
بسم الله الرحمن الرحيم

Abnormal Uterine Bleeding (AUB)

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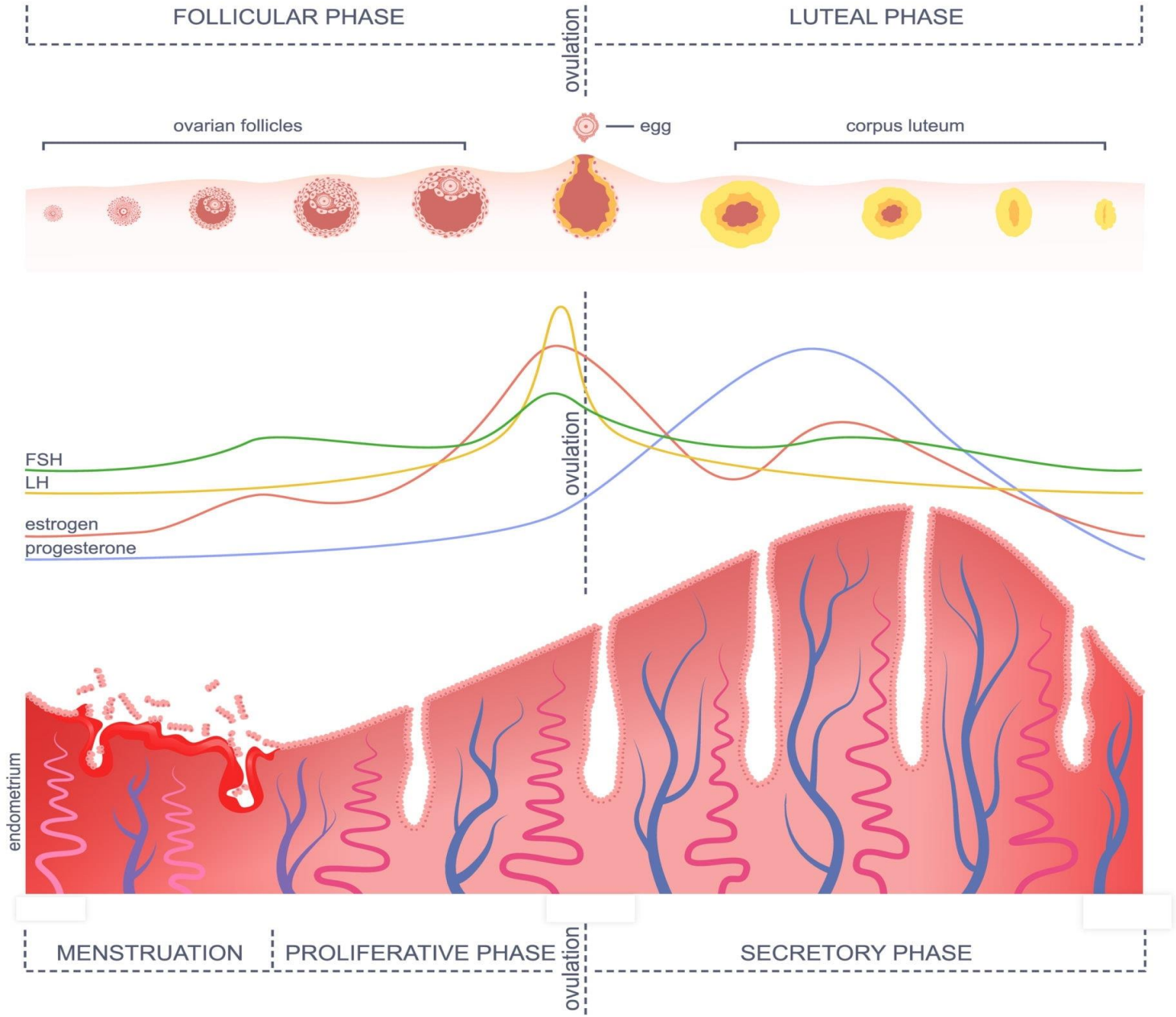
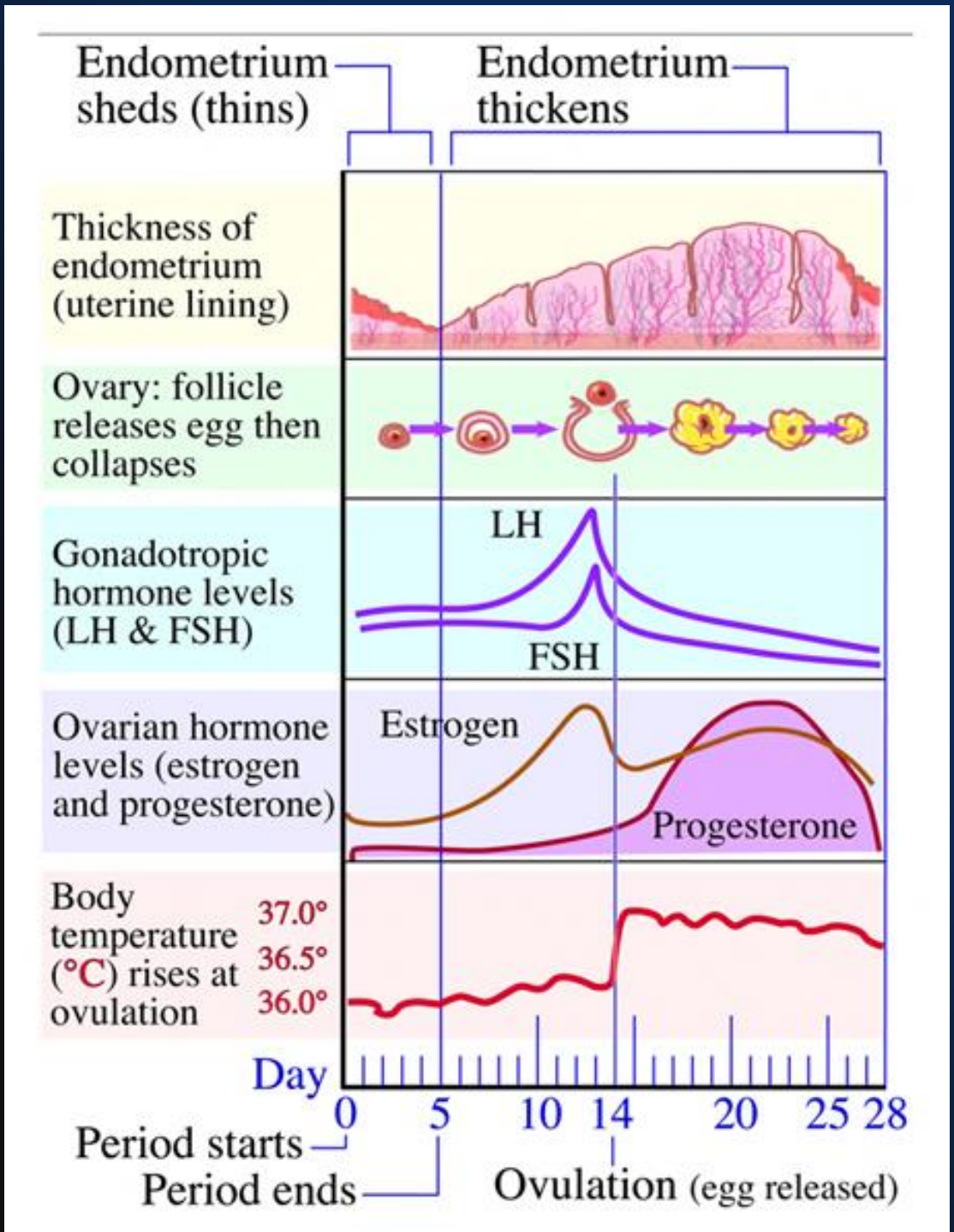
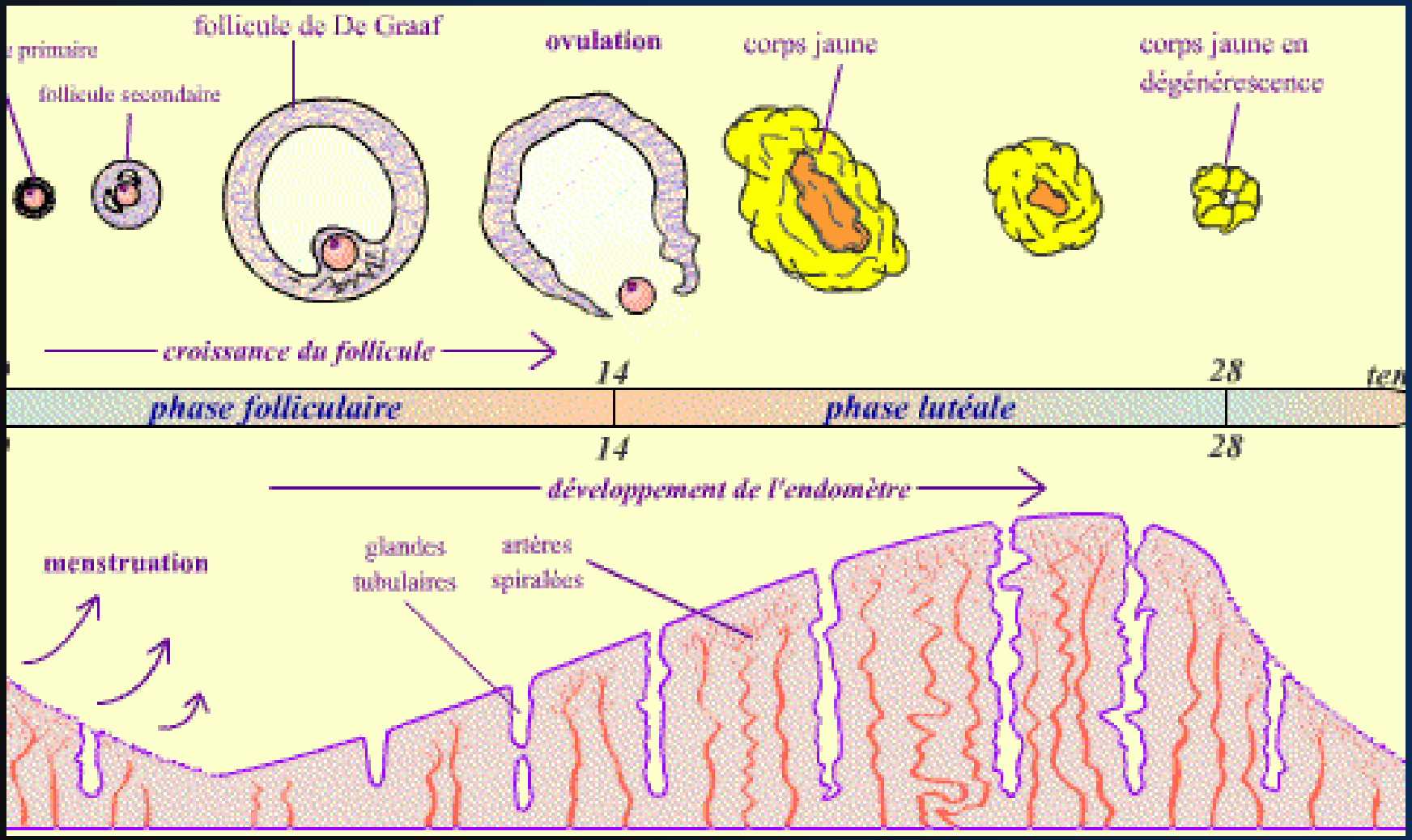
MENSTRUAL CYCLE




Endometrium sheds (thins)
Endometrium thickens
Thickness of endometrium (uterine lining)
Ovary: follicle releases egg then collapses
Gonadotropic hormone levels (LH & FSH)
LH
FSH
Ovarian hormone levels (estrogen and progesterone)
Estrogen
Progesterone
Body temperature (°C) rises at ovulation
37.0°
36.5°
36.0°
Day
0
5
10
14
20
25
28
Period starts
Period ends
Ovulation (egg released)


follicule de De Graaf
ovulation
corps jaune
corps jaune en dégénérescence
follicule secondaire
croissance du follicule
14
28
phase folliculaire
phase lutéale
14
28
développement de l'endomètre
menstruation
glandes tubulaires
artères spiralées

Abnormal Uterine Bleeding

Dysfunctional Uterine Bleeding

Definitions

Normal:

Mean interval is 28 days +/- 7 days.

Mean duration is 4 days.

More than 7 days is abnormal.

Average blood loss with menstruation is 35-50cc.

More than 80 cc is abnormal.

95% of women lose <60cc.

تشخیص مهم است:

- سن خردسالی
- سن بلوغ
- سن باروری
- سن پیش از منوپوز
- سن پس از منوپوز
- سن پیری

Abnormal uterine bleeding

Best Pract Res Clin Obstet Gynaecol. 2016 Jul; 34: 54–65.
doi: [10.1016/j.bpobgyn.2015.11.012]

- AUB was redefined by Fédération International de Gynécologie et d'Obstétrique (FIGO) in 2009 by the FIGO Menstrual Disorders Group (FMDG). This was in order to standardise definitions, nomenclature and the underlying categories of aetiology. It was hoped that this would facilitate ease of investigation and comparison of similar patient populations and thereby aid research and improve evidence-based care; this would also be a practical tool for assessing contributing aetiologies.
- Chronic AUB was defined as 'bleeding from the uterine corpus that is abnormal in volume, regularity and/or timing that has been present for the majority of the last 6 months'. Values out with the accepted 5–95th percentiles indicated abnormality.

Suggested Normal limits for menstrual parameters. Adapted from Fraser et al.

Clinical Parameter	Descriptive term	Normal limits (5–95th percentiles)
Frequency of menses (days)	Frequent Normal Infrequent	<24 38–24 38<
Regularity of menses, cycle to cycle (Variation in days over 12 months)	Absent Regular Irregular	No bleeding Variation ± 2–20 days Variation >20 days
Duration of flow (days)	Prolonged Normal Shortened	>8.0 8.0–4.5 <4.5
Volume of monthly blood loss (mL)	Heavy Normal Light	>80 80–5 <5

Abnormal uterine bleeding

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- With regard to volume, however, both the Royal College of Obstetricians and Gynaecologists (RCOG) and American College of Obstetricians and Gynecologists (ACOG) prefer the patient-centred definition of **HMB**, ‘excessive menstrual blood loss which interferes with a woman's physical, social, emotional and/or material quality of life’, as an indication for investigation and treatment options. As such, objective measurements of volume are usually the preserve of research studies and surrogates such a pictorial blood-loss assessment chart (PBAC) scores are not recommended in routine clinical practice.

FIGO classification of cause: ‘PALM-COEIN’

- Once bleeding is defined as being abnormal, the acronym PALM-COEIN is now being increasingly used for categorising causes:
- **P**olyp, **A**denomyosis, **L**eiomyoma, **M**alignancy (and hyperplasia), **C**oagulopathy, **O**vulatory disorders, **E**ndometrial, **I**atrogenic and **N**ot otherwise classified.
- The ‘PALM’ are assessed visually (imaging and histopathology) and the ‘COEIN’ are non-structural.

PALM & COEIN

Polyp
Adenomyosis
Leiomyoma
Malignancy & hyperplasia

Submucosal
Other

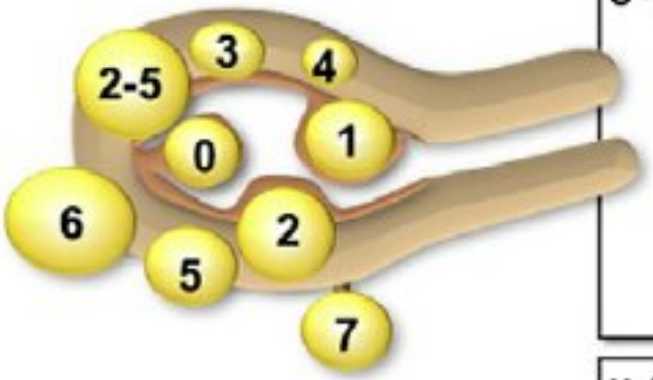
Coagulopathy
Ovulatory dysfunction
Endometrial
Iatrogenic
Not yet classified

Polyp
Adenomyosis
Leiomyoma
Malignancy & hyperplasia

Smucosal
Other

Coagulopathy
Ovulatory dysfunction
Endometrial
Iatrogenic
Not yet classified

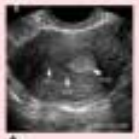
Leiomyoma subclassification system

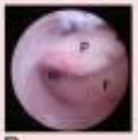


SM - Submucosal	0	Pedunculated intracavitary
	1	<50% intramural
	2	≥50% intramural
O - Other	3	Contacts endometrium; 100% intramural
	4	Intramural
	5	Subserosal ≥50% intramural
	6	Subserosal <50% intramural
	7	Subserosal pedunculated
	8	Other (specify e.g. cervical, parasitic)

Hybrid leiomyomas (impact both endometrium and serosa)	Two numbers are listed separated by a hyphen. By convention, the first refers to the relationship with the endometrium while the second refers to the relationship to the serosa. One example is below	
	2-5	Submucosal and subserosal, each with less than half the diameter in the endometrial and peritoneal cavities, respectively.

P **Polyp**


A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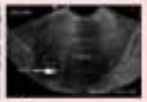
A **Adenomyosis**


C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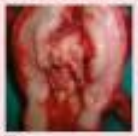
L **Leiomyoma**


E

M **Malignancy**


F

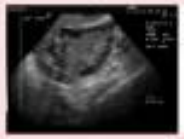

G

A: USS view of polyp
B: Hysteroscopic view of polyp
C: MRI of adenomyosis
D: USS of adenomyosis
E: Hysterectomy specimen containing fibroids
F: Hysterectomy specimen containing endometrial cancer
G: Histology of endometrioid carcinoma
H: Excessive bruising
I: USS of polycystic ovary
J: Progesterone receptor localisation in secretory phase
K: levonorgestrel-releasing intrauterine system (LNG-IUS)
L: Doppler USS of AV malformation
M: Doppler USS of endometrial pseudo-aneurysm

C **Coagulopathy**


H

O **Ovulatory**


I

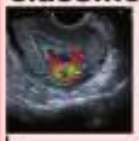
E **Endometrial**

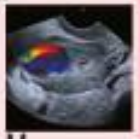

J

I **Iatrogenic**


K

N **Not otherwise classified**


L


M

Polyps

- Endometrial polyps are epithelial proliferations arising from the endometrial stroma and glands. The majority are asymptomatic. The contribution of polyps to AUB varies widely ranging from 3.7% to 65%, but it is widely accepted.
- The incidence of polyps as with fibroids increases with age and both pathologies may frequently co-exist, or suspected polyps visualised on transvaginal ultrasound scanning (TV-USS) may be mistaken for SM fibroids and vice-versa.

Adenomyosis (AUB-A)

- The relationship between adenomyosis and AUB remains unclear, particularly with regard to wide variations in histopathological diagnosis reflecting variations in criteria used and also improved radiological diagnosis.
- Typically, adenomyosis is associated with increasing age and may co-exist with fibroids. Furthermore, adenomyosis may be both focal and diffuse and it may be harder to establish diagnosis if fibroids are also present.

Malignancy (AUB-M)

- Endometrial cancer is the most common gynaecological malignancy in the western world.
- Historically, endometrial cancer has rarely occurred in premenopausal women; however, with increasing obesity and rising prevalence of the metabolic syndrome, the endocrine-driven subset of endometrial malignancy has markedly increased in frequency.
- Between 1992–1994 and 2009–2011, the European age-standardised rates of uterine cancer in the UK have increased by 48%. With the reclassification by the WHO from hyperplasia to endometrial intraepithelial neoplasia (EIN), the current prevalence of premalignant disease is unknown.
- The evaluation of the endometrium may be affected by distortion of the uterine cavity by fibroids, and as such, the co-existing pathology may delay diagnosis.

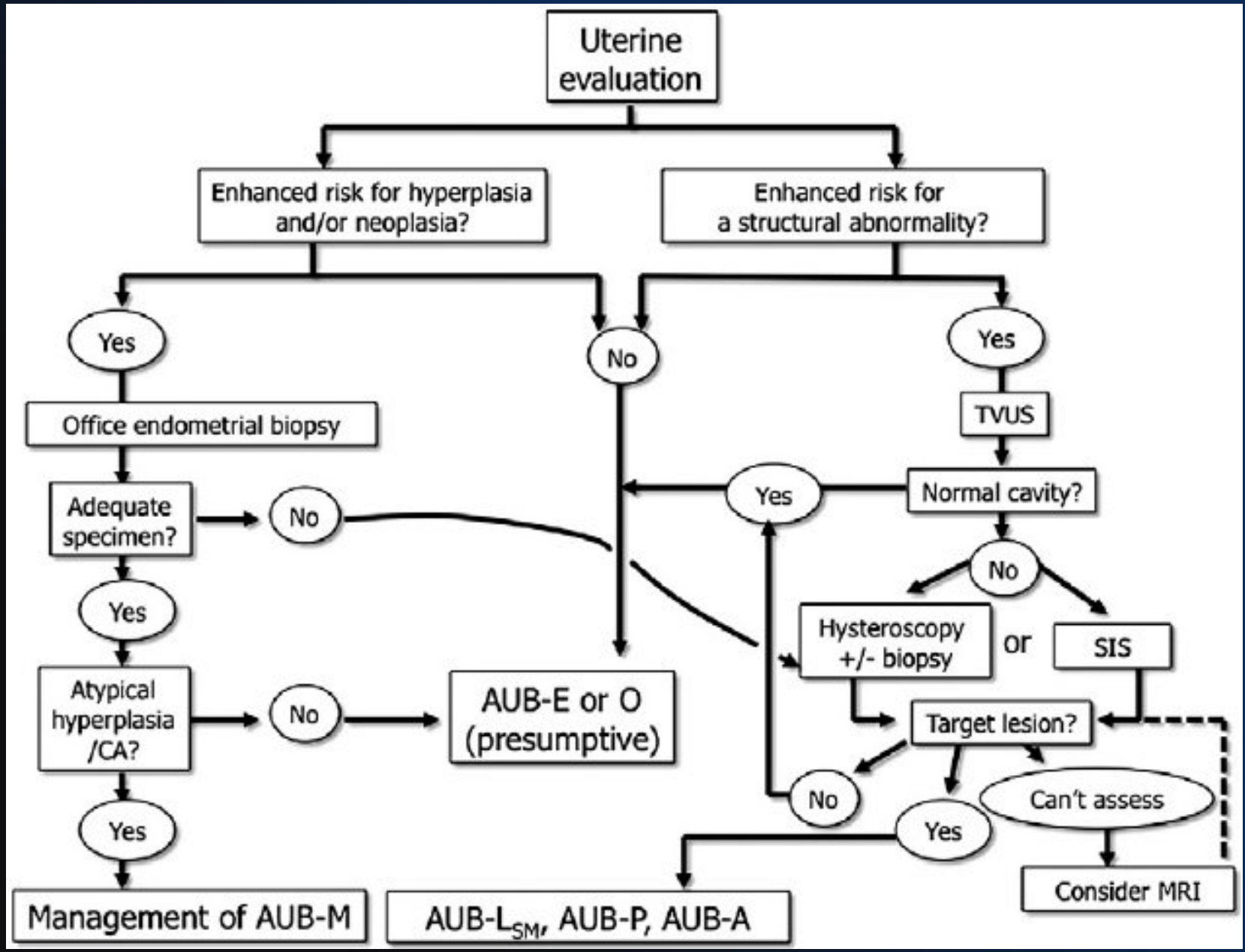
Incidence of Endometrial Cancer in Premenopausal Women

2.3/100,000 in 30-34 yr old

6.1/100,000 in 35-39 yr old

36/100,000 in 40-49 yr old

Ref: ACOG Practice Bulletin


Uterine evaluation
Enhanced risk for hyperplasia and/or neoplasia?
Enhanced risk for a structural abnormality?
Yes
No
Yes
Office endometrial biopsy
TVUS
Adequate specimen?
No
Yes
Normal cavity?
Yes
No
Yes
Hysteroscopy +/- biopsy
or
SIS
Atypical hyperplasia /CA?
No
AUB-E or O (presumptive)
Target lesion?
Yes
No
Can't assess
Consider MRI
Management of AUB-M
AUB-L$_{SM}$, AUB-P, AUB-A

Malignancy (AUB-M)

- The diagnosis of cervical cancer should be considered, particularly with persistent intermenstrual bleeding, and rarely ovarian cancer may present with AUB.
- Uterine sarcoma have been reported as rare (3–7/100,000 in the USA) but maybe a cause of AUB-M. A recent meta-analysis reported that leiomyosarcoma are unexpectedly diagnosed following surgery for anticipated ‘benign’ myomas in 2.94 per 1000 women (one in 340 women).
- Race is the only commonality between leiomyosarcoma and leiomyoma with black women having an approximately twofold increased risk.
- The risk of development of leiomyosarcoma is reported to increase with age with <1 case per 500 among women aged under 30 years to one in 98 among women in the age range 75–79 years.
- Other risk factors for uterine leiomyosarcoma include the long-term use of Tamoxifen, previous pelvic radiation therapy and rare inherited disorders such as hereditary leiomyomatosis and renal cell carcinoma (HLRCC)

Coagulopathy (AUB-C)

- Coagulopathies are reported to affect 13% of the women presenting with HMB. The majority of these women suffer from Von Willebrand disease.
- Systemic disorders of haemostasis may be identified in 90% of women using a structured history

Ovulatory (AUB-O)

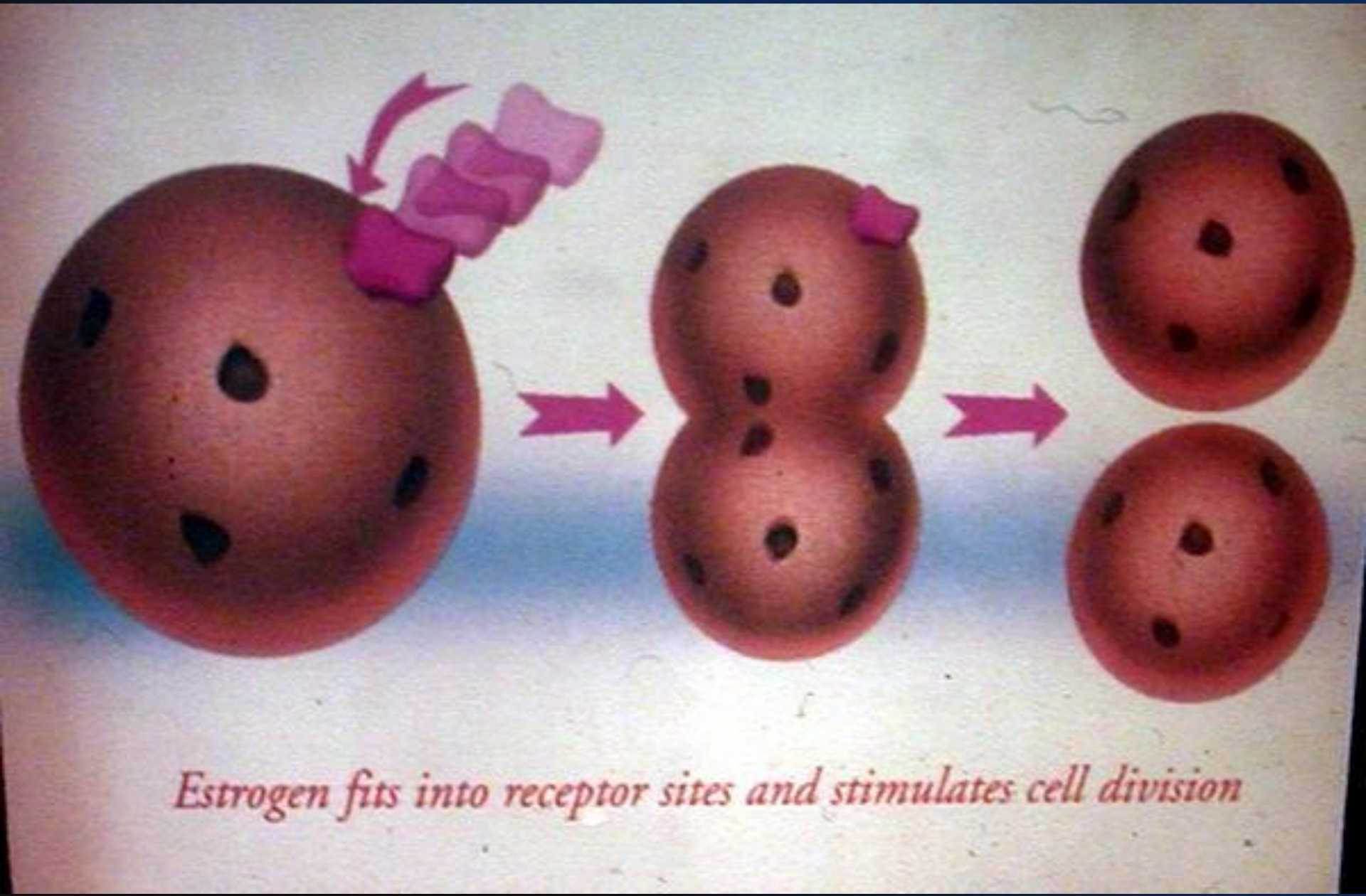
- Anovulatory cycles may contribute to AUB by unopposed oestrogen effects on the endometrium causing marked proliferation and thickening resulting in HMB along with an altered frequency of menstruation. This is observed at the extremes of reproductive age.
- The latter include polycystic ovarian syndrome (PCOS), hyperprolactinaemia, hypothyroidism as well as factors such as obesity, anorexia, weight loss, mental stress and extreme exercise.
- Typically, women in this group have menstrual cycles that fall out with 38 days or have a variation of >21 days. Drugs that affect dopamine levels, with their attendant effects on the HPO axis, also currently fall under this category rather than AUB-I. In women with fibroids, the co-existing ovulatory dysfunction may exacerbate menstrual loss.
- The FIGO AUB classification system is a dynamic system with feedback and contemporary debate informing future revisions. The position of drug therapies affecting AUB is currently under review with regard to whether anticoagulant/antiplatelet therapies and drugs affecting the HPO axis may be better placed in ‘AUB-I’.

Endometrial (AUB-E)

- AUB that occurs in the context of a structurally normal uterus with regular menstrual cycles without evidence of coagulopathy is likely to have an underlying endometrial cause.
- Hypoxia, inflammation, haemostasis and angiogenesis all play crucial roles in the shedding and subsequent scarless repair of the functional upper layer of the endometrium.
- Perturbation of local glucocorticoid metabolism, aberrant prostaglandin synthesis and excessive plasminogen (resulting in premature clot lysis) have all been implicated in AUB.
- AUB-E may be implicated in many women with AUB, but a lack of clinically available specific tests or biomarkers means that practical testing for such disorders is not yet feasible. As such, diagnosis depends on careful history taking and exclusion of other contributors. The high prevalence of potential endometrial dysfunction means that it is highly likely that those with AUB-L will often have an element of AUB-E contributing to increased/aberrant menstrual blood loss with its attendant implication for therapy.

Iatrogenic (AUB-I)

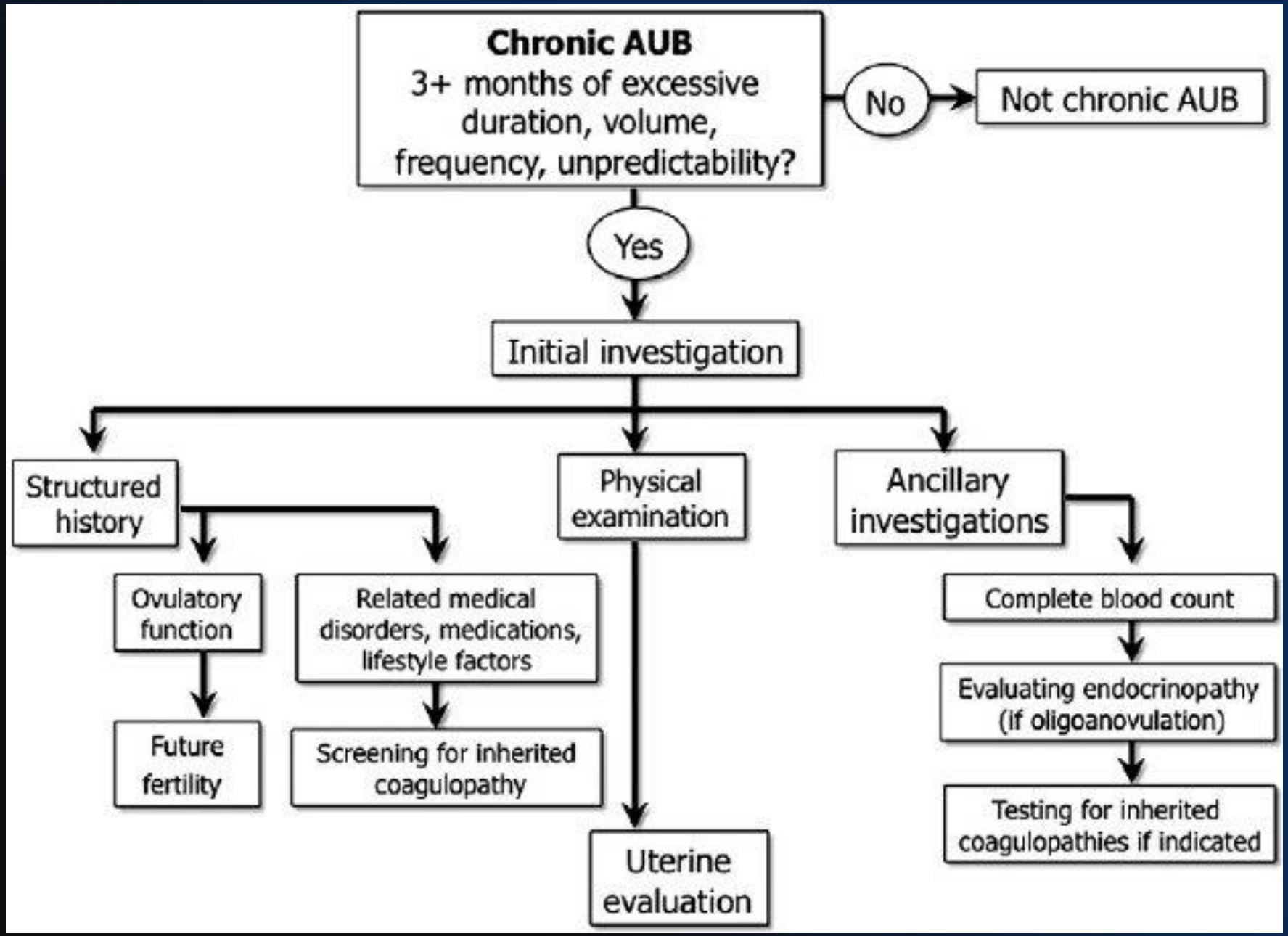
- Iatrogenic causes of AUB include exogenous therapy than may lead to unscheduled endometrial bleeding. This is typically associated with continuous oestrogen or progestin therapy (systemic or intrauterine delivery routes) or those interventions that act on ovarian steroid release such as gonadotropin-releasing hormone (GnRH) agonists and aromatase inhibitors. Selective oestrogen receptor modulators (SERMs) and more rarely selective progesterone receptor modulators (SPRMs) may cause AUB through direct action on the endometrium.
- The use of an intrauterine device (IUD) may cause a low-grade endometritis which may also contribute to AUB.



Estrogen fits into receptor sites and stimulates cell division

Not otherwise classified (AUB-N)

- It is inevitable that there will be pathologies that are either rare or poorly defined that do not easily fit within the categories described earlier. Examples include arteriovenous malformations, endometrial pseudoaneurysms, myometrial hypertrophy and chronic endometritis (not precipitated by an IUD). All of these can co-exist with AUB-L.
- The planned regular review of the FIGO PALM-COEIN classification system every 3–5 years through FIGO will allow reassessment, in particular, of this category. Further areas considered for future sub-classification include AUB-P and AUB-A.


Chronic AUB
3+ months of excessive duration, volume, frequency, unpredictability?
No
Not chronic AUB
Yes
Initial investigation
Structured history
Physical examination
Ancillary investigations
Ovulatory function
Related medical disorders, medications, lifestyle factors
Future fertility
Screening for inherited coagulopathy
Uterine evaluation
Complete blood count
Evaluating endocrinopathy (if oligoanovulation)
Testing for inherited coagulopathies if indicated

Specific treatment options for individual PALM-COEIN causes of AUB.

AUB Sub-classification	Specific treatment
Polyp	Resection
Adenomyosis	Surgery: hysterectomy; adenomyomectomy (not frequently performed)
Malignancy	Surgery +/− adjuvant treatment High-dose progestogens (if surgery not possible) Palliation (including radiotherapy)
Coagulopathy	Tranexamic acid DDVAP
Ovulation	Lifestyle modification Cabergoline (if hyperprolactinaemia) Levothyroxine (if hypothyroid)
Endometrial	Specific therapies await further delineation of underlying mechanisms
Iatrogenic	Refer to FSRH CEU guidance on problematic bleeding with hormonal contraception [56]
Not otherwise classified	Antibiotics for endometritis Embolisation of AV malformation

Common Terminology

Descriptive Term	**Bleeding pattern**
Menorrhagia	Regular cycles, prolonged duration, excessive flow
Metrorrhagia	Irregular cycles
Menometorrhagia	Irregular, prolonged, excessive
Hypermenorrhea	Regular, normal duration, excessive flow
Polymenorrhea	Frequent cycles
Oligomenorrhea	Infrequent cycles

Definitions

Menorrhagia:

Prolonged > 7 days or > 80 cc occurring at regular intervals.

Menorrhagia occurs in 9-14% of healthy women.

Synonymous with hypermenorrhea

Definitions

Metrorrhagia:

Uterine bleeding occurring at irregular but frequent intervals.

Definitions

Menometrorrhagia:

Prolonged uterine bleeding occurring at irregular intervals.

Definitions

Oligomenorrhea:

Infrequent uterine bleeding varying between 35 days and 6 months.

Definitions

Amenorrhea:

No menses for 6 months.

Hallberg, *et al*., 1966:

40% of women with blood loss >80cc considered their flow to be small or moderate. 14% of women with <20cc loss thought their flow was heavy.

Chimbira, *et al*., 1980 :

One third of light menses were actually <80cc and one-half of those believed to be heavy were >80cc.

Etiologies

- Organic
  - Systemic
  - Reproductive tract disease
  - Iatrogenic
- Dysfunctional
  - Ovulatory
  - Anovulatory

Systemic Etiologies

- Coagulation defects
- Leukemia
- ITP
- Thyroid dysfunction

Claessens, *et al*., 1981:

In a 9 year review of 59 cases of acute menorrhagia in adolescents it was discovered that 20% had a primary coagulation disorder.

Routine screening for coagulation defects should be reserved for the young patient who has heavy flow with the onset of menstruation.

Ref: Comprehensive Gynecology, 4th edition

Von Willebrand's Disease is the most common inherited bleeding disorder with a frequency of 1/800-1000.

Ref: Harrison's Principles of Internal Medicine, 14th edition

Wilansky, *et al*., 1989 :

Hypothyroidism can be associated with menorrhagia or metrorrhagia.

The incidence has been reported to be 0.3-2.5%.

Most Common Causes of Reproductive Tract AUB

- Pre-menarchal
  - Foreign body
- Reproductive age
  - Gestational event
- Post-menopausal
  - Atrophy

Reproductive Tract Causes

- Gestational events
- Malignancies
- Benign
  - Atrophy
  - Leiomyoma
  - Polyps
  - Cervical lesions
  - Foreign body
  - Infections

Reproductive Tract Causes

- Gestational events
  - Abortions
  - Ectopic pregnancies
  - Trophoblastic disease
  - IUP

Reproductive Tract Causes

- Malignancies
  - Endometrial
  - Ovarian
  - Cervical

Karlsson, *et al*., 1995:

10% of women with postmenopausal bleeding will be diagnosed with endometrial cancer and an equal number with hyperplasia.

Reproductive Tract Causes of Benign Origin

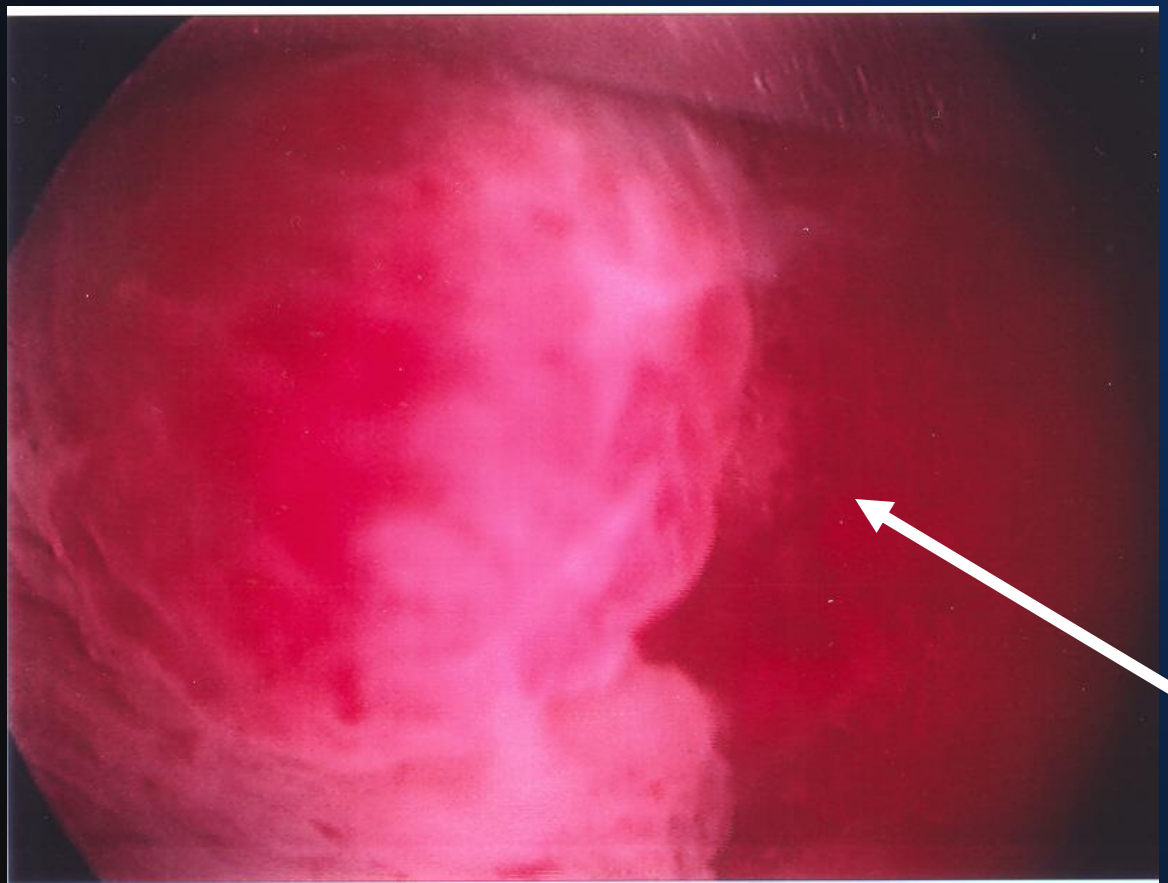
- Atrophy
- Leiomyoma
- Polyps
- Cervical lesions
- Foreign body
- Infection

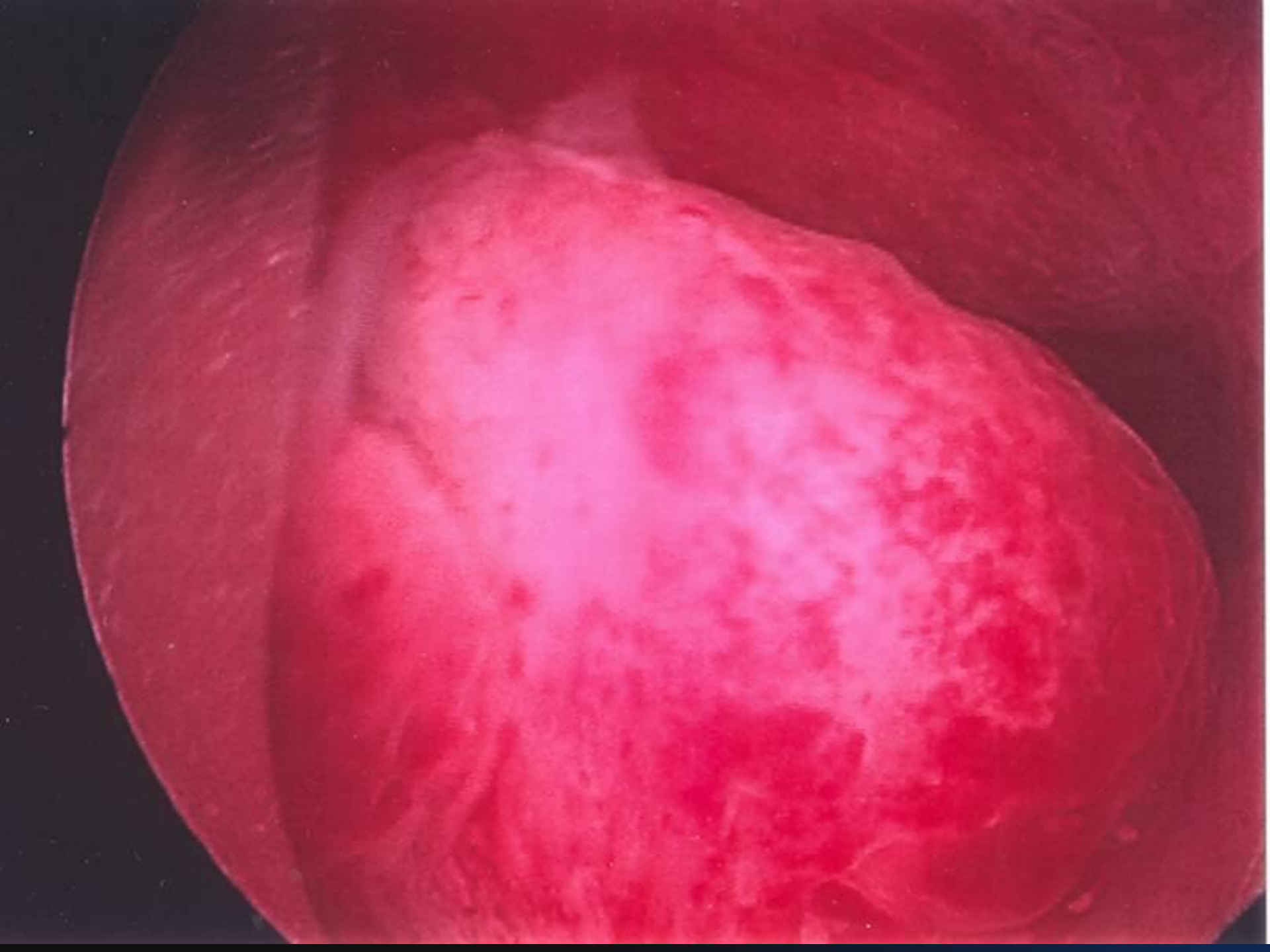
Polyps

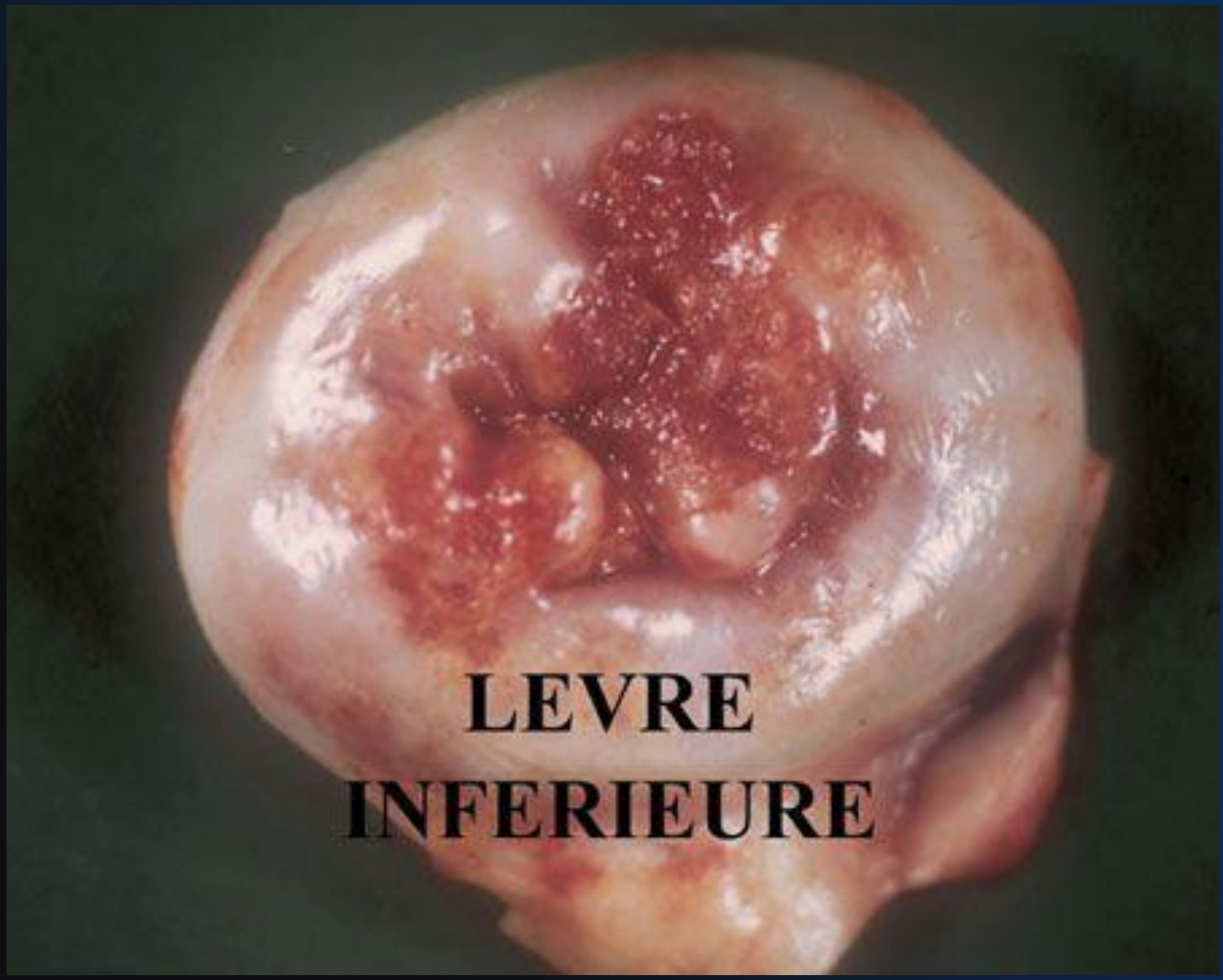
- Endometrial
  - Intermenstrual bleeding
  - Irregular bleeding
  - Menorrhagia
- Cervical
  - Intermenstual spotting
  - Postcoital spotting

Karlsson, *et al*., 1995:

60% of women with PMB will be found to have atrophy. 10% will have polyps and 10% will have hyperplasia.



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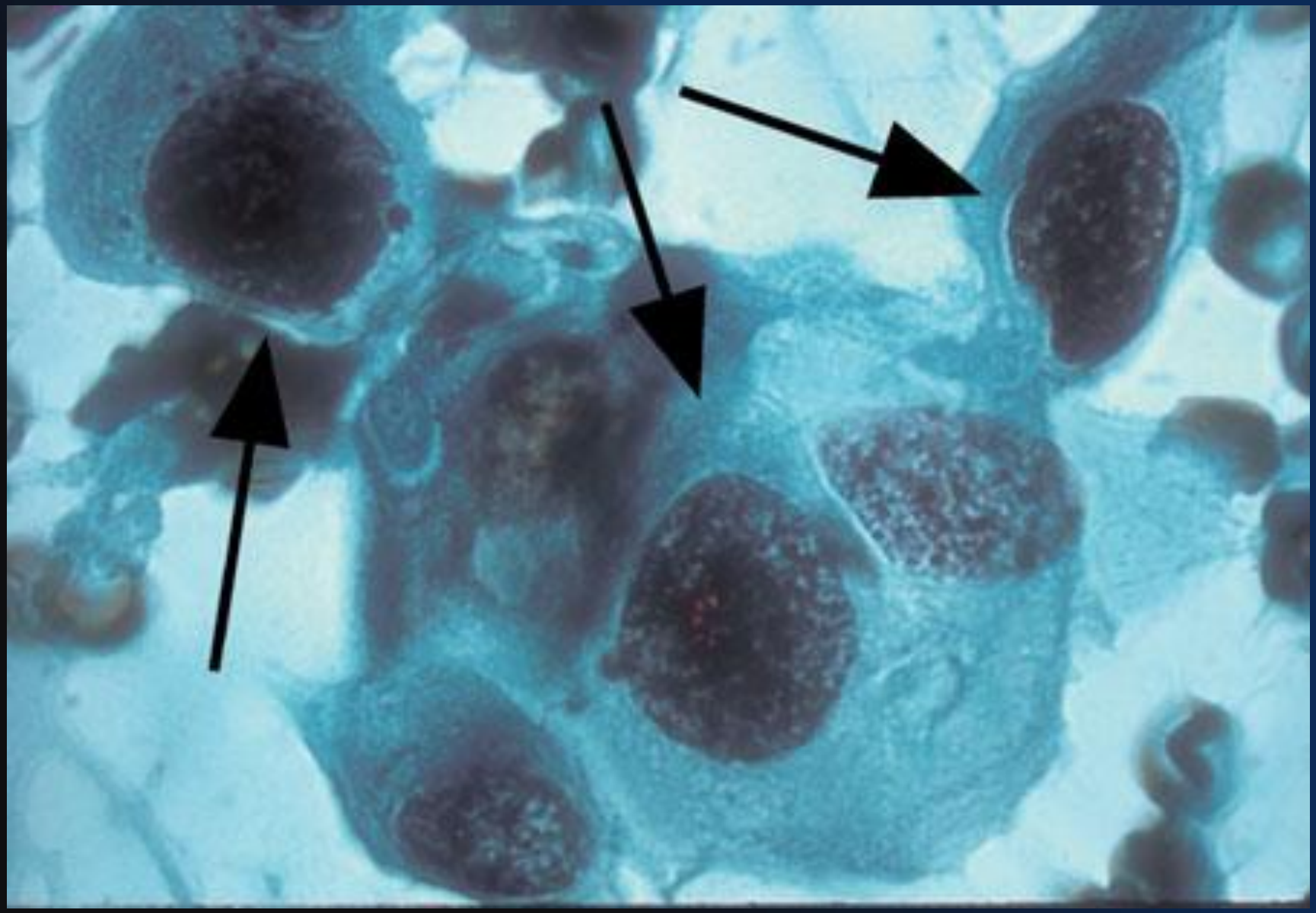


Proposed Etiologies of Menorrhagia with Leiomyoma

- Increased vessel number
- Increased endometrial surface area
- Impeded uterine contraction with menstruation
- Clotting less efficient locally

Leiomyoma in any location is associated with increased risks of gushing or high pad/tampon use.

Ref: Wegienka, *et al*., 2003

Infectious causes

- PID
  - fever, pelvic discomfort, CMT, adnexal tenderness, or atypically
  - Can cause menorrhagia or metrorrhagia
  - More common during menstruation
- Trichomonas
- Endocervicitis

Pelvic Inflammatory Disease

- Definition:
- Pelvic Inflammatory Disease (PID) is any acute, subacute, recurrent, or chronic infection of the oviducts, and ovaries, with adjacent involvement.

Pelvic Inflammatory Disease

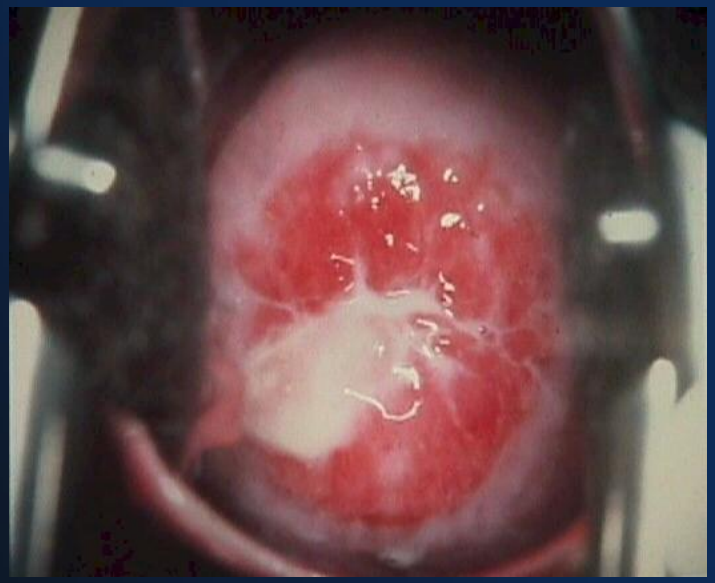
- Sites:
- It includes inflammation of :
- cervix (cervicitis)
- uterus (endometritis)
- fallopian tubes (salpingitis) and
- ovaries (oophoritis)
- the connective tissue lying between the broad ligaments (parametritis)

Pelvic Inflammatory Disease

- Cervicitis.

Definition:

inflammation of the cervix.



Pelvic Inflammatory Disease

- Causative organisms:
- gonococcus,
- streptococcus,
- staphylococcus,
- aerobic organisms,
- anaerobic organisms,
- herpes virus,
- chlamydia.

Pelvic Inflammatory Disease

- Forms of cervicitis--
- 1- Acute
- 2- Chronic

Pelvic Inflammatory Disease

- Acute cervicitis.
- Symptoms.
- Purulent, foul smelling vaginal discharge.
- Itching and/or burning sensation.
- Red, edematous cervix.
- Pelvic discomfort.
- Sexual dysfunction > infertility.

Pelvic Inflammatory Disease

- Acute cervicitis.
- Assessment.
- Physical examination.
- Cultures for N. gonorrhea are positive greater than 90% of the time.
- Cytologic smears.
- Cervical palpation reveals tenderness.
- Management - based on culture results.

Pelvic Inflammatory Disease

- Chronic cervicitis.
- Symptoms.
- Cervical dystocia--difficult labor.
- Lacerations or eversion of the cervix.
- Ulceration vesicular lesions (when cervicitis results from Herpes simplex

Pelvic Inflammatory Disease

- Assessment.
- Physical examination.
- Chronic cervicitis, causative organisms are usually staphylococcus or streptococcus.

Pelvic Inflammatory Disease

- Management - manage by cauterization, cryotherapy, conization (excision of a cone of tissue).

Pelvic Inflammatory Disease

- Endometritis

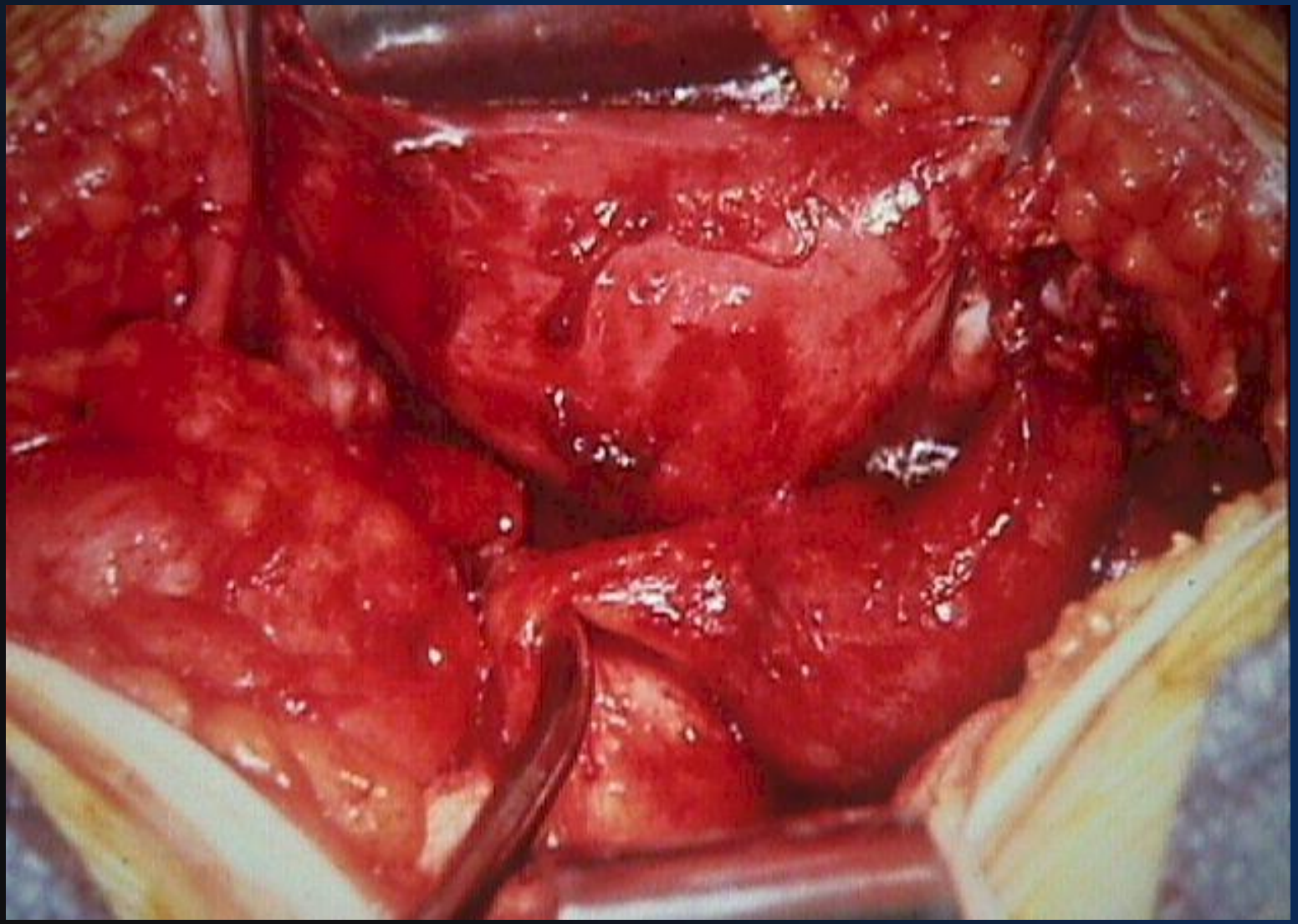
- Definition - inflammation of the endometrium.

Pelvic Inflammatory Disease

- Etiology - produced by bacterial infection most commonly staphylococci, colon bacilli, or gonococci, trauma, septic abortion.
- Sites - uterine ligaments, (uterosacral, broad, round) and ovaries, (extra uterine locations).

NOTE

- Endometriosis - ectopic endometrium located in various sites throughout the pelvis or on the abdominal wall.



Pelvic Inflammatory Disease

- Endometriosis
- Symptoms.
- Low back and low abdominal pain.
- Dysmenorrhea.
- Menorrhagia.
- Pain on defecation, constipation.
- Sterility.

Pelvic Inflammatory Disease

- Endometriosis
- Assessment.
- Physical examination.
- Vaginal cultures.
- Management
- based upon culture results.

Pelvic Inflammatory Disease

- Salpingitis and Oophoritis.
- Definition - infection of the fallopian tubes and ovaries.
- History - usually recent sexual intercourse, insertion of an IUD, or a recent childbirth or abortion, gonococcus, chlamydia, streptococcus, and anaerobes have been implicated as causative organisms

Pelvic Inflammatory Disease

- Salpingitis and Oophoritis.
- Signs and symptoms.
- Lower abdominal pain sometimes with signs and symptoms of acute abdomen can be unilateral or bilateral.
- Fever.
- Severe pain with palpation of the cervix, uterus, and adnexa (Chandelier sign).
- Purulent cervical discharge.
- Leukocytosis.

Pelvic Inflammatory Disease

- Salpingitis and Oophoritis.
- Assessment.
- Physical examination.
- Gonorrhea culture.
- Test for chlamydia.

Pelvic Inflammatory Disease

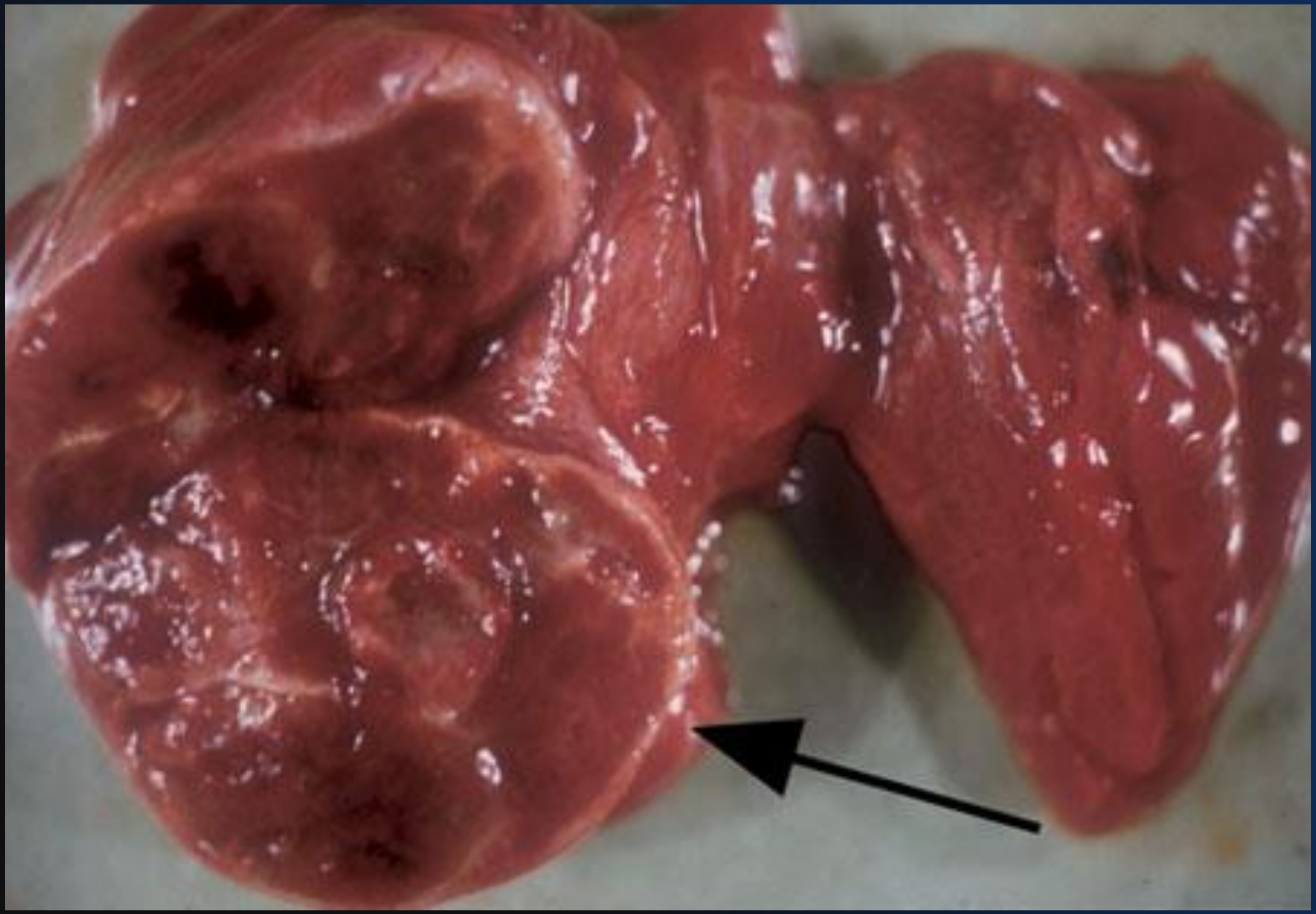
- Salpingitis and Oophoritis
- Complications.
- Tubal abscess.
- Infertility (common)

Pelvic Inflammatory Disease

- Salpingitis and Oophoritis
- Management.
- IV fluids to correct dehydration.
- NG suction in the presence of abdominal distention or ileus.
- Manage the associated symptoms.
- Bedrest and restrict oral feedings.

Endocrine abnormalities

- Hyperthyroidism
  - Amenorrhea
  - Oligomenorrhea
    - most common
  - Hypermenorrhea
  - Polymenorrhea,
- Hypothyroidism
  - Amenorrhea
  - Oligomenorrhea
  - Polymenorrhea
  - Menorrhagia
  - Occurs more frequently with severe hypothyroidism



Iatrogenic Causes of AUB

- Intra-uterine device
- Oral and injectable steroids
- Psychotropic drugs

Contraceptive Bleeding

- OCP's
  - Lower dose contraceptives
  - Skipped pills
  - Altered absorption / metabolism
- Depo Provera
  - 50% irregular bleeding after first dose
  - 25% after a year
- Norplant
  - 30% have regular cycles
  - 66% have regular cycles by the 5th year of use

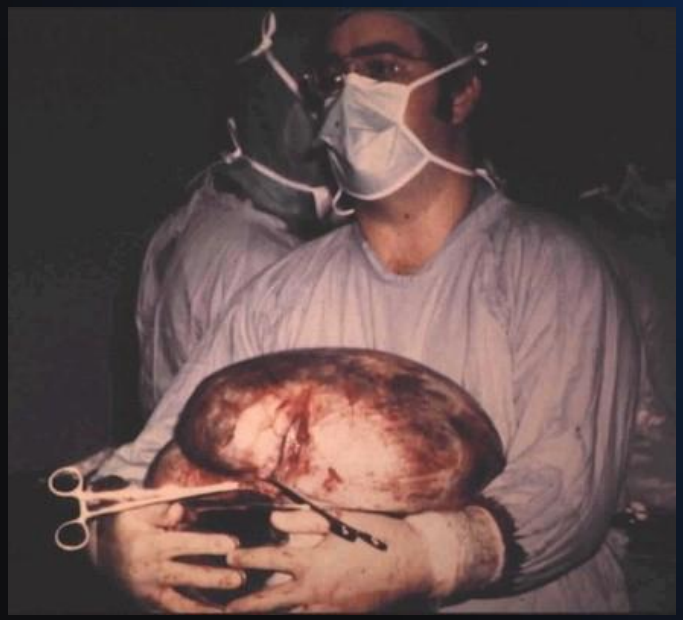
DUB

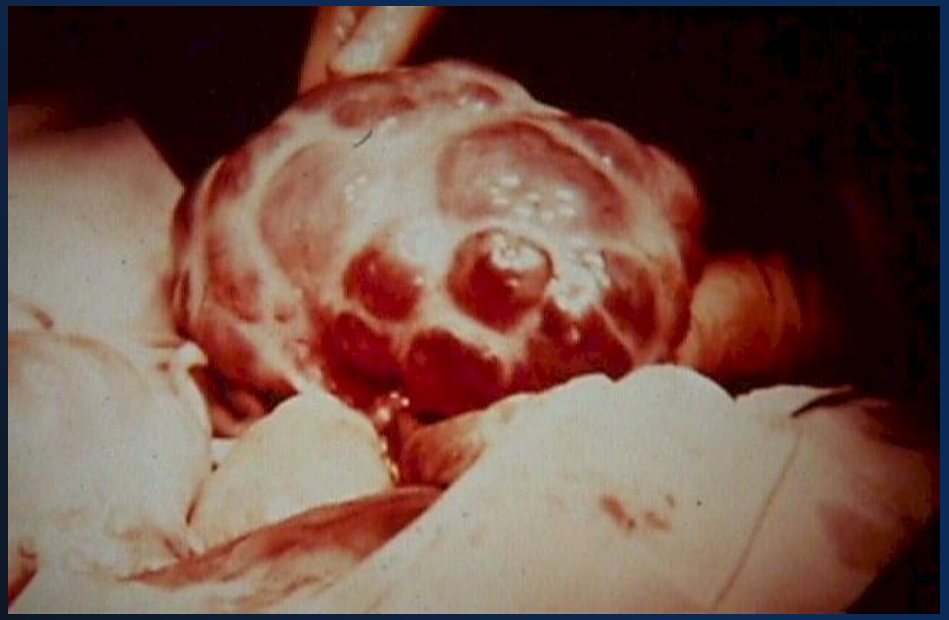
Abnormal uterine bleeding for which an organic etiology has been excluded. It is either ovulatory or anovulatory in origin.

To determine if DUB is ovulatory or anovulatory….

- History
- Daily basal body temperature
- Luteal phase progesterone
- Luteal phase EMB (Endometrial Biopsy)

Ovarian Cyst





Ovarian Cyst

- Ovarian cysts are usually nonneoplastic sacs on an ovary that contain:
- fluid or
- semisolid material.

Ovarian Cyst

- Ovarian cysts are frequently asymptomatic, but the pressure of an abnormal mass may cause:
- discomfort,
- aching, or
- heaviness to the pelvic region and on abdominal organs.

Ovarian Cyst

- Sudden or sharp pain may indicate:
- rupture,
- hemorrhage, or
- torsion of cyst.
- Fever, leukocytosis or s/s of shock may be present.

The majority of dysfunctional AUB in the premenopausal woman is a result of anovulation.

With anovulation a corpus luteum is NOT produced and the ovary thereby fails to secrete progesterone.

However, estrogen production continues, resulting in endometrial proliferation and subsequent AUB.

Ref: Comprehensive Gynecology, 4th edition

PGE_2 → vasodilation

$PGF_{2\alpha}$ → vasoconstriction

Progesterone is necessary to increase arachidonic acid, the precursor to $PGF_{2\alpha}$.

With decreased progesterone there is a decreased $PGF_{2\alpha}/PGE_2$ ratio.

Since vasoconstriction is promoted by PGF2α, which is less abundant due to the decrease in progesterone, vasodilation results thereby promoting AUB.

Evaluation and Work-up:

Early Reproductive Years/Adolescent

- Thorough history
- Screen for eating disorder
- Labs:
  - CBC, PT, PTT, bleeding time, hCG

One should consider an EMB for adolescents with 2-3 year history of untreated anovulatory bleeding in obese females < 20 years of age.

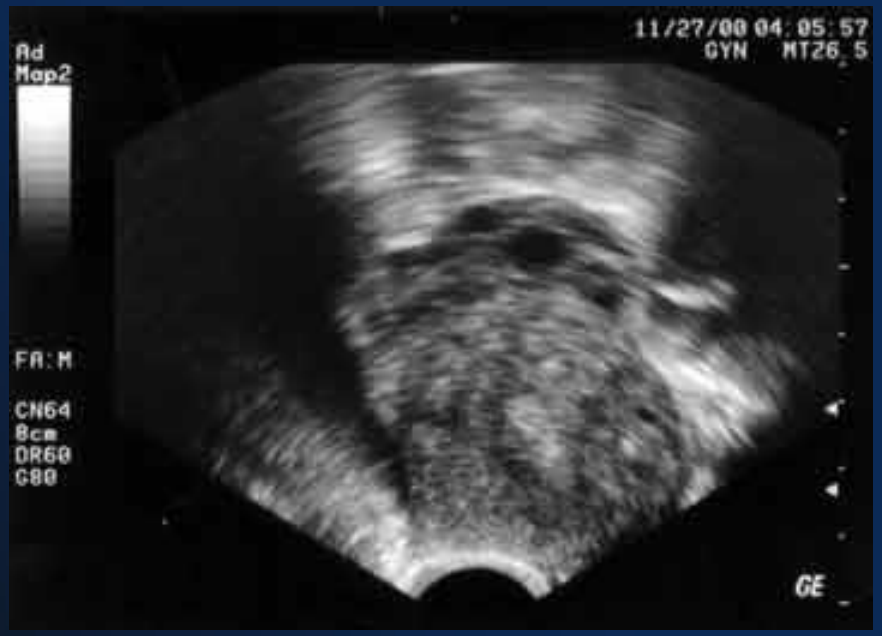
Ref: ACOG Practice Bulletin #14, March 2000

Laboratory studies

- CBC
- Urine or serum pregnancy test
- TSH
  - symptoms consistent with hypo/hyperthyroidism
  - women presenting with a change from a normal menstrual pattern
- PT, PTT, and bleeding time.
  - adolescents presenting with menorrhagia at menarche
- PCOS/Adult-onset CAH
  - LH, FSH, testosterone, androstenedione, basal 17-hydroxyprogesterone (17-HP)

Ultrasound

- Evaluate ovaries for PCOS
- Evaluate for fibroids
- Evaluate endometrial stripe



Evaluation and Work-up:
Women of Reproductive Age

- hCG, LH/FSH, CBC
- Cervical cultures
- U/S
- Hysteroscopy
- EMB (Endometrial Biopsy)

Evaluation and Work-up: Post-menopausal Women

- FSH/LH
- Transvaginal U/S
- EMB
- Hysteroscopy with endometrial sampling

Karlsson, *et al*., 1995:

An endometrial cancer is diagnosed in approximately 10% of women with PMB.

Gull, *et al*., 2003:

PMB incurs a 64-fold increased risk for developing endometrial CA.

Not a single case of endometrial CA was missed when a <4mm cut-off for the endometrial stripe was used in their 10 yr follow-up study.

Gull, *et al*., 2003:

There was no increased risk of endometrial cancer or atypia in those women who did not experience recurrent PMB in their 10 year follow-up.

Further, no endometrial cancer was diagnosed in women with recurrent PMB who had an endometrial stripe width of <4mm on their initial scan.

However, 3 women with stripe width of 5-6mm developed recurrent PMB and were diagnosed with endometrial cancer within 3-5 years.

Good, 1997:

The stripe thickness measures between 4-8mm in women on cyclic HRT and about 5mm if they are receiving combined HRT.

EMB

Complications rare.

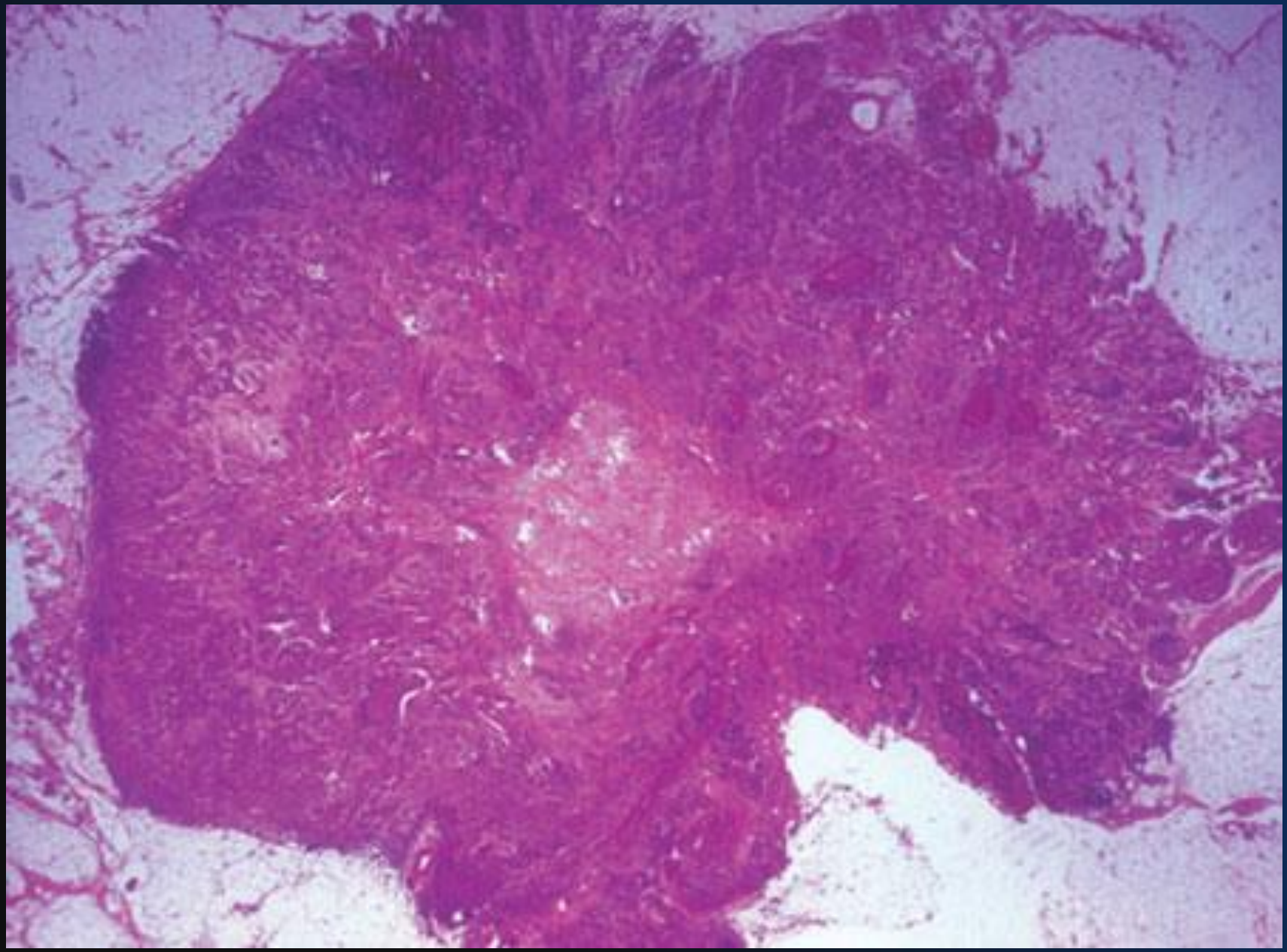
Rate of perforation 1-2/1,000.

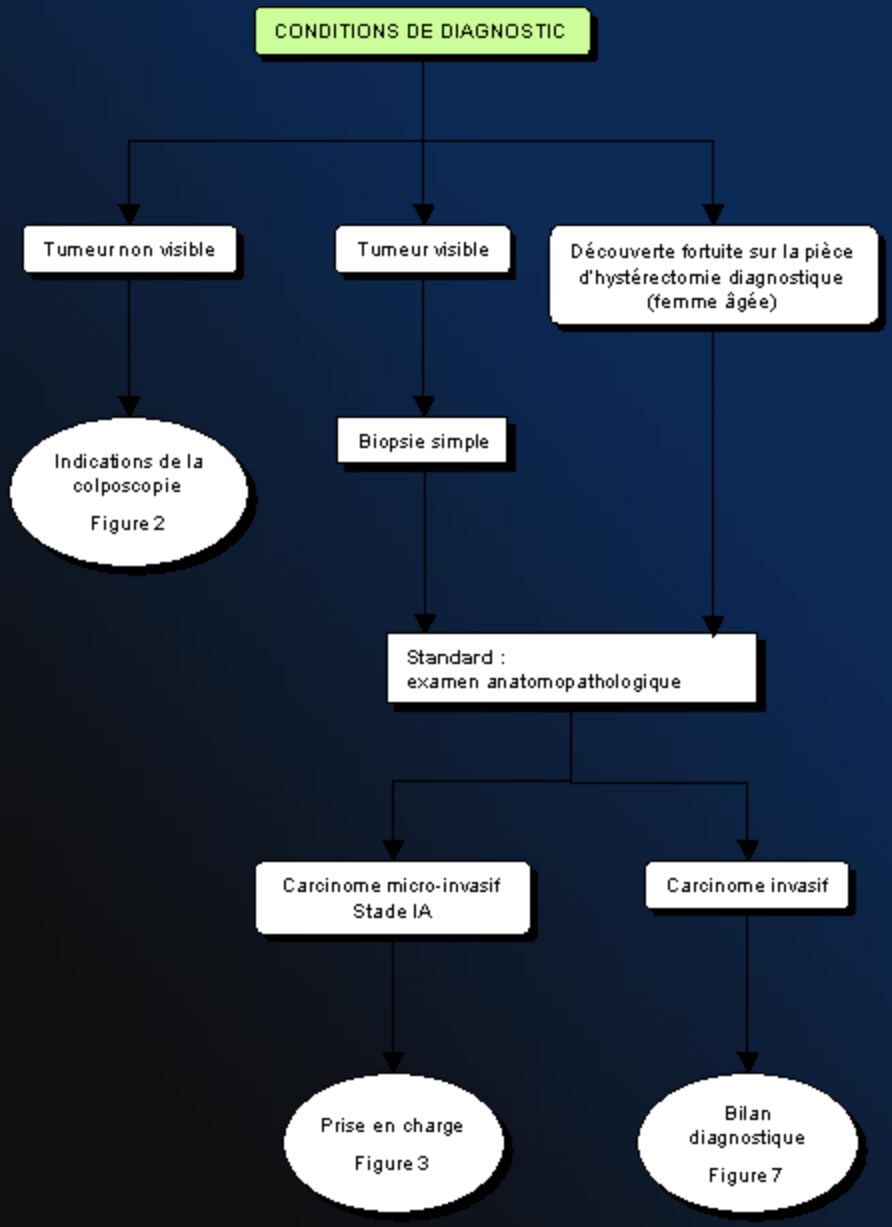
Infection and bleeding rarer.

Ref: Comprehensive Gynecology, 4th ed.

EMB

- Sensitivity 90-95%
- Easy to perform
- Numerous sampling devices available




CONDITIONS DE DIAGNOSTIC
Tumeur non visible
Tumeur visible
Découverte fortuite sur la pièce d'hystérectomie diagnostique (femme âgée)
Indications de la colposcopie
Figure 2
Biopsie simple
Standard : examen anatomopathologique
Carcinome micro-invasif Stade IA
Carcinome invasif
Prise en charge
Figure 3
Bilan diagnostique
Figure 7

Incidence of Endometrial Cancer in Premenopausal Women

2.3/100,000 in 30-34 yr old

6.1/100,000 in 35-39 yr old

36/100,000 in 40-49 yr old

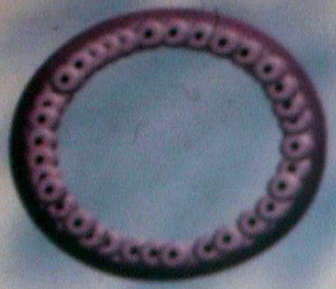
Ref: ACOG Practice Bulletin #14, 2000

Therefore, based upon age alone, an EMB to exclude malignancy is indicated in any woman > 35 years of age with AUB.

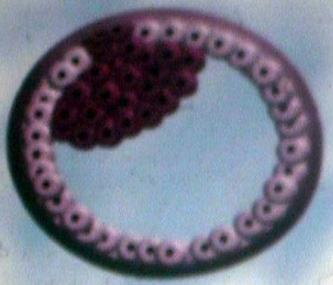
Ref: ACOG Practice Bulletin #14, March 2000

Endometrial Cancer Risk Factors

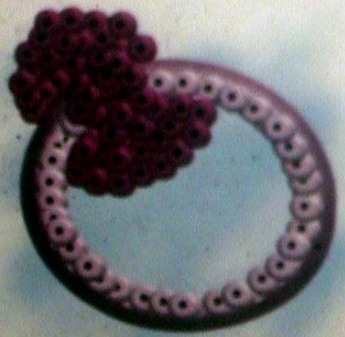
- Nulliparity: 2-3 times
- Diabetes: 2.8 times
- Unopposed estrogen: 4-8 times
- Weight gain
  - 20 to 50 pounds: 3 times
  - Greater than 50 lbs: 10 times!



Normal duct



In situ cancer



Invasive cancer

Possible Path Reports with EMB:

- Proliferative, secretory, benign, or atrophic endometrium
- Inactive endometrium
- Tissue insufficient for evaluation
- No endometrium seen

Possible Path Reports with EMB:

- Simple or complex hyperplasia WITHOUT atypia
- Simple or complex hyperplasia WITH atypia
- Endometrial cancer

Management

Prior to initiation of therapy:

pregnancy and malignancy must be ruled out.

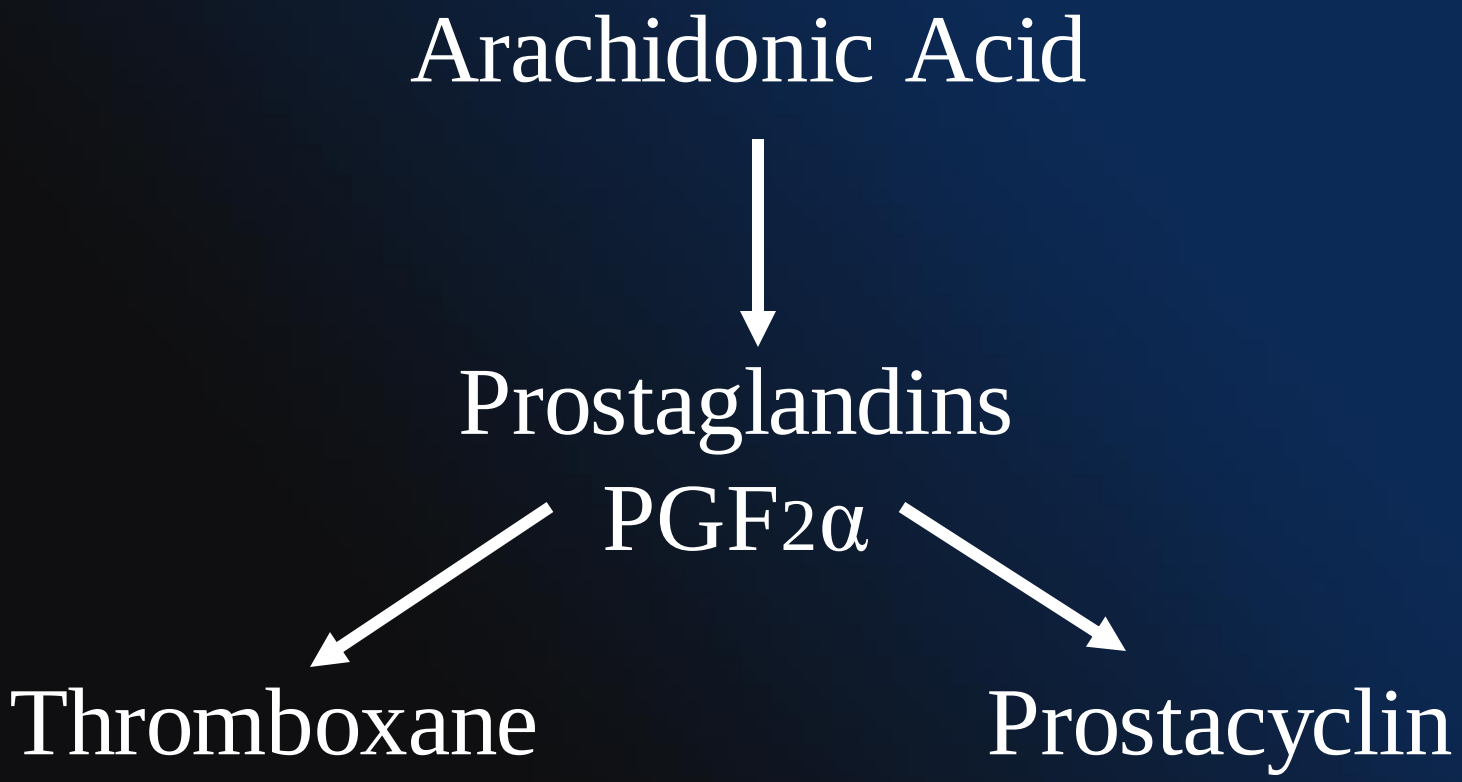
Management Options:

- Progestins
- Estrogen
- OCs
- NSAIDs
- Antifibrinolytics
- Surgical

Progestins:
Mechanisms of Action

- Inhibit endometrial growth
  - Inhibit synthesis of estrogen receptors
  - Promote conversion of estradiol → estrone
  - Inhibit LH
- Organized slough to basalis layer
- Stimulate arachidonic acid formation

Management: Progesterone Cyclooxygenase Pathway



Adolescent anovulatory patients are ideally suited for progestins as the development of the immature hypothalamic-pituitary axis is not impeded.

Progestins are the preferred treatment for those women with anovulatory AUB.
Cyclic progesterone is not recommended for ovulatory AUB.

Consider a progestational IUD as a viable option in the management of anovulatory/ovulatory AUB.

Progestational Agents

- Cyclic medroxyprogesterone (Provera®) 2.5-10mg daily for 10-14 days
- Continuous Provera® 2.5-5mg daily
- Progesterone in oil, 100mg every 4 weeks
- DepoProvera® 150mg IM every 3 months
- Progestasert® IUD (12 months)
- Mirena® IUD (5 years)

Progestins

- induce withdrawal bleeding
- decrease the risk of future hyperplasia and/or endometrial cancer
- continued for 7-12 days each cycle
- Medroxyprogesterone 10 mg x 10 days monthly common regimen
- norethindrone acetate (Aygestin), norethindrone (Micronor), norgestrel (Ovrette), and micronized progesterone (Prometrium, Crinone)

Endometrial Hyperplasia

It is reasonable for you to initiate a progestational agent if an EMB path report indicates simple hypersplasia WITHOUT atypia. Provera® 5-10 mg daily with a f/u plan for an EMB in 6 months. Referral is prudent if bleeding persists or worsens.

Management: Estrogen

Conjugated estrogens given IV in 25mg doses every 6 hours should be effective in controlling heavy bleeding. This is followed by PO estrogen.

Management: Estrogen

For less severe bleeding, PO Premarin® 1.25mg, 2 tabs QID until bleeding ceases.

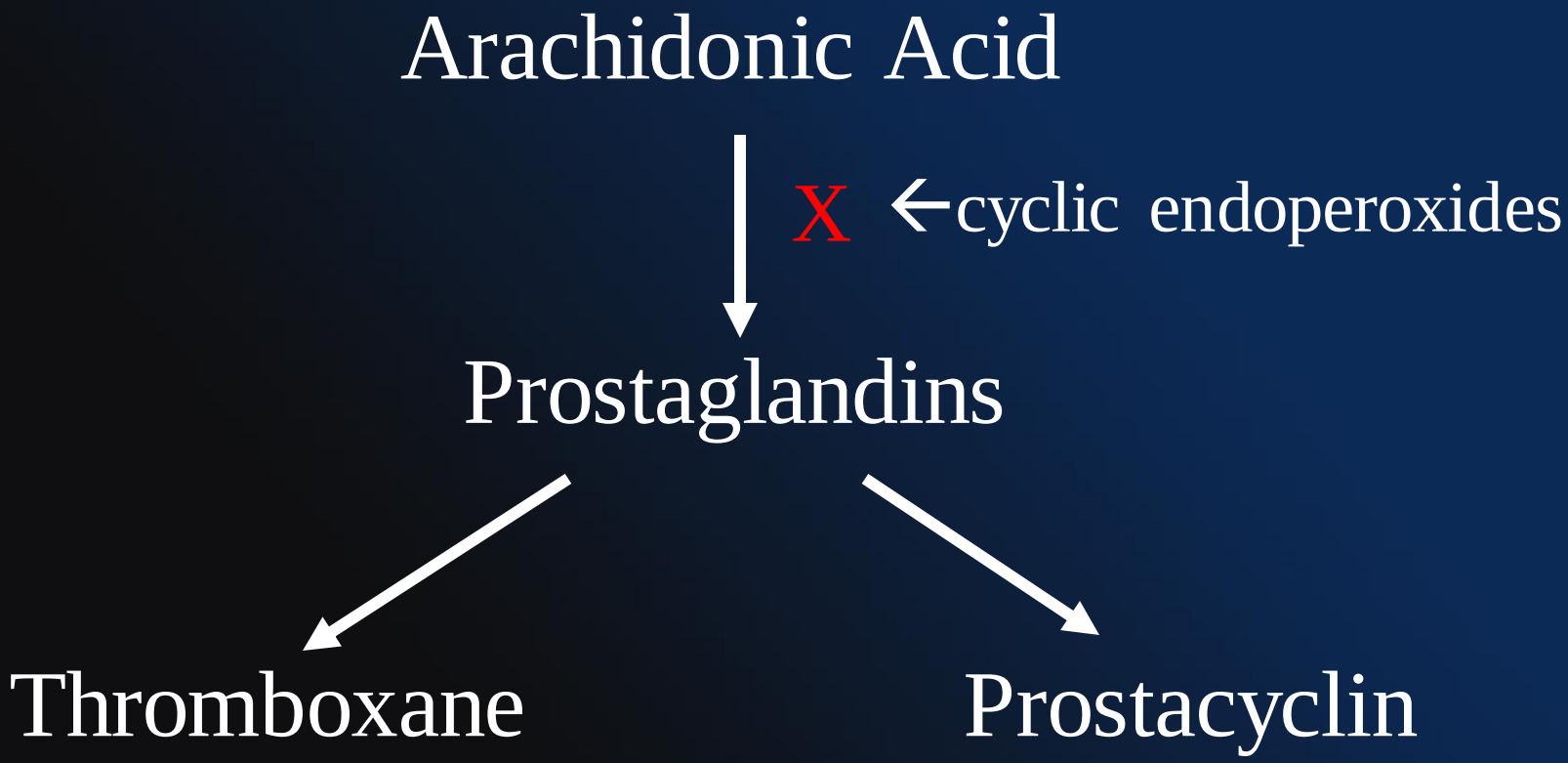
Estrogen

- will temporarily stop most uterine bleeding, no matter what the cause
- dose commonly used is 25 mg IV of conjugated estrogen every four hours, or 2.5 mg p.o. QID
- Nausea limits using high doses of estrogen orally, but lower doses can be used in a patient who is hemodynamically stable

Oral Contraceptives

- option for treatment of both the acute episode of bleeding and future episodes of bleeding as well as prevention of long term health problems from anovulation
- triphasil norgestimate/ethinyl estradiol combination is what has been studied in a double-blind, placebo-controlled study
- various oral contraceptives have been used for decades
- Acute bleeding: 50mcg tab QID for one week after bleeding stops

Management: NSAIDs
Cyclooxygenase Pathway



Prostaglandin Synthetase Inhibitors

- mefanamic acid, ibuprofen, and naproxen
- Blood loss can be cut in half
- many of the studies completed in women with ovulatory cycles
- does not address the issues of future noncyclic bleeding and decreasing future health risks due to anovulation

Antifibrinolytics: Tranexamic Acid Cyklokapron®

- Used extensively in Europe
- Mainstay of treatment of ovulatory AUB in most of the world
- Reduces blood loss by 45-50%
- Non-FDA labeled indication

Antifibrinolytics

1 gram P.O. every 6 hours for 3-7 days at onset of menses

Contraindications include: acquired defective color vision, active intravascular clotting process and subarachnoid hemorrhage

Surgical Options:

- Laser ablation
- Thermal ablation
- Resection
- Hysterectomy

Endometrial Ablation

- electrocautery, laser, cryoablation, or thermoablation
- all result in destruction of the endometrial lining
- outcomes are not well studied for women with anovulation
- most women will not experience long term amenorrhea after treatment
- risk of endometrial cancer is not eliminated

Comparison of Ablative Techniques

	Amenorrhea	Satisfaction
Laser/resection	45%[1]	90%[1]
Thermal ablation	15%[2]	90%[2]

[1]Aberdeen Trial Group, 1999
[2]Meyer et al., 1998

Summary

- Think coagulation defect in the menarchal adolescent patient with severe menorrhagia
- Gestational events are the single most likely cause of AUB in reproductive age women
- 35 yrs and older with AUB → EMB
- If Rx estrogen be sure to screen for contraindications

Summary

- Most common cause of AUB in post-menopausal women is atrophy
- TVS is an excellent screening tool for the evaluation of PMB
- Women with recurrent PMB require definitive F/U
- Endometrial CA risk factors: age, obesity, unopposed estrogen, DM, and ↑BP
- Hysteroscopy is the “gold standard”


به امید موفقیت و سعادت شما