

# Progesterone

# What is Menopause?

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- Please review the first video in this series “Physiology of Menopause”
- Ovarian reserve (fertility) declines with age
- Ova maturation and release are the key contributors to estradiol (E2) and progesterone (P) levels throughout the fertile years
  - E2 and P have *numerous* actions in the body
- Ovarian fertility cycle stops at age 45-55
- Ovarian ova production stops, **E2 and P drop to minimal levels**
- Systems that benefitted from E2 and P **experience functional decline**

# What is Progesterone?

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- Progesterone is an ovarian hormone
- Pro-gest: promotes gestation
- Most important role is to partner with estrogen to prepare the endometrium for implantation (conception)
- Estrogen causes growth and proliferation in many tissues, especially the endometrium
- Progesterone “Opposes” estrogen: stabilizes growth, keeps endometrium from breaking down in the luteal phase
- Estradiol = bricks, Progesterone = mortar

# Benefits Of Progesterone (Outside Of Fertility)

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## Most clinically important action:

- Protects against endometrial cancers

## Support for other significant clinical complaints:

- Sleep
- Mood
- Memory
- Bone health
- Cardiovascular health

# Does Progesterone Have a Downside?

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- Oral progesterone can cause drowsiness
  - Taking at night can turn this into a benefit
- Some studies find that progesterone and its metabolites promote **negative mood** symptoms
- In some women, progesterone can cause nausea and bloating
  - It has diuretic properties, but rebound water retention is not uncommon
  - This occurs most frequently in the 3-4 days prior to menses or with oral supplementation

# Menopause Clinical Concerns

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- Low E symptoms:
  - Hot flashes (76.1%)
  - Insomnia, disrupted sleep (65.7%)
  - Low libido/Vaginal dryness (58.9%/55.8%)
  - Depression/Irritability/Anxiety (46.2%/45.1%/30.5%)
- Low P symptoms:
  - Difficult to define due to its persistent coexistence with E
  - Hot flashes, sleep disturbances, irritability and anxiety improve with P replacement
  - Low P in the presence of high or higher E2 increases the risk of endometrial cancers

# Benefits of HRT: Progesterone

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- Used to reduce endometrial cancer risk with E2 replacement
- Often not given post hysterectomy
- Oral progesterone taken at bedtime promotes sleep through alpha-pregnenediol (GABA agonist)
- Some find improved metabolism, reduced water retention
- Oral progesterone can cause moodiness and bloating in some women
- Vaginal progesterone may be a better option in some cases
  - Concentrates in the endometrium
  - Protection without side effects

# Progesterone HRT

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- Protection of the endometrium with E2 HRT:
  - 200 mg oral bioidentical progesterone daily (nightly)
  - 100 mg vaginal bioidentical progesterone daily (nightly)
- If the patient is post-hysterectomy:
  - Oral progesterone can help with sleep, but dosing is tailored to patient preference
  - Vaginal progesterone is not needed post hysterectomy
  - Transdermal: it is not known how well transdermal P absorbs
    - Dose based on symptoms



# Progesterone Metabolism

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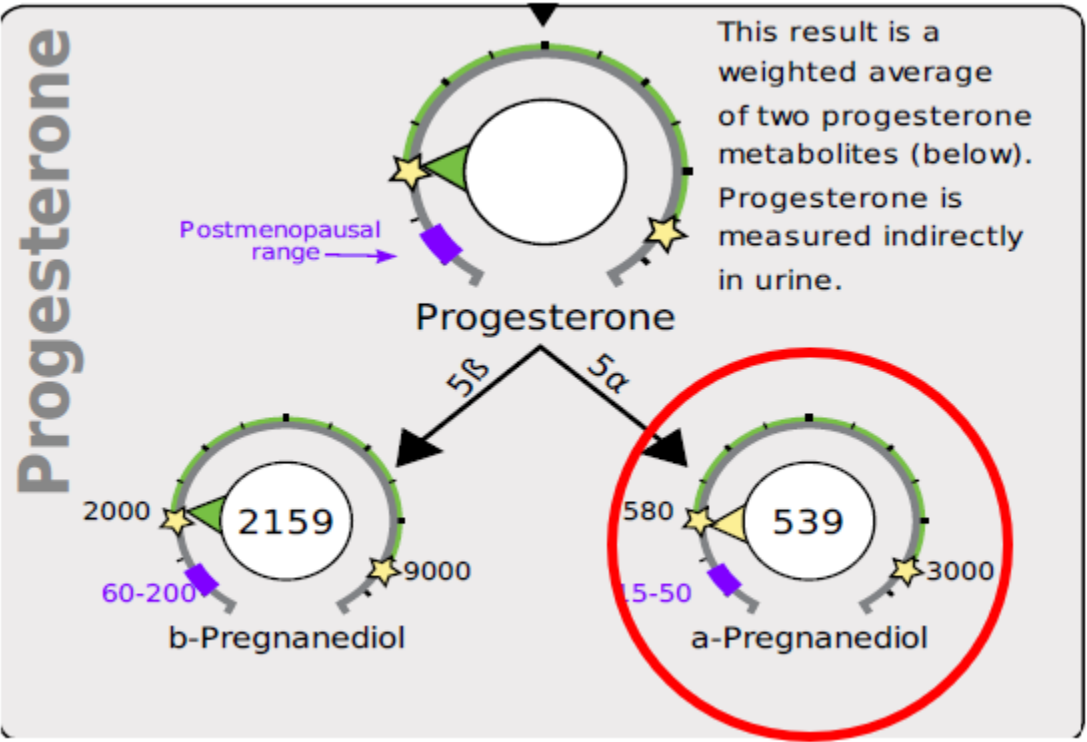
- Liver is responsible for progesterone metabolism and the half life is only about 5 minutes
- Progesterone is primarily metabolized into
  - 5a-dihydroprogesterone (by 5a-reductase)
  - 5b-dihydroprogesterone (by 5b-reductase)
  - These are further metabolized into allopregnanolone and pregnanolone, then they undergo further reduction, conjugation (glucuronidation and/or sulfation) and are excreted by the kidneys into urine
- Alpha metabolites of progesterone can bind to the GABA receptor and may support sleep and relaxation
- Urinary progesterone metabolite levels strongly correlate with serum when progesterone is not being supplemented

# Progesterone Monitoring

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- Monitoring supplemented progesterone levels is not necessary
- 200 mg oral or 100 mg vaginal has been shown to protect the endometrium, regardless of circulating levels
- Metabolites: If using oral progesterone for sleep and it's not working, checking urinary alpha-pregnane-20-one may reveal low metabolism through the 5 $\alpha$ -reductase pathway
- If found to be low, consider increasing the dose of progesterone or using other types of GABA support, like L-theanine

# Progesterone Monitoring



# Thank You!

If you are interested in learning more about hormones, each week we hold one-hour long mentorship sessions! Once you are a registered DUTCH provider, you can book these through our online scheduling link. Please call to get registered today.

**For questions, contact:**

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