial uterine surgery including classical cesarean section or myomectomy
- Uterine anomaly such as septate, bicornuate, or unicornuate uterus
- Relative contraindications: postmenopausal state, uterine cavity length greater than 10 cm to 12 cm, severe myometrial thinning, or severe uterine retroflection or anteflexion.

TECHNIQUE

- First Generation Technique – Resectoscopic Endometrial Ablation

Performed under hysteroscopic guidance using a rollerball, monopolar, or bipolar loop electrode. The endometrium is desiccated to the level of the basalis layer using thermal energy. The major disadvantage to resectoscopic endometrial ablation is operator expertise and safety.

- Second Generation Techniques – Non-resectoscopic Systems

Do not require the use of a resectoscope to accomplish the destruction of the endometrium. The devices used are global and treat the whole endometrial cavity. Second-generation techniques include thermal fluid, microwave or bipolar radiofrequency electrical energy, laser thermotherapy, and cryoablation. These are easy to use, safe, and outcomes are similar to resectoscopic techniques.

Both first and second generation are found to have equal efficacy in outcomes.

COMPLICATIONS

- Distention fluid overload
- Infection
- Uterine trauma: cervical laceration, perforation of the uterus.
- Lower tract thermal injury: burns of the cervix, vagina, and vulva
- Pregnancy-related complications including premature birth, abnormal placentation, intrauterine growth restriction, malpresentation, and perinatal mortality
- Obstructed hematometra leading to cyclic pain due to residual endometrium
- Post ablation tubal sterilization syndrome is seen in patients who had a prior bilateral tubal ligation and endometrial ablation – cyclic pelvic pain due to endometrial regrowth and distension of the uterine cornua with blocked fallopian tubes.
- Subsequent difficulty evaluating the endometrium due to scarring and changes seen on imaging after ablation can lead to missed or delayed diagnosis of uterine carcinoma.
- Reoperation with definitive hysterectomy within 5 years due to bleeding and/or pain

3. UTERINE ARTERY EMBOLIZATION (Refer to page ….)

4. MR GUIDED FOCUS ULTRASOUND (Refer to page…)

5. RADICAL TREATMENT

Hysterectomy is the most common gynaecological procedure in the world for management of AUB.

Over 60% patients with AUB end up having hysterectomy within 5 years from the diagnosis. About one-third of hysterectomies are avoidable.

With newer modalities available, hysterectomy should be the last option. However, still hysterectomy is the treatment of choice in patients not responding to other forms of treatment, who have severe symptoms and have completed family.

Treatment should be tailored depending on the impact of related symptoms, fertility requirements and cavity distortion-

Symptoms/Uterine cavity distortion	AUB only	AUB with pressure symptoms, family complete and no desire to retain fertility	AUB symptoms and fertility desire/subfertility
No cavity distortion	UAE EA Hysterectomy	UAE MRgFUS Myomectomy Hysterectomy	Myomectomy UAE (evidence needed) MRgFUS
Cavity distortion	TCRF UAE Hysterectomy	UAE Myomectomy Hysterectomy	TCRF Myomectomy UAE (evidence needed)

Whitaker L, Critchley HO. Abnormal uterine bleeding. Best Pract Res Clin Obstet Gynaecol. 2016 Jul;34:54-65. doi: 10.1016/j.bpobgyn.2015.11.012. Epub 2015 Nov 25. PMID: 26803558; PMCID: PMC4970656

Different types of hysterectomy that can be done in AUB as per underlying cause

Supracervical or subtotal hysterectomy -removal of body of the uterus, keeping the cervix in place.

Total hysterectomy-removal of the body uterus and cervix.

Radical hysterectomy -removal of uterus with cervix, bilateral parametrium, and the upper1-2cm of the vagina. Radical hysterectomy is done when we suspect carcinomas (AUB-M)

Types of Hysterectomy depending on the route of surgery-

Open Abdominal Hysterectomy- This is the most common type, accounting for about 54% of hysterectomies done for all non-cancerous (benign) conditions.

Minimally invasive procedure (MIP) Hysterectomy-Several approaches can be used for a minimally invasive procedure:

- Vaginal hysterectomy
- Laparoscopic hysterectomy
- Laparoscopic-assisted vaginal hysterectomy
- Robot-assisted laparoscopic hysterectomy

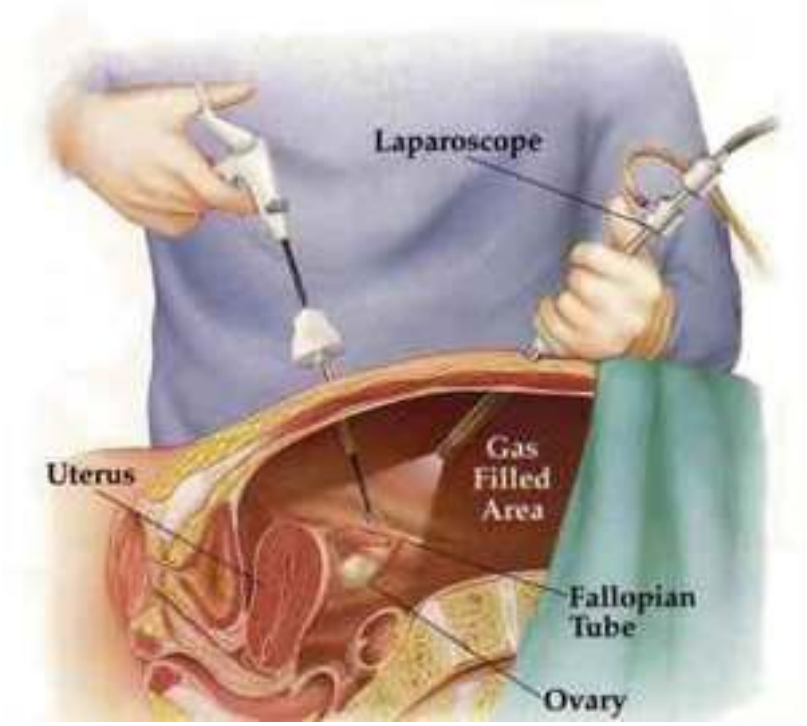

Fig: Laparoscopic hysterectomy

Comparison of MIP Hysterectomy and Abdominal Hysterectomy

Using minimally invasive approach to remove the uterus has several benefits, when compared to the more traditional open surgery. In general, an MIP allows for faster recovery, shorter hospital stays, less pain and scarring, and a lower chance of infection.

Risks of Hysterectomy

- Urinary incontinence
- Vaginal prolapse
- Recto-Vaginal/ Vesicovaginal fistula formation
- Chronic pain, Wound infections, blood clots, haemorrhage, reactions to anaesthesia, and injury to surrounding organs

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CHAPTER 10

AUB IN ADOLESCENCE

INTRODUCTION-

Abnormal uterine bleeding (AUB) refers to uterine bleeding in a nonpregnant female that is abnormal in volume, frequency, duration, and/or regularity.

Due to immaturity of the hypothalamic-pituitary-ovarian (HPO) axis, AUB is common in adolescents, anovulation being accountable for approximately 80 percent of cases. During the evaluation, pregnancy, trauma, sexually transmitted diseases and underlying bleeding disorders must be ruled out.

PATHOPHYSIOLOGY -

With anovulatory cycles, unopposed estrogen stimulates the endometrium, leading to a sustained proliferative phase rather than maturing to a secretory endometrium. Estrogen levels ultimately cannot sustain the hyperplastic endometrial lining, leading to irregular, sometimes heavy, menstrual bleeding.

EVALUATION

Detailed menstrual history taking is the first and most important part of evaluation.

Initial screening for an underlying disorder of haemostasis in patients with excessive menstrual bleeding should be structured by the medical history.

A positive screening result comprises the following circumstances:

• Heavy menstrual bleeding since menarche
• One of the following conditions: – Postpartum haemorrhage – Surgery-related bleeding – Bleeding associated with dental work
• Two or more of the following conditions: – Bruising, one to two times per month – Epistaxis, one to two times per month – Frequent gum bleeding – Family history of bleeding symptoms

It is also desirable to use objective method of assessing bloos loss-PBAC. (Refer to page…)

General examination is must to see for signs of pallor, hepatosplenomegaly, signs related to hormonal disorders like hirsutism, acanthosis nigricans. Gynaecological examination is not needed unless some problem related to pregnancy is considered as differential diagnosis.

Ultrasound is not mandatory as majority of these AUB are because of anovulatory cycles followed by bleeding disorders. Wherever it is needed USG should be done to rule out pelvic pathology. Transabdominal route is preferred in adolescent girls.

LABORATORY TESTS

The minimum laboratory evaluation should include; complete blood count, peripheral blood smear, ferritin level, Endocrine evaluation for hyperprolactinemia, thyroid disorders and PCOS, Coagulation studies prothrombin time, activated partial thromboplastin time and fibrinogen. Adolescents at risk of bleeding disorders should undergo testing for vWD.

Anovulatory uterine bleeding classification as per severity as follows-

Mild anovulatory uterine bleeding Longer than normal menses (>7 days) or shortened Cycles (<3 weeks) for more than 2 months Haemoglobin ≥ 12 g/dl/mildly decreased (10-12g/dl)
Moderate anovulatory uterine bleeding Moderately prolonged or frequent menses every one to three weeks Haemoglobin >10 g/dl
Severe anovulatory uterine bleeding Heavy bleeding that causes decrease in haemoglobin to less than 10 g/dl, may or may not cause hemodynamic instability

MANAGEMENT -

Mild Anovulatory uterine bleeding

Reassurance, NSAIDs can be used. Menstrual cycle diary to be maintained

Moderate Anovulatory uterine bleeding –

These adolescents are managed on an **outpatient basis**. In addition to iron supplementation, hormonal therapy is necessary to stabilize endometrial proliferation and shedding

In case of active bleeding-

Combined estrogen-progestin oral contraceptives are better choice. Monophasic COCs, containing at least 30 μg of ethinyl E2, are preferred to prevent breakthrough bleeding.

Dosage Schedule- Dose is one pill every 8–12 hours until the bleeding stops, then to continue with one pill per day for a total of at least 21 days. 4–8 mg of ondansetron can be given if nausea occurs with high doses of E2. At the end of 21 days, seven days of placebo or pause should be given. COCs treatment is continued for 3–6 months until the haemoglobin level reaches ≥12 g/dl.

In absence of active bleeding or having a contraindication for estrogen therapy - progestin-only hormone therapy can be used. Micronized oral progesterone (200 mg/day), medroxyprogesterone (10 mg/day), norethindrone acetate (2.5–5 mg/day), depot medroxyprogesterone acetate (DMPA) or a levonorgestrel-releasing intrauterine device are available options. The last two options are for those who need contraception or cannot take pills.

Dosage Schedule-Oral progestin is given for 12 days every month and bleeding occurs 2–7 days after cessation. If bleeding does not start within one week the patient should be re-evaluated.

Severe Anovulatory uterine bleeding-

Indications for hospitalization
• hemodynamic instability,
• hemoglobin concentration <7 g/dL or <10 g/dL with active heavy bleeding
• symptomatic anemia, and
• need for intravenous conjugated estrogen (eg, cannot take oral medications or continued bleeding after 24 hours of estrogen-progestin combination therapy)

Management –

The patient should be hospitalized and monitored. Blood products should be arranged. OCPs containing High doses of oestrogen (35–50 µg ethinyloestradiol) should be used because OCPs promote rapid endometrial regrowth to cover denuded epithelial surfaces.

Dosage Schedule-

ESTROGEN THERAPY-
The treatment with high-dose oestrogen is continued at 6-hour intervals until the severity of the bleeding decreases. The dose is then decreased within 1 week as follows: One pill every 6 hours for 2 days, then every 8 hours for 2 days, then every 12 hours for 2 days and finally 1 pill daily for a minimum of 6 months. 4–8 mg of ondansetron can be given if nausea occurs with high doses of E2.
Intravenous (IV) conjugated oestrogen treatment (25 mg at intervals of 4–6 hours) maximum 6 doses may be considered for patients who cannot tolerate high-dose oral oestrogen therapy.

PROGESTERONE THERAPY-
Medroxyprogesterone acetate (MPA, 20–40 mg) and norethindrone acetate (NETA, 5–10 mg) are administered three times per day for 7 days. When the bleeding stops, the progesterone dose is decreased to every 12 hours for 2 weeks. Thereafter, therapy is maintained with the cyclic use of MPA (10 mg/d) and NETA (5 mg/d) for 12 days per month and between the same dates in every month

There may be a need for hemostatic agents such as tranexamic acid, aminocaproic acid and desmopressin, if bleeding exceeds 24 hours despite high dose COCs or there is a known platelet dysfunction.

If hormonal and hemostatic treatment fail to lessen bleeding in 24–36 hours, examination under anaesthesia, endometrial sampling and therapeutic curettage may be necessary.

MANAGEMENT ALGORITHM

CLINICAL HISTORY - Age of menarche

Initial screening of underlying bleeding disorder on history

• Sexual activity

Physical examination

• Vital signs and BMI

• General examination

Laboratory analysis for all adolescents

• hCG, CBC, TSH, S.Ferritin

If signs of PCOS- Testosterone(free/Total), DHEAS, S. Prolactin

If sexually active: Gonorrhoea/ Chlamydia NAAT

If history suggestive of bleeding include tier 1 testing:

• VWF Ag. WWF activity, factor VIll assay, PT/PTT

Imaging usually not needed. Consider if bleeding or pain not controlled

Hemodynamically stable- OUTPAIENT MANAGEMENT

• Consider antiemetic
• Start COC (if no contraindication) or Progesterone taper
• Schedule follow-up appointment within 7 days
• Return if no improvement within 24 hours
• Start oral iron, consider stool softener

Hemodynamically unstable- INPATIENT MANAGEMENT

• Consult Hematologist, Pelvic Ultrasonography
• Blood transfusion-hemodynamically unstable

ESTROGEN THERAPY-

Tolerating PO- begin COC taper

Not tolerating PO-I/V Conjugated Equine Estrogen (Premarin 25 mg IV every 4-6 hours, maximum 6 doses), when bleeding slows or stops, then start COC tapers, Begin antiemetic

PROGESTIN THERAPY-• PO medroxyprogesterone

High dose (60-80 mg) bid until bleeding stops then begin progestin taper

ESTROGEN CONTRAINDICATION

• Migraine with aura
• Hypertension
• Prior DVT/PE
• Congenital cardiac anomalies
• Increased risk for blood clots

Medical treatment regimen for heavy menstrual bleeding -

Drug	Dose Schedule	Suggested Dose
Conjugated equine estrogen	25 mg IV	Every 4-6 hours for 24 hours
Combined oral contraceptives	Monophasic COCs that contain 30-50 micrograms of ethinyl estradiol	Every 6-8 hours until cessation of bleeding
Medroxyprogesterone acetate	20 mg orally	Three times per day for 7 days
Tranexamic acid	1.3 g orally or 10 mg/kg IV (maximum 600 mg/dose)	Three times per day for 5 days (every 8 hours)

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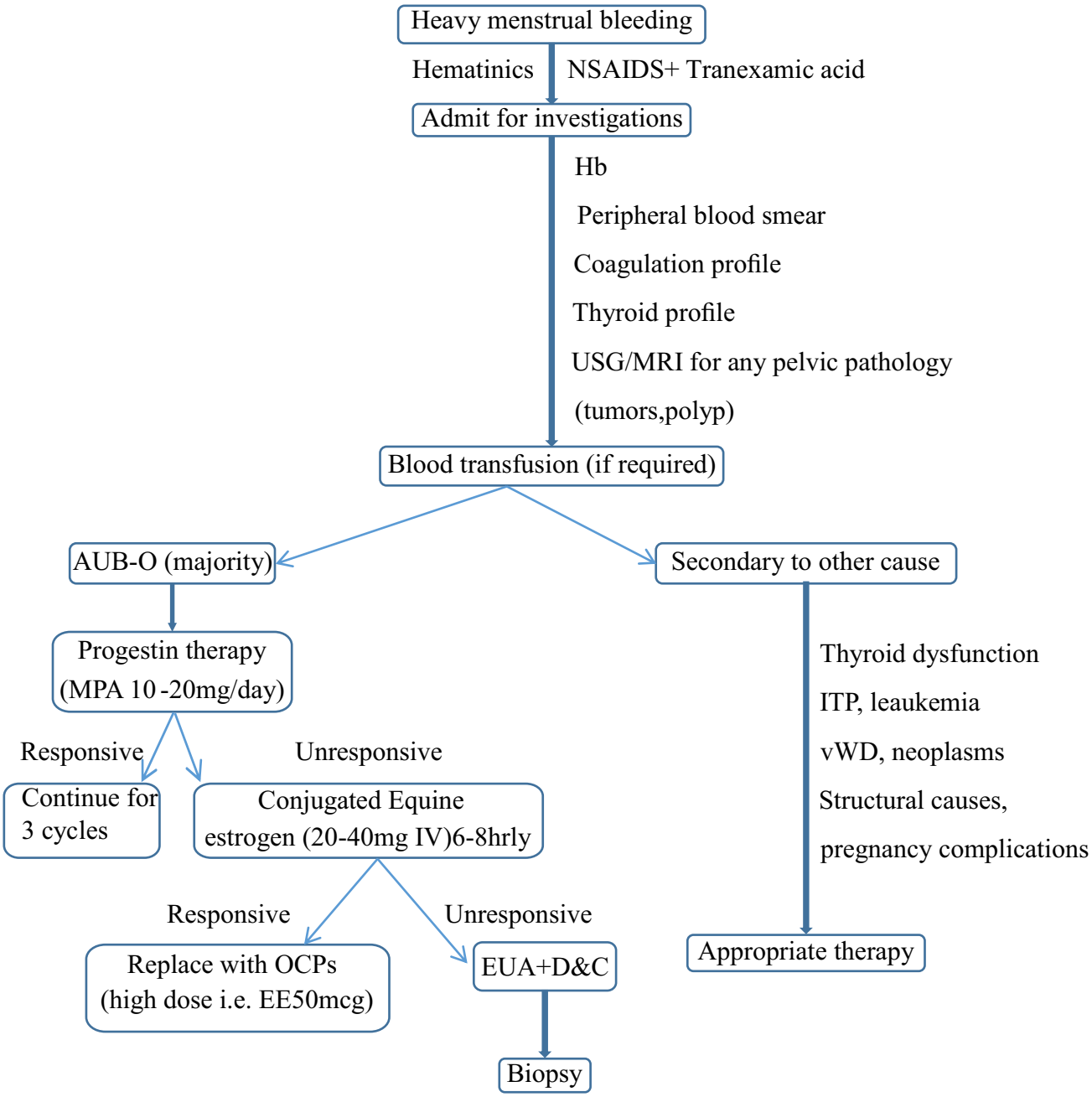
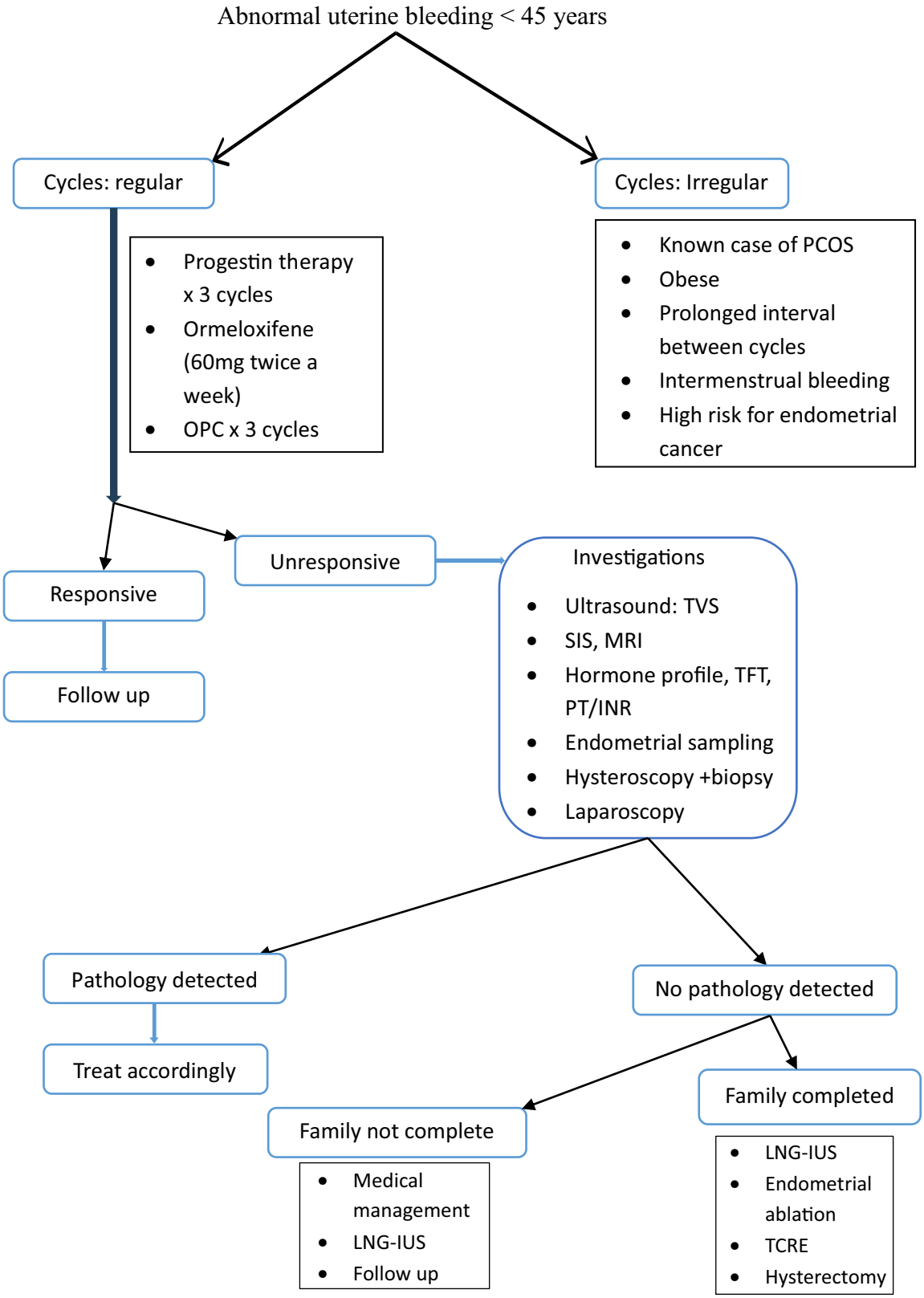
Annexures

FLOWCHARTS FOR MANAGEMENT

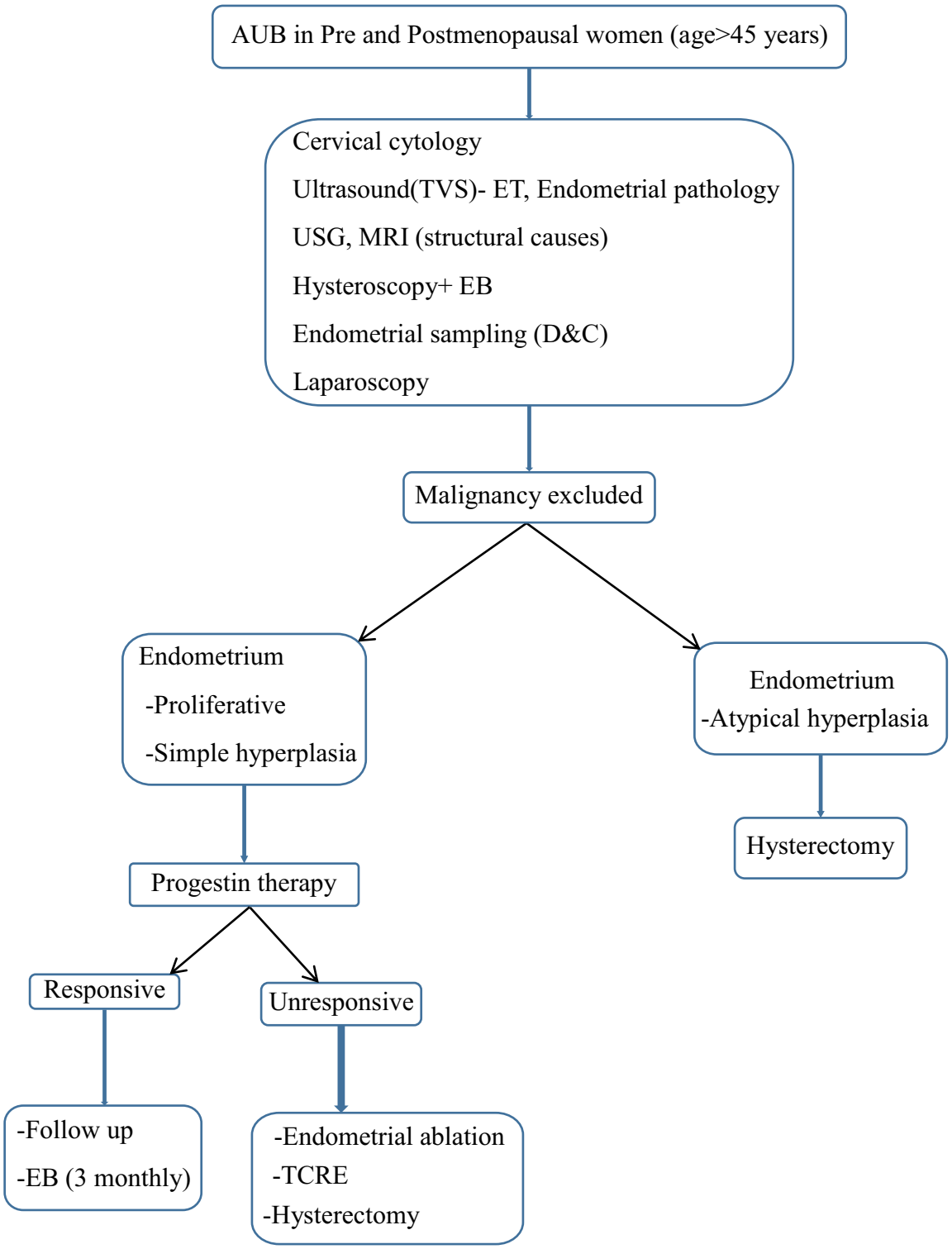
MANAGEMENT PROTOCOL OF PUBERTY MENORRHAGIA



MANAGEMENT PROTOCOL OF AUB IN REPRODUCTIVE AGE WOMEN



MANAGEMENT PROTOCOL OF AUB IN PERIMENOPAUSAL WOMEN



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