REPRODUCTIVE MENTAL HEALTH

Reproductive mental health refers to the diagnosis, treatment, and prevention of mental illness related to specific phases of the reproductive life cycle, including the menstrual cycle, pregnancy, postpartum, and perimenopause. These stages represent windows of increased risk for exacerbation of or new-onset mental illness. There are biological, psychological, and sociocultural factors that contribute to the etiology of mental illness during the reproductive life cycle. From a biological perspective, hormonal and physiologic changes associated with different times of reproductive transition can provoke or contribute to mental illness, as can genetic predisposition. Other factors that make women more susceptible to mental illness during these windows are cultural expectations around women's roles, lack of guaranteed paid parental leave, and financial stressors. Maternal health disparities, prominent in the United States, especially among Black women, also contribute to increased risk of perinatal mental illness.

Overall, women have a higher prevalence of mental illness than men, with rates of 22.3% versus 15.1%, respectively. Perinatal depression affects anywhere from 10-20% of women in the United States, and up to 19.2% of women have a depressive episode in the first 3 months postpartum. Depression is one of the most common complications of childbirth, and suicide is now one of the leading causes of death postpartum. Hormonal changes across the reproductive lifespan that contribute to the increased risk of mental illness in women are not only common, but potentially predictable and treatable, making reproductive mental health an imperative area of training for all mental health providers.

The field of reproductive mental health also encompasses care for people identifying as trans and non-binary, as well as fathers, but more research in these areas is needed. The data regarding mental illness at times of specific stages in the reproductive life cycle for individuals who do not identify as cisgender women is limited. For the purpose of this work, the term "women" will be used when referring to research data collected from cisgender females. However, it is widely recognized that not all individuals assigned female sex at birth identify as women. Our use of the term "women" does not discount the impact of reproductive transitions on the mental health of all people.

History and DSM Classification

Reproductive mental health is a developing field. Historically, data driven research on mental health problems in women has been lacking, and for centuries the term "hysteria" was used to describe unexplained physical or behavioral symptoms in female patients. The term "hysterical neurosis" was removed from the Diagnostic and Statistical Manual of Mental Disorders (DSM) when DSM-III was published in 1980 and attention to mental illness during pregnancy and postpartum started to grow, spurred by national and international organizations including the Marcé Society (founded in 1980) and Postpartum Support International (founded in 1987). After the 1993 NIH Revitalization Act mandated the inclusion of women and minorities in federally funded research, publications on postpartum depression and other conditions related to reproductive mental health grew exponentially. The field has expanded rapidly since the early 2000s, with U.S. fellowships in women's mental health growing from 1 available in 2002 to 16 available in 2023.

Previously, following common clinical practice, physicians typically stopped psychiatric medications during pregnancy due to concern for fetal teratogenicity, with little known about the risks of untreated mental illness for both mother and child. However, starting in the 2000s, the standard of care evolved as research established fetal risks associated with untreated perinatal depression and anxiety, including earlier delivery, low birth weight, preeclampsia, stays in the neonatal intensive care unit, and Cesarean sections. Simultaneously, large scale registries tracking outcomes in pregnant patients has provided reassuring safety data for a large number of older psychiatric medications taken in pregnancy. With this data, clinicians have been able to have more informed discussions with patients, weighing the risks of untreated mental illness against the risks of medications in both pregnancy and breastfeeding. Aligned with this changing standard of care, the American College of Obstetricians and Gynecologists (ACOG) position statement now recommends starting or continuing medications during pregnancy for the treatment of moderate-to-severe mental illness in pregnant patients.

Also reflecting the rapidly evolving pace of reproductive psychiatry, there are several distinct and well-established clinical entities including postpartum depression, postpartum psychosis, and premenstrual exacerbation, not yet recognized by the DSM in its 5th revised edition. That edition does refer to premenstrual dysphoric disorder in the depressive disorders section and lists “with peripartum onset” as a specifier in the depressive disorders and bipolar disorder sections, but otherwise does not align entirely with clinical practice.

Measures and Assessment

There exist several instruments for the clinical assessment of mental illness presenting at different stages of the reproductive life span. Starting with menarche and evaluation for pre-menstrual dysphoric disorder, the Daily Record of Severity of Problems (DRSP) allows for

prospective logging of mood and physical symptoms throughout the menstrual cycle. The DSM requires patients to have at least two symptomatic cycles to meet criteria for PMDD. Used during pregnancy and postpartum, the Edinburgh Postnatal Depression Scale (EPDS) is a 10-item self-report questionnaire developed in 1987, validated throughout the world for screening and detection of perinatal depression. The Perinatal Obsessive-Compulsive Scale (POCS) has been validated for detection of obsessive-compulsive disorder during the perinatal period, highlighting typical intrusive thoughts, such as fear of having an unhealthy baby at birth, contamination, the baby being taken away, and infant death. While there is one recently developed rating scale for the detection of perimenopausal depression, the Meno-D, many clinicians currently use the psychological/psychosocial domains of more broad-based menopausal symptom assessments, such as the Menopausal Rating Scale (MRS) or Menopause-Specific Quality of Life (MENQOL). Validated rating scales specific to other mental health conditions at these various times of reproductive transition remain in the development phase.

Biological Factors

Hormones, including but not limited to estrogen and progesterone, act as neurotransmitters in brain systems intimately tied to mood and play a key role in the development or exacerbation of mental illness during times of reproductive transition. Initially, researchers suspected individual pathology to be related to abnormal levels or misfunctioning of hormones. However, this hypothesis has been challenged. In a landmark study using exogenously administered hormones and hormone blockers, women with a history of postpartum depression were found to be uniquely sensitive to normal hormone add back, which disproportionately provoked psychiatric symptoms in them, as compared to women without a history of postpartum depression, who did not experience psychiatric symptoms under these

conditions. Prevailing theory now recognizes a subset of women who are more vulnerable to symptoms caused by normal hormonal fluctuations that occur during the reproductive cycle. As such, women who experience significant premenstrual symptoms are more likely to experience postpartum symptoms as well as perimenopausal symptoms.

Other biological factors relevant to the development and exacerbation of mental illness in the reproductive life cycle are still being researched. One factor that may play a strong role in triggering or maintaining anxiety and depression symptoms postpartum or during perimenopause is sleep disruption. Causes of sleep disruption during these windows of time are multifactorial, including hormonal fluctuations, breastfeeding, and societal expectations. Women who experience postpartum depression exhibit poorer sleep quality than postpartum women without depression. More research is needed.

Psychosocial Factors

Multiple psychosocial factors contribute to the onset or exacerbation of depression and anxiety symptoms in women at times of reproductive transition. These factors include episodic stressors (such as major life or traumatic events), chronic stressors (such as parenting stress or financial strain), unsatisfactory interpersonal relationships with partners and family, and lack of social support. Intimate partner violence can start or escalate during pregnancy and is associated with negative maternal and newborn outcomes, necessitating universal screening for IPV and early intervention when identified. Gendered expectations that women take on the bulk of childcare can also confer risk; in opposite-sex couples, women's dissatisfaction with their postpartum role can negatively impact individual and couple well-being. In addition, rigid expectations around infant feeding may contribute to postpartum depressive symptoms, fueled by societal and cultural pressure with little consideration or support for logistical challenges of

breastfeeding (especially in the workplace) or its impact on mental health or sleep. Themes identified in men with paternal postpartum depression consist of adhering to traditional male stereotypes such as providing for the household instead of assisting with childcare, repression of feelings, and feeling overwhelmed or neglected by their partner. Research has shown that longer duration of parental leave for men and women can decrease the risk of depression, distress, and burnout. However, there is currently no policy mandating paid parental leave in the United States.

Treatment

Premenstrual dysphoric disorder (PMDD) is defined by mood symptoms that cause functional impairment during the luteal phase of the menstrual cycle. There is significant evidence that antidepressants such as selective serotonin reuptake inhibitors (SSRIs) and serotonin and norepinephrine reuptake inhibitors (SNRIs) can buffer the mental health symptoms caused by hormonal fluctuations. More specifically, SSRIs have been found to reduce premenstrual irritability and mood symptoms in as little as 10 hours, operating more quickly than in major depressive disorder and generalized anxiety disorder. For PMDD, SSRIs are considered a first line treatment and come with various dosing options, including symptom-triggered, luteal phase, or taken continuously throughout the month. Symptom-triggered dosing involves taking medication only at the onset of symptoms, while luteal phase dosing is a preventative treatment taken for two weeks prior to onset of menses.

When treating perinatal mental illness, basic principles include an individualized consideration of severity of illness, maximizing behavioral and somatic treatments and interventions, minimizing the number of fetal exposures (counting both medications and illness as exposures), using older medications that have more available safety data than newer

medications, treating to full remission of symptoms, and anticipating that doses of medications may need to be increased throughout pregnancy. For moderate-to-severe depressive symptoms in pregnancy and postpartum, treatment with antidepressant medications is recommended. There is strong evidence to show that first-trimester exposure to most older antidepressants and antipsychotics do not increase the risk of fetal malformations when controlling for the confounding effects of underlying maternal mental illness. Risks of mood stabilizers in pregnancy vary by agent, and these risks need to be weighed for each individual against the risks of decompensated serious mental illness. Valproic acid is one of the few medications where the risks of use in pregnancy, including neural tube defects and long-term behavioral and neurodevelopmental disorders, are increasingly considered unacceptable. Since over 50% of pregnancies are unplanned, prescribing valproic acid is generally contraindicated in all reproductive age women unless no alternatives exist and reliable birth control methods are in place.

To limit the number of exposures in pregnancy for patients who have been successfully treated with psychotropic medications in the past, it is recommended to use previously effective medications, rather than starting new agents with unknown efficacy and to limit the number of medications. Untreated or undertreated mental illness is also considered an adverse exposure, thus medications should be titrated to achieve remission if possible. Dose increases or higher than average doses may be required by the physiologic changes of pregnancy, such as increased circulating blood volume and the impact of hormonal changes on metabolic enzymes, and should be driven by clinical assessment of worsening symptoms. Most older antidepressants are generally transferred in small amounts in breastmilk and are considered reasonable to use during breastfeeding.

Perimenopause is defined as the 4-8 years (on average) of menstrual irregularity leading up to the complete cessation of menstruation. During this window of time, women are at increased risk of a recurrence of or new onset depression. In general, perimenopausal depression is treated with the same medications that treat other types of depression, specifically medications that have previously been helpful for a woman. In addition to depression, perimenopause can cause a host of somatic symptoms that are important to identify and treat. These include vasomotor symptoms, commonly referred to as hot flashes, difficulty sleeping, difficulty concentrating, vaginal dryness and urinary problems, fatigue, and joint and muscle pain. Many symptoms of depression and perimenopause overlap, including depressed mood, irritability, insomnia, impaired sexual function, and cognitive changes. Although estrogen is the first-line treatment for vasomotor symptoms secondary to perimenopause, SSRIs and SNRIs have also been shown to be effective in treating vasomotor symptoms, as well as anxiety and depressive symptoms in perimenopause. If a woman is also experiencing chronic pain, SNRIs, effective in treating both depression and anxiety as well as chronic pain, may be a first choice.

Conclusion

Reproductive mental health is an emerging field that focuses on the identification and treatment of mental illness at times of reproductive transition, including the menstrual cycle, pregnancy, postpartum, and perimenopause. These windows of transition represent times of increased risk for new onset and exacerbation of mental illness, largely driven by sensitivity to hormonal fluctuations and psychosocial stressors. Current literature suggests that SSRIs and SNRIs can greatly buffer psychiatric symptoms due to hormonal fluctuations, though research and treatment options in this area continue to grow.

It is important to note that the inclusion of reproductive mental health training in psychiatry residency programs is inconsistent and often inadequate or altogether absent. This results in heterogeneity among psychiatric providers in terms of prescribing practices and management of these conditions. There is a significant need for adequate training in recognition and management of reproductive psychiatric conditions so that the standard of care is more uniformly applied.

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FURTHER READINGS

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