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

“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.”


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**Overall Benefits of Hormone Therapy (HT)**

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


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**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)


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**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

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**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


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This table contains summary data, not head-to-head comparisons.

<table>
<thead>
<tr>
<th>Coronary Heart Disease</th>
<th>Micronized Progesterone (MP)</th>
<th>Medroxyprogesterone Acetate (MPA)</th>
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</thead>
<tbody>
<tr>
<td>Breast Cancer</td>
<td></td>
<td>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</td>
</tr>
<tr>
<td>Rossouw JE, <em>et al.</em> <em>JAMA</em> 2002;288(3):321-33. Fournier A, <em>et al.</em> <em>Breast Cancer Res Treat</em> 2008;107(1):103-11.</td>
<td>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</td>
<td></td>
</tr>
</tbody>
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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

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<th>Transdermal estrogen</th>
<th>Oral estrogen</th>
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<tbody>
<tr>
<td><strong>Risk of stroke</strong></td>
<td>Transdermal estrogen does not increase risk of VTE</td>
<td>Increased risk of stroke with oral HT, including low-dose estrogen, estrogen alone or combined estrogen plus progestin oral</td>
</tr>
</tbody>
</table>

| | NOTE: All these references are observational studies. |  |
| | NOTE: This reference is a nested case control study. |  |

| **Cardiovascular risk** | Decreased CV risk in patients with metabolic syndrome | Oral estrogen can elevate triglyceride levels |
| | Triglycerides decreased |  |
| | Less favourable for HDL and LDL changes |  |
| | | CEE has a favourable effect on HDL-C |

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<th>Contraindications to HT</th>
<th>Non-contraindications to HT</th>
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<tbody>
<tr>
<td>- Unexplained/undiagnosed vaginal bleeding prior to investigation</td>
<td>- Smoking</td>
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<tr>
<td>- Known or suspected breast carcinoma</td>
<td>- Diabetes</td>
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<td>- Acute liver disease</td>
<td>- Hypertension</td>
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<td>- Active thromboembolic disease (estrogen only)</td>
<td>- Migraine</td>
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<td>- Pregnancy</td>
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NOTE: These contraindications do not refer to local vaginal hormone therapy.