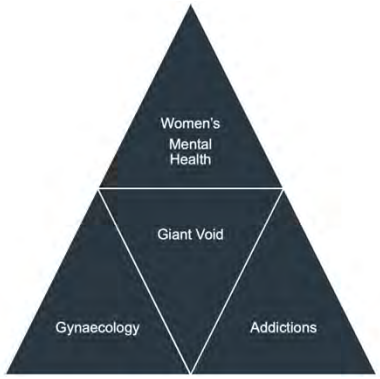
The Bermuda Triangle: Sex Hormones, Mental Illness & Addiction

Resilience through Connection

1

Why is There so Little Research on This????



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What We're Going to Cover

- Why are mental health problems so common in women at menarche and menopause?
- The impact on oestrogen and progesterone on neurotransmitter systems.
- Normal hormone variability across the menstrual cycle.
- Normal hormone variability in perimenopause and menopause.
- The consequences of this for women's mental health: ADHD, Depression, Psychosis and Addiction.
- Practical approaches to managing this.

3

If You Learn One Thing….

- Sex hormones impact mental health.
- Levels of sex hormones vary hugely across women's lives from menarche to menopause.
- There is a lack of awareness, research and education about this.
- This has a global impact on women's health.

4

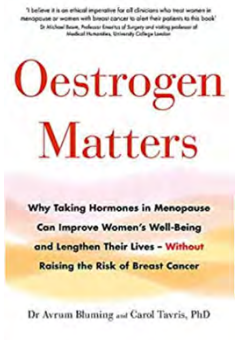
Basic Science of Sex Hormones in Women

Resilience through Connection

5

Oestrogen Matters- So Does Progesterone

- Oestrogen is produced by the ovaries at ovulation.
- It's a hormone with many effects on mind and body.
- It strengthens the heart, bones, muscles and skin.
- It reduces the risk of developing depression, psychosis and dementia in later life.
- It improves the symptoms of ADHD.
- Oestrogen protects both brain and the body.
- This is why hormone health is such a big deal.



6

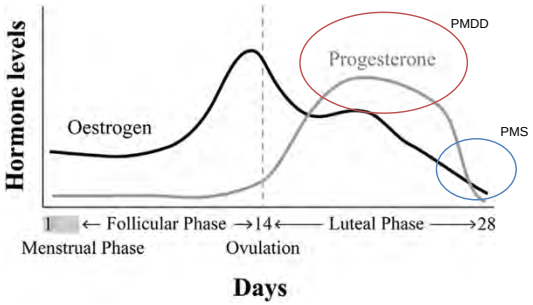
Hormonal Impact on Mood Across the Cycle

High Oestrogen= better mood, concentration and focus (days 12-15)

High Progesterone = calmer mood, less anxiety (most women) (days 16-26)

High Progesterone in women under stress = increased cortisol and probably PMDD (days 16-26)

Withdrawal of Oestrogen and Progesterone = anxiety, emotional dysregulation, lowered mood, brain fog PMS (days 26-28)

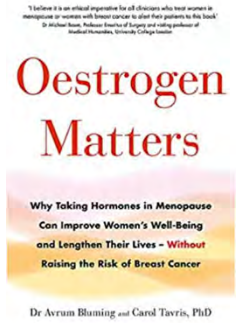


7

Oestrogen and Neurotransmitters

- Both oestrogen and progesterone are known to interact with several neurotransmitter systems, including noradrenaline, serotonin, acetylcholine and dopamine (DA).
- In particular, oestrogen has a special impact on the dopaminergic system.
- It **increases** the synthesis, release, re-uptake and turnover of DA, affects downstream targets of its receptor and modifies basal firing rates of dopaminergic neurons.

Front. Neurosci., 13 July 2017. Sec. Neuroendocrine Science Volume 11 - 2017



8

Progesterone has Major Brain Impacts

- Progesterone is present during days 14-28 and during pregnancy.
- It's metabolized to allopregnanolone and pregnanolone.
- By binding to GABA-R receptors, allopregnanolone has sedative, anxiolytic, anti-convulsant and neuroprotective properties.
- Progesterone via allopregnanolone, influences emotion processing.
- It is a likely causal factor for the mood symptoms experienced by women with premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD).
- Synthetic progestogens play a role for the mental side effects that have been noted by some hormonal contraceptive users.

9

Progesterone: Friend or Foe

Progesterone withdrawal just before and during menstruation, or post partum mimics alcohol withdrawal

This is a high-risk time for relapse of any mental health condition

For some women progesterone does not reduce anxiety via allopregnanolone

- Oestrogen can prevent depression, in perimenopause (JAMA 2019)

In women under chronic stress allopregnanolone is metabolised to cortisol

These women are likely to experience pre-menstrual dysphoric disorder

Their mood and anxiety are worse during day 14-28 when progesterone levels are high

Progesterone – Friend or foe?, Frontiers in Neuroendocrinology, Volume 59, 2020, 100856, ISSN 0091-3022, https://doi.org/10.1016/j.yfrne.2020.100856.

10

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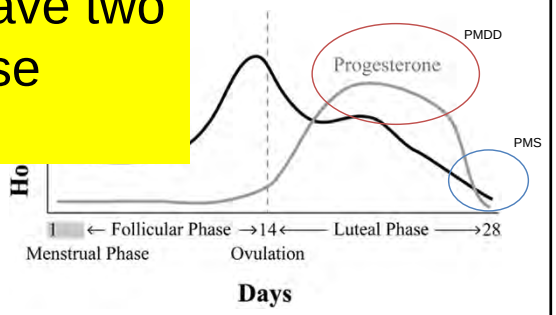
You have two of these slides



11

Depression and Sex Hormones

12

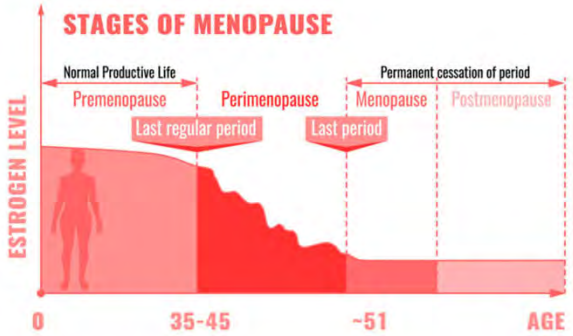
Women and Depression

- Depression is the biggest cause of disease burden worldwide in women. ~ *WHO*
- Women are 1.7 x more likely to be depressed than men.
- These sex differences occur only between ages 15-65.
- Are our sex hormones making us depressed?

Menarche and Depression

- Before puberty, boys and girls have similar rates of depression.
- After puberty, depression is more than **twice** as prevalent in young women as men (age 14-25).
- **Young women are at the greatest risk of depression of any social group globally.**

Average Oestrogen Levels Across the Lifespan

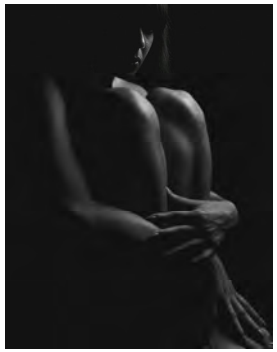


Perimenopause and Depression

- Average age: 45-50
- 1 in 6 women develops depression for the first time in perimenopause.
- Anxiety, insomnia, poor concentration, brain fog, panic attacks and memory issues are common.
- Menopause is when periods stop- average age is 51.

Menopause and Depression

- In perimenopause and menopause, fluctuations in oestrogen increase sensitivity to psychosocial stress.
- This has a priming effect on the development of depression.
- There is a further priming effect on relapse or development of addiction.
- https://rdcu.be/dLQ3L
- Oestrogen may be an effective treatment for perimenopausal depression.



17

Sex Hormones and Schizophrenia

18

Women and Schizophrenia

- Generally, schizophrenia affects men slightly more frequently than women, with a ratio of nearly 1.4:1 (*Jongsma et al. 2019*).
- The peak age of onset for men with schizophrenia is between 20 and 29 years. For women, this peak occurs about 5 years later between ages 20 and 39 (*Giordano et al. 2021*)
- Women show higher incidence rates after the age of 40 (*Van Der Werf et al. 2014*) which may be related to decreased oestrogen levels after menopause.

19

Schizophrenia in the Reproductive Years

- Earlier menarche — that is, earlier rise of oestrogen levels — seems to be associated with a later onset of schizophrenia (*Cohen et al. 1999; Kiliçaslan et al. 2014*).
- Psychotic symptoms often deteriorate premenstrually or perimenstrually (*Handy et al. 2022; Reilly et al. 2020*).
- The postpartum period and menopause, both marked by declining estrogen levels are associated with increased risk of first episode psychosis or relapse (*Seeman 1986; Seeman 1996*).

20

Menopause and Schizophrenia

- After menopause, women with pre-existing chronic schizophrenia tend to experience a worsening of their condition, leading to an increased requirement for antipsychotic medication.
- Oestrogen has neuroprotective effects and appears to delay the onset of psychosis.
- Reduction in oestrogen levels around menstruation, postpartum and in menopause are associated with increased psychotic symptoms.
- **Oestrogen is an effective treatment for schizophrenia**. *(Kulkarni since 1996)*

Female Hormones and ADHD

Women's Lifespan Experiences of ADHD

ADHD symptoms fluctuate significantly during a lifetime, with impulsivity and hyperactivity often giving way to disorganization and emotional dysregulation over time. According to the 1500 women who answered ADDitude's 2023 survey, the most problematic ADHD symptoms during each stage of life are as follows (in order of severity):

- 0-9: Emotional dysregulation, inattention/distractibility, and social struggles
- 10-19: Procrastination, emotional dysregulation, and time-management difficulties
- 20-39: Procrastination, overwhelm, and time-management difficulties
- 40-59: Overwhelm, brain fog and memory issues, and time-management difficulties
- 60+: Brain fog and memory issues, procrastination, and overwhelm

Menopause and ADHD

- Clinicians and women report frequent "unmasking" or even emergence of ADHD symptoms during menopause.
- An ADDitude survey of 1500 women with ADHD symptoms in 2023 found that 94% reported worsening ADHD symptoms during perimenopause and menopause.
- 50% of women with ADHD experienced "life altering symptoms in perimenopause" (*ADDitude 2024*).
- 83% developed new ADHD symptoms (*ADDitude 2024*).

Augmenting Stimulant Treatment in Luteal Phase

- Premenstrual worsening of depressive and ADHD symptoms represent a treatment challenge. In our adult ADHD clinic, we noted several women describing exacerbation of their ADHD and depressive symptoms in the premenstrual week and/or insufficient effect of their established dosage of psychostimulant.
- This community case study of nine consecutive women being treated for ADHD and co-occurring conditions (including depression and premenstrual dysphoric disorder), reports our local experience of increasing the individually prescribed psychostimulant dosage during the premenstrual period.
- All nine women experienced improved ADHD and mood symptoms with minimal adverse events. Premenstrual inattention, irritability and energy levels improved, and now resembled the other non-premenstrual weeks more closely.

Front Psychiatry. 2023; 14: 1306194.

25

Lisdexamfetamine for Healthy Women at Menopause

- Thirty-two healthy perimenopausal and early postmenopausal women experiencing mid-life-onset executive function difficulties as measured using the Brown Attention Deficit Disorder Scale (BADDS) were administered LDX 40–60 mg/day for 4 weeks in this double-blind, placebo-controlled, cross-over study.
- **Diagnosis of lifetime ADHD was exclusionary.**
- Analyses revealed a significant effect of LDX treatment over placebo for total BADDS scores ($p = 0.0001$) and for four out of the five BADDS subscales (all $p < 0.004$).

Psychopharmacology 232, 3091–3100 (2015). https://doi.org/10.1007/s00213-015-3953-7

26

What Does All This Mean for Addictions?

Resilience through Connection

27

Sex Hormones and Addiction

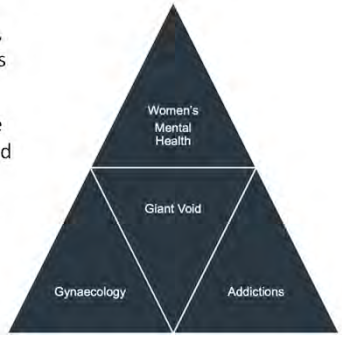
- Fluctuations in sex hormones have a big impact on women's mental health across the lifespan.
- Variations across the menstrual cycle between the age of 15-45 increase risk of depression.
- The peri-menstrual phase is a risk factor for increased stress, anxiety and relapse into substance use for many women.
- Postpartum and perimenopause are also high risk phases for relapse.

28

The Bermuda Triangle: Lack of Research!

- Thirty-four articles examining alcohol use, cannabis use, nicotine use, caffeine use, and gambling behavior across menstrual cycle phase met inclusion criteria.
- Consistent with self-medication theory, strong evidence indicated that nicotine use increased premenstrually and menstrually.
- Other factors increasing both nicotine and alcohol use premenstrually and menstrually include having a premenstrual dysphoric disorder diagnosis or having premenstrual syndrome.

Arch. Womens Ment. Health 2021 Joyce et al



Key Clinical Recommendations

The key clinical recommendations are to ensure that a **menstrual history is taken in all women who present with any mental health condition** to determine whether there is an association between their menstrual cycle and the severity of their symptoms.

It is also important to recognize the likelihood of **relapse or new onset of mental illness during perimenopause,** especially among women with a history of exacerbated symptoms during the menstrual cycle or postpartum period

Arch. Women's mental health 2024 Mu, Kulkarni

Approaches to Hormone Health for All Women

- Educate yourself about menopause- 51% of your patients go through it.
- Consider, discuss and signpost for HRT in every woman over 40.
- Explore cyclical variations in mood and ADHD symptoms- Flow app or similar.
- Do not dismiss individual responses across the cycle and lifespan in different women.

The Case for Hormone Replacement Therapy (HRT)

- Replaces your body's natural oestrogen with identical hormones.
- Gives you even oestrogen levels across the monthly cycle.
- Does not replace contraception and must be taken with progesterone to protect the womb.
- Consider referral to gynaecologist alongside standard addictions programme.

Thank you ~ Questions?

We'd love your Feedback!

Scan QR code