UTERINE DYSFUNCTION

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THE MOST TRADITIONAL UTERINE DYSFUNCTION

For at least two thousand years of European history until the late nineteenth century uterine dysfunction was called **HYSTERIA**

- (from the Greek ὑστέρα "hystera" = uterus)
- commonly attributed to [Hippocrates](https://en.wikipedia.org/wiki/Hippocrates)
- variety of illness symptoms, such as suffocation and Heracles' disease supposedly caused by the movement of a woman's uterus to various locations within her body as it became light and dry due to a lack of bodily fluids.
- Recommends pregnancy to cure such symptoms, because intercourse will "moisten" the womb and facilitate blood circulation within the body.
A case of uterine dysfunction 17\textsuperscript{th} century

Do the doctors know what to do???
WHAT IS UTERINE DYSFUNCTION?

- Menstrual blood loss > 80 mls?
- Disabling period cramps causing work or school absence?
- 19 weeks miscarriage?
- Preterm labour at 27 weeks?
- Failure to progress in term labour at 5cm?
- Preeclampsia?
- Massive postpartum haemorrhage?
- Pelvic organs prolapse?
- Anorgasmia?
What is the principal uterine function?

- The primary function of the uterus is in reproduction:
  - Sperm transport
  - Preparation for pregnancy
  - embryo implantation and early nourishment
  - development of placenta
  - to provide a safe and nourishing environment for the fetus until maturity and growth potential are reached
  - safe delivery of the baby
  - Safe for mother delivery of placenta
Uterine dysfunction definition

- Dysfunctional uterus would then be a very broad range of problems covering most of fertility, obstetrics and gynaecology!
Uterine dysfunction….

What shall we talk about?
Where do the uteruses come from?

- Reproductive tract in amphibians, reptiles, birds and monotremes: oviducts empty into terminus of large intestine with ureters – cloaca
- Marsupial and placental mammals – distal oviducts acquire rich blood supply and thickness, becoming uteruses
- Entirely new structure develops – vagina
- Linked to adaptive evolution of HoxA-11 and HoxA-13 genes coding transcription factors “redesigned toolbox”
- HoxA-11 also linked to development of placenta and prolongation of pregnancy in placentals c/w marsupials
Spot the difference
Evolution among the placentals

- Variation of how deep the embryo sinks into the uterus: epithelochorial, endothelochorial, and hemochorial
- First two do not menstruate and have triggered decidualisation on contact with embryo
- Hemochorial (most primates) undergo spontaneous decidualisation in anticipation of pregnancy.
- Ensures thick decidua for proper placental development and protects the woman from excessive trophoblast invasion!
- The consequence of spontaneous decidualisation is menstruation with associated symptomatology
Menstrual dysfunction

- Normal menstruation lasts 2 to 7 days
- Occurs between 21 to 35 days
- Results in blood loss of 30 mL per period
- Abnormalities:
  - Oligomenorrhea
  - Polymenorrhea
  - Menorrhagia: technically > 80 mL blood loss or > 7 days of flow
  - Metrorrhagia
Menstrual dysfunction

- 50% of women presenting with menorrhagia has bleeding within normal range but unacceptable to them
- Objective measurement of menorrhagia is clinically meaningless outside the context of research
- Treat the patient, not the definition
Scope of the problem

• DUB occurs in 10% to 30% of reproductive age women
• 1 in each 20 women a year seeks GP advice with heavy periods
• 22% of referrals to gynaecologist
• Age distribution
  • < 20 y - 20% of cases
  • 20 – 40 y - 40% of cases
  • >40 y - 40% of cases
American approach: “AUB” abnormal uterine bleeding. PALM-COEIN classification

**PALM:**
Structural causes
- Polyp
- Adenomyosis
- Leiomyoma
- Malignancy
  - *example: AUB-A*

**COEIN:**
Nonstructural causes
- Coagulopathy
- Ovulatory dysfunction
- Endometrial
- Iatrogenic
- Not yet classified
  - *published Am J Obstet Gynecol 2011*
SAFETY FIRST

• Exclude
  • Obvious gross pathology
  • Pregnancy
  • Malignancy
  • STDs
  • Systemic disease
SAFETY FIRST

- Detailed history
- Abdominal palpation
- Bimanual examination
- Speculum examination
- PAP smear
- Endocx swabs
- bHCG, FBC, TSH, P21 +-further endocrinology
  +- coagulation studies
- Ultrasound scan
- +-Endometrial biopsy
Endometrial biopsy

• The incidence of endometrial cancer increases with age
• 13-18 years: 0.2 per 100,000 women
  • The rare cases had obesity and 2-3 years of abnormal bleeding
• 19-34 years: 1.6% - on average still low risk; biopsy when no response to treatment or a high risk presentation
• 35-44 years: 6.2% - biopsy mandatory
Endometrial biopsy

- Type of biopsy depends on ultrasound appearance of endometrium
- Uniform low risk appearance: Pipelle –
  - samples 4% of endometrium
  - Pipelle sensitivity 68%
- High risk appearance or localised pathology require hysteroscopy D&C
- some would do sonohysterography
Treatment steps

cOC, Cyklokapron, Ponstan

Mirena

Endometrial ablation, UA embolisation

Hysterectomy - supracervical - total

Effectiveness

Invasiveness, side effects
COC

- Stabilise endometrium, reduce thickness
- Increase levels of factor VIII and vWF
- Supress androgen production, increase SHBG
- Mainstay of treatment of DUB caused by anovulation, PCOS, with acne/hirsutism, coagulopathy
- Also provides reliable contraception
- Courses up to 120 days
- Weight management, diet, exercise
COC

Cochrane review: only one study found comparing COC, mefenamic acid, naproxen and danazol

• Reduction in measured blood loss
  • COC 43%
  • Danazol 49%
  • MFA 38%, Naproxen 39%

• All results highly significant, no difference between the groups

Cyklokapron inhibits fibrinolysis

- tissue plasminogen activator

- PLASMINOGEN $\rightarrow$ PLASMINE

- Cyklokapron
  - blocks lysine sites on plasminogen, preventing plasmine formation
  - Lowers endometrial tPA activity
Cyklokapron

- Effective with many pathologies
- Used iv after various surgical procedures
- Oral form for menorrhagia
  - Scandinavia 70s
  - UK 80s
  - Australia 90s
  - USA 2009
- Effect dose dependent
  - 3900mgs – 39% reduction in menstrual blood loss
  - 1950mgs – 25%  *Obstet Gynecol 116(5), Nov 2010*
- Establish cause !!!
Cyklokapron

- Side effects: venous and arterial thrombosis
  - But in Sweden available o/c, recent study no increased risk of VTE

- Recommended dosage Australia:
  - 1.0 – 1.5 g (2-3 tab) 4 x per day FOR THE FIRST FOUR DAYS OF A PERIOD
  - USA 650mgs tabs – 3 to 6 once daily for up to 5 days
Progestins

• Levonorgestrel IUCD
  • Reduction of blood loss 79-96%
  • Australia: very low cost
  • Significantly superior to oral progestins including QoL *N Eng J Med* 2013 Jan 10;368(2):128-37
  • If inserted as a “bridge” before hysterectomy, 64% women cancelled surgery *Lahteenmaki BMJ* 1998
  • Satisfaction rates and QoL similar to surgery both at 1 and 5 years *Lethaby, Cochrane Database of Systematic Reviews* 2005

• Cyclical oral progestins, various regimes D5-26, or 1-10 each month etc
Progestins

• Discontinuation rates

• Mirena: discontinuation rate at 12 months: 23-30%, by 5 years up to 60%  
  *Ewies, Gynecol Endocrinol 2009*

• Oral progestins discontinuation rate 78%  
  *Lethaby, Cochrane Database of Systematic Reviews 2005*
Endometrial ablation

- Attractive philosophy: remove what is the actual problem i.e. bleeding endometrium
- Evolution from 80s – 1st, 2nd and 3rd generation methods
- Current favourite: radiofrequency ablation “Novasure”
  - Few contraindications: cCS/myomectomy scar, cavity distortion,, cavity >12 cm or <4cm, neoplasia
  - No endometrial preparation required
  - No risk of fluid retention: continuous suction
  - Active bleeding is not a limiting factor
  - In-built safety systems pre and intraoperative
  - Typical amenorrhea rate 50-60% at 12 months and overall improvement and satisfaction rate 92%

Endometrial ablation

- Satisfaction rate when compared with Mirena is similar, despite lower effectiveness and more side effects in Mirena patients

  Beumont, Cochrane Database of Systematic Reviews CD001017
  Lethaby, Cochrane Database of Systematic Reviews CD000249

* Multicentre Randomised Trial started 2013, M. Herman et al, BMC Women’s Health 2013, 13:32
Endometrial ablation does not address primary pathology f.ex. Anovulation

- Long term risk of occult uterine malignancy while assessment of endometrium by U/S, biopsy, and hysteroscopy is difficult if not impossible
- Number of cases reported, 87% had risk factors for endometrial ca. *Alhilli, J Minim Inv Gynecol 2011*
- Women at risk of endom ca shold be offered progestins or hysterectomy
Uterine artery embolisation

- Minimally invasive alternative to hysterectomy
- Requires specialised interventional radiology techniques
- EMMY TRIAL 5 y outcomes:
  - Patient satisfaction 85% vs 89% in hysterectomy group
  - No differences in urinary and anal symptomatology
  - No differences in QoL scores
  - Fewer patients menopausal 35% vs 47% after hysterectomy
  - 28% of UaE underwent hysterectomy *Am J Obstet Gynecol 2010*

- SAN report 76 UAEs, f-up 12-24 months
  - 93% SUCCESS FOR MENORRHAGIA
  - HYSTERECTOMY OR REPEAT UAE 5%
    *Liang et al, Aust NZ J Obstet Gynecol April 2012*
HYSTERECTOMY REVISITED: 
DISPELLING THE MYTHS

• Does hysterectomy cause pelvic organ dysfunction?
• Prolapse: v. low incidence of advanced prolapse <3%, no difference SCH or TAH Persson et al, BJOG Nov 2013
• Urinary symptomatology
  – Reduction in SI, urgency, frequency, nocturia, hesitancy and incomplete emptying
  – Desire to void and max bladder capacity much higher by UD
  – No differences between TAH and SCAH
    – Thakkar et al, NEJM 2002;347:1318-1329
• Bowel function
  – Transient negative effect at 6 weeks
  – Then progressive improvement in GI QoL above preop values Lashen et al, Europ J Gast Hepatol 2013, 25:1217-1222
  – Anecdotal and individual patient reports may not be reliable b/o high prevalence of bowel dysfunction in patients with gynaecological symptoms Heaton, Gut 1993;34:1108-1111
HYSTERECTOMY REVISITED: SEXUAL FUNCTION

• Systematic review: most studies showed no change or an enhancement of sexuality following hysterectomy

• The largest prospective study: ”Maryland Women’s Health Study” 1299 women, f-up 24 months:
  • Significant improvement in frequency of sexual activity
  • Improvement in dyspareunia, orgasm, libido and vaginal dryness
    Kjerulff et al, J Urol 2002;167:2088-2092

• Postulated orgasmic advantage of conserving cervix with surrounding uterovaginal nerve plexus

• Subsequent research failed to reproduce these findings
HYSTERECTOMY REVISITED: SEXUAL FUNCTION

- **POOR OUTCOME**
  - Negative expectations of sexual recovery
  - Psychiatric morbidity
  - Depression
  - Unsatisfactory preoperative relations
  - Poor knowledge of reproductive function
  - Negative partner’s attitude
  - Unemployment

- **Positive outcome**
  - Healthy relationship
  - Satisfactory sexual life before surgery
  - High level of sexual desire and orgasmic response
  - Good general health
  - Freedom from stress
  - Absence of financial worry

- *Rhodes, JAMA 1999*
- *Darling, J Sex Res 1993*
Spot the difference!

Before treatment

After treatment
• Systematic review on quality of life and satisfaction, comparing various treatment for dysfunctional bleeding: Broelmann et al, Gynecol Surg 2010

• “In conclusion, the fundamental question if patients have a better quality of life if they choose a minimal invasive alternative or hysterectomy remains unresolved. Some do and some do not”.

• As QoL depends on the extent to which patients’ expectations are matched by reality, adequate information beforehand is of utmost importance
ENDNOTE

- INFORMATION, INDIVIDUALIZATION AND FREEDOM OF CHOICE BEST SERVE OUR PATIENTS