

Tips and Tricks for the Perimenopause

(Answers to 22 Questions in 22 Minutes in '22)



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Everyday Gynaecology CME

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Learning Objectives

To increase your confidence in treating the perimenopausal patient by:

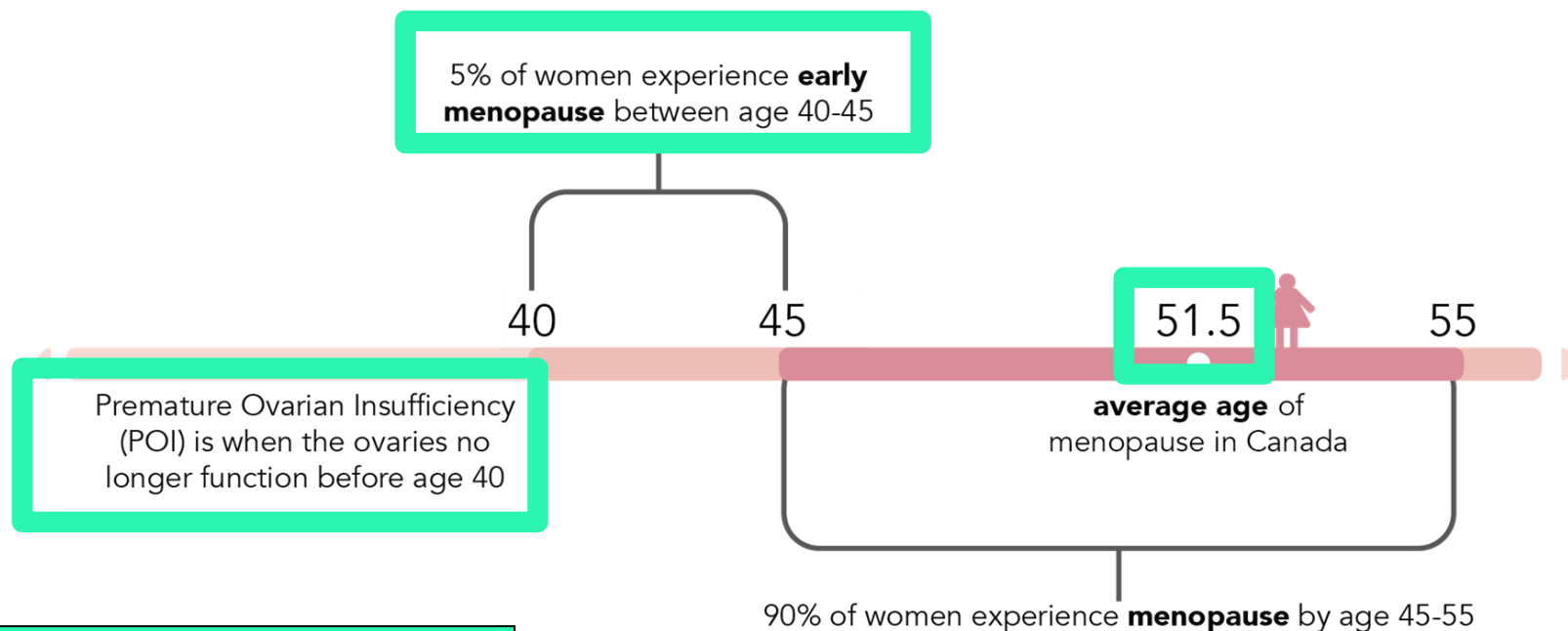
1. Reviewing 22 relevant facts about perimenopause in 2022.
 - Definition and Physiology
 - Gynaecologic Considerations
 - Management Approach
2. Providing '*Toolkit Tips*' that you can apply in your own practice when considering different options.

Toolkit Tips

Question 1:

What is menopause?

Menopause occurs when the ovaries decrease their functioning and no longer release eggs. Usually, menopause is diagnosed after someone has gone 12 months without a menstrual period.



Toolkit Tips

Different types of menopause:

Surgical, Induced, POI, Early, Natural Menopause

Question 2:

What is perimenopause?

STRAW +10

Standardized Staging System for Reproductive Aging

Stage	-5	-4	-3b	-3a	-2	-1	+1 a	+1b	+1c	+2
Terminology	REPRODUCTIVE				MENOPAUSAL TRANSITION		POSTMENOPAUSE			
	Early	Peak	Late		Early	Late	Early			Late
					Perimenopause					
Duration	variable				variable	1-3 years	2 years (1+1)	3-6 years	Remaining lifespan	
PRINCIPAL CRITERIA										
Menstrual Cycle	Variable to regular	Regular	Regular	Subtle changes in Flow/ Length	Variable Length Persistent ≥7- day difference in length of consecutive cycles	Interval of amenorrhea of ≥60 days				
SUPPORTIVE CRITERIA										
Endocrine			Low	Variable	↑ Variable	↑ >25 IU/L**	↑ Variable	Stabilizes		
FSH			Low	Low	Low	Low	Low	Very Low		
AMH			Low	Low	Low	Low	Low	Very Low		
Inhibin B			Low	Low	Low	Low	Very Low	Very Low		
Antral Follicle Count			Low	Low	Low	Low	Very Low	Very Low		
DESCRIPTIVE CHARACTERISTICS										
Symptoms						Vasomotor symptoms Likely	Vasomotor symptoms Most Likely			Increasing symptoms of urogenital atrophy

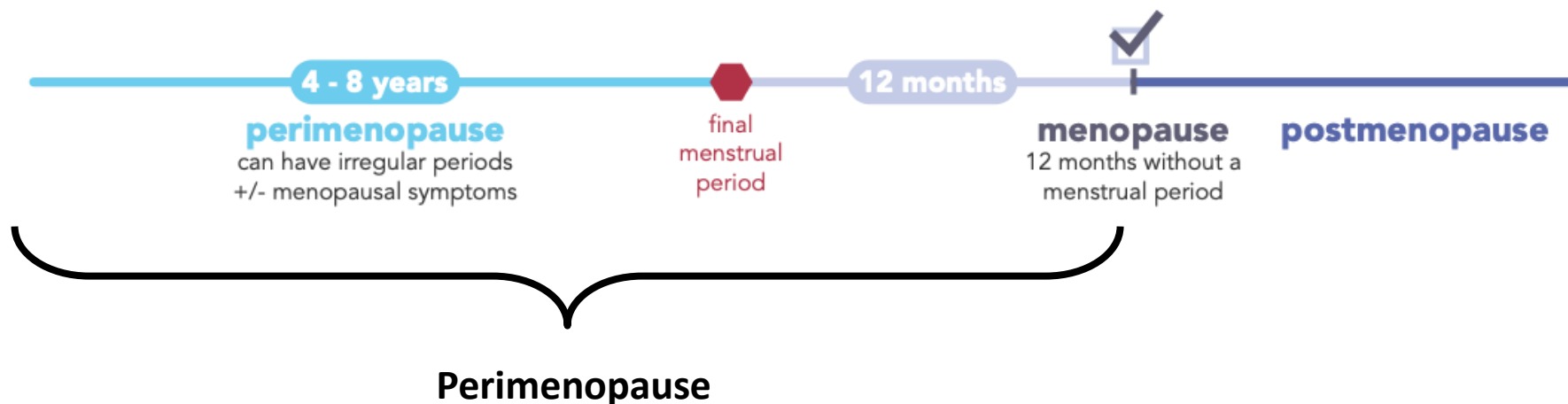
* Blood draw on cycle days 2-5 ↑ = elevated

**Approximate expected level based on assays using current international pituitary standard⁶⁷⁻⁶⁹

Question 2:

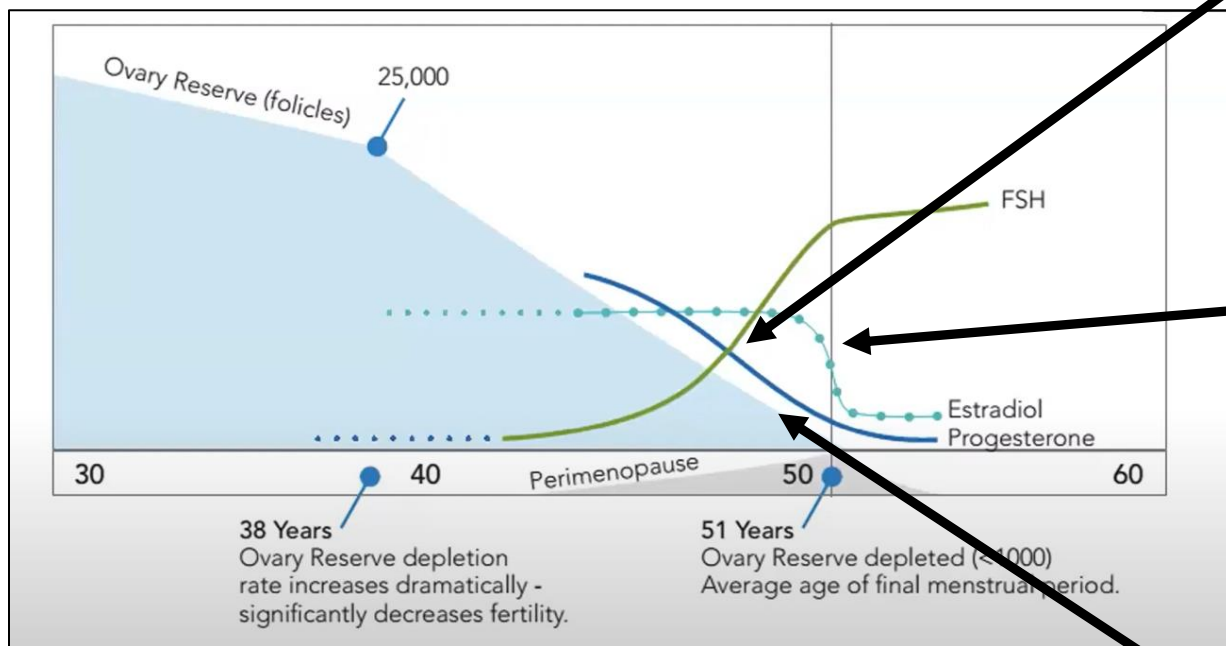
What is perimenopause?

Perimenopause precedes natural menopause and occurs during a time of fluctuating hormones. People may experience irregular periods and menopausal symptoms. It can last **4 to 8 years** and typically starts with changes in the length of time between periods and ends 1 year after the final menstrual period.



Question 3:

How do I explain the endocrinology to patients?



Ovaries stop being as responsive to FSH so your brain works a bit harder by releasing **more FSH** to help you ovulate. Ovarian response to FSH is inconsistent.

Without the consistent ovarian response to FSH, follicle development **decreases** so you don't make as much **estrogen**. **This is what is giving you the symptoms associated with low estrogen.**

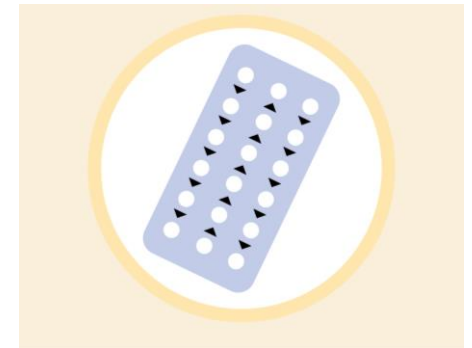
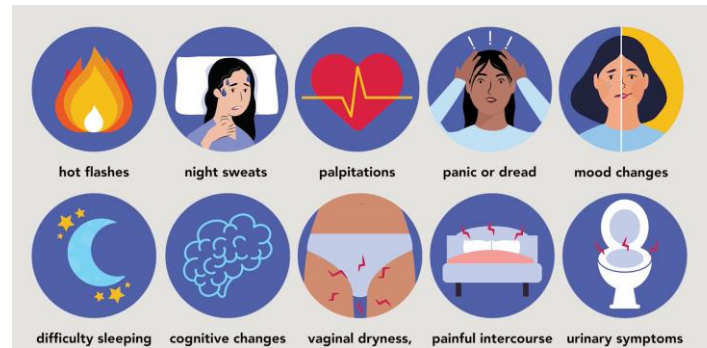
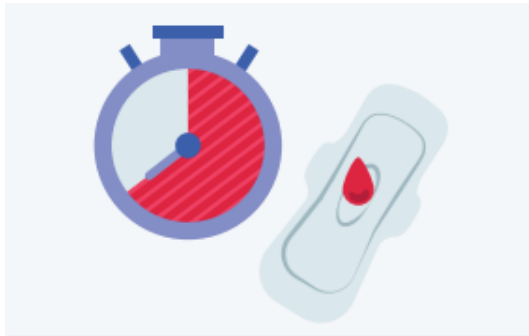
Because you aren't ovulating as much, you don't have a lot of **progesterone** circulating to stabilize your endometrial lining. **This is what may be giving you abnormal bleeding, usually referred to as anovulatory cycles.**

Toolkit Tips

"Checking Hormones" or "Seeing Where you Are" isn't typically helpful.

Question 4:

What are common gynaecologic considerations in perimenopausal patients?



Toolkit Tips

- ✓ Bleeding Pattern Changes
- ✓ Menopausal Symptoms
- ✓ Contraception

Question 5:

What's a *NORMAL* period?

REGULARITY



Periods occur every
24 – 38 days

DURATION



Periods last
from 4.5 – 8 days

FLOW

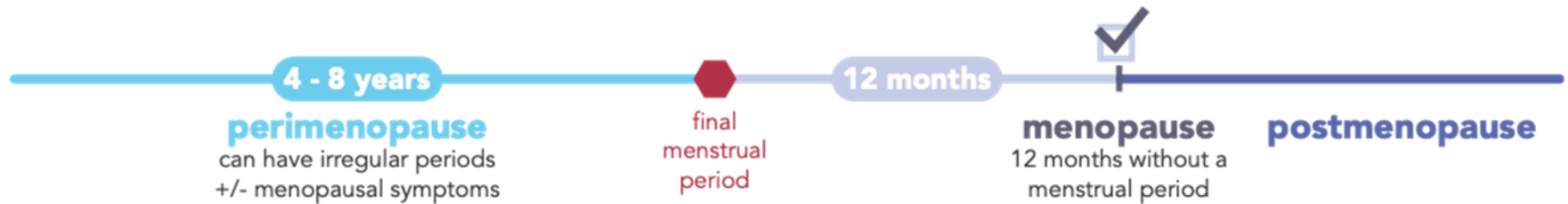


Flow does not
impact your daily life

Overall, normal menstruation exists on a spectrum with some people having lighter or heavier periods than others, and variation from cycle to cycle

Question 6:

What happens to bleeding in perimenopause?

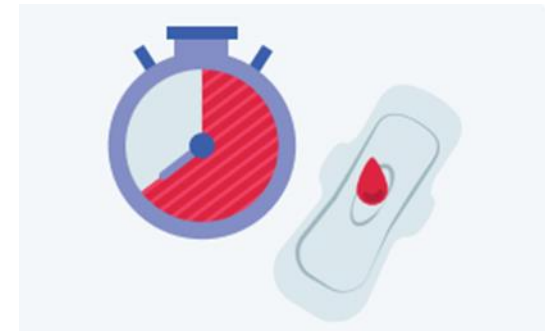


EARLY PERIMENOPAUSE

- Variable length of flow
- Persistent difference of ≥ 7 day in length of consecutive cycles

LATE PERIMENOPAUSE

- Interval of amenorrhea of ≥ 60 days

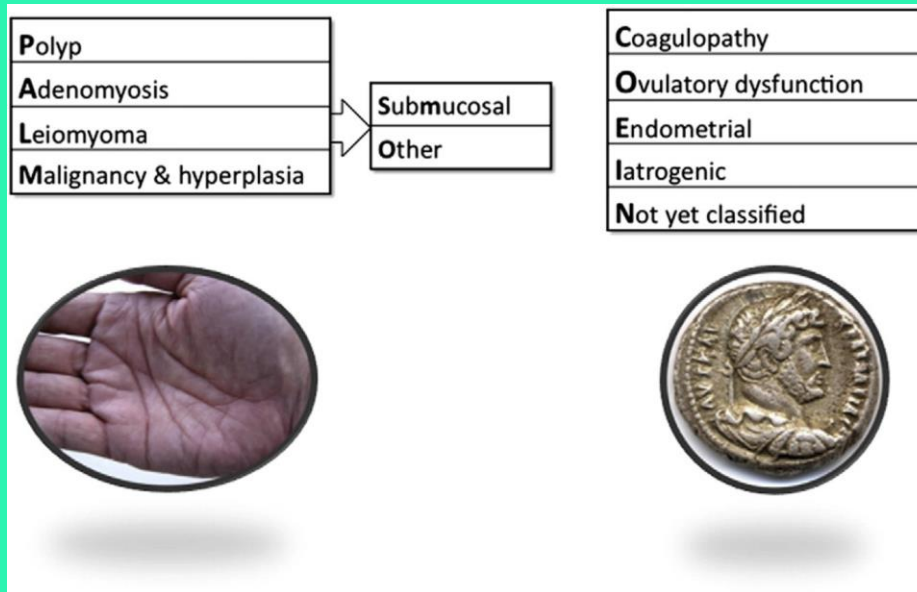


Question 8:

What is the DDX for abnormal uterine bleeding?

Toolkit Tips

- ✓ **PALM COEIN causes of abnormal uterine bleeding in nonpregnant, premenopausal women**



- ✓ **Bleeding caused by structural pathology measurable through imaging or histopathology**

versus

- ✓ **Bleeding unrelated to structural abnormalities**

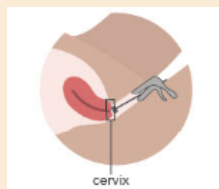
Question 9:

What are initial steps for AUB work-up?

History

Physical Examination

Pap Test

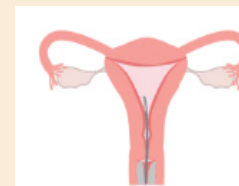


Labs



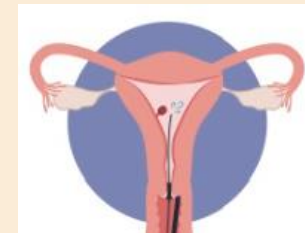
- CBC, ferritin, TSH, β hcg, Prolactin, Vaginal C&S, Urine GC/Chlamydia, Bleeding disorder investigations

Endometrial Sampling (e.g., EMBx or D&C)



- Age > 40
- Unexpected response to medical management
- Persistent AUB
- Family History of endometrial CA or Lynch Syndrome
- **Risk Factors:** Obesity, PCOS, Unopposed Estrogen, Bioidentical MHT, Tamoxifen use
- **If worried, you should do it or refer for one.**

Diagnostic Imaging



- Pelvic/TVUS
- Sonohysterogram
- \pm MRI

Question 10: What's Next?

Benign Conditions

- *Structural (GYN)*: Polyps, fibroids, adenomyosis, vaginal and cervical causes (polyps, lacerations)
- *Structural (non-GYN)*: GU, GI
- *Systemic*: Thyroid Dysfunction, Coagulopathy

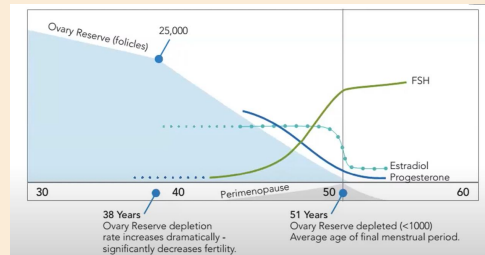
Pre-Malignant & Malignant Conditions

- *GYN*: Endometrial, Cervical, Synchronous Ovarian, Vulvar, Vaginal
- *Non-GYN*: GU, GI

Manage Structural Pathology or Systemic Condition

Hormonal Changes

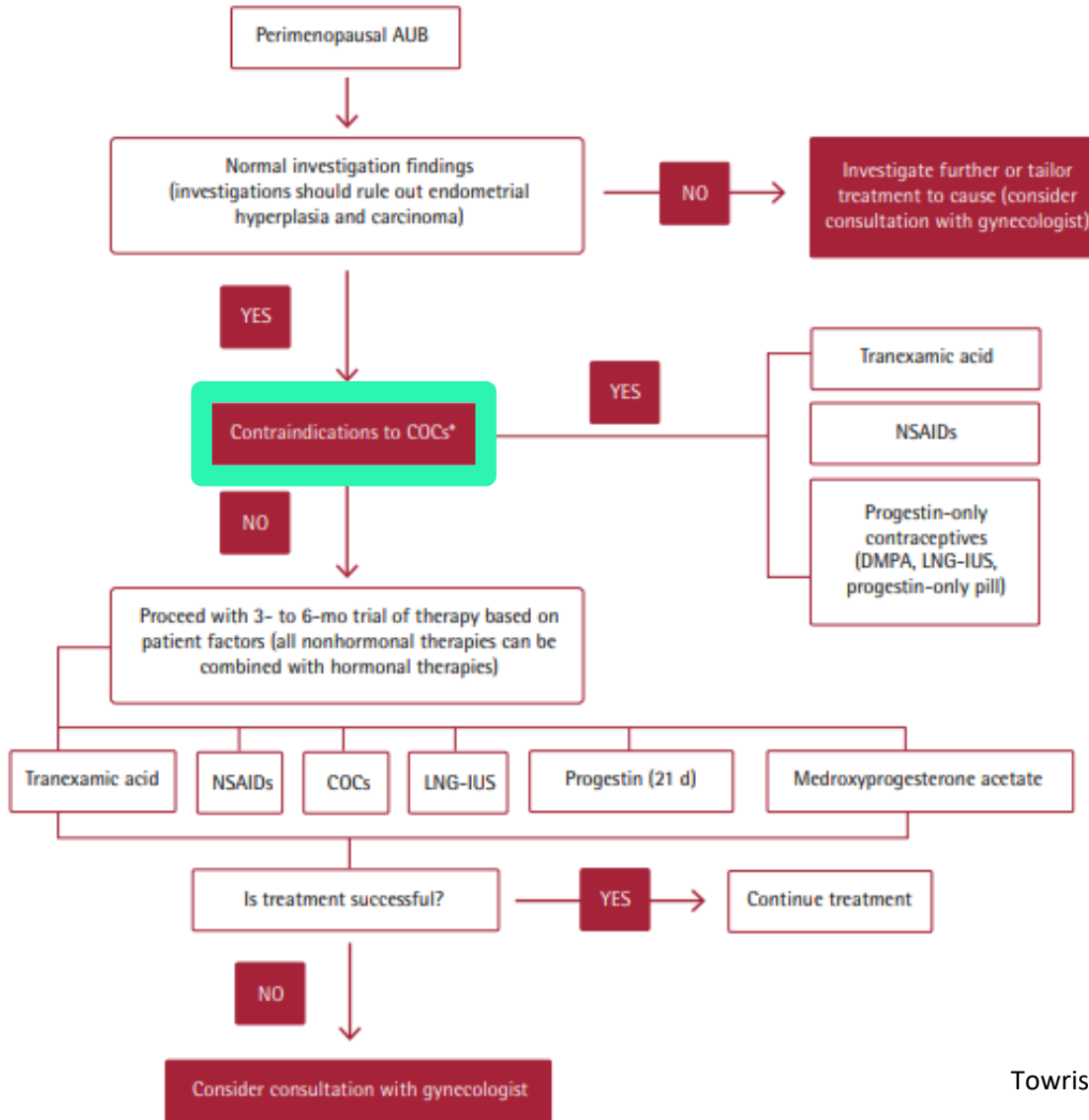
- Ovulatory Dysfunction



Manage Anovulatory Cycles

Question 11:

Some 'go-to' office medical management options?



Tranexamic Acid 1g po TID
“take while bleeding for up to 5 days per cycle”

Typical NSAID Dosing:
 Naproxen 500mg po BID
 Ibuprofen 600-1200 mg PO daily
 Mefenamic Acid 500 mg daily
“start on first day of your period and take for 3-5 days”

First-Line Hormonal:

First Line: **LNG-IUS (52mg)**

Second Line: **Combined Hormonal Contraceptive**
 *ANY type of CHC will be effective

Question 11:

Some 'go-to' office medical management options?



Manage AUB

Third-Line Hormonal:



Injected Progestins

i.e. Depot medroxyprogesterone acetate (DMPA)

150mg intramuscular injection every 90 days



Cyclic Oral Progestins

i.e. Norethisterone (or Norethindrone) acetate / NETA

5mg taken TID for 21 days monthly
(from day 5 to day 26 of menstrual cycle)

A note about oral progestins

Taking lower dose NETA for 7-11 days per month (cyclic luteal phase progestins) is not effective for treating heavy menstrual bleeding; higher doses taken for 21 days per month is required to manage heavy flow (long-cycle progestin)

Fourth-Line Hormonal:



Danazol

100 – 400mg PO once daily



GnRH Agonists

i.e. Leuprolide acetate (*Lupron*)

Administered as a monthly intramuscular injection for 3 to 6 months

A note about "add-back" therapy

If Lupron is used long term (> 6 months), "add-back" hormone therapy (estrogen with progestin OR progestin-only pill) should be prescribed for patients to protect against bone loss and manage the unwanted side effects

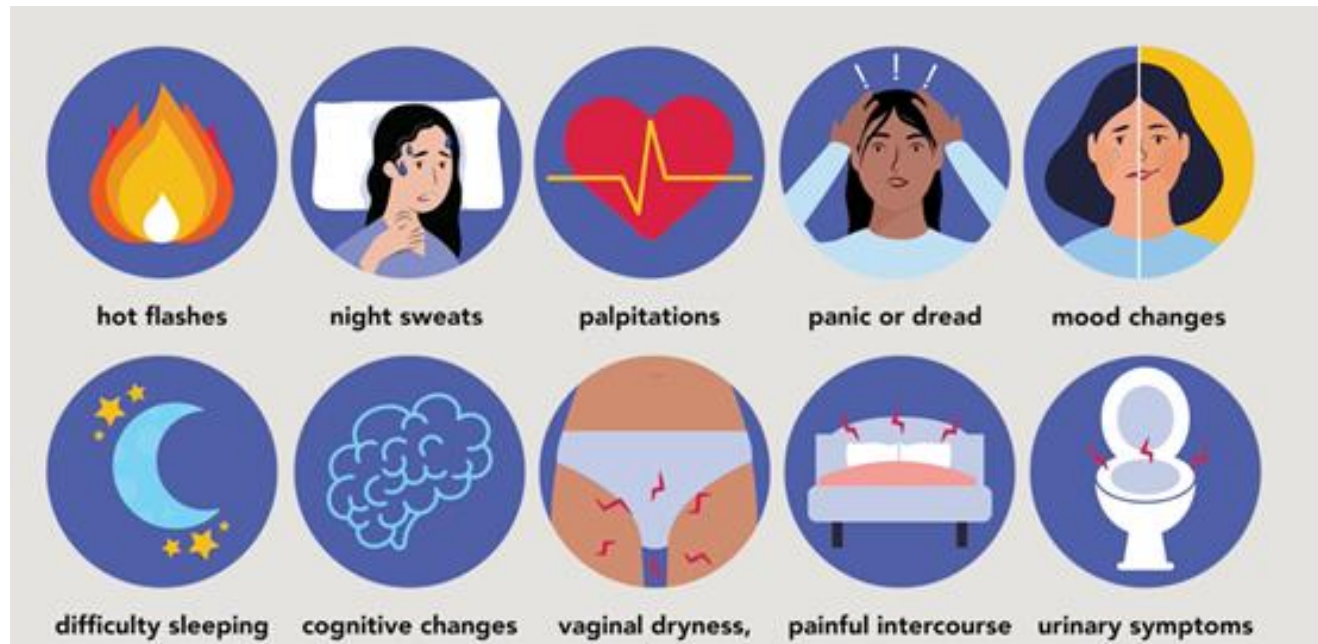
High Dose Oral Progestins

NETA 5mg po (OD to TID)

MPA 5-30mg/day

Question 12:

What are common menopausal symptoms?



Toolkit Tips

- ✓ Many symptoms arise during perimenopause. Important to screen for symptoms especially mood and vasomotor symptoms ***at the time of perimenopause.***

Question 13:

What are some important counselling points?

SYMPTOM	COUNSELLING POINTS
Vasomotor Symptoms	<ul style="list-style-type: none">• 75% of women will suffer from them with 20% of women rating flushes as severe and causing significant impairment.• Risk factors include smoking, obesity, physical inactivity.• 10% of women with have VMS for longer than 10 yrs.• MHT is most effective treatment but symptoms return in 50% of women who stop the medication.
Vaginal Dryness	<ul style="list-style-type: none">• Proper term is Genitourinary Syndrome of Menopause (GSM).• It is very treatable, usually happens later.
Low Libido	<ul style="list-style-type: none">• Multifactorial and affects up to 50% of people• Dyspareunia secondary to atrophy is treatable.
Weight Gain	<ul style="list-style-type: none">• Average weight gain is 2.3kg (5lbs), usually related to aging and activity changes. Usually distributed centrally.
Sleep	<ul style="list-style-type: none">• Affects 30% of menopausal people• <i>Causes:</i> night sweats, RLL, overactive bladder, etc.
Cognitive Changes	<ul style="list-style-type: none">• Forgetfulness and difficulty concentrating (“brain fog”)• Can worsen in the first year after LMP
Mood	<ul style="list-style-type: none">• Depression affects women > men and depressive symptoms can increase during the menopausal transition.• CBT and antidepressants are first-line treatments. MHT may be helpful for people with both VMS and mood concerns.

Question 14:

What are treatment options for VMS?

1) Lifestyle modification

no harm and low cost

CBT

Weight Loss

Paced Respiration

2) Nonprescription Treatments

little potential for harm, but often ineffective

Soy (s-equol)

Black Cohosh

3) Non-hormonal Prescription Drugs

great choice when MHT is contraindicated

4) Menopause Hormone Therapy

most effective (90% effective)

Toolkit Tips

Treating Vasomotor Symptoms

Remember 4 broad categories of treatment. What has your patient tried and what do they want?

Question 15:

What are some non-hormonal prescription options?

Category Generic Name (Brand Name)	Dosages and frequency for vasomotor symptom management
Citalopram (<i>Celexa</i>)	10, 20 mg oral daily
Escitalopram (<i>Cipralex</i>)	10, 20 mg oral daily
Paroxetine (<i>Paxil</i>)	10, 20 mg oral daily
Desvenlafaxine (<i>Pristiq</i>)	100–150mg oral daily
Venlafaxine (<i>Effexor</i>)	37.5, 75 mg oral daily
Gabapentin (<i>Neurontin</i>)	300–900 mg oral once daily at night
Pregabalin (<i>Lyrica</i>)	150–300 mg oral daily
Clonidine (<i>Dixarit</i>)	0.05 mg oral twice daily
Oxybutynin Immediate-Release	2.5, 5 mg oral twice daily

Question 15:

What are some non-hormonal prescription options?

Toolkit Tips **SSRIs**

Look at medications the patient is already on. Avoid Paxil in women taking Tamoxifen. High doses of SSRI medications can make vasomotor symptoms worse.

Toolkit Tips **Clonidine**

Small dosing – *watch the decimal!*
Discontinuing clonidine at higher doses can lead to rebound hypertension among other symptoms.

Toolkit Tips **Oxybutynin**

Initial Prescription: 2.5mg po BID
Watch for **side effects**: dry mouth, eyes, nose or skin; nausea and urinary retention.
New warnings about cognitive impairment due to anticholinergic activity on the CNS leading to central side effects.

Toolkit Tips

1. Writing the first Rx for Gabapentin

Gabapentin 100mg po QHS
Increase by 100mg po QHS q3-4 nights until a maximum dose of 900mg po QHS is reached.
Mitte: 270 x 100mg tablets (1 month)

2. FDA Warning

Respiratory depression can occur when Gabapentin or Pregabalin is taken with other medications that depress the CNS (ie. Opiates), women who have respiratory issues or in the elderly.

Question 16:

What about Menopausal Hormone Therapy (MHT)?

- 1 Bothersome vasomotor symptoms (VMS)
- 2 Significant sleep or mood disturbances
- 3 Genitourinary syndrome of menopause (GSM)
- 4 Prevention of bone loss in postmenopausal women at high risk of developing or have osteoporosis
- 5 Hypoestrogenism caused by hypogonadism, premature surgical menopause or premature ovarian insufficiency (POI)

Toolkit Tip

GSM is typically treated with **LOCAL** therapies.
Other indications are managed with **SYSTEMIC** MHT.

Question 17:

Who cannot take *SYSTEMIC MHT*?

Contraindications to estrogen

- Undiagnosed abnormal vaginal bleeding
- Known, suspected, or history of breast cancer
- Known or suspected estrogen-dependent cancers (i.e., endometrial, ovarian)
- Coronary heart disease
- Active or history of venous thromboembolism
- Active or history of stroke
- Active liver disease
- Known or suspected pregnancy

Contraindications to progestogen

- Undiagnosed abnormal vaginal bleeding
- Current or history of breast cancer

Toolkit Tips

NOT on this list:

migraines, controlled hypertension,
smoking

Question 18:

How do I start my perimenopausal patient on MHT?

Estrogen Generic Name (Brand Name)	Typical Estrogen Starting Doses	Continuous Progesterone Regimen	Cyclic Regimen Progesterone Regimen
Conjugated Estrogen (<i>Premarin</i>)	0.3 mg OD 0.625 mg OD	Medroxyprogesterone Acetate (<i>Provera</i>) 2.5 mg OD	Medroxyprogesterone Acetate (<i>Provera</i>) 5 mg PO OD for 12-14 consecutive calendar days each month
17 β Estradiol (<i>Estrace</i>)	0.5 mg OD 1 mg OD		
17 β Estradiol (<i>Estradot</i>) <i>Patch changed twice/week</i>	25 mcg 37.5 mcg 50 mcg 75 mcg*	OR	OR
17 β Estradiol (<i>Estrogel</i>)	1 ppd OD 2 ppd OD	Micronized Progesterone (<i>Prometrium</i>) 100 mg PO or PV OD	Micronized Progesterone (<i>Prometrium</i>) 200 mg PO or PV for 12-14 consecutive calendar days each month
17 β Estradiol (<i>Divigel</i>)	0.25 mg sachet OD 0.5 mg sachet OD	OR	
		Levonorgestrel IUD (<i>Mirena</i>)	

*Typically requires more progesterone than listed in far column

Estrogens

Toolkit Tips
Oral Estrogens

Many patients prefer once daily dosing. **ODSP** will cover generic *Premarin* (0.625mg tablet) and *Estrace* (0.5mg, 1mg and 2mg tablets).
Downsides: VTE/stroke risk, first-pass at liver

Estrogen Generic Name (Brand Name)	Typical Estrogen Starting Doses	Continuous Progesterone Regimen	Cyclic Regimen Progesterone Regimen
Conjugated Estrogen (<i>Premarin</i>)	0.3 mg OD 0.625 mg OD	Medroxyprogesterone Acetate (<i>Provera</i>) 2.5mg OD	Medroxyprogesterone Acetate (<i>Provera</i>) 5 mg PO OD for 12-14 consecutive calendar days each month
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Toolkit Tips
Transdermal Estrogens

Best option for women who are smokers or have migraines, hypertriglyceridemia, malabsorption syndromes, metabolic syndrome or hypertension.

Toolkit Tips
Gels

Estrogel (80g canister): 64 actuations
 Daily application to >2000 cm² and let dry for 2 minutes after application.
Divigel (30 sachets in a box)
 Consider when the Rx will need a refill.

Toolkit Tips
Patches

i.e. Estradot (8 patches/box)

Change patch twice per week with lower abdomen or buttock application. Check patch site for irritation in patients with ongoing symptoms.

Estradot is a matrix patch, which can be cut in women wanting to wean off hormone therapy.
 (ie. 25 mcg patch → 12.5 mcg patch)

Progesterones

Toolkit Tips
Progesterones

This can be the hardest to ‘get right.’

A good ‘go-to’ option is a micronized progesterone (*Prometrium*) because it can be given orally or vaginally. Orally is great for women with sleep concerns. Vaginally can be helpful for patients with mood dysfunction.

Toolkit Tips

Message to your patient about Progesterone:

Estrogen is going to help your symptoms the most. However, if you still have a uterus and you have been prescribed a stand-alone estrogen, it is important you take a progesterone to protect the lining of the uterus from developing precancer or cancer cells.

Estrogen Generic Name (Brand Name)	Typical Estrogen Starting Doses	Continuous Progesterone Regimen	Cyclic Regimen Progesterone Regimen
Conjugated Estrogen (<i>Premarin</i>)	0.3 mg OD 0.625 mg OD	Medroxyprogesterone Acetate (<i>Provera</i>) 2.5mg OD	Medroxyprogesterone Acetate (<i>Provera</i>) 5 mg PO OD for 12-14 consecutive calendar days each month
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Toolkit Tips

Medroxyprogesterone Acetate

All strengths of the generic tablets are covered by ODSP.

Medroxyprogesterone acetate was the same progesterone in the WHI trial.

Question 19:

How do I explain risks of systemic MHT?

There was a large study published in 2002 called the WHI Trial that made women very nervous. However, a **closer look at the data showed hormone therapy isn't as harmful as was initially thought** and several studies have shown significant benefit with respect to systemic hormone therapy, meaning hormones given by mouth or through the skin as a patch or gel. While every patient has individualized risks and every regimen carries different risks, generally:

Breast Cancer: Risk of breast cancer among the average patient is 63 cases per 1000 women. If we have you a combined estrogen and progesterone regimen, we increase that risk by approximately 1 case per 1000 women with each year of use. This is the same risk brought on by being obese or drinking 1-2 glasses of wine per night.

Stroke: Risk of stroke increases after the age of 60. If you start HRT before the age of 60, your risk of stroke is not really increased. Our counselling may be slightly different when speaking to patients with a history of migraines.

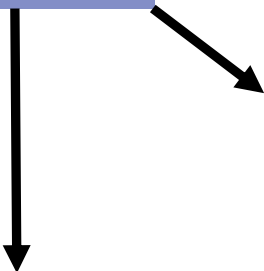
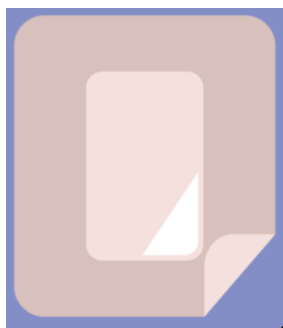
Heart Attack: As long as you are starting systemic hormone therapy within 10 years of your final period and before the age of 60, your risk of heart attack is not increased. In fact, starting estrogen in that time period likely offers cardiovascular protection in a healthy patient. However, we are not prescribing estrogen for that indication at the moment.

Blood Clot: Your absolute risk of blood clot is very low. Starting systemic estrogen increases that risk in the first 1-2 years of use. If you are a smoker or overweight, it is reasonable to consider an estrogen through the skin as risks of blood clot are lower in those using transdermal estrogens.

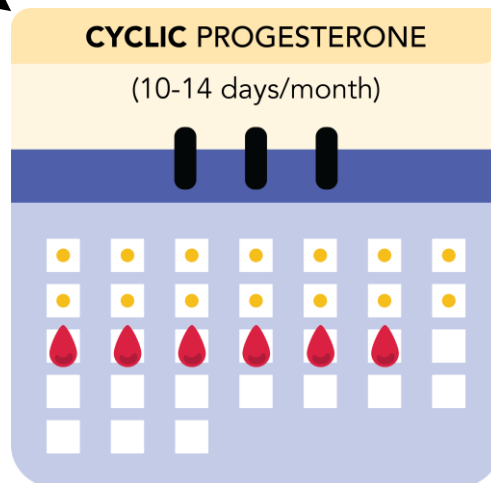
Question 20:

What progesterone components of systemic MHT is best for perimenopausal women?

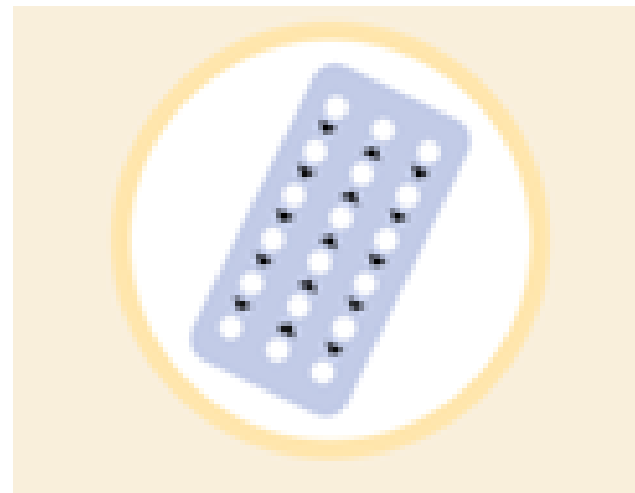
Estrogen (pill, patch, gel)



Levonorgestrel IUD



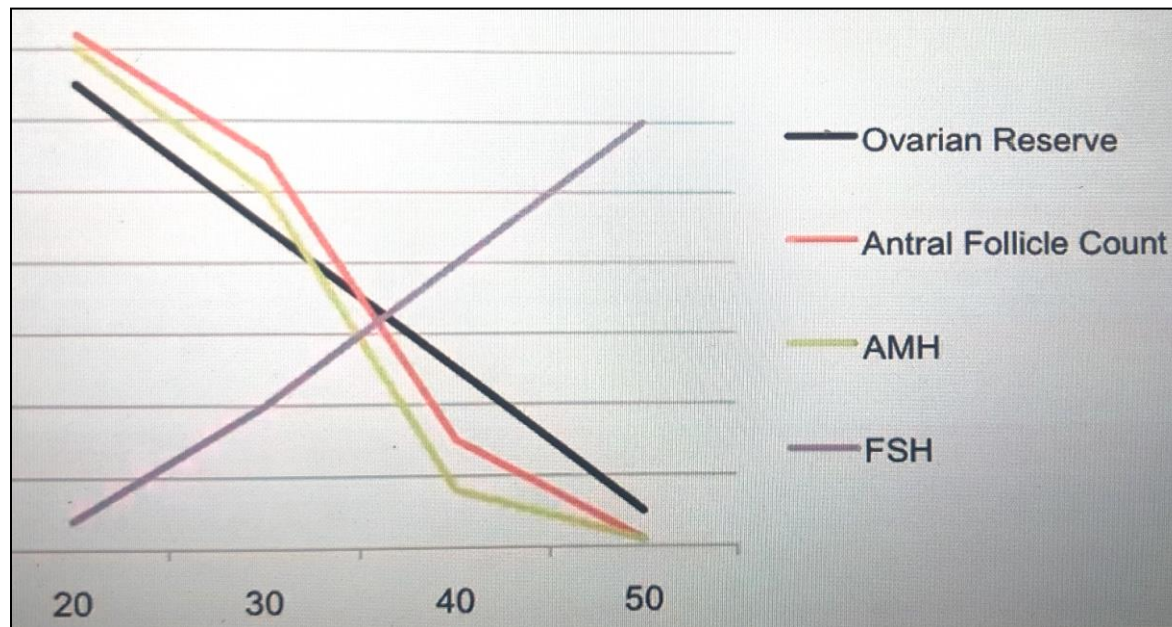
Cyclic Progesterone



Toolkit Tip
*OCP may also be an option
e.g., LoLo OCP*

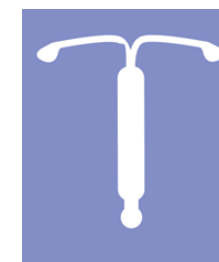
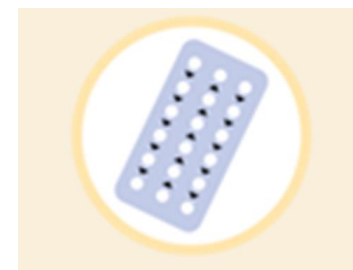
Question 21:

What about contraception?



Age (years)

"You need to use an effective, safe, and appropriate method of birth control until menopause is confirmed if you don't want to get pregnant at midlife."



Toolkit Tip

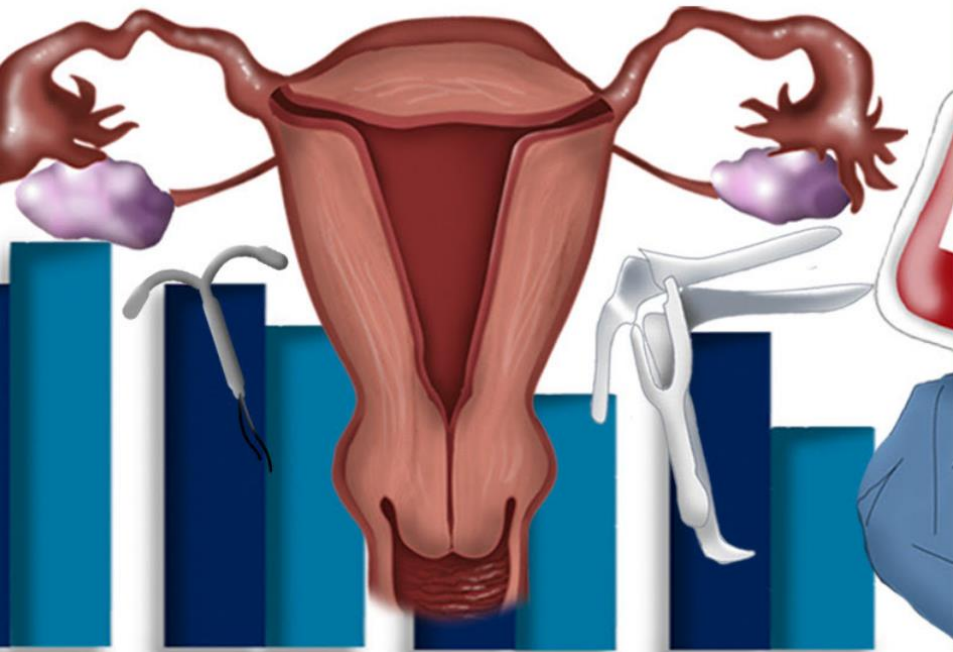
In real life, coital frequency and ovarian reserve decrease as women age. Therefore, contraceptive methods with lower inherent efficacy may be acceptable to your patient.

Question 21:

Any new resources available?



[Home](#) [About the Project](#) [For Surgeons](#) [For Patients](#) [QI Projects](#) [Publications](#) [Project Funding](#) [Who We Are](#) ▼



GYNAECOLOGY QUALITY IMPROVEMENT COLLABORATION

Hysterectomy
Complication Prediction
Tool

Patient Handout
Project



Toolkit Tip

www.GYNQI.com

Question 22:

Any new resources available?



Patient Handout Project

We wanted to create a place for patients to access reliable, evidence-based information related to gynaecologic care. We also hope gynaecologists can use these resources as they counsel patients in the clinic or hospital setting.

In this collaboration, Staff Gynaecologists have partnered with Obstetrics and Gynaecology residents and University of Toronto medical students to create a unique collection of patient handouts. We look forward to building and updating these resources over time. You can search your topic of interest and click the image to view your desired handout.

GENERAL GYNAECOLOGY

COMMON GYNAECOLOGIC CONDITIONS

MENOPAUSE

VULVA

GYNAECOLOGIC SURGERY

PREPAR

Search here...

General Gynaecology

Menopause



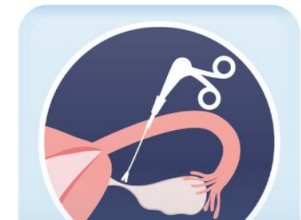
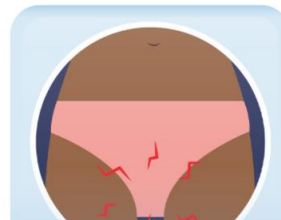
Introduction to Menopause



Vasomotor Symptoms of Menopause



Cost of VSM Treatments



Question 22:

Any new resources available?

Genitourinary Syndrome of Menopause



Genitourinary Syndrome of Menopause (GSM) is caused by low estrogen levels in the tissues of the urinary tract and the female genital tract. The symptoms of GSM can vary between patients and may affect the vulva and vagina, urinary function, and sexual function.



Genital Symptoms

Dryness, burning, and irritation of the genital area (vulva and vagina)



Sexual Symptoms

Lack of lubrication, discomfort or pain, and impaired function during sex

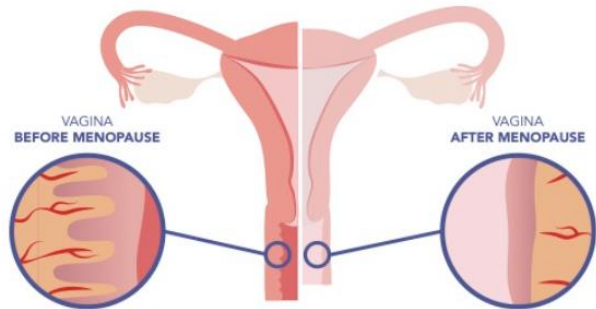


Urinary Symptoms

Urgency, burning, and recurrent urinary tract infections

GSM is very common and can impair quality of life, sexual function, and relationships with partners

Without adequate and timely treatment, GSM can become a chronic concern with longstanding functional and structural changes in the urogenital tissues that can be difficult to reverse.



Prior to menopause, the vagina is well-lubricated and thickened

After menopause, vaginal tissues become thin, dry, and brittle

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