Recognizing the Menopause Transition

The menopause transition is an opportunity for women to make healthy changes in their life

What is perimenopause?

- A natural part of aging that lasts an average of five years
- The transition period leading up to menopause that can be challenging and disorienting for many women
- Most women experience the physical and emotional changes of perimenopause in their late 40s or early 50s when:
  - Their monthly cycle begins to change
  - Estrogen and progesterone production becomes unpredictable
  - The number of stored eggs in the ovaries decreases
- Each woman experiences menopausal transition differently – some women may have many difficulties and others may be symptom-free

Menopausal Symptoms

Menstrual cycle
Irregular periods or variable length
Changes in bleeding patterns (heavier or lighter flow)

Urogenital symptoms
Vaginal dryness
Vulvovaginal atrophy
Sexual dysfunction and change in sexual desire
Bladder control
Recurrent urinary tract infections

Sleep
Disruptions of normal sleep patterns
Insomnia

Vasomotor symptoms
Hot flashes, night sweats
May be accompanied by mood swings, sweating, palpitations

Mood & cognition
Mood swings including sudden irritability, tearfulness, anxiety, depression, lack of motivation / energy, disruption of sleep patterns
Memory change (e.g., memory loss, impaired concentration)

Other symptoms
Weight gain
Fatigue / lack of energy
Aches / joint pain

Menopausal symptoms may vary over time

Prevalence of menopausal symptoms among women as they advance from pre-menopause to post-menopause in population studies.

Symptoms	Pre-menopause	Perimenopause	Post-menopause
Lack of energy	43%	43%	43%
Depression	26%	38%	32%
Aches / joint pain	41%	53%	57%
Insomnia	31%	38-39%	43%
Memory change	31%	44%	42%
Vasomotor	10%	42-58%	41-48%
Vaginal dryness	3%	21%	32%
Bladder control issues	12%	14%	26%
Sexual dysfunction		42%	88%
Dry mouth	18%	23%	29%

Adapted from: Dennerstein et al., 2000; Woods et al., 2005; Asplund et al., 2005.

Menopause Management Algorithm

General Health Assessment

Pap test, bimanual breast exam, mammogram, 10-year fracture risk, CV risk profile (blood pressure, lipids, fasting glucose), thyroid function, bowel cancer screening, safe sex, influenza shot

Symptomatic

Intolerable menopausal symptoms interfering with quality of life

Evaluate Diet & Lifestyle Elements

- Stress management
- Sleep hygiene
- Diet (Eating Well With Canada's Food Guide)
- Smoking cessation
- Regular exercise (30 min 3x/week)
- Alcohol and caffeine consumption

Hot Flashes

- Lifestyle: dressing in layers, cool showers, ceiling fan, paced breathing, weight management, smoking cessation
- Hormonal therapies*: estrogens, progestins
- Non-hormonal prescription therapies: gapapentin, clonidine, Bellergal, SSRI / SNRI

Vaginal Symptoms

- Lifestyle: Kegel exercises, continued regular intercourse
- Lubricants / moisturizers
- Local hormone therapy: vaginal estrogen (if urogenital symptoms are the only complaint)
- Systemic HT if other symptoms present (such a hot flashes)

*The most commonly prescribed hormone is estrogen (ET) either alone or combined with a progestin (EPT) for women with a uterus.

Complementary and alternative medicine: Long-term safety and efficacy data are lacking for complementary and alternative medicine including herbal remedies, vitamin E and acupuncture as well as bioidentical hormone therapy / progesterone cream.

Contraindications to estrogen and progestin use	
Unexplained vaginal bleeding prior to investigation	
Known or suspected breast carcinoma	
Undiagnosed vaginal bleeding	
Acute liver disease	
Active thromboembolic disease (estrogen only)	
Pregnancy	
Use estrogen with caution	**Use progestin with caution**
History of cardiovascular disease and hypertriglyceridemia	History of thromboembolic disorders
Risk of recurrence of breast cancer is unknown	

These are general recommendations that must be modified according to individual clinical situations and desires of the woman after she has been fully assessed and informed of all the available treatment options.

References:

Society of Obstetricians and Gynaecologists of Canada (SOGC). Canadian Consensus Conference on Menopause, 2006 Update. JOGC 2006;28:S1-S112.
Dennerstein L, Dudley EC, Hopper JL, et al. A prospective population-based study of menopausal symptoms. Obstet Gynecol 2000;96(3):351-8.
Woods NF, Mitchell ES. Symptoms during the perimenopause: prevalence, severity, trajectory, and significance in women's lives. Am J Med 2005;118 (Suppl 12B):14-24.
Asplund R, Aberg AG. Oral dryness, nocturia and the menopause. Maturitas 2005;50(2):86-90.

Transdermal Estrogen and Micronized Progesterone: A First-line Hormone Therapy Option

Updated June 2012

"Individualization is of key importance in the decision to use HT and should incorporate the woman's health and quality of life priorities as well as her personal risk factors such as risk of venous thrombosis, CHD, stroke, and breast cancer."

North American Menopause Society. *Menopause* 2012;19(3):257-71.

Overall Benefits of Hormone Therapy (HT)

- ↓ Vasomotor symptoms
- ↓ Risk of osteoporotic fractures
- ↓ Urogenital atrophy
- ↓ Somatic pain, arthralgia
- ↓ Risk of colorectal cancer
- Mood stabilization

Reid RL, et al. *J Obstet Gynaecol Can* 2009;31(1 Suppl 1):S1-S48.
Rossouw JE, et al. *JAMA* 2002;288(3):321-33.

SOGC Menopause and Osteoporosis Update 2009: Recommendations for Systemic Hormone Therapy

- HT should be prescribed at the appropriate dose, route and duration according to symptoms and to achieve treatment goals
- Primary indication for HT: Management of moderate to severe menopausal symptoms (Grade A)
- Vaginal therapy for vaginal symptoms only
- Prolonged therapy may be offered with appropriate assessment and counselling
- HT should **not** be prescribed for primary or secondary prevention of cardiovascular disease or primary prevention of dementia (Grade A)

Reid RL, et al. *J Obstet Gynaecol Can* 2009;31(1 Suppl 1):S1-S48.

Micronized Progesterone

- Metabolized primarily by the liver
- Beneficial effects of metabolites:
  - Sedation (may improve sleep)
  - Anti-aldosterone-like properties (may reduce fluid retention)
- Adverse effects of metabolites:
  - May cause nausea and dizziness
  - Contraindicated in patients with peanut allergy

Progestogen Indications

- Endometrial protection from unopposed ET
- Not necessary with standard doses of vaginal ET (including vaginal ring)
- Progestogen not generally indicated with ET post-hysterectomy

North American Menopause Society. *Menopause* 2012;19(3):257-71.

This table contains summary data, *not* head-to-head comparisons.	Micronized Progesterone (MP)	Medroxyprogesterone Acetate (MPA)
Coronary Heart Disease		
Rosano GM, et al. *J Am Coll Cardiol* 2000;36(7):2154-9. **Collins P. *Br J Obstet Gynaecol* 1996;103 Suppl 13:68-71.**	MP does not counteract estrogen-mediated effects on blood vessels	MPA may negate the beneficial effects of estrogen on the blood vessels
The Writing Group for the PEPI Trial. *JAMA* 1995;273(3):199-208.	In a woman with a uterus, CEE with cyclic MP has the most favourable effect on HDL-C	
Breast Cancer		Continuous Combined Estrogen therapy used with MPA for 5 years has been associated with an increased risk of breast cancer HR 1.26; 95% CI 1.00 to 1.59
Rossouw JE, et al. *JAMA* 2002;288(3):321-33.		
Fournier A, et al. *Breast Cancer Res Treat* 2008;107(1):103-11.	Estrogen in combination with micronized progesterone is not associated with an increased risk of breast cancer Estrogen/progesterone RR 1.00; 95% CI 0.83 to 1.22 Estrogen/dydrogesterone RR 1.16; 95% CI 0.94 to 1.43	

Transdermal Estrogen

Both oral and transdermal HT are systemic. The key differences between oral and transdermal therapy is their metabolism:

- Orally-administered HT must go through **first-pass metabolism** in the digestive tract and the liver before entering the circulation.
- Transdermal preparations enter directly into the circulation.

May be prescribed as a first-line therapy for any woman. For women with underlying medical conditions, transdermal HT may be the preferred route of administration. Consider:

- Higher risk of DVT or PTE
- Gall bladder disease
- High triglyceride levels
- Hypertension

Clinical Pearls

- Total surface area gel spread determines level of circulating estrogen, i.e., ↑ surface area ↑ level
- Surface area of patch determines rate of absorption and circulating levels of estrogen
- Gives a steady state (e.g., shift work)
- Compliance (e.g., GI intolerance, daily pill usage)

To maintain stable levels:

- The gel must be applied **to same surface area** with regular frequency, as prescribed
- The patch can be rotated to different areas with regular frequency, as prescribed

Tapering down transdermal estrogen:

- Surface area of the same dose of gel can be decreased, or decrease the number of pumps
- All matrix patches can be cut down as necessary to decrease surface area for absorption
- Reservoir patches cannot be cut

This table contains summary data, *not* head-to-head comparisons.	**Transdermal estrogen**	**Oral estrogen**
Risk of stroke **Santen RJ, et al. *J Clin Endocrinol Metab* 2010;95(7 Suppl 1):s1-s66.** **Canonico M, et al. *Circulation* 2007;115(7):840-5.** **Scarabin PY. *Lancet* 2003;362(9382):428-32.** **NOTE: All these references are observational studies.** **Renoux C, et al. *BMJ* 2010;340:c2519.** **NOTE: This reference is a nested case control study.**	Transdermal estrogen does not increase risk of VTE	Increased risk of stroke with oral HT, including low-dose estrogen, estrogen alone or combined estrogen plus progestin oral
Cardiovascular risk **Chu MC, et al. *Am J Obstet Gynecol* 2008;199(5):526.e1-e7.** **Lewandowski KC, et al. *J Clin Endocrinol Metab* 2006;91(8):3123-30.** **Sanada M, et al. *Menopause* 2004;11(3):331-6.** **Modena MG, et al. *Am J Med* 2002;113(4):331-4.** **Walsh BW, et al. *N Engl J Med* 1991;325(17):1196-204.** **The Writing Group for the PEPI Trial. *JAMA* 1995;273(3):199-208.**	Decreased CV risk in patients with metabolic syndrome Triglycerides decreased Less favourable for HDL and LDL changes	Oral estrogen can elevate triglyceride levels CEE has a favourable effect on HDL-C

Contraindications to HT	**Non-contraindications to HT**
• Unexplained/undiagnosed vaginal bleeding prior to investigation • Known or suspected breast carcinoma • Acute liver disease • Active thromboembolic disease (estrogen only) • Pregnancy	• Smoking • Diabetes • Hypertension • Migraine

NOTE: These contraindications do not refer to local vaginal hormone therapy.

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