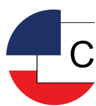
An Approach to the Diagnosis and Management of Benign Uterine Conditions in Primary Care



Centre for Effective Practice

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Glossary of Abbreviations

▲	Increase
▼	Decrease
AUB	Abnormal uterine bleeding
BMD	Bone mineral density
BMI	Body mass index
CAD	Coronary artery disease
CHF	Congestive heart failure
CPP	Chronic pelvic pain
d	Day
D+C	Dilatation and curettage
DHEAS	Dehydroepiandosterone sulfate
DMOS	Dimethyl sulfoxide
ds	Disease
DUB	Dysfunctional uterine bleeding
GnRH	Gonadotropin releasing hormone
h/hr	Hour
HT	Hormone therapy
HTN	Hypertension
Hx	History
IBD	Inflammatory bowel disease
IUS	Intrauterine system
NSAID	Non-steroidal anti-inflammatory drug
PCOS	Polycystic ovarian syndrome
PE	Pulmonary embolism
PID	Pelvic inflammatory disease
PMHx	Past medical history
RCT	Randomized control trial
R/O	Rule out
sc	Subcutaneous
STI	Sexually transmitted infection
sTSH	Sensitive thyroid stimulating hormone
SBE	Subacute Bacterial Endocarditis
TENS	Transcutaneous electro-nerve stimulator
U/S	Ultrasound

An Approach to the Diagnosis and Management of Benign Uterine Conditions in Primary Care was developed by Family Physicians:

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Medications Used for Treatment of Benign Uterine Conditions

Medication	Indication	Dose	Length of treatment	Possible side-effects	Contraindications	Cost For 30 tablets, approx. in Canadian $, excluding dis-pensing fee.
Danazol (Cyclomen®)	Fibroids Endometriosis Abnormal uterine bleeding Chronic pelvic pain	Fibroids 100 - 200mg OD Endometriosis 600 - 800mg OD Abnormal uterine bleeding 200 mg OD	6 months maximum	▲ with ▲ doses Androgenic, menopausal (see GnRH), lipid changes, liver disease, muscle cramps, break through bleeding, need barrier contraception	Undiagnosed vaginal bleeding, genital neoplasia, impaired hepatic/renal/ cardiac function, pregnancy, attempt at pregnancy, lactation, porphyria, active thrombosis or thromboembolic disease	100 mg - $40 200 mg - $70
Estrogen IV Premarin®	Acute severe menorrhagia due to anovulation	25mg IV q6hr up to 4 doses	Until symptoms resolve (for shortest duration possible)	Headache, nausea, increased risk of stroke, PE, DVT.	Venous thrombosis or thrombophilia	Available in hospital/ emergency department
GnRH agonists Leupride acetate (Lupron®) Naferelin (Synarel®) Goserelin (Zoladex®)	Fibroids Endometriosis Chronic pelvic pain	Leupride acetate (Lupron®) 3.75mg/ month or 11.25mg/3 months IM, Naferelin (Synarel®) 200ug/d intranasal bid, Goserelin (Zoladex®) 3.6mg sc monthly or 10.8mg sc q3 months)	6 months maximum alone, longer with add-back therapy (estrogen + progesterone similar to HT)	Menopausal symptoms 80-90% (hot flashes, vagi-nal dryness etc.) irregular bleed-ing, need barrier contraception, possible bone den-sity loss if used > 6 months without add-back HT	Pregnancy, breast feeding, undiagnosed vaginal bleeding	Lupron® 3.75mg/month - $400 Synarel® 200 mg - $360 Zoladex® 3.6 mg - $450
Oral Iron (ferrous fumarate, ferrous gluconate, ferrous sulfate)	Anemia secondary to menorrhagia	300mg 1 tab after a meal for 1 week, then increase slowly to 1 tablet tid.	Until anemia resolves and AUB treated	GI (nausea, epigastric distress, constipation or diarrhea)	Hemochromatosis	Over the counter $7 for 90 tablets
Non-steroidal anti-inflammatory drugs (NSAIDs)	Dysfunctional uterine bleeding, endometriosis, adenomyosis, dysmenorrhea, chronic pelvic pain	Mefenamic acid (Ponstan®) 500 mg tid Naproxen: (Naprosyn® 250 bid-qid, Anaprox® 275-500 bid) Ibuprofen (Advil®, Motrin®) 400 mg q4-6h Sodium diclofenac (Voltaren®)50 mg tid	Start as soon as mild cramps of dysmenorrhea begins. Use regularly even if pain is completely relieved, until a few days after onset of menses	Nausea, GI upset, diarrhea, dizziness, headache, rashes, GI bleed	Acute peptic ulcers or hx of ulcers, active IBD, hypersensitivity to NSAIDs, caution in patients with asthma, nasal polyps, renal ds, liver ds, CHF, HTN, pregnancy	Mefenamic acid 250 mg - $11 Naproxen 250 mg - $4 500mg - $7 Sodium Diclof-enac 50 mg - $13 Ibuprofen 400 mg - $1.50

Medication	Indication	Dose	Length of treatment	Possible side-effects	Contraindications	Cost For 30 tablets, approx. in Canadian $, excluding dispensing fee.
Hormonal contraceptives	Dysfunctional uterine bleeding, dysmenorrhea, endometriosis fibroids adenomyosis	Use monocyclic compound cyclically 21d on/7d off or continuously every day without stopping.	Unlimited	Breakthrough bleeding, bloating, nausea, headache, breast tenderness, weight gain	Hx/active thromboembolic disorder, cerebrovascular disorder, CAD, DVT, acute liver disease, breast cancer, migraine with aura, diabetes with renal, vascular or neuro complications, undiagnosed abnormal vaginal bleeding, pregnancy, uncontrolled HTN, smoker >35 years old,	1 month - $14
Oral Progestins Provera® Megace® Prometrium® Norlutate®	Anovulatory menorrhagia endometriosis	Cyclically 10-14d during luteal phase. Provera 5-20mg, Prometrium 2-3 tabs x 100mg; Micronor 1 tab daily Norlutate® or Megace®	Unlimited	Abnormal uterine bleeding, breast tenderness, fluid retention, acne, nausea, headaches, depression	Undiagnosed vaginal bleeding/ breast disease (including cancer), pregnancy, severe liver disease, depression Prometrium®: peanut allergy	Medroxy-progesterone 5 mg - $8 Micronor® $17 Norlutate® $26 Prometrium® 100 mg - $30
Injectable Medroxy-progesterone (Depo-Provera®)	Fibroids, dysfunctional uterine bleeding endometriosis	150mg IM q3 months Tip: May ▼ interval if ++ breakthrough bleeding	Unlimited Has been associated with possible loss of bone density in young women. This may be prevented by adding low-dose estrogen (premarin 0.3mg, estrace 0.5mg, Estrogel 1 pump/d, estradiol patch 25ug) BMD not reliable in women under age 30.	Bloating, weight gain, depression, irregular bleeding, amenorrhea, ▼ BMD with long term use	Same as above for oral progestins and possible decreased bone mineral density.	$30/injection
Intrauterine Levonorgestrel releasing system (Mirena® IUS)	Dysfunctional uterine bleeding endometriosis adenomyosis fibroids	20ug/d	5 years then replace with new device	Breakthrough bleeding, amenorrhea, perforation, expulsion, pain, rarely progesterone side-effects from systemic absorption	Pregnancy, undiagnosed uterine bleeding, uterine abnormalities that distort cavity, uterine/cervical malignancy, acute liver ds, immunodeficiency, leukemias	$350/device
Tranexamic acid (Cyclokapron®)	Menorrhagia secondary to dysfunctional uterine bleeding, adenomyosis, anovulation.	500mg-1500mg q 6-8 h PRN Maximum daily dose: 6gm	1-4 days	GI(nausea, vomiting, diarrhea, dyspepsia), occasional disturbance of colour vision	History, risk or active thromboembolic disease (DVT, PE) Acquired colour vision disturbance	500 mg - $60

Steps to manage: Fibroids

Bottom Line

Asymptomatic fibroids do not require treatment. Many medical therapies and several procedures can be tried, with none proving superior. Choice of treatment will depend on symptoms, patient preference, availability of procedure, other health factors and fertility issues.

Definition

Benign smooth muscle tumours of the uterus also called leiomyomas, myomas. Prevalence 20-40% of women. Most asymptomatic (no treatment required). Malignancy risk: 1.7/100,000 women

1

Symptoms

- Abnormal bleeding
- Anemia
- Dyspareunia
- Bladder dysfunction
- Pelvic pressure
- Increased abdominal girth (if large)
- Rarely infertility
  - fibroids cause 2-3% of infertility
  - usual submucosal

Risk Factors

- Obesity
- FHx
- Black
- Nulliparity
- Early menarche and late menopause

2

Physical Examination

- Pelvic and abdominal exam is accurate for detecting fibroids when uterus size > 12 weeks

3

Investigation/Treatment Principles

- Goal of treatment is to alleviate menorrhagia and/or pelvic pressure due to fibroids if symptomatic
- Rapid growth of fibroids needs to be investigated, especially in post-menopause

Menorrhagia

- CBC, TSH, ferritin, beta HCG

MRI

- If fibroid is rapidly growing or suspicious in appearence

Ultrasound

- Useful to confirm diagnosis, r/o ovarian or other pathology
- Transabdominal better > 12 weeks size, transvaginal < 12 weeks

4

Fibroids & Pregnancy

No need to remove prior to conception unless infertility or problematic during previous pregnancy. During pregnancy, 80% of fibroids remain unchanged. Slight ▲ preterm labour/ post-partum sepsis. >20cm more likely to cause pain due to degeneration or placental abruption. Bottom Line: Fibroids during pregnancy need ▲ surveillance, but no treatment.

Medical Therapy

- No treatment necessary unless symptomatic or rapid growth
- No evidence to use NSAID, HT, oral progestins (i.e. Provera®)
- To treat menorrhagia without affecting size of fibroid
  - Cyclokapron®
  - Hormonal contraceptives
- To decrease size/treat menorrhagia (risk of amenorrhea)
  - Regrowth occurs when medications are stopped
  - Depo-Provera®: some evidence prevents fibroids from developing
  - Mirena® IUS: higher risk expulsion, modest ▼ size
  - GnRH agonists: useful pre-op to help anemia, decrease fibroid size, decrease blood loss and perimenopausally to avoid surgery, maximum use is 6 months unless "add-back" therapy (similar to HT)
  - Cyclomen® (danazol): ▼ size 20-57%, only use for 6 months due to side effects

5

Further Evaluations/Surgical Treatments

(see Table A on page 5)

- Uterine Artery Embolization
- Myolysis
- Myomectomy
- Hysterectomy

Indicated for rapid growth, possible malignancy or poorly controlled symptoms require further investigation

Supporting table for: Fibroids

Table A ▸ *Other Options*

Uterine Artery Embolization *(UAE)*

- Performed by interventional radiologist using angiography to catheterize both uterine arteries and inject tiny beads (usually polyvinyl alcohol) to interrupt blood supply to fibroids.
- Done under local anesthesia plus sedation. Medication is necessary to control pain after UAE.
- Fibroids infarct/degenerate leading to decrease volume 40-60%, menorrhagia improved 64-96%
- Not considered first line for infertility. New evidence suggests it's safe for pregnancy but may ▲ placenta problems.
- Perioperative risks 1-2%: infection, bleeding, reaction to dye, incomplete occlusion, misembolization of non-target organ, hematoma at puncture site.
- Post embolization syndrome up to 40% (pain, malaise, anorexia, vomiting, low grade fever, leukocytosis), ovarian failure up to 10% (higher risk >age 45), amenorrhea (transient 15%, permanent: 3-8%), expulsion of myoma 5%, hysterectomy (1-2%) and mortality 0.1-0.2/1000

Myomectomy

- Fibroids are removed surgically via hysteroscope (submucous), laparoscope (subserous) or open (multiple, deep fibroids)
- Recommended procedure for infertility
- Hemorrhage is common (up to 20% need transfusion), small risk of immediate hysterectomy
- Occurrence of new fibroids is high (35% hysteroscopic, 50% laparoscopic, 27% open)
- 10% of women will go on to hysterectomy within 5-10 years

Myolysis *(not yet available in Canada)*

- Energy delivered to myomas to desiccate/disrupt their blood supply using laser, coagulation or cryotherapy
- Usually performed laparoscopically. Procedure now being developed to be accomplished by intra-uterine ultrasound guidance for submucous fibroids.
- Better for smaller and fewer fibroids, no pregnancy desired
- Reduces size 10-55%
- Complications : infection, bacteremia, bleeding (<1%), adhesions

Notes:

Steps to manage: Pre-Menopausal Abnormal Uterine Bleeding *(AUB)*

Bottom Line

AUB requires a stepwise approach to rule out pregnancy, systemic, iatrogenic and genital tract disease before it is called dysfunctional uterine bleeding (DUB). Endometrial sampling should be considered for women at high risk for endometrial hyperplasia and carcinoma (age>40, anovulatory DUB, PCOS, obesity etc.). Several medical and surgical options are available for treatment.

Definitions

Abnormal Uterine Bleeding: any *persistent* change in menstrual period frequency, duration or amount ± breakthrough bleeding.
Dysfunctional Uterine Bleeding: excessively heavy, prolonged or frequent bleeding of uterine origin which is not due to pregnancy or to recognizable pelvic or systemic disease.

1 Presentation/History

- Amount of blood loss (see Table B)
- Ovulatory vs anovulatory (see Table B)
- Rule out pregnancy/desire for pregnancy
- Psychosocial issues (i. e. stress, depression)
- Medications causing bleeding (see Table C)
- Intrauterine device (IUD)
- Systemic causes (see Table D)
- Family Hx (bleeding disorder, blood clots)

2 Physical Examination

- Thyroid, abdominal, skin (pallor, striae, ecchymosis)
- Pap + swabs
- Pelvic/bimanual exam
  - detect genital tract pathology (fibroids, polyps etc.)
  - if abnormal, consider transvaginal U/S

3 Investigation/Treatment Principles

- CBC, ferritin, TSH
- coagulopathy work-up if family history or bleeding dyscrasia
- pelvic ultrasound
- endometrial biopsy

Endometrial Cancer Risk Factors

- BMI > 40
- AGE > 40
- Diabetes
- Anovulatory cycle/PCOS
- Tamoxifen
- Family history of endometrial or colon cancer

Endometrial Biopsy

- Sensitivity to detect abnormalities 81-96%
- Adequate sample obtained > 85%
- Hyperplasia without atypia
  - treat with Provera 10 mg 5-90 days
  - repeat biopsy 3-6 months
- Atypia/Cancer - refer to Gynecology

If Anovulatory /PCOS there is a long term risk of endometrial hyperplasia/cancer requiring endometrial protection with hormonal contraceptives, Mirena®, cyclic progestins (i.e. Provera® 5-10mg for 10-14 days/month)

OHIP billing codes for endometrial biopsy

Z770 + E542

4 Medical Therapy

Non Hormonal

- NSAIDs
- Cyclokapron®
  - anti-fibronolytic that reduces blood loss
  - taken only when bleeding

Hormonal

- hormonal contraceptives
- Mirena®
- Depo-Provera®

5 Further Evaluations/ Surgical Treatments

If not previously done:

- Transvaginal ultrasound
- Endometrial Biopsy
- Saline Infusion Sonohysterogram

Gynecology Consult

- Hysteroscopy, endometrial ablation, hysterectomy

Note: D+C is no longer a treatment option for AUB since it has no long term benefit

Management of Acute Bleeding

If stable: Hormonal contraceptive 2-4 pills/d for 7 days, then 1 pill/d for 2 weeks. (unstable see page 7)

Supporting tables for: Pre-Menopausal Abnormal Uterine Bleeding

Table B ▸ *Amount of blood loss*

- Menorrhagia is defined as total blood volume > 80 mL
- 60% of patients overestimate blood loss
- Flooding
- Changing soaked thick pad < q1h
- Changing pad during sleep
- Social impact
- Fatigue, pallor
- Postural hypotension

Clinical Presentation

Ovulatory	***Anovulatory***
Cyclical bleeding	Irregular bleeding
Premenstral symptoms	Minimal pain
Midcycle pain	Higher risk of endometrial hyperplasia, or cancer
Dysmenorrhea	

Table C ▸ *Medications/iatrogenic causes*

- Anticoagulants
- ASA
- Herbs: ginseng, ginkgo, soy products
- Phenothiazines
- SSRI, TCA
- Tamoxifen- requires endometrial sampling
- Corticosteroids
- Thyroxine
- Contraceptive
  - OCP, Depo-Provera, IUD

Table D ▸ *Further investigation on high clinical suspicion*

Systemic Causes	Initial Investigations
Thyroid disease (hyper or hypo)	sTSH
Polycystic ovary syndrome	Free testosterone, DHEAS, LH:FSH>2:1, Transvaginal U/S
Coagulopathies, Leukemia, Thrombocytopenia	CBC, INR, PTT, Bleeding time
Pituitary adenoma or hyperprolactinemia	Fasting prolactin
Hypothalamic suppression ▸ stress, weight loss ▸ excessive exercise ▸ eating disorder	Measure weight/BMI
Hepatic disease	LFTs, INR
Renal disease	Creatinine
Adrenal hyperplasia	DHEAS, free testosterone
Cushing's disease	24 hour urine free cortisol Overnight dexamethasone suppression test
Tumours: - gynecological, hormonally active	U/S, CT, MRI. Refer to specialist

Table E ▸ *Further Evaluations and Surgical Treatments*

Further Evaluations: *Saline Infusion Sonohysterogram (SIS)*

- Good for detecting submucous fibroids and polyps
- 5 to 15 mL of sterile saline instilled in the endometrial cavity
- Can be uncomfortable, suggest NSAID prior

Further Evaluations: *Hysteroscopy*

- Good for submucous fibroids, polyps and biopsy under direct visualization
- Usually under general anesthetic but some doing office procedure
- Cavity needs to be filled with liquid (glycine) or less often gas (CO2)
- Small risk of perforation, infection, fluid overload/gas embolism

Surgical Treatments: *Endometrial Ablation or Hysterectomy*

Endometrial Ablation

- Hysteroscopic guidance or blind
- Small risk of perforation, fluid overload (if used), does not protect against future uterine cancer

Hysterectomy

- Major surgical procedure
- May be done vaginally, abdominally or by laparoscopy

Management of acute bleeding:

- If unstable, send to Emergency
- Conjugated equine estrogen (CEE or Premarin®)25mg IV q6h x 4 doses, or until bleeding subsides
- If severe menorrhagia, refer to a specialist
- Once bleeding has subsided, oral hormonal therapy is continued for 2-3 weeks with:

  a) conjugated estrogen 2.5-10 mg daily along with oral progesterone (Provera® 10 mg) for the last 10 days OR

  b) Ovral (50ug) 2 tab po BID x 2d, then 1 tab BID x 2d, then 1 tab od x 9d

All regimens should be followed by cyclic hormonal contraceptive or cyclic progestin for 4-6 months.

Notes:

Steps to manage: Post-Menopausal Abnormal Uterine Bleeding

Bottom Line

The most common cause of AUB in post menopausal women are endometrial and vaginal atrophy. Initial investigation of the endometrium can include either a transvaginal ultrasound or endometrial sampling.

Definition

Vaginal bleeding ≥ 12 months after the cessation of menses or unpredictable bleeding > 12 months on hormone therapy.

1 Presentation/History

- Amount/frequency of blood loss
- Medications causing bleeding:
  - HT, Anticoagulants, ASA and Tamoxifen

Differential Diagnosis	*Frequency*		
Atrophic Vaginitis	59%	Hormonal effect	7%
Endometrial Polyp	12%	Cervical Cancer	2%
Endometrial Hyperplasia	10%	Other	<1%
Endometrial Cancer	10%		

Source: Karlsson et al 1995

2 Physical Examination

- General exam:
  - Stigmatae of liver disease
  - Ecchymosis
- Pap + swabs
- Pelvic exam
  - external genitalia
- atrophic/infectious vaginitis
- cervical polyps
- uterine size, contour

3 Investigation/Treatment Principles

CBC, ferritin, TSH

- if iron deficient, treat with iron supplementation
- if evidence of coagulopathy (bruising, bleeding elsewhere) do INR, PTT, bleeding time, von Willebrand screen

Evaluate the Endometrium/Uterine Cavity

- Either endometrial biopsy, transvaginal ultrasound or both can be done to initially assess the endometrium
- Can base choice of first investigation upon patient preference, physician comfort with procedure, U/S availability

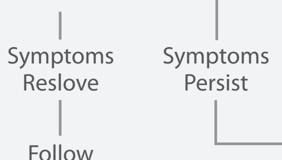
Transvaginal Ultrasound

- Sensitivity 96% for detecting endometrial carcinoma
- If endometrial echo (EE) (double thickness) < 5mm and symptoms resolve ▸ watch
- If endometrial echo (EE) (stripe, double thickness) ≥ 5mm or symptoms persist need endometrial evaluation

Endometrial Biopsy

- Sensitivity to detect abnormalities 81-96%
- Adequate sample obtained > 85%

Results of Biopsy



Unable to perform
Tips: Table F
Inadequate Sample
→ ***Transvaginal*** U/S (See box above)

Hyperplasia without Atypia
→ Treat with Provera® 10mg-20mg anywhere from 5-90 days Repeat biopsy 3-6 months

Hyperplasia with Atypia/ Cancer
→ Gyne Consult

OHIP billing codes for endometrial biopsy

Z770 + E542

4 Medical Therapy

- Topical estrogen therapy for vaginal atrophy (creams, tablets, vaginal ring)
- If on HT
  - After r/o pathology adjust HT by trial and error
  - Increase estrogen and/or decrease progesterone if EE <= 5mm
  - Decrease estrogen and/or increase progesterone if EE >5mm
  - Vary dosing schedule (cyclic vs. continous)

5 Further Evaluations/ Surgical Treatments (see Table E on page 7)

- Saline infusion sonohysterogram (SIS)
- Hysteroscopy
- Removal of polyp
- Hysterectomy

Table F ▸ *Tips for a difficult endometrial biopsy* (i.e. previous failed attempt, likely to have stenotic os)

Prior to biopsy	At time of biopsy
▸ Have patient insert 2 x 200 ug misoprosol (Cytotec®) tablets deep in her vagina 4 -12 hours before procedure ***Warning: this is an off label use and can cause severe cramping*** More effective in pre-menopausal patients ***OR*** ▸ Advance sterile dilator, pipelle or swab covered with Xylocaine® jelly 2% to area of stenosis and hold several seconds ***OR*** ▸ Insert an osmotic laminaria (seaweed) 3 mm size 4-6 hours prior to biopsy	▸ Biopsy sampler/pipelle ▸ Place in freezer to stiffen ▸ Lubricate tip with sterile topical anesthetic ▸ Uterine sound - gently probe cervix prior to biopsy ▸ Cervical dilators/os finders ▸ Tenaculum ▸ grasp anterior lip of the cervix to help stabilize it and straighten the cervical canal

Notes:

OHIP billing codes for laminaria insertion

G362 + E870

(If MD supplies laminaria)

Steps to manage: Endometriosis

Bottom Line

If fertility is not desired currently and there are no pelvic masses present, a trial of medical therapy can be started without a diagnostic laparoscopy first. Consider continuous monophasic hormonal contraceptives +/- NSAIDs followed by a second line therapy if no response after 3-6 months, as all hormonal treatments are equally effective in reducing pain.

Definition

Presence of endometrial tissue outside the uterus. Prevalence about 10% (additional facts, see Table G).
Etiology (several theories, see Table G).

1 Presentation/History

History

- Pelvic pain begins premenstrual
- Deep dyspareunia
- Infertility
- Menstrual irregularities
- Backache
- Family history
- Dysmenorrhea
- Pain or rectal bleeding with defecation

Rule out other causes of pelvic pain:

- Interstitial cystitis
- PID
- Adhesions
- Irritable bowel/IBD
- Ovarian cyst
- Psychosocial contributors (i.e. abuse, depression)
- Adenomyosis (see Table L on page 13)

2 Physical Examination

- Often normal
- Pelvic tenderness
- Nodularity
- Adnexal masses
- Decreased uterine mobility

Initial Investigations

- Urinalysis
- Pap + swabs
- Menorrhagia: CBC, ferritin, TSH
- Pelvic ultrasound: transvaginal + transabdominal

3 Investigation/Treatment Principles

Incidental Finding (i.e. discovered at tubal ligation)

- No need to treat unless symptomatic

Suspected Endometriosis

- Can begin medical therapy without laparoscopy first
- History, physical and lab/imaging investigations accurate 80% of the time

Infertility

- No medical treatments for endometriosis have been proven to improve fertility
- Requires laparoscopic resection/ablation

4 Medical Therapy

Symptoms recur in 37-74% after stopping medications

Trial of First Line

- NSAIDs improve pain 72%
- Hormonal contraceptives: continous monophasic (satisfaction 60 - 70%)
- Relaxation techniques, exercise may help
- Manage pain

Trial of Second Line

- Progestins (satisfaction 80-90%) Mirena® IUS, Depo-Provera®, Oral progestins
- GnRH analogs (▼ pain up to 90%) Lupron®, Zoladex®, Synarel®. Maximum 6 months but if effective consider long term treatment with add-back" therapy (similar to HT)
- Cyclomen® (danazol) 600-800 mg/day (symptoms improve 80-90%). Maximum 6 months (due to long term androgenic side effects)

5 Further Evaluations/ Surgical Treatments

Diagnostic Laparoscopy

- Pain does not always correlate with severity of finding
- Of all lesions seen and biopsied, only 45% confirmed to be endometriosis

Therapeutic Laparoscopy

- Excision, ablation, adhesion lysis, cyst removal
  - success rate 45-85%
  - recurrent rate 40-60%

Hysterectomy

- Reserved for intractable pain, treatment failures, side effects of medications
- Adding oophorectomy to hysterectomy
  - ▼ recurrence rate from 62 ▸ 10%
  - ▼ re-operation rate from 31 ▸ 4%
  - need HRT in premenopausal until reach (average) menopause age

Therapeutic Laparoscopy

Unless pregnancy is desired, therapeutic laparoscopy should be immediately followed by ovarian suppression by hormonal contraceptives to prevent recurrence.

Supporting Table for: Endometriosis

Table G ▸ *Endometriosis Facts*

- Etiology: several theories
  - Retrograde menstrual flow implants on the peritoneal surface
  - Coelomic metaplasia (peritoneal cells change into endometrial glandular cells)
  - Hematological/lymphatic spread.
- Most asymptomatic, symptoms usually improve after menopause
- Classification based on laparoscopic visualization: minimal (stage I), mild (stage II), moderate (stage III) and severe (stage IV)

Notes:

Steps to manage: Chronic Pelvic Pain

Bottom Line

The 4 most common causes are: Irritable Bowel Syndrome, Interstitial Cystitis, Endometriosis and Adhesions. Treatment can be initiated without performing a laparoscopy first as they benefit a variety of causes of Chronic Pelvic Pain that worsen with menstruation.

Definition

Non-menstrual pain > 6 months causing functional disability. Prevalence: 5-20%.

1

Presentation/History

History

- Pain: timing, aggravating/relieving, dyspareunia (superficial vs. deep)
- Previous evaluation/medications/therapies/response
- Screen for depression (present in 60% of chronic pelvic pain sufferers)
- Quality of life, sexual dysfunction
- PMHx: obstetrical, sexual, STI/PID, contraceptive methods, surgeries, injuries
- Hx physical/sexual abuse
- Urinary/Bowel symptoms
- Family Hx (especially 4 most common causes, see below)

4 Most Common Causes

(for other causes see Table H, for diagnosis, investigation and treatment see Tables I, J and K)

- Irritable Bowel Syndrome (IBS)
- Interstitial Cystitis (IC)
- Endometriosis (see page 10 and 11)
- Adhesions

Systems as source of pain: Gastrointestinal 38%, Urinary 31%, Gynecological 20%
25-50% of women have > 1 organ system involved and experience higher pain scores

Talking Tip: Ask about physical/sexual abuse

"Although it can be difficult to talk about, some women who have chronic pelvic pain have been hurt or abused physically or sexually at some earlier time in their lives. I'm wondering if anything like this has ever happened to you?"

2

Physical Examination

- Abdominal, MSK, CNS
- Pelvic exam: do a vaginal exam first to eliminate abdominal sources of pain, then bimanual exam for masses, nodularity, rectal exam to detect uterosacral ligament nodularities

Initial Investigations

- Pap + swabs
- Transvaginal pelvic U/S
- betaHCG
- Urinalysis + culture
- Laparoscopy is optional (see treatment principles below)

3

Treatment Principles

- Multidisciplinary approach proven beneficial
  - combinations of medical, surgical, nutrition, physical therapy and psychotherapy
- Can treat pain itself (analgesics, pain relieving modalities) and/or underlying cause
- Can treat with chronic pain medications such as antidepressants, anticonvulsants, muscle relaxants, etc.
- Very little evidence to support any treatment
- GnRH analogues (Lupron®, Zoladex®, Synarel®) help pain that varies with menstrual cycle (endometriosis, pelvic congestion, IBS, IC, post-oophorectomy ovarian remnant/ post-hysterectomy ovarian retention syndrome)
- Some experts suggest trying GnRH without performing a laparoscopy first

4

Medical Treatments

- First line: acetaminophen, ASA, NSAIDs
- Second line: hormonal contraceptive (continuous, monophasic), continuous progestins, GnRH analogues
- Refractory pain: TCAs, SNRIs, Opioids

Surgical Treatments

- Presacral neurectomy only helps midline dysmenorrhea
- Hysterectomy and oophorectomy relieves pain 60-95%
- Less efficacious if age<30, no clear pelvic pathology or psychological problems

Supporting Table for: Chronic Pelvic Pain

Table H ▸ *Other causes of Chronic Pelvic Pain* *(Level A evidence)*

Malignancies	***Gastrointestinal***	***Urinary***
▸ Bladder, gynecologic, colon	▸ Constipation ▸ IBD	▸ Radiation cystitis ▸ Urethral syndrome
Gynecological	***MSK***	***Other***
▸ Adenomyosis (see Table L) ▸ Post-hysterectomy ovarian retention/ post-oophorectomy ovarian remnant syndromes ▸ Pelvic congestion syndrome ▸ PID ▸ Tuberculous salpingitis	▸ Abdominal wall myofascial pain (trigger points) ▸ Coccygeal/back pain ▸ Fibromyalgia ▸ Neuralgia ▸ Pelvic floor myalgia ▸ Levator ani or piriformis syndrome ▸ Peripartum pelvic pain syndrome ▸ Pubic symphysitis	▸ Abdominal cutaneous nerve ▸ Entrapment in surgical scar ▸ Depression ▸ Somatization disorder

Table I ▸ *Irritable Bowel Syndrome*

Consider if:

Rome II Criteria for Irritable Bowel Syndrome:

At least 12 weeks (need not be consecutive) in the preceeding 12 months of abdominal discomfort or pain that has 2 of 3 features:

1. Relieved with defecation
2. Onset associated with a change in frequency of stool
3. Onset associated with a change in stool form or appearance

The following symptoms are not essential for the diagnosis, but their presence increases diagnostic confidence and may be used to identify subgroups of irritable bowel syndrome:

- Abnormal stool frequency (more than 3 per day or fewer than 3 per week)
- Abnormal stool form (lumpy, hard or loose, watery) in more than 25% of defecations
- Abnormal stool passage (straining, urgency, or feeling of incomplete evacuation) in more than 25% of defecations
- Passage of mucus in more than 25% of defecations
- Bloating or feeling of abdominal distention in more than 25% of days

Modified from Thompson WG, Longstreth GF, Drossman DA, Heaton KW, Irvine EJ, Muller-Lissner Sa. Functional bowel disorders and functional abdominal pain.

Gut 1999;45(Suppl 2):1143-7.

Investigation

Work up needed for alarm symptoms (i.e. bleeding, thin stools, etc.)

- Age>50 consider colonoscopy

Rule out other GI causes:

- Common: IBD, celiac, lactose intolerance
- Less common: fructose intolerance, microscopic colitis, chronic infection, bacterial overgrowth, chronic pancreatitis

Treatment

- Diet: decrease lactose, sorbitol, caffeine, fructose
- Constipation: increase fiber (Metamucil®), stool softener (docusate sodium)
- Osmotic laxatives (lactulose, milk of magnesium, sorbitol)
- Diarrhea: loperamide, cholestyramine
- Antigas: Beno®, Gas-X®
- Antispasmodics: Dicetel®, dicylomine (Bentylol®), hyscomine (Levsin®)
- Librax®
- TCA
- Peppermint Oil

Table J ▸ *Interstitial Cystitis*

Consider if:	Treatment
▸ Urgency, frequency, suprapubic pain, nocturia, dysuria, ▸ Urine C+S negative	▸ Dietary modifications (elimination of aggravators) ▸ Stress management ***Pentosan polysulfate*** (Elmiron®) ***Antihistamines*** (hydroxyzine) ***Amitriptyline*** ▸ Intravesical instillations DMSO/other agents ▸ Hydrodistention of bladder/TENS/acupuncture/ sacral neuromodulation
Investigations	
▸ No single diagnostic test: rule out other pathology ▸ Voiding diary ▸ Urine microscopy and culture ▸ Urine cytology ▸ Cystoscopy ▸ Intravesical KCL sensitivity test	

Table K ▸ *Adhesions*

Consider if:		Investigations

▸ Past surgery
▸ Previous infection
  ▸ PID
  ▸ Appendicitis
	▸ IBD
	▸ Endometriosis
	▸ Pain is positional
		▸ Laparoscopy

		Treatments
		▸ Adhesiolysis for severe lesions

Table L ▸ *Adenomyosis*

Definition: *Ectopic endometrial glands and stroma within the myometrium surrounded by myometrial hypertrophy.*

- Two types: diffuse (distributed throughout the myometrium) and focal, which occurs as adenomyomas (nodules of hypertrophic myometrium and ectopic endometrium, often difficult to distinguish from fibroids)
- Though sometimes referred to as endometriosis interna, uterine endometriosis, or internal endometriosis, it is not endometriosis. They are separate conditions.
- Difficult to diagnose as mostly a pathological diagnosis by microscopic exam of the uterine wall from hysterectomy specimens (endometrial biopsy not helpful), though MRI and transvaginal ultrasound starting to become accurate.
- Cause unknown but there appears to be increase risk if history of uterine trauma (childbirth, pregnancy terminations, Caesarian sections,)
- Usually age> 30, disappears after menopause
- Symptoms: menorrhagia, dyspareunia, dysmenorrhea, pelvic pain
- Signs: symmetrically enlarged, tender uterus
- Treat depending on symptoms (not radiological findings) with NSAIDs, hormonal contraceptive, Mirena® IUS, GnRH agonists
- Some trials showing a response to uterine artery embolization
- Endometrial ablation not recommended.
- Last resort: hysterectomy

Notes:

Steps to manage: Pelvic Organ Prolapse

Bottom Line

Women are often reluctant to discuss prolapse symptoms. While no RCT's exist for treatment, pessaries are a good option for those who wish to avoid surgery.

Definition

Descent of pelvic organs towards or into the vagina.

- Anterior: cystocele (bladder, most common), urethrocele (urethra)
- Middle: uterus, vault (post hysterectomy)
- Posterior: rectocele (rectum), enterocele (small bowel, omentum)

1 Presentation/History

Prevalence = 50% of parous women. Most asymtomatic

History

- Urinary frequency, urgency
- Bulge/lump in vagina
- Pelvic pressure/heaviness
- Incontinence of urine or stool
- Difficulty with defecation/constipation
- Dyspareunia
- Need to insert fingers in vagina to void/defecate

Risk Factors

- Childbirth
- Constipation
- Age
- Pelvic surgery
- Chronic cough
- Obesity
- Raised intraabdominal pressure

2 Physical Examination

- Bimanual + speculum exam at rest and with straining
- If prolapse not obvious: repeat with patient standing with one foot on chair
- Urine culture
- Pelvic U/S or cystography
- If history of urinary incontinence, urodynamic testing

3 Treatment Principles

- Most asymptomatic and no treatment needed
- Trial of lifestyle modification may be beneficial
  - kegel exercises
  - weight loss
  - smoking cessation
  - treatment of constipation
  - electical stimulation/biofeedback

Tips for speculum exam for prolapse:

- Turn regular speculum 90° (watch urethra) to see anterior/posterior
- Remove one blade from the double speculum and use single blade applied anteriorly and posteriorly

4 Medical Therapy

- Local estrogen for vaginal atrophy may relieve urinary urgency/frequency and improve results from kegel exercises, pessary or surgery
- Consider a pessary
  - shaped device usually made of silicone and left in the vagina
  - different types for cystocele, stress incontinence, uterine prolapse, rectocele or combinations, and for post-hysterectomy vault prolapse.
  - fit by trial and error with fitting rings similar to diaphragm fitting
  - most common is ring to treat symptomatic uterine prolapse or cystocele
  - removed regularly for cleaning by patient or health care professional
  - see patient every 3 - 6 months to check for vaginal erosions

OHIP billing codes for pessary fitting

G398 (per 12 months)

G358 (per 3 months)

This is the code to use to remove, clean, reinsert pessary and check for vaginal lesions

5 Further Evaluations/ Surgical Treatments

- Pelvic organ prolapse surgeries have a success rate 65-90%, re-operation rate 30%
- When more than one compartment involved, need a combination of surgeries
- Correcting cystocele can unmask stress incontinence (unkink urethra, easier to leak)
- can check for this prior to surgery by correcting prolapse during pelvic exam and observing for urinary incontinence when coughing.
- Some operations may predispose to prolapse in another compartment

- Can use fascia/mesh/tape/suture to suspend organs through abdomen, vagina or laparoscopic approach
- For uterine prolapse, vaginal hysterectomy is treatment of choice
  - to conserve uterus: sacrohysteropexy uses Y-shaped graft to attach uterus to sacrum
- Complications include hemorrhage, hematoma, nerve damage, voiding difficulties, recurrence of prolapse, dyspareunia, mesh erosion

Grades of Pelvic Organ Prolapse

1. Mild descent of uterus, cystocele or rectocele, usually asymptomatic and found incidentally on exam
2. Descent of uterus, cystocele or rectocele above introitus, also usually asymptomatic
3. Descent of uterus, cystocele or rectocele to introitus
4. Descent of uterus, cystocele or rectocele beyond introitus

Procidentia: total prolapsed of uterus

Table M ▸ *Pessary Tips*

- Two types: supportive for milder prolapses and space occupying for higher grades
- Cost: $88C delivered to your office
- For women with atrophic changes, the vagina can be prepared with 2 g estrogen 2-3 x/wk for a month prior to insertion
- Aim for the largest size that fits comfortably
- Examiners fingers should pass easily between pessary and vagina wall
- After fitting the pessary in the office, have patient walk around and try to urinate/defecate
- Women can remove, wash with mild soap and/or water and replace the pessary weekly or monthly (or it can be cleaned by a health care professional every 3-6 months)
- No evidence or concensus on which pessary is best, how often to clean or visit health professional
- Must keep the vagina lubricated with estrogen or Trimosan (supplied by Milex)
- Adverse effects: discharge, odour, pain, bleeding, failure to reduce prolapse, expulsion
- Long term use has a risk of vaginal erosion, therefore vaginal exams should be performed every 3-12 months
- Forgotten pessaries: if pessary is fixed in place, apply estrogen cream 2 gm every second day for 2 weeks to help loosen before removal
- Change a pessary at around 5 years or when it wears out

Table N ▸ *Pessary Companies* *(available 2010)*

Milex (Cooper Surgical, Inc.)	1-800-243-2974	www.coopersurgical.com
Superior Medical Limited	1-800-268-7944	www.superiormedical.com

Notes:

Investigations and Surgical Options for Benign Uterine Conditions

Endometrial Ablation

- Indication: menorrhagia
- Entire endometrium and 3mm of myometrium are destroyed
- Contraindicated in patients who want to preserve their fertility
- Can be done under hysteroscopic guidance using laser, radiofrequency, electrical (+ rollerball), hydrothermablation (hot glycine, good for congenital abnormalities or fibroids)
- Can be blind procedure (non-hysteroscopic, no distension with fluid/gas) procedure
  - Thermal balloon catheter (balloon conforms to shape of cavity, filled with heated water)
  - Radiofrequency, Laser, microwave, cryoablation
- Amenorrhea 35%-71% , higher rates > 40 years old
- Ongoing or worse dysmenorrhea possibly due to adenomyosis
- Pregnancy can occur post procedure (0.7%) therefore need contraception
- Complications (1-5%): perforation 0.76%, fluid overload (if used), does not protect against future uterine cancer, mortality 2-3/10,000
- Procedure usually lasts approximately 5 years
- 10-20% go on to hysterectomy
- 10-16% repeat ablation

Endometrial Sampling

- Do betaHCG before

Endometrial biopsy

- Office procedure using small catheter with internal plunger which creates suction to sample endometrial lining
- Adequate sample obtained 87-97% of the time
- Detects 67-96% of endometrial carcinomas
- Diagnostic accuracy > dilation and curretage (D + C)

Hysteroscopic directed biopsy

- Usually done under general anesthetic, can do under local
- Hysteroscope enters through cervix to see the lining of the uterus
- Allows direct visualization of abnormalities (polyps, hyperplasia) and biopsy
- Better than D + C for diagnosis of lesions (see hysteroscopy)

Dilation and Curettage (D + C)

- Done under general anesthetic (sometimes local) to sample the endometrium
- Can miss pathology up to 10% of the time
- Often now done with hysteroscopy to increase yield
- No longer a treatment for abnormal uterine bleeding (effects not long-lasting)

Hysteroscopy

- Done in the office, under general anesthesia or conscious sedation by gynecologist
- Good at detecting submucous fibroids and polyps and for biopsy under direct visualization
- Cavity needs to be filled with liquid (glycine) or less often now, gas (CO_2)
- Risks: perforation, infection, bleeding, fluid overload/gas embolism.

Hysterectomy

- Done through the vagina, abdomen or laparoscopy-assisted
- Vaginal route preferred if feasable due to lower morbidity (vaginal 24%, abdominal 43%)
- Laparoscopic procedure: little advantage as complication rates not lower and procedure time lengthened (but recovery time and length of hospital stay is shorter)
- Partial (subtotal) hysterectomy leaves cervix therefore ongoing Pap smear surveillance required
- Conserving ovaries is preferred unless indication is for endometriosis, chronic pelvic pain
- Sometimes ovaries left in place fail to function post hysterectomy
- Can stop pap smear screening in women with total hysterectomy for benign reasons and no cervical intraepithelial neoplasia on pathology
- Patients with fibroids, menorrhagia, endometriosis very satisfied
- Chronic pelvic pain 74%-90% are pain-free at 1 year
- Complications: postop infections, fever, hemorrhage, injury to bowel, bladder, ureter, thromboembolic events, pneumonia, constipation, vaginal vault prolapse
- 90% patients have improved/same sexual function post hysterectomy
- No proven advantage to partial hysterectomy for sexual response
- Mortality 5-16/10,000

Laparoscopy

- For diagnosis of endometriosis: positive predictive value of 45%
- Surgical treatment of endometriosis: removal (excision), destruction (ablation, endocoagulation, electrocautery, laser vapourization), division of adhesions, removal of cysts
- 0.06% risk of major complication

Ultrasound

Transvaginal

- Detects leiomyoma, endometrial thickening, polyps, diffuse adenomyosis
- Measure double thickness endometrial echo in mm
- Post-menopausal women with vaginal bleeding and an endometrial lining thickness > 5mm require investigation
- Pre-menopausal patient expert opinion suggests lining >10-12 mm (done first half of the menstrual cycle) requires further investigation
- Can miss endometrial polyps, submucous fibroids (better visualized with transvaginal sonohysterogram)

Transabdominal

- Generally not the best modality for pelvic pathology
- Consider if virginal
- Good for fibroids greater than 12 weeks size

Sonohysterogram (SHG) / hysterosonogram / saline infusion study (SIS)

- Ultrasound visualization of uterus after instillation 5 -15 mL sterile saline into endometrial cavity
- Indicated for irregular bleeding, infertility, some intrauterine abnormalities found on ultrasound
- Good for detecting submucous fibroids, polyps
- Can be painful, helpful to take NSAID before
- SBE prophylaxis is recommended for those at risk

Best Articles and Guidelines for Benign Uterine Conditions

Fibroids

Best Article:

Evans P, Brunsell S. Uterine Fibroid Tumors: Diagnosis and Treatment. American Family Physician 2007;75:1503-8

Best Guideline:

SOGC Clinical Practice Guidelines. The Management of Uterine Leiomyomas. JOGC May 2003.

Pre-Menopausal Abnormal Uterine Bleeding

Best Article:

Telner D, Jakubovicz D. Approach to diagnosis and management of abnormal uterine bleeding.
Canadian Family Physician 2007;53:58-64

Best Guideline:

SOGC Clinical Practice Guidelines. Guidelines for the Management of Abnormal Uterine Bleeding. JOGC August 2001

Post-Menopausal Abnormal Uterine Bleeding

Best Article:

Telner D, Jakubovicz D. Approach to diagnosis and management of abnormal uterine bleeding. Canadian Family Physician 2007;53:58-64

Best Guideline:

Investigation of Post-Menopausal Bleeding Scottish Intercollegiate Guidelines Network Publication No. 61
September 2002 available at: *http://www.sign.ac.uk/guidelines/fulltext/61/index.html*

Endometriosis

Best Article:

Farquhar C. Endometriosis. BMJ 2007:334;249-53

Best Guideline:

Jackson B, Telner D. Managing the misplaced. Canadian Family Physician 2006;52:1420-1424

Chronic Pelvic Pain

Pain assessment forms:

One page symptom sheet available at:
http://www.obgyn.net/ENGLISH/PUBS/FEATURES/CARTER/SYMPTOMS_checklist.pdf
Detailed history/physical form available at: *http://pelvicpain.org/pdf/FRM_Pain_Questionnaire.pdf*

Best Articles:

Ortiz D. Chronic Pelvic Pain in Women. American Family Physician 2008;77(11):1535-1542
Bordman R, Jackson B. Below the belt: approach to chronic pelvic pain. Canadian Family Physician 2006;52:1556-1562

Best Guideline:

SOGC Clinical Practice Guidelines. Consensus Guidelines for the Management of Chronic Pelvic Pain. JOGC
Aug 2005/Sept 2005 (2 part series)

Pelvic Organ Prolapse

Best Articles:

O'Neil B, Gilmour D. Approach to urinary incontinence in women. Canadian Family Physician 2003;49:611-618
Thakar R. Stanton S. Management of genital prolapse. BMJ. 2002; 324(7348):1258-62

Best Guideline:

SOGC Clinical practice guidelines. Conservative Management of Urinary Incontinence. JOGC Dec 2006

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