New classification of Abnormal Uterine Bleeding: Why is it necessary?

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Abnormal Uterine Bleeding

- Common condition: 33% of all gynae visits to GPs (Coulter et al. BMJ 1992)
- Fe Def anaemia
- Negative impact on QOL – social, sexual and occupational activities
- Financial burden: patient, health system and country’s economy
  - USA costs: $2000 /patient/year (Cote I et al. 2002)
AUB

- **Terminology:**
  - Poorly defined - archaic terms
  - Inconsistent use in different countries / textbooks
  - Suspect clinical management
  - Difficulty in interpretation of basic science research

- **Wide spectrum of causes**
  - >1 cause in a given women
  - Some perceived causes found maybe asymptomatic
FIGO

- 2004 – FIGO menstrual disorders group
- Washington meeting: Feb 2005
- Reporting – 2007 - Published simultaneously in Fertil Steril and Hum Reprod journals
- FIGO acceptance: Nov 2009
- Published Feb/April 2011
A process designed to lead to international agreement on terminologies and definitions used to describe abnormalities of menstrual bleeding

Fraser IS, Critchley HOD, Munro MG, Broder M

*Fertil Steril* 2007; 87(3): 466-76

Can we achieve international agreement on terminologies and definitions used to describe abnormalities of menstrual bleeding?

Fraser IS, Critchley HOD, Munro MG, Broder M

*Hum Reprod* 2007; 22(3): 635-43
SPECIAL COMMUNICATION

FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age

Malcolm G. Munro a,b,*, Hilary O.D. Critchley c, Michael S. Broder d, Ian S. Fraser e; for the FIGO Working Group on Menstrual Disorders

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b Kaiser Permanente, Los Angeles Medical Center, Los Angeles, USA
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d Partnership for Health Analytic Research, Beverly Hills, USA
e University of Sydney, Queen Elizabeth II Research Institute for Mothers and Infants, Sydney, Australia

<table>
<thead>
<tr>
<th>Polyp</th>
<th>Coagulopathy</th>
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<tbody>
<tr>
<td>Adenomyosis</td>
<td>Ovulatory dysfunction</td>
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<tr>
<td>Leiomyoma</td>
<td>Endometrial</td>
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<td>Malignancy &amp; hyperplasia</td>
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FIGO acceptance: Nov 2010; e-pub in Feb 2011; print published in April 2011
Terminology abandoned by FIGO

Munro et al. Int J Gynecol Obstet 2011; 113: 3-13

Dysfunctional uterine bleeding/Functional uterine bleeding
Menorrhagia (including idiopathic menorrhagia, essential menorrhagia, ovulatory menorrhagia, anovulatory menorrhagia, polymenorrhagia, epimenorrhagia)
Menorrhoea (including epimenorrhea, hypermenorrhea, hypomenorrhoea, polymenorrhea)
Menometrorrhagia
Metorrhagia
Metropathia hemorrhagica
Oligomenorrhea
Uterine haemorrhage
Justification for discontinuing use of the term *menorrhagia*

- Confusing term with Latin & Greek roots used to describe some aspect of HMB
- **USA:** used equally as a symptom, a sign, or a diagnosis
- Used solely as a symptom or sign in most other parts of the world
- **USA:** solely to describe “regular” heavy bleeding
- Some Drs: encompasses prolonged (not necessarily heavy) bleeding
- Most women: complaint of merely “heavy” (not excessive) bleeding
- **Women:** in most countries do not understand the term *menorrhagia*

*Fraser. Fertil Steril* 2007
Justification for discontinuing “dysfunctional uterine bleeding”

- Generally used as a diagnosis of exclusion and admission of ignorance of underlying mechanisms
- USA: used as a symptom, a sign, and a diagnosis
- In most countries: used mainly as a diagnosis
- USA: refers solely to anovulatory (i.e., irregular) bleeding, which is not necessarily heavy
- In most countries: is used to describe both ovulatory (regular) or anovulatory (irregular) bleeding
- The term is not understood by women

Fraser. Fertil Steril 2007
Terminology
History taking for AUB symptoms

Simple descriptive terminology
Understandable to women
Capable of translation into other languages

<table>
<thead>
<tr>
<th>Volume</th>
<th>Heavy</th>
<th>Normal</th>
<th>Light</th>
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<td>Regularity</td>
<td>Irregular</td>
<td>Regular</td>
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</tr>
<tr>
<td>Frequency</td>
<td>Frequent</td>
<td>Normal</td>
<td>Infrequent</td>
</tr>
<tr>
<td>Duration</td>
<td>Prolonged</td>
<td>Normal</td>
<td>Shortened</td>
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<tr>
<td>Other</td>
<td>Intermenstrual, Premenstrual, Post-coital, Unscheduled bleeding (in association with the use of sex steroids)</td>
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### Suggested “normal limits” for uterine bleeding in the mid-reproductive years


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<th>Menstrual parameter</th>
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<th>Normal and abnormal limits</th>
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<td>Frequency</td>
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<td>Light</td>
<td>&lt;5 ml</td>
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Investigations
Applicability & Practicality worldwide

- Washington (2005) – general agreement
  - Hb &/or Hct measurement
  - US evaluation of uterus for myomas
  - Endometrial cavity assessment - hysteroscopy or SIS
  - Assessment for Coagulopathies:
    - Structured history screening
    - PT, APTT, Fibrinogen, VWF, F VIII
FIGO Classification System

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Polyps (AUB-P)

- Polyps (endometrial and cervical)
- Diagnosis: using imaging (ultrasound), hysteroscopy or histology
- Categorized: absent or present (AUB-P)
- Caution: although often asymptomatic, polyps may play some role in AUB
- Allows for future development of a subclassification for clinical or investigative use
  - Polyp dimensions, location, number, morphology, histol.
Adenomyosis (AUB- A)

- Wide range in reported prevalence: 5 – 70%
- Included in the classification – cos have both US and MRI –based diagnostic criteria
- Worldwide- US is much more accessible
- TVUS comparable to MRI
  - 80% sensitivity and 80% specificity
Adenomyosis (AUB- A)

- **TVUS criteria**
  - Globular uterine configuration
  - Poorly defined endometrial-myometrial junction
  - Myometrial echogenic linear striations
  - Thickening of the myometrium
  - Assymetry of the anterior-posterior myometrial thickness
  - Irregular myometrial cystic spaces
  - Heterogenous myometrial echotexture
Sonographic findings of Adenomyosis

A - Heterogenous myometrium
B – Anechoic lacunae
C – Linear striations
D – Increased myometrial echotexture
E – Indistinct endomyometrial junction
Sonographic findings of Adenomyosis

Color Doppler: vessels following normal course through an indistinct mass
Leiomyoma (AUB – L)

- Historically: a number of unproven hypotheses
  - Increased endometrial surface area
  - Presence of a fragile and engorged plexus of perimyoma vasculature
  - Myomas bleed (solid and avascular)
  - Myomas contribute to genesis of AUB even when they do not involve the endometrial cavity
Leiomyoma (AUB – L)

- Search for biochemical mechanisms:
  - Release antigenic and growth factors – VEGF, BFGF, TGF-β (impairs local endometrial haemostasis)
- Until then: submucous myomas cause bleeding
  - Site of bleeding is adjacent &/or overlying endometrium
  - Less commonly: blood vessels that surround tumour
- Primary: presence or absence of leiomyoma
- Secondary: position – submucous or other
- Tertiary: limited to LSM that could be seen with hysteroscope
Hysteroscopy
Malignancy and Hyperplasia (AUB – M)

- Relatively uncommon
- Hyperplasia may occur as a result of prolonged estrogen exposure - due to chronic anovulation
- If confirmed AUB-M, then sub-classify using appropriate WHO or FIGO system for endometrial hyperplasia or malignancy
Coagulopathy

- Most common is von Willebrand Disease
- Prevalence: 13% with HMB
- Not clear how often these abn cause or contribute to AUB
- Screening using a structured history: Approx 90% may be identified
- Positive screen: consult haematologist &/or test for von Willebrand factor and ristocetin cofactor
Coagulopathy (AUB-C)
Structured history screening

1. HMB since menarche
2. One of the ff:
   1. PPH
   2. Surgical related bleeding
   3. Bleeding associated with dental work
3. Two or more of the ff. symptoms:
   1. Bruising 1-2 times/month
   2. Epistaxis 1-2 times/month
   3. Frequent gum bleeding
   4. Family history of bleeding symptoms
Ovulatory disorders

- Manifest in unpredictable timing and variable amount of flow and in some instances HMB
- Due to anovulation: absence of cyclical progesterone. Occurs at extremes of reprod. life
- In later reproductive years related to disturbed ovulations – “luteal out-of-phase” events
- Endocrinopathies: PCOS, hypothyroidism, hyperprolactinaemia, weight changes
- Medications: gonadal steroids, drugs affecting dopamine metabolism
Endometrial dysfunction (AUB-E)

- A diagnosis of exclusion
- Patient has predictable and cyclic bleeding typical of ovulatory cycles
- Mechanism: a primary disorder of the endometrium
  - Disturbances of metabolic molecular pathways – tissue fibrinolytic activity, prostaglandins, inflammatory and vasoactive mediators
  - No tests available yet
Iatrogenic (AUB-I)

- Include medication and intrauterine devices
- Directly impact on endometrium, may interfere with coagulation or influence ovulation
- Gonadal steroid therapy (E, P A) – unscheduled bleeding = “breakthrough bleeding”
  - Related to compliance – missed, delayed or erratic use
- Also anticonvulsants, antibiotics, smoking
- Anticoagulant related AUB – in AUB-C category
Not otherwise classified (AUB-N)

- Other uterine entities not yet described

- Maybe defined in the future:
  - biochemical or
  - molecular biological assays

- Not conclusively demonstrated:
  - chronic endometritis
  - AV malformations
  - myometrial hypertrophy
Notation: each case has 1 identified abnormality
Notation: >1 positive category
The three stage classification system for leiomyoma

<table>
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<tr>
<th>Primary</th>
<th>Secondary</th>
<th>Tertiary</th>
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<td>Submucous</td>
<td>0 Pedunculated intracavity</td>
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<td>OR</td>
<td>OR</td>
<td>1 ≤50% intramural</td>
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<td>Present</td>
<td>Other</td>
<td>2 &gt;50% intramural</td>
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<td></td>
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<td>3 Intramural but contacts endometrium</td>
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<tr>
<td></td>
<td></td>
<td>4 Intramural</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5 Subserous ≥50% intramural</td>
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<td>6 Subserous &lt;50% intramural</td>
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<tr>
<td></td>
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<td>7 Subserous pedunculated</td>
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<td></td>
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<td>8 Other (eg cervical parasitic)</td>
</tr>
</tbody>
</table>
Guidelines for Investigation

- **General assessment**
  - Not related to pregnancy
  - Not emanating from cervix or another location
  - Evaluate for anaemia – Hb

- **Determine ovulatory status**
  - Predictable cyclic menses every 22-35 days

- **Screening for systemic disorders of haemostasis**
  - Structured history: 90% sensitivity
  - Positive screen: von Willebrand factor, haematologist
Guidelines for Investigation

- Evaluation of the endometrium
  - Endometrial sampling if risk factors, persistent on Rx
  - TVUS - endometrial thickness

- Evaluation of structure of endometrial cavity
  - To identify polyps, submucous myomas
  - TVUS is not 100% sensitive – small lesions undetectable
  - If suboptimal – proceed to SIS or hysteroscopy

- Myometrial assessment
  - US and +/- hysteroscopy
  - MRI (not feasible everywhere) – leiomyoma or adenomyosis
Initial Evaluation

Chronic AUB
3+ months of excessive duration, volume, frequency, unpredictability?

No → Not chronic AUB

Yes ➔ Initial investigation

- Structured history
  - Ovulatory function
    - Future fertility
  - Related medical disorders, medications, lifestyle factors
    - Screening for inherited coagulopathy
- Physical examination
- Ancillary investigations
  - Complete blood count
  - Evaluating endocrinopathy (if oligoanovulation)
  - Testing for inherited coagulopathies if indicated

Uterine evaluation
Uterine Evaluation
Int J Gynecol Obstet (2011): 113: 3-13

Uterine evaluation

Enhanced risk for hyperplasia and/or neoplasia?

Yes
Office endometrial biopsy
Adequate specimen?
Yes
Atypical hyperplasia/CA?
Yes
Management of AUB-M

No
AUB-E or O (presumptive)

No

No

Enhanced risk for a structural abnormality?

Yes
TVUS
Normal cavity?
Yes
Hysteroscopy +/- biopsy
or
SIS
Target lesion?
No
Can’t assess
Consider MRI
Yes

No

AUB-LSm, AUB-P, AUB-A
Putting PALM-COEIN into practice
Abnormal uterine bleeding: advantages of formal classification to patients, clinicians and researchers

MAYANK MADHRA¹, IAN S. FRASER², MALCOLM G. MUNRO³,⁴ & HILARY O. D. CRITCHLEY¹

Case 1

- 37 yr nullip
- Regular HMB with severe menstrual pain
- No intermenstrual / postcoital bleeding
- Barrier contraception/ no surgical hx
- Exam: normal BMI, palpable lower central mass
- No abnormality of lower genital tract
- US: 10 cm antero-fundal uterine mass, cannot define origin nor clearly image endometrium. Ovaries normal
- Classify according to PALM-COEIN
Case 1: PALM-COIEN Classification after Hx, exam and US

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<th>Abnormal Uterine Bleeding Classification</th>
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<th>Absent</th>
<th>Unknown</th>
<th>History</th>
<th>Drug History</th>
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<th>Histology</th>
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<td>Polyps (Endometrial)</td>
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Case 1: Further investigation

- Non-structural causes unlikely: “C” – screening Q in history negative and thus marked absent
- Structural causes (PALM)- require further investigation
- Ix: depends on preferences and resources available
- Why not “M”: risk of hyperplasia/malignancy is low cos <40 yrs and regular (cyclic) bleeding.
- Perform MRI:
  - Normal endometrial cavity
  - 12cm transmural lesion with characteristics consistent with adenomyosis
- Update classification: AUB-A
# Final classification

**AUB- A**

## Abnormal Uterine Bleeding Classification

<table>
<thead>
<tr>
<th>Condition</th>
<th>Type</th>
<th>Present</th>
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<th>History</th>
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Case 2

- 25 yr old P1 G1 – previous CS
- Cyclical predictable HMB with cycle length -29 days
- No significant past medical / family history
- Rx: COC – contraception & improved HMB
- Now symptoms changed: heavier menses & developed inter-menstrual bleeding. No changes in her medication
- Abd and Gynae exam: NAD
- US : 3cm subserous fibroid (type 5), ET = 25mm, ovaries normal
- Hysteroscopy & Bx: solitary 2.5cm fundal endometrial polyp & no submucous fibroids (alternative: contrast infusion ultrasound)
- Histology: benign polyp
- PALM-COEIN classification: - AUB-P
# PALM-COEIN classification

## AUB-P

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<th>Hysteroscopy</th>
<th>Histology</th>
<th>Other</th>
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Nomenclature & classification of AUB

Abnormal Uterine Bleeding (AUB)

- Acute
- Intermittent
- Chronic

Frequency
Regularity
Duration
Volume

Polyp
Adenomyosis
Leiomyoma
Malignancy

Coagulopathy
Ovulatory dysfunction
Endometrial
Iatrogenic
Not otherwise classified
Summary

- New Classification
  - Optimising patient management
  - Improving research design of trials
  - Enabling valid interpretation of clinical trials
  - Single language for medical training

- An evolving classification
  - Similar to FIGO classification of Gynae cancers
  - 3 yearly reporting
Conclusions
Abnormal Uterine Bleeding

FIGO nomenclature
and
PALM-COEIN classification
FIGO nomenclature & PALM-COEIN classification

- Simplified and unified terminology
- Allows clear focus of treatment concepts
- Facilitates clinical and scientific research collaboration
- Provides the basis to structure more effective clinical teaching
FIGO nomenclature

&

PALM-COEIN classification

- Serves to enhance and clarify communication within and between specialties

- Presently the advantages and benefits over current practice remains to be fully realized

- Accrual of benefits will be in proportion to its adoption
Thank you