

The Role of Reproductive Psychiatry in Women's Mental Health

Emily C. Dossett

Introduction

Reproductive psychiatry is a medical specialty focusing on psychiatric symptoms during times of hormonal change. Worldwide, women bear a disproportionately large burden of mental illness, with rates of depression that are twice as high as those in men and elevated levels of almost all anxiety disorders (World Health Organization, 2009). This gender divide begins in puberty as young women undergo menarche, and it continues until menopause is reached. For the 30–40 years between these milestones, women experience hormonal fluctuations monthly with their menstrual cycle; significant hormonal shifts with each pregnancy and postpartum period; and erratic hormone changes during perimenopause. Many women experience infertility or pregnancy loss as well. All of these hormonal shifts can leave women vulnerable to psychiatric symptoms of mood, anxiety, and thought disorders (Brizendine, 2006).

Reproductive psychiatry is a specialized field of medicine that seeks to understand and treat such disorders. It is a relatively new discipline, since many years of stigma and lack of focused attention on female-specific health needs have prevented research and education in women's mental health (World Health Organization, 2009). This chapter describes the training, education, and research opportunities in reproductive psychiatry as well as the role of the specialist in women's health care. Evolving theories of mental illness and their connection to times of reproductive change, as well as how to assess these conditions, are reviewed. Treatment recommendations, including medications and other evidence-based interventions, are described as well as the informed consent process. The goal is for each reader to develop a stronger understanding of what reproductive psychiatrists do and what needs to be done to further our knowledge in this area.

E.C. Dossett, M.D., M.T.S. (✉)

Assistant Clinical Professor, Department of Psychiatry and Biobehavioral Sciences and Department of Obstetrics Gynecology, Keck School of Medicine, Los Angeles, University of Southern California Medical Center, Pasadena, CA, USA

e-mail: edossett@gmail.com

Reproductive Psychiatry as a Clinical Specialty

The reproductive psychiatrist's role includes evaluation and diagnosis; informed consent and medication management; psychotherapy or collaboration with a therapist; and close teamwork with the patient's family and other health care providers. Understanding how psychiatric disorders may present differently during times of hormonal change is a key component of this field. The reproductive psychiatrist trains not only in the medication management of these mood-related disorders but in psychotherapeutic approaches as well. Decisions about medication are an integral part of any treatment plan but are especially important when mood, anxiety, or psychotic symptoms become so severe that a woman's ability to care for herself or others is impeded. When focused on the peripartum, reproductive psychiatry attends to treatment decisions that minimize the risk for both mother and child, often in situations with "no perfect solution" (Wisner et al., 2000; Wisner, Sit, & Moses-Kolko, 2006). These complicated decisions require careful psychiatric assessment and a fully informed conversation about risks and benefits of medication use, which is often beyond the scope of a general practitioner or even a psychiatrist without specialized training in assessment, diagnosis, and treatment during times of reproductive change.

However, this specialized training can be difficult to obtain, as the American Board of Psychiatry and Neurology does not offer any official fellowships or certifications in reproductive psychiatry. The closest match would be a subspecialty in psychosomatic medicine, "a subspecialty that involves the diagnosis and treatment of psychiatric disorders and symptoms in medically complex patients," including "high-risk pregnancies," among many other medical conditions (www.abpn.org/sub_psyched.html). However, how much exposure to reproductive psychiatry a fellow in psychosomatic medicine receives depends on where he or she is training. Similarly, whether or not an interested medical student or psychiatric resident is able to learn about reproductive psychiatry is dependent on what educational or clinical opportunities exist where he or she is training. Anecdotally, most medical school programs offer at most one to two lectures on women's mental health, and even psychiatric residencies may offer only a few hours of teaching on the subject. Fortunately, 1-year post-residency research and/or clinical fellowships are emerging around the country at universities with a strong interest in reproductive psychiatry, such as Brigham and Women's Hospital at Harvard Medical School (<http://www.brighamandwomens.org>) and the University of Illinois in Chicago (<http://www.psych.uic.edu>).

Once formal training is complete, reproductive psychiatrists practice in a variety of settings. Many are in private practice, and most engage in medication management, psychotherapy, or both. Some work in hospital settings as consultation-liaison psychiatrists, serving as a bridge between psychiatry and obstetrics or gynecology. Increasingly, reproductive psychiatrists are working as consultants in primary care settings, as health care moves more toward providing specialty care, including mental health care, in outpatient "medical homes" (Baker-Ericzen et al., 2012; Yawn et al., 2012). Finally, reproductive psychiatrists often work in academic settings, where they perform research, teach medical trainees, and treat patients.

An up-to-date knowledge of psychiatric medications and their safety profile in general, and even more specifically during times of hormonal change, is essential. This can be accomplished in numerous ways. Several professional organizations offer yearly conferences that provide continuing medical education. The North American Society for Psychosocial Obstetrics and Gynecology, or “NASPOG,” brings together psychiatrists, psychologists, obstetricians–gynecologists, and other professionals interested in the intersection of mental and reproductive health (www.NASPOG.org). NASPOG is the North American branch of the Marcé Society, an international group dedicated to women's mental health. The American Psychiatric Association offers multiple courses on reproductive psychiatry during their annual meeting. Postpartum Support International, or PSI, is the largest lay-volunteer organization dedicated to perinatal mental health, and their annual conference typically offers psychosocial and medical training.

Medical journals, such as the *Archives of Women's Health*, publish articles on the latest research on many aspects of reproductive psychiatry, including medication use, psychotherapy, and other evidence-based interventions. More and more non-specialty journals, such as the *Journal of the American Medical Association* (JAMA) or the flagship journals in both psychiatry and obstetrics–gynecology, publish papers relevant to women's mental health. Online resources, such as *Journal Watch* (www.jwatch.org), summarize these findings into quickly read and easily understood e-mails that arrive regularly and help keep practitioners up to date. Blogs, such as Massachusetts General Hospital's Center for Women's Mental Health, also offer regular updates on treatment recommendations. Staying abreast of research on psychotropic medications is particularly important for the reproductive psychiatrist, as this is where much of their practice lies. Medication management is also where some of the largest clinical, as well as social, psychological, and ethical, challenges emerge.

Mood and Anxiety: What Is the Biology Behind It?

Every woman who faces mood and anxiety symptoms during times of reproductive change wants to know *why*. What is the connection between her brain, body, and hormones that has gone awry? There are several possible theories. The longest held is the “monoamine neurotransmitter” theory of depression. This theory looks at the influence of chemical messengers, called neurotransmitters, in the brain. Serotonin, norepinephrine, and dopamine are the most well-understood neurotransmitters. For many years, researchers have looked at the connection between depression and possible dysregulation of these “brain messengers” (Stahl, 2000). In addition, there is a growing understanding of the association between depression and hormonal systems in the body, as well as outside influences, that affect gene expression and how the brain itself grows and evolves (Massart, Mongeau, & Lanfumey, 2012).

For women, it has long been suspected that there is an additional link between hormones and mood, but the relationship has remained elusive. However, research is starting to reveal a possible connection, and we are learning more and more about

the variety of ways that serotonin seems to have a close relationship to estrogen (Lokuge, Frey, Foster, Soares, & Steiner, 2011). Serotonin seems to need estrogen to do its job well. Clinically, it is important to note that women seem to struggle most with psychiatric symptoms during times when estrogen levels fall most rapidly: premenstrually; in the postpartum; and off and on throughout perimenopause (Brizendine, 2006; Bromberger et al., 2010). These rapid fluctuations appear to influence how well serotonin works and, subsequently, how a woman feels. Additionally, each woman responds to the shifts in hormones differently. This is why two women may have the same hormone levels, as measured in blood tests, but very different mood or anxiety symptoms.

A third rapidly evolving theory of mental illness involves immune system activation. Immune system activation means being in a “proinflammatory” state. Inflammation plays a pivotal role in the development of depression and anxiety in general (Harrison, 2013). For women specifically, research points to immune system dysregulation as a possible factor in perinatal mood and anxiety disorders. A normal pregnancy appears to shift between both pro- and anti-inflammatory states. For instance, it has long been thought that a woman’s immune system becomes more subdued in pregnancy in order to protect the developing fetus from being rejected by the very womb that holds it. New research shows even more subtle and complex immune changes during the normal course of a woman’s pregnancy (Chen, Liu, & Sytwu, 2012). If that complexity is derailed and shifts toward more inflammation, perinatal mood and anxiety disorders may result (Bergink et al., 2013). Interestingly, elevated inflammation is also linked to common medical problems in pregnancy, including preeclampsia, preterm delivery, and gestational diabetes. If depression is possibly caused by abnormal changes in a woman’s inflammatory state, then all these processes may, in fact, be linked. Extensive research is currently looking into the connection between both physical and mental health in pregnancy, with a possible common denominator of a dysregulated immune system (Osborne & Monk, 2013). In the future, we may be able to promote treatments for depression that target inflammation. For now, however, medications based on the monoamine hypothesis of anxiety and depression remain the mainstay of treatment.

The Psychiatric Assessment

How does this understanding of biology present in “real life,” in the faces and voices of women who are suffering? The women who present with symptoms in my office are usually in the grips of raw emotion: tears that seem to come from nowhere; terror at facing another night fighting for sleep; and despair that she will ever “feel like normal” again. Sometimes there is even suicidality, brought on by intense feelings of hopelessness and helplessness. A husband, partner, or mother sometimes accompanies her; sometimes she is nursing a newborn; sometimes she is very much alone. A psychiatrist’s office is often the last stop in a long line of efforts to heal, particularly if she is pregnant or nursing, and the possibility of needing medication is fraught with

challenges. Women often struggle greatly with the stigma of mental illness as well as with their own guilt and shame around possibly needing psychiatric help.

Before making any decision about medication, however, a careful assessment is always needed. The first question in any assessment is what each woman is feeling and what her primary concerns may be. Is she struggling with monthly mood changes around her menstrual cycle? Is she planning a pregnancy, pregnant already, or newly postpartum? Is she caught in the ups and downs of perimenopausal hormonal shifts? In the midst of these biological realities, is she facing social and psychological transitions as momentous as moving through adolescence, becoming a mother, or watching her grown children leave home? How does she describe and experience all these changes?

Questions about safety are of utmost importance. Is she truly safe, or is suicide a real possibility? Is she having thoughts of harming others, including her own child? It is imperative that the reproductive psychiatrist talk directly and openly with a woman about any unusual thoughts she might be having and if any thoughts or images feel out of control. Studies indicate that suicide is a leading cause of death in women during the first year after delivering a child, with one study demonstrating that suicide accounts for 28 % of maternal deaths (Almond, 2009; Oats, 2003). Similarly, for women suffering from postpartum psychosis, rates of infanticide are roughly 4 %, making the diagnosis a medical emergency (Spinelli, 2009). When assessing safety in any woman, having the input of a loved one that can verify and add information, as well as provide support, is enormously helpful.

Another objective for the initial evaluation is to assess “functioning.” In other words, can she sleep? Can she eat, shower, and brush her teeth? Is she able to study for school, go to work, or care for her children? Or is her illness and its accompanying symptoms so pronounced that she cannot get out of bed, keep food down, or manage the basics of her day-to-day routine?

Once her concerns have been reviewed, safety has been established, and basic functioning evaluated, symptoms need to be assessed. She should be carefully and thoroughly asked about symptoms of depression, mania, anxiety, panic attacks, obsessions, compulsions, psychosis, eating disorders, substance use, or any other upsetting or disruptive symptoms. This can be challenging, particularly in pregnancy, as many of the symptoms of a “normal” pregnancy can mimic depression. For instance, four of the nine criteria necessary for a diagnosis of major depressive disorder—sleep disruption, appetite disruption, low energy, and poor concentration—are often experienced by pregnant or postpartum women who, in fact, have no depression at all (American Psychiatric Association, 2013). In this situation, looking for other symptoms, such as profound low mood, agitation, a feeling of disconnection from the pregnancy or the infant, or excessive anxiety, can be helpful.

Other helpful tools are screening tests. The Edinburgh Postnatal Depression Screen, EPDS, has been used for years to detect depression and anxiety in perinatal women (Cox, Holden, & Sagovsky, 1987). The EPDS3, a shortened version consisting of only three questions, can pick up on excessive anxiety (Swalm, Brooks, Doherty, Nathan, & Jacques, 2010). More recently, the Patient Health Questionnaire-9, or PHQ9, has been shown to work with most adults, including

pregnant or postpartum women (Davis, Pearlstein, Stuart, O'Hara, & Zlotnick, 2013; Sidebottom, Harrison, Godecker, & Kim, 2012). Asking only the first two questions of the PHQ9, a test called the "PHQ2," can be used quickly and easily done in a busy prenatal or primary care office (National Centre for Health and Clinical Excellence, 2007). Several other screening tools exist as well, such as the Postpartum Depression Screening Scale (PDSS) and the Center for Epidemiological Studies Depression Scale (CES-D).

Current guidelines from both the American College of Obstetrics and Gynecology (ACOG) and the American Academy of Pediatrics (AAP) recommend screening in each trimester and again at frequent intervals in the postpartum, including during well-child checks (ACOG National Committee for Quality Assurance, & Physician Consortium for Practice Improvement, Committee Opinion, 2012; Earls, & Committee on Psychosocial Aspects of Child and Family Health American Academy of Pediatrics, 2010). On the other hand, the US Preventive Services Task Force only recommends screening if there are referrals for women who screen positive (US Preventive Services Task Force, 2009). This debate will continue until we have enough resources for all women to receive quality mental health care; for now, however, screening tools can help distinguish between a fairly normal pregnancy and one marked by depression and anxiety.

For all women, it is also important to look more specifically at her past reproductive psychiatric history. If she is newly postpartum and struggling with depression, did she also feel this way in previous pregnancies? If she is going through perimenopause and feels tense and irritable, did she also feel this way prior to the onset of her periods? New research suggests that there may be a subset of women who are genetically predisposed to more intense psychiatric symptoms during times of hormonal change (Bath et al., 2012; Epperson & Bale, 2012). Similarly, their mothers and sisters may feel this way; consequently, taking a good family history becomes essential.

Many women also want to have their hormone levels tested, with the hope that this will explain their psychiatric symptoms. In reality, research has not yet demonstrated a link between specific hormone levels and mental illness. What seems to matter, as mentioned previously, is the rate of change of reproductive hormones (such as estrogen or progesterone) as they fluctuate up or down. However, testing for thyroid dysfunction can be helpful and should be part of any women's assessment. Thyroid dysregulation is common in women of childbearing age, and it can often present as anxiety, low mood, sluggishness, or other symptoms that mimic mood or anxiety shifts (De Groot et al., 2012). Making sure that a woman's thyroid function is good can help reduce the need for further psychiatric management, if, in fact, this is the underlying cause of her symptoms.

Additional medical work-up includes ensuring that she is not on any medications that cause or worsen psychiatric symptoms. These include beta blockers, a family of blood pressure medications that make women feel tired; opiates, which also cause lethargy; hormone-based drugs, such as oral contraceptives or infertility medications, that can trigger mood swings; or even tamoxifen, a breast cancer prevention drug that sometimes has neurocognitive symptoms as side effects (Danaher et al., 2012). Gathering an exhaustive list of all medications a woman may be taking, including over-the-counter, herbal, and vitamin supplements, is important so that

their possible interactions and safety can be assessed. In addition, assessing substance use is of critical importance: alcohol and drug use clearly affect a woman's mood, anxiety levels, and cognition.

Putting together the pieces to this puzzle provides reproductive psychiatrists with the information they need to make effective treatment decisions. Information from the assessment can be organized into "the four Ps:"

- Predisposing factors
- Precipitating factors
- Perpetuating factors
- Protective factors

Predisposing factors are long-standing issues that put a woman at higher risk for psychiatric symptoms and include family history, history of substance use, and chronic medical problems, to name a few. Precipitating factors send women "over the edge" into more severe symptoms. Examples are new-onset intimate partner violence, the death of a loved one, or even a pregnancy or a delivery itself. Perpetuating factors are aspects of her life that will cause her symptoms to continue or worsen if left unchecked; examples include lack of social support, chronic financial stress, or ongoing violence. Finally, protective factors draw on a woman's own strengths and can lessen symptoms or prevent them from developing. Protective factors can include physical health, sobriety, a strong community of support, and love of children or family members. Looking closely at "the four Ps" helps the reproductive psychiatrist organize a treatment plan into interventions that reduce chronic risk factors, ameliorate the current crisis, and build on a woman's individual resources.

In general, medications are reserved for women who have symptoms that are moderate to severe and impact functioning. They are used if a woman is so ill that she feels suicidal. Medications are often typically clinically necessary when a woman experiences psychiatric symptoms of mania, psychosis, obsessions, compulsions, or panic attacks. Therapy is essential with all of these conditions as well, and with many patients psychotherapy should be a front-line treatment; in other patients, however, medications are necessary for stability and even to save lives (Yonkers et al., 2009). When a woman is faced with needing medication while she is pregnant or nursing, treatment decisions grow even more complicated.

Why Do Medications Cause Fear?

The possibility of medication, particularly during pregnancy or lactation, strikes fear in many women. Pregnant women are often told that psychiatric medications should be stopped at all costs, regardless of which medication it is or why it was prescribed. Well-meaning physicians give this advice frequently, and the media often presents frightening information out of context. Television advertisements for class-action lawsuits blast scary messages about antidepressant use in pregnancy, urging women to call "1-800-BAD-DRUG." A Google search for "antidepressants and pregnancy" turns up a website for law firms promising "National Assistance for

Birth Defects from Antidepressant Use.” Parenting websites lead with articles such as “Common Antidepressants Too Risky During Pregnancy, Researchers Say.” To be fair, many articles with more positive or nuanced approaches are regularly published as well, but for a woman who is already fearful, the negative headlines prove the most eye-catching.

There are general struggles and doubts around medication use that extend beyond possible harm to a developing fetus or a breastfeeding baby. Women who use medications for any reason, are often reluctant, and understandably so, to try psychiatric medications. Many women worry about side effects. They may have had negative experiences in the past with medications, or they may be struggling with their current regimen. Other women do not like the idea of having to take a medication to address mood or anxiety. They want to be able to “do it themselves” and believe that taking medication is not addressing the root problem. They often will express the belief that taking medication feels like a moral failing or character flaw. Sometimes women worry that psychotropic medications are addictive and that if they start, they will need to take them for the rest of their life. More commonly, no matter what phase of life a woman is in, she worries about being judged.

Some of these concerns are valid. Many women do have side effects, though the majority are mild and pass within a few days of taking them. However, there are rare, but serious, side effects with most drugs. Some medications are addictive and need to be carefully monitored and used for short periods of time. Aside from these more practical concerns, the underlying question is really one about what mental illness actually *is*. Is it a disease, with symptoms to be addressed with pharmaceuticals? Or is it a choice, one that if she just worked a little harder she could overcome? Does it mean that a woman has failed in some way; that she is simply not strong enough, smart enough, or savvy enough to move forward on her own? And for the woman who is pregnant or breastfeeding, the doubts and questions are even more profound. Does taking medication mean that she can also be a good mother?

From the moment of conception, if not before, the vast majority of women want to be the best mother possible. Pregnant and postpartum mothers are understandably frightened by the idea that they could harm their child by choosing to take a medication with any degree of risk. This terror comes not only from worry about the baby but also from the scary thought that the mother has somehow failed from the very beginning if she is suffering from depression or anxiety. In other words, she believes the message that “good mothers do not get depressed” and the corollary message that needing medication solidifies that failure (Los Angeles County Perinatal Mental Health Task Force, 2013). Underneath it all, many women perceive the message that should she continue an antidepressant in pregnancy or lactation, she is choosing her happiness over her baby’s health, and she is somehow a “bad mother.” The question that many women in this situation ask is the following: “Can I even be a good mother?”

The short answer is *yes*, she can. In fact, women who are happy and healthy are often able to be better mothers (Pearson et al., 2013; Sandman, Davis, Buss, & Glynn, 2012). Making a choice to take care of oneself is surprisingly difficult in our world, particularly for women, but is often the right one for making sure that one’s

baby is happy and healthy. Medications, though not without their own risks, can be one tool to accomplish this. They are not appropriate for everyone, nor are they “happy pills” that will wipe away all problems. They should only be taken after full informed consent. They should not medicate away normal emotions but instead should simply put a floor under depression and a ceiling on anxiety so that symptoms do not become devastating. They should help a woman feel more in control of her emotions. They should help her body start sleeping, eating, and concentrating again. Most importantly, they should free her from the torment and exhaustion that mental illness can cause, so that she can turn her attention to the most important task at hand: taking care of herself, her family, her work, and her life.

Classes of Medication

Antidepressants

The most commonly prescribed antidepressants are the selective serotonin reuptake inhibitors, SSRIs. The first SSRI was fluoxetine, or Prozac, which was released onto the market in 1987. Fluoxetine was relatively effective and much safer than previous antidepressants, which had burdensome side effects (such as following strict diets to avoid dangerous rises in blood pressure) or could be fatal in overdose. After fluoxetine, other SSRIs were developed in rapid succession: paroxetine (Paril), sertraline (Zalofs), fluvoxamine (Luvox), citalopram (Cerexa), and escitalopram (Lexapro). As of 2008, one in ten Americans over the age of 12 takes an antidepressant. Women are 2½ times more likely to take one than men, and 23 % of women in their forties and fifties take an antidepressant (Pratt, Brody, & Gu, 2011). The proportion of pregnancies with any antidepressant use increased from 5.7 % of pregnancies in 1999 to 13.4 % in 2007; the majority of these were prescribed an SSRI (Cooper, Willy, Pont, & Ray, 2007). SSRIs are believed to work by modulating the amount of serotonin available to neurons.

Antidepressants in other families target different neurotransmitters. For instance, the serotonin norepinephrine reuptake inhibitors, SNRIs, target both serotonin and norepinephrine. These medications include venlafaxine (Effexor), desvenlafaxine (Pristiq), and duloxetine (Cymbalta) as well as an older family of medications called tricyclic antidepressants (TCAs). Both SSRIs and SNRIs are effective for depression as well as a variety of anxiety disorders, including generalized anxiety disorder, panic disorder, and obsessive-compulsive disorder. Since many women experience anxiety and depression symptoms together, medications that treat both types of symptoms with one pill are extremely useful.

Other antidepressants work in more unique ways. Bupropion (Wellbutrin), a commonly used antidepressant that also has effectiveness for smoking cessation, seems to facilitate dopamine function. Dopamine is linked to motivation, energy, and a sense of well-being. A number of antidepressants are simply labeled “other” because they do not fit neatly into a particular class. These include mirtazapine, trazodone, and atomoxetine.

Mood Stabilizers

Mood stabilizers treat symptoms of both depression and mania. As our understanding of mood disorders grows, more people seem to suffer from both high mood as well as low mood than previously thought. Most people with bipolar disorder do not have full-blown manic episodes of euphoric mood, extreme grandiosity, or profound behavioral changes. Instead, diagnoses such as bipolar II or cyclothymia describe symptoms of mood swings, irritability, decreased need for sleep, a pressured sense of purpose, thought, speech, and impulsive behavior that can occur in varying degrees and for varying lengths of time (American Psychiatric Association, 2013). At the same time, most people with bipolar disorder spend more time depressed than “up” in their mood (Kupka et al., 2007).

Regardless of presentation, mood stabilizers are the treatment of choice for bipolar disorder, even bipolar depression. Lithium was the first mood stabilizer, and it remains the gold standard for bipolar disorder type I. However, it can be complicated to monitor and becomes toxic easily. Other well-known mood stabilizers include carbamazepine (Tegregol), valproic acid (Depakote), and lamotrigine (Lamictal). These are also used for epilepsy, and much of the safety data that we have for them comes from studies done on pregnant women with seizure disorders. Increasingly, a class of medications called atypical antipsychotics is also used to manage mood instability.

Antipsychotics

Atypical antipsychotics are the newest generation of medications targeting psychosis and, as described above, some mood symptoms. “Psychosis” is not a disorder, but a set of symptoms based on disturbed thoughts and perceptions. Hearing voices, feeling paranoid, and holding delusional beliefs are a few manifestations of psychosis and can be present in a variety of disorders, including postpartum psychosis. Atypical antipsychotics work quickly to manage these symptoms and can be very effective. The main challenge is weight gain; atypicals, as they are called, can lead to obesity as well as diabetes and cholesterol problems (McCloughen & Foster, 2011; Pramyothin & Khaodhiar, 2010). All patients want to avoid this, but particularly women who are pregnant or who are already struggling with weight.

Older antipsychotics, or “typical antipsychotics” since they were developed first, have been in use for nearly six decades. However, they are often considered “second line” to atypicals because of side effects. These side effects include neuromuscular abnormalities, tremor, and motor tics, some of which last a lifetime, as well as weight gain and sedation. Nonetheless, in reproductive psychiatry, typical antipsychotics have the advantage of years of safety data in pregnant and postpartum women. For this reason, plus the fact that atypicals can be so challenging for weight management, typical antipsychotics are still used at times, including occasionally with pregnant women who are psychotic.

Antianxiety Medications

Many antidepressants also work effectively to treat anxiety. These include most of the serotonin- or norepinephrine-based medications. Ideally this allows a woman that is suffering from both anxiety and depression to take a single drug to address both sets of symptoms. However, most of these medications can take up to 6 weeks to take effect, and many women cannot tolerate symptoms of anxiety without relief for that long. In this case, shorter acting, more temporary agents can be helpful.

Benzodiazepines work much more quickly and on an “as-needed” basis for more intense symptoms of anxiety, such as panic attacks. Common benzodiazepines include diazepam (Valium), alprazolam (Xanax), lorazepam (Ativan), and clonazepam (Klonopin). They generally take effect within a few minutes to an hour and provide relief from anxiety; in addition, they can be helpful with insomnia, particularly if it is driven by anxiety. However, they are also potentially addictive and should only be used on a short-term basis or on infrequent occasions.

Additional Psychotropic Medications

The armamentarium of psychotropic medications is much broader than that of those listed above, and medications from other branches of medicine are often used to treat psychiatric symptoms as well. Buspirone is an alternative antianxiety medication. Gabapentin is often used for anxiety, as well. Stimulants can be used to treat attention-deficit disorder, ADD. Naltrexone has some evidence for its use to treat substance-abuse disorders (Pettinati, O'Brien, & Dundon, 2013). New medications are constantly researched and often released to the market. Even as this book goes to press, new research continues to provide glimpses into potential medications that work in novel ways and may be even more effective.

Evidence-Based Interventions

Psychotherapy

Medications are certainly not the only type of treatment available and, in fact, are most effective when used in conjunction with psychotherapy (Yonkers et al., 2009). For many women, psychotherapy is much preferred. Interpersonal psychotherapy, whether individual or group, works well for perinatal women as they transition into motherhood and for perimenopausal women as they are often navigating changes in their own family status during the same time of life (Sockol, Epperson, & Barber, 2011). In addition, cognitive-behavioral therapy can be effective for symptoms of anxiety and depression (O'Mahen, Himle, Gedock, Henshaw, & Flynn, 2013). In general, if a patient needs to take medication, ideally she should be in therapy as well.

Omega-3 Fatty Acids

Omega-3 fatty acids, often referred to as “fish oils,” decrease inflammation in a variety of ways. As mental health has increasingly been linked to increased inflammation, research into omega-3 fatty acids as a possible treatment has increased (Deligiannidis & Freeman, 2010). Modest efficacy has been shown for doses upwards of 3,000 mg a day for general depression and anxiety (Dennis & Dowswell, 2013; Luberto, White, Sears, & Cotton, 2013). Data is sparse for treatment of premenstrual or perimenopausal mood symptoms with omega-3s, though one study did show a decrease in hot flashes (Lucas, Asselin, Merette et al., 2009). For perinatal mood and anxiety disorders, data are mixed. Studies showing the most efficacy tend to use docosahexaenoic acid, DHA, and eicosapentaenoic acid, EPA, in a ratio of roughly 1:2. For women taking prenatal vitamins, DHA is often already included; taking a supplement may be necessary to reach the recommended doses. In addition, pregnant or nursing women should choose a form of fish oil that is low in mercury in order to avoid toxicity.

Folate

Folate is a B vitamin that is important for a variety of reasons, including healthy cell division and metabolism of amino acids. Folate is naturally present in some foods, and folic acid is the form of folate used in supplements. Recent research into the use of folate to help treat depression has been encouraging. Folate itself is not an antidepressant, but individuals with higher folate levels seem to respond better to antidepressants. Current recommendations suggest adding 15 mg of L-methyl folate a day to one’s antidepressant dose (Papakostas et al., 2012). For pregnant women, prenatal vitamins typically contain 400 µg (or 0.4 mg) of folic acid to prevent two common central nervous system malformations, spina bifida and anencephaly. Folate supplementation may then achieve two goals: reducing the risk of birth defects as well as increasing the efficacy of antidepressants.

Calcium Carbonate

Calcium carbonate, 1,200 mg a day, can be effective for treating premenstrual mood and anxiety symptoms, though data is sparse. While not as effective as an antidepressant, some studies have shown effectiveness with premenstrual tiredness, appetite changes, and depressive symptoms (Ghanbari, Haghollahi, Shariat, Foroshani, & Ashrafi, 2009; Yonkers, Pearlstein, & Gotman, 2013). For women who would like a non-psychotropic approach to premenstrual symptoms, calcium carbonate is an option.

Exercise

Exercise is a well-established way to improve mood, anxiety, and physical health. For premenstrual symptoms, exercise reduces personal stress, anxiety, tension, and depression as well as breast tenderness, fluid retention, and cramps (Deligiannidis & Freeman, 2010). The ACOG recommends 30 min of moderate exercise most days for pregnant women, unless there is a clear medical reason not to do so (American College of Obstetrics and Gynecology, 2002, reaffirmed 2009). For perimenopausal women, moderate aerobic exercise three times a week improves sleep quality, insomnia, and depression; however, it does not seem to have an effect on hot flashes or other vasomotor symptoms (Sternfeld et al., 2014).

Acupuncture

Increasingly, women seek acupuncture for a variety of symptoms, including anxiety, depression, and infertility. Acupuncture consists of the placement of needles throughout the bodies' channels, or "meridians," to facilitate the flow of *qi* and relieve symptoms. Along with herbal medications, acupuncture is an essential modality in traditional Chinese medicine. While it is extremely difficult to study using Western methods of randomized, controlled trials, anecdotally some women report relief from symptoms with acupuncture (Luberto et al., 2013). One consideration for the reproductive psychiatrist is any potential interaction between Chinese herbal medicine and psychotropic medications. Very little data is available on possible changes in drug metabolism or serum levels when these two approaches are used together. This is not to say that the two approaches are incompatible, but rather close symptom control and, when necessary, serum level monitoring of psychotropics are important.

Bright Light Therapy

Bright light therapy was initially evaluated in the treatment of seasonal affective disorder, and it has shown some effectiveness in treating depression as well. Bright light therapy consists of spending a set amount of time each day, often half an hour, in front of a "light box" that provides 10,000 lx white light. For premenstrual disorders, small studies have shown reduction in depression as well as irritability and physical symptoms (Lam et al., 1999; Parry, Mahan, Mostofi, Lew, & Gillin, 1993). Small trials have also been modestly effective for perinatal depression; at this point larger studies are needed as well as guidelines regarding use in women with bipolar depression (Dennis & Dowswell, 2013). To date, there are no available data on bright light therapy in depressed perimenopausal women.

Brain Stimulation Therapies

Brain stimulation therapies involve activating the brain through electricity, magnets, or implants in order to treat mood symptoms. The oldest, best researched is electroconvulsive therapy, ECT. Since the late 1930s, this technique has been used to treat severe, seemingly intractable cases of mood and psychotic disorders. ECT consists of inducing a seizure in a patient under a controlled setting. ECT is not contraindicated in pregnancy, and rates of success are often higher than for pharmacotherapy (Anderson, 2009; Dierckx, Heijnen, van den Broek, & Birkenhager, 2012). However, side effects of headache and short-term memory loss, as well as the stigma attached to ECT, prevent its more widespread use.

Newer brain stimulation therapies include repetitive transcranial magnetic stimulation, or rTMS; vagus nerve stimulation; magnetic seizure therapy; and deep brain stimulation. Many of these are still considered experimental, but rTMS is gaining traction as a treatment option (Hovington, McGirr, Lepage, & Berlim, 2013). It also induces electrical activity in the brain, similar to ECT, but in a much more targeted way with fewer side effects. Data thus far have been somewhat mixed, but increasingly more positive as the technique is refined. A series of case studies in pregnant women demonstrate safety and efficacy; the next step is more large-scale studies (Zhang, Liu, Sun, & Zheng, 2010). This is a particularly attractive option because it might reduce the need for medication and therefore creates less of an exposure for the developing fetus.

Hormonal Therapies

A logical treatment option for psychiatric symptoms around times of hormonal fluctuation is to use hormones themselves. Despite the rationality of this, data remains mixed for most studies examining this approach. For premenstrual mood symptoms, the oral contraceptive pill may benefit some women; for others, however, it seems to make depression or irritability worse (Rapkin & Winer, 2008). Trials of estrogen for postpartum women have been promising in reducing depression symptoms, based on the theory that adding estrogen immediately after delivery lessens the significant drop in reproductive hormones that occurs within hours after birth and may be responsible for postpartum depression. However, these have not been explored in larger trials and are not currently standard practice (Moses-Kolko, Berga, Kairo, Sit, & Wisner, 2009). Using hormone replacement therapy provides relief to many, but not all, women undergoing the menopausal transition. This approach can be used alone or with serotonergic and noradrenergic antidepressants as well as psychological supports (Soares, 2013). However, there can be health concerns with hormone replacement therapy that make collaboration with a gynecologist important.

The Decision-Making Process

Since many treatment options exist, sorting through which ones are potentially most helpful requires careful assessment and a clear sense of what the goal of treatment is for each woman. If medications do seem appropriate, a few simple rules can help determine which ones to use. If a woman has tried medication in the past, it is helpful to look and see how she responded. If a particular medication worked, then it may be worth trying it, or a medicine in the same family, again. Another guideline is monotherapy or the idea that one medication is preferable to multiple. The principle of monotherapy is particularly important to consider for pregnant or nursing women in order to minimize the number of drug exposures to the fetus or the infant. However, this may not suffice for all women, and current psychiatric guidelines often suggest adding in a second medicine to augment one that may only be partially effective (Gaynes et al., 2012). When choosing doses, one maxim is “start low, go slow, but go!” This teaches to start at a low dose and increase slowly to try and find the lowest possible effective dose. However, it is important to “go,” in other words, to treat until the medication is effective.

For many women, a pre-pregnancy consultation can be enormously helpful in educating a woman and her family about the risks and benefits of medication use so that she can plan ahead for the safest possible perinatal period. A thorough treatment plan is based on the biopsychosocial model. Biological recommendations may include whether or not to use medications or supplements, check thyroid function, or address other medical conditions. Psychological support through individual or group therapy should be strongly considered. Finally, social aspects of care need to be included, such as how to increase social support or connect with other new mothers. A written summary of this information ensures that the potential mother is clear on her options and the risks and benefits they involve. In addition, this written report can be shared with her obstetrician and her child's pediatrician after delivery.

Vignettes

What do these treatment choices look like in real life? The following vignettes describe common situations seen in reproductive psychiatry.

Vignette 1

Sarah is a 23-year-old woman who comes in to your office because she feels “crazy” right before her period. For five days before her period starts, she becomes full of rage and weepy, to the point that she must take time off work and her boyfriend has threatened to leave her. The rest of the month, she feels well. She is stable in her mood, with no profound anxiety or tension. She sleeps, eats, and concentrates well, and has no suicidal thoughts or other concerning symptoms. However, she is worried that her premenstrual symptoms are causing serious damage to her life. She wants you to check her hormone levels and help her in any way you can.

Many women have questions about their hormone levels and whether or not they are “off.” However, there is little evidence to support checking hormone levels in

order to explain psychiatric symptoms. What matters is an individual woman's response to her hormone fluctuations. Many women like Sarah feel mood and anxiety symptoms acutely during these times of flux, but there is no lab value that corresponds with this. The more important questions focus on symptoms and, in the case of premenstrual disorders, on whether she truly feels these symptoms just during the luteal phase (the time in her menstrual cycle directly before her period actually starts) or whether she actually feels them to some degree all month.

The best way to determine this is by tracking her moods as well as when her period starts and stops. In order to have a true diagnosis of premenstrual dysphoric disorder, such tracking must happen for 2 months and demonstrate that symptoms are isolated to the luteal phase (American Psychiatric Association, 2013). This is important because it determines the course of treatment. If symptoms are solely in the luteal phase, then many women benefit from intermittent dosing of SSRI medications (Rapkin & Winer, 2008). This means that she can take an SSRI from the time immediately before her symptoms typically start until they end, usually right after her period begins. She does not need them the rest of the month, and she typically does not have side effects associated with starting or stopping the medication. On the other hand, if she is having symptoms all month, with a worsening before her period, she needs "continuous dosing" of an SSRI. This means taking the medication all month. Some women do well with the same dose all month. Other women find that they are stable on a lower dose for most of the month but require a temporary increase in dose during the luteal phase in order to best contain symptoms.

SSRIs are not the only option for women with premenstrual mood and anxiety symptoms. Some women benefit from oral contraceptive pills. If they do, this is a streamlined way to control symptoms as well as to provide birth control, if desired. Other women feel poorly on OCPs, and prefer the antidepressant route. Which one to try first depends mostly on patient preference, on past experience with the types of medications, and on how effective the two different treatments are for the individual woman.

For women with milder symptoms, the ACOG recommends moderate exercise, a complex-carbohydrate diet, and reducing alcohol and caffeine use (American College of Obstetricians and Gynecologists, 2011). Calcium carbonate can also be effective in alleviating milder symptoms.

For the patient described above, however, her symptoms are more severe. Tracking reveals that they are isolated to the 5 days before the onset of her period and she opted for intermittent dosing with fluoxetine. She also began taking calcium supplements and trying to implement diet and exercise changes, though these were challenging during a time of the month when she did not feel well physically. However, her efforts paid off. She responded well, and her work life and relationship both improved.

Vignette 2

Melinda is a 28-year-old woman who calls for an appointment because she is three months pregnant. She was previously taking an antidepressant, but tapered off because she wanted to become pregnant and her obstetrician told her that antidepressants were harmful to the baby. She was only off the medication a few weeks before she became pregnant. Melinda did well initially, but over the past month she has become increasingly more sad, anxious,

and fearful. She thinks constantly about possible negative outcomes with the baby. She ruminates on this at night and finds herself unable to sleep. She feels as if she has “knots in her stomach,” and her weight has dropped to the point that her obstetrician is worried. She began seeing her therapist again, who advised that she seek care from a reproductive psychiatrist as well.

Melinda's situation is common: well-intentioned advice from care providers often guides women to stop their medications. Unfortunately, rates of relapse are high; one study showed that nearly 70 % of women who were doing well on antidepressants but stopped because of pregnancy relapsed. Over half of these women relapsed early, in the first trimester (Cohen et al., 2006). This is the case with Melinda.

At this point, the decision of whether or not to restart medications should be based on an evidence-based, well-thought-out risk–benefit analysis. This should include the risks of untreated illness as well as the risks of medications themselves. It is this risk of untreated illness that is often left out of the equation: women are usually told of risks of medication use but not of poor outcomes that are associated with untreated mood and anxiety disorders in pregnancy.

Melinda's visit with a reproductive psychiatrist began with a careful assessment of her symptoms and her current history. She relapsed before when tapering off antidepressants, and many of the symptoms she is feeling now are consistent with how she has felt in the past. This is significant because the risks of untreated depression and anxiety are well documented, and research on this topic continues to grow. Untreated depression makes it much harder for pregnant or postpartum women to take care of themselves, even with such basics as eating, sleeping, or getting good medical care. Women with depression in pregnancy are at risk for delivering prematurely (Grigoriadis et al., 2013; Straub, Adams, Kim, & Silver, 2012) as well as for having small-for-gestational-age babies (Grote et al., 2010; Hosseini et al., 2009). In addition, an expectant mother's depression and anxiety in pregnancy may impact the developing fetus' own stress management system, and infants are born with more irritability, jitteriness, and a higher likelihood of experiencing anxiety themselves (Sandman et al., 2012; van der Wal, van Eijdsden, & Bonsel, 2007). Finally, untreated depression in pregnancy is one of the biggest risk factors for postpartum anxiety and depression, with research indicating that women with antenatal depression are 5 times more likely to develop postpartum depression (Milgrom et al., 2008; Topiwala, Hothi, & Ebmeier, 2012). Postpartum mood and anxiety disorders are serious illnesses, leading to poor bonding between mother and child, less breastfeeding (Ystrom, 2012), and even high rates of suicide (Almond, 2009; Oats, 2003).

However, these risks of untreated illness need to be weighed against the risk of medication use (Byatt, Deligiannidis, & Freeman, 2013; Koren & Nordeng, 2012). It is notoriously difficult to assess data in this field, as ethical constraints prevent testing drugs on pregnant or nursing women (Einarson, Kennedy, & Einarson, 2012; Palmsten & Hernandez-Diaz, 2012). As a result, all the data we have tends to emerge after the fact, i.e., once a medication has already been on the market for many years. In addition, it is very difficult to tease out the risks of medication use versus all the risks of untreated depression. These include both the biological

effects of depression on the body as well as behavioral risks such as poor appetite, disrupted sleep, and possible alcohol or drug use. Even with these challenges, however, new research continues to change the way reproductive psychiatry is practiced, making any recommendations on medication use obsolete before this book goes to press.

However, while specific recommendations are beyond the scope of this chapter, the basic framework on how to weigh the risks or the benefits of medications in pregnancy remains the same. While we have more information on SSRIs than other drug classes (and thus, the information below focuses on SSRIs), this framework applies to any medication. There are four major areas to consider. First are concerns concentrated mostly in the first trimester, namely, birth defects or pregnancy loss. For SSRIs specifically, data is mixed on these topics, but most articles are more reassuring, with the risks of medication not appearing to exceed the standard risks of pregnancy (Ross et al., 2013; United States Food and Drug Administration, 2013). However, there are other studies that do show patterns of elevated risk for various birth defects (Malm, Artama, Gissler, & Ritvanen, 2011), though these are different in design and the results are hard to generalize.

The second set of concerns centers on any medical issues for either mother or infant closer to the time of delivery. A well-described “poor neonatal adaptation syndrome” affects roughly 5–10 % of all babies, but that number increases to 10–30 % in babies exposed to SSRIs in utero. Common symptoms include respiratory distress, jitteriness, irritability, alterations in blood glucose, and, very rarely, seizures; these are transient, with no known long-lasting effects, and usually resolve with observation or symptomatic management (Maschi et al., 2008). Preterm delivery is a concern with SSRIs as well (Suri et al., 2011; Yonkers et al., 2012), though some studies show rates fairly equivalent to those seen with untreated depression (Wisner et al., 2009). Another potential medical issue, though again with some studies showing an association and others not, is persistent pulmonary hypertension of the newborn (PPHN). This more serious respiratory illness is linked to a variety of risk factors, and exposure to SSRIs in pregnancy appears to increase the risk from roughly 1/1,000 to 2/1,000 (Kieler et al., 2012). Third are questions about more long-term developmental issues, such as whether in utero exposure affects intelligence, language, or behavior. The majority of these studies with SSRIs are reassuring, with no differences between infants exposed to antidepressants in utero versus unexposed.

Finally, the possibility of breastfeeding should be considered from the very beginning. Ideally, if medications are indicated, she should be on the same agent in pregnancy through delivery, and into the postpartum. The first few days and weeks postpartum, when breastfeeding is established, are of the most high risk for mood and anxiety symptoms, and a woman should move into this time period without having to change medications for drug safety reasons during lactation. This minimizes her risk of relapse, plus decreases the number of exposures for the infant. For many women, a pre-pregnancy consultation can be enormously helpful in educating her

and her family about the risks and benefits of medication use so that she can plan ahead for the safest possible perinatal period.

In Melinda's case, no pre-pregnancy consultation was available; she is already pregnant and needing to make treatment decisions. She knows from past experience that her symptoms will continue unless she treats them with antidepressants. She is worried about taking any sort of medication during pregnancy, but she is also worried about her weight loss, anxiety, and inability to sleep. After much thought, she decides to restart the antidepressant. This time, her obstetrician is supportive, as she has seen firsthand how ill Melinda becomes when untreated.

Melinda does not want to rely on medication alone, however, and she inquires into other treatments that might help keep her healthy and stable in pregnancy. Her reproductive psychiatrist advises her that there are measures that pregnant and postpartum women can take to address anxiety and depression. Melinda talks further to her obstetrician, and she begins a supplemental fish oil capsule along with her prenatal vitamins. She starts prenatal yoga as well as half-hour walks in her neighborhood several times a week. Most importantly, she finds a therapist trained in perinatal mood and anxiety disorders, and she starts seeing her on a regular basis. After a few weeks of these efforts, along with antidepressant use, her mood is brighter, her anxiety lower, and her weight gain and sleep are back on track. She plans on continuing the medication throughout pregnancy and into the postpartum, and she is already talking to her psychiatrist about making sure that her medication choice will be safe while breastfeeding.

Vignette 3

Tracy is a 32-year-old woman who gave birth to her second child three weeks ago. She felt happy and grounded after her first baby was born, with no anxiety or depression at all. However, this time, she is frantic with worry. She wakes up in the night with "cold sweats" and feeling as if, "I have electrical currents running through my body." She has frequent diarrhea and can barely eat. She is trying to nurse her baby, however, and feels pressure to breastfeed exclusively, "because I did it the first time around." She does not want to take medication, but she is desperate. Her therapist advised her to come in for a consultation.

Tracy arrives at your office slightly disheveled and exhausted appearing, with dark circles under her eyes. She continually jiggles her foot up and down, and she is struggling to sit still long enough to nurse her baby, who is crying. Tracy herself begins crying when she describes her symptoms. Her appetite has plunged; she is up hours every night, even after her children are asleep; and she cannot focus on simple tasks. She feels anxious constantly, with spikes upward into panic several times daily.

You carefully assess for manic symptoms, particularly given her agitation and inability to sleep. The practitioner should always ask about elevated or irritable mood, impulsive behavior, racing thoughts, or feelings of grandiosity. She says that while her mind is "spinning"—a common symptom with anxiety—she does not have these other experiences. She denies hearing voices, feeling paranoid, or other signs of paranoia. She also clearly denies thoughts or plans of suicide. She also denies any plan or intention to harm or kill her infant, though at times she has unbidden "images" of this that cause her even more anxiety.

Tracy had read about the “Baby Blues” online and was hoping for the first 2 weeks that this was causing her feelings. However, now that 3 weeks have passed and her symptoms are getting worse, not better, she is worried about more serious illness. Her therapist, who is trained in perinatal mood and anxiety disorders, has diagnosed her with postpartum depression and anxiety, and you concur. In addition, you are worried about panic attacks and possible OCD given the intrusive and upsetting images that she is describing. Because of your thorough screen of symptoms, you are able to rule out mania and psychosis as possible diagnoses. Tracy is also very clear that she is not using alcohol or illicit drugs.

Tracy initially declined medication when her therapist had recommended it, but today in your office, she is ready to discuss it further. Her main concern is breastfeeding: she really feels committed to continuing but is worried about transfer of any medication to the baby. You discuss at length the available medications that are known to have minimal transfer to the infant (Lanza di Scalea, 2009). One such medication in particular is helpful for sleep and appetite, as well as anxiety and depression, and this is the one you agree on together. You also discuss flexibility in breastfeeding, and she acknowledges that the pressure she feels to nurse exclusively is worsened by her anxiety and vice versa.

You recommend ongoing therapy to address this dilemma as well as work on her relationship with her new baby and how to incorporate him into her life. Other supportive measures include omega-3 fatty acids, and you give Tracy a handout on which ones are the most reliably safe and effective. You also discuss at length ways to ensure that she have a break from childcare so that she can rest, engage in moderate exercise, and allow time to heal. She agrees to discuss this with her husband and gives you permission to speak to him as well.

When you see her again for a follow-up appointment in 2 weeks’ time, she is already showing signs of improvement, and you continue the current treatment plan.

Vignette 4

Janet is a 51-year-old woman who comes into your office at the advice of her therapist, who she just started seeing recently. She sought care because her own mother had a psychotic break at age 50, and she is worried this will happen to her. She herself has experienced no psychosis, and has no other psychiatric history. However, she has had times filled with rage and profound irritability for the past three years. During this time, she has also had weight gain, insomnia, poor concentration, and difficulty with short-term memory and word-finding. She initiated therapy because she is “normally happy,” but has found it increasingly hard to get out of the bed in the morning.

Janet begins the session describing the intense irritability that seems to be worsening; she cannot stand how guilty she feels after she lashes out at her husband or daughter. She feels as if “I have PMS all the time.” Her period is very erratic; the last time was 6 months ago. She tried to use black cohosh, a herbal medication often recommended for perimenopause (Deligiannidis & Freeman, 2010). She felt as if it helped initially, but her symptoms have worsened to the point that the herb is no longer effective. She wants to discuss different treatment options for how she is feeling.

You begin with a conversation about whether she is more interested in addressing her symptoms through hormone replacement therapy or through psychotropic

medication. Because of a history of blood clots with one of her pregnancies, she is wary of any hormonal treatment. In addition, because of her family's mental health history, she is more interested in a psychiatric approach. She has never tried any sort of psychotropic medication before.

Given her mother's mood and psychotic symptoms, you screen carefully for bipolar disorder and psychosis in Janet. Antidepressants can sometimes make these symptoms worse, and a mood stabilizer or an antipsychotic would be more appropriate if any such symptoms were present. However, she denies any such symptoms. Her main complaints remain irritability, insomnia, weight gain, and poor concentration. Janet is pleased to hear that certain antidepressants have also been approved for hot flashes associated with perimenopause, as she is also suffering from these multiple times daily.

Together you decide on a trial of a serotonergic-based medication. She tries it for roughly 2 weeks but found herself feeling sedated and gaining even more weight. After more discussion, you agree to switch to a different family of medications, one that acts on both serotonin and norepinephrine. This family of medicine also has good evidence for containing mood and anxiety symptoms associated with perimenopause (Soares, 2013). Fortunately, she responds well this time, with the more tolerable side effect of a slight headache that resolves after a few days. She starts to feel better within a month, with much reduced irritability, better sleep, and improved concentration.

However, once her main symptoms are better contained, she also starts to mourn the loss of her own mother's mental health as well as the fact that her only daughter is about to leave for college. She and her husband are arguing more as well, after nearly 25 years of marriage. You recommend individual as well as family therapy, and she readily agrees. Six months later, she is much more stable in terms of her relationships as well as perimenopausal symptoms.

Conclusion

An emerging awareness of the scope and depth of reproductive mental illness has led to a dramatic increase in research, education, and clinical resources; however, there is much more to do, and we have a long way to go. To date, there are very few training programs specifically for reproductive psychiatry, and there is no officially recognized subspecialty in this field within psychiatry. Mental health care remains difficult to access for most people, but the specialized care of a reproductive psychiatrist can feel unattainable. The media, and even the medical establishment itself, continues to endorse the idea that psychiatric medications, regardless of the type of medication or the severity of illness that they are treating, should be stopped without question in pregnancy or postpartum. Stigma, financial and insurance constraints, and lack of education still prevent many women from seeking help. Despite these

challenges, reproductive psychiatrists can provide the much-needed care to vulnerable and suffering women, and this exciting field is becoming more acceptable and available with each passing year.

Resources

- <http://www.brighamandwomens.org>—The teaching hospital for Harvard Medical School.
- www.jwatch.org—An online resource provided by the New England Journal of Medicine. Journal Watch reviews a broad base of scientific research to present important clinical findings and commentary.
- www.marcesociety.com—The Marcé Society is a research organization dedicated to increasing awareness, understanding, prevention, and treatment of mental illness related to childbearing.
- www.motherisk.org—Motherisk is a clinical research and teaching program at the Hospital for Sick Children in Toronto, Ontario, Canada, that provides information and guidance to pregnant or breastfeeding women and to health care professionals regarding risks to the fetus from exposure to drugs, chemicals, diseases, radiation, and environmental agents.
- www.NASPOG.org—The NASPOG was formed as a collaboration among obstetrician–gynecologists, psychiatrists, and psychologists with the mission of fostering scholarly scientific and clinical study of the biopsychosocial aspects of obstetric and gynecologic medicine.
- www.postpartum.net—Postpartum Support International brings together families, communities, and professionals working to support families during pregnancy, pregnancy loss, and the postpartum period in an effort to increase awareness about perinatal illness.
- www.psych.org—The American Psychiatric Association is a medical specialty organization representing more than 33,000 psychiatric physicians from the USA and around the world with the goal of insuring effective and appropriate treatment for all individuals with mental disorders.
- <http://www.womenandinfants.org>—Women and Infants Hospital is the teaching hospital of the Warren Alpert Medical School of Brown University. Their Center for Women’s Behavioral Health specializes in outpatient care for a wide range of behavioral health issues, including mood and anxiety disorders during pregnancy and the postpartum period, substance abuse, psychiatric complications from medical disorders, crisis management and anxiety and depression stemming from pregnancy loss, infertility, a cancer diagnosis, trauma, or other crises.
- www.womensmentalhealth.org—The Massachusetts General Hospital Center for Women’s Mental Health is a perinatal and reproductive psychiatry information center. The website provides a range of current information that includes new research findings in women’s mental health and how these studies inform current clinical practice.

References

- ACOG National Committee for Quality Assurance, Physician Consortium for Practice Improvement. Committee Opinion. (2012). Maternity care: Performance Measurement Set Measure #3: Behavioral health risk assessment.
- Almond, P. (2009). Postnatal depression: A global public health perspective. *Perspectives in Public Health, 129*(5), 221–227.
- American College of Obstetricians and Gynecologists. (2011). FAQ057: Premenstrual syndrome.
- American College of Obstetrics and Gynecology. (2002). *Exercise during pregnancy and the postpartum period*. Washington, DC: Committee on Obstetric Practice. Reaffirmed 2009.
- American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Retrieved from <http://dx.doi.org/10.1176/appi.books.9780890425596.910646>
- Anderson, E. L. (2009). ECT in pregnancy: A review of the literature from 1941–2007. *Psychosomatic Medicine, 71*, 235–242.
- Baker-Ericzen, M. J., Duenas, C., Landsverk, J. A., Connelly, C. D., Hazen, L., & Horwitz, S. M. (2012). A collaborative care telemedicine intervention to overcome treatment barriers for Latina women with depression during the perinatal period. *Families, Systems & Health, 30*(3), 224–240.
- Bath, K. G., Chuang, J., Spencer-Segal, J. L., Amso, D., Altemus, M., McEwen, B. S., & Lee, F. S. (2012). Variant brain-derived neurotrophic factor (Valine66Methionine) polymorphism contributes to developmental and estrous stage-specific expression of anxiety-like behavior in female mice. *Biological Psychiatry, 72*, 499–504.
- Bergink, V., Burgerhout, K. M., Weigelt, K., Pop, V. J., de Wit, H., Drexhage, R. C., ... Drexhage, H. A. (2013). Immune system dysregulation in first-onset postpartum psychosis. *Biological Psychiatry, 73*(10), 1000–1007.
- Brizendine, L. (2006). *The female brain*. New York, NY: Broadway Books.
- Bromberger, J. T., Schott, L. L., Kravitz, H. M., Sowers, M., Avis, N. E., Gold, E. B., ... Matthews, K. A. (2010). Longitudinal change in reproductive hormones and depressive symptoms across the menopausal transition: Results from the Study of Women's Health Across the Nation (SWAN). *Archives of General Psychiatry, 67*(6), 598–607.
- Byatt, N., Deligiannidis, K. M., & Freeman, M. P. (2013). Antidepressant use in pregnancy: A critical review focused on risks and controversies. *Acta Psychiatrica Scandinavica, 127*(2), 94–114.
- Chen, S.-J., Liu, Y.-L., & Sytwu, H.-K. (2012). Immunologic regulation in pregnancy: From mechanism to therapeutic strategy for immunomodulation. *Clinical & Developmental Immunology, 2012*, 1–10. Article ID:258391.
- Coern, L. A., Grether, J. K., Yoshida, C. K., Odouli, R., & Hendrick, V. (2011). Antidepressant use during pregnancy and childhood autism spectrum disorders. *Archives of General Psychiatry, 68*(11), 1104–1112.
- Cohen, L. S., Altshuler, L. L., Harlow, B. L., Nonacs, R., Newport, D. J., Viguera, A. C., ... Stowe, Z. N. (2006). Relapse of major depression during pregnancy in women who maintain or discontinue antidepressant treatment. *Journal of the American Medical Association, 295*(5), 499–507.
- Cooper, W. O., Willy, M. E., Pont, S. J., & Ray, W. A. (2007). Increasing use of antidepressants in pregnancy. *American Journal of Obstetrics & Gynecology, 196*, 544.e1–544.e5.
- Cox, J. L., Holden, J. M., & Sagovsky, R. (1987). Detection of postnatal depression: Development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry, 150*, 782–786.
- Danhauer, S. C., Legault, C., Bandos, H., Kidwell, K., Constantino, J., Vaughan, L., ... Shumaker, S. (2012). Positive and negative affect, depression, and cognitive processes in the cognition in the Study of Tamoxifen and Raloxifene (Co-STAR) trial. *Neuropsychology Development and Cognitive Section B. Aging Neuropsychology and Cognition, 20*(5), 532–552.
- Davis, K., Pearlstein, T., Stuart, S., O'Hara, M., & Zlotnick, C. (2013). Analysis of brief screening tools for the detection of postpartum depression: Comparisons of the PRAMS 6-item instrument, PHQ-9, and structured interviews. *Archives of Women's Mental Health, 16*(4), 271–277.

- De Groot, L., Abalovich, M., Alexander, E. K., Amino, N., Barbour, L., Cobin, R. H., ... Stagnaro-Green, A. (2012). Management of thyroid dysfunction during pregnancy and postpartum: An Endocrine Society clinical guideline. *Journal of Clinical and Endocrinology Metabolism*, 97(8), 2543–2565.
- Deligiannidis, K., & Freeman, M. (2010). Complementary and alternative medicine for the treatment of depressive disorders in women. *Psychiatry Clinics of North America*, 33(2), 441–463.
- Dennis, C. L., Dowswell, T. (2013). Interventions (other than pharmacological, psychosocial or psychological) for treating antenatal depression. *Cochrane Database Systematic Reviews*, (4), CD006795. doi: [10.1002/14651858.CD006795.pub3](https://doi.org/10.1002/14651858.CD006795.pub3).
- Dierckx, B., Heijnen, W. T., van den Broek, W. W., & Birkenhager, T. K. (2012). Efficacy of electroconvulsive therapy in bipolar versus unipolar major depression. *Bipolar Disorder*, 14(2), 146–150.
- Earls, M. F., & Committee on Psychosocial Aspects of Child and Family Health American Academy of Pediatrics. (2010). Incorporating recognition and management of perinatal and postpartum depression into pediatric practice. *Pediatrics*, 126(5), 1032–1039.
- Einarson, T. R., Kennedy, D., & Einarson, A. (2012). Do findings differ across research design? The case of antidepressant use in pregnancy and malformations. *Journal of Popular Therapy Clinical Pharmacology*, 19(2), e334–e348.
- Epperson, C. N., & Bale, T. L. (2012). *BDNF Val66Met* polymorphism and brain-derived neurotrophic factor levels across the female life span: Implications for the sex bias in affective disorders. *Biological Psychiatry*, 72, 434–436.
- Gaynes, B. N., Dusetzina, S. B., Ellis, A. R., Hansen, R. A., Farley, J. F., Miller, W. C., & Sturmer, T. (2012). Treating depression after initial treatment failure: Directly comparing switch and augmenting strategies in STAR*D. *Journal of Clinical Psychopharmacology*, 32(1), 114–119.
- Ghanbari, Z., Haghollahi, F., Shariat, M., Foroshani, R., & Ashrafi, M. (2009). Effects of calcium supplement therapy in women with premenstrual syndrome. *Taiwan Journal of Obstetrics & Gynecology*, 48(2), 124–129.
- Grigoriadis, S., VonderPorten, E. H., Mamisashvili, L., Tomlinson, G., Dennis, C. -L., Koren, G., ... Ross, L. E. (2013). The impact of maternal depression during pregnancy on perinatal outcomes: A systematic review and meta-analysis. *Journal of Clinical Psychiatry*, 74(4), e321–e341.
- Grote, N. K., Bridge, J. A., Gavin, A. R., Melville, J. L., Iyengar, S., & Katon, W. J. (2010). A meta-analysis of depression during pregnancy and the risk of preterm birth, low birth weight, and intrauterine growth restriction. *Archives of General Psychiatry*, 67(10), 1012–1024.
- Harrison, N. (2013). Inflammation and mental illness. *Journal of Neurological Neurosurgical Psychiatry*, 84(9), e1.
- Hosseini, S. M., Bigian, M. W., Larkby, C., Brooks, M. M., Gorin, M. B., & Day, N. L. (2009). Trait anxiety in pregnant women predicts offspring birth outcomes. *Paediatric Perinatal Epidemiology*, 23(6), 557–566.
- Hovington, C. L., McGirr, A., Lepage, M., & Berlim, M. T. (2013). Repetitive transcranial magnetic stimulation (rTMS) for treating major depression and schizophrenia: A systematic review of recent meta-analyses. *Annals of Medicine*, 45(4), 308–321.
- Kieler, H., Artama, M., Engeland, A., Ericsson, O., Furu, K., Gissler, M., ... Haglund, B. (2012). Selective serotonin reuptake inhibitors during pregnancy and risk of persistent pulmonary hypertension of the newborn: A population based cohort study from the five Nordic countries. *British Medical Journal*, 344, d8012.
- Koren, G., & Nordeng, H. (2012). Antidepressant use during pregnancy: The risk-benefit ratio. *American Journal of Obstetrics & Gynecology*, 207(3), 157–163.
- Kupka, R. W., Altschuler, L. L., Nolen, W. A., Suppes, T., Luckenbaugh, D. A., Leverich, G. S., ... Post, R. M. (2007). Three times more days depressed than manic or hypomanic in both bipolar I and bipolar II disorder. *Bipolar Disorder*, 9(5), 531–535.
- Lam, R. W., Carter, D., Misri, S., Kuan, A. J., Yatham, L. N., & Zis, A. P. (1999). A controlled study of light therapy in women with late luteal phase dysphoric disorder. *Psychiatry Research*, 86(3), 185–192.

- Lanza di Scalea, T. (2009). Antidepressant medication use during breastfeeding. *Clinical OBGYN*, 52(3), 483–497.
- Lokuge, S., Frey, B. N., Foster, J. A., Soares, C. N., & Steiner, M. (2011). Depression in women: Windows of vulnerability and new insights into the link between estrogen and serotonin. *Journal of Clinical Psychiatry*, 72(11), 1563–1569.
- Los Angeles County Perinatal Mental Health Task Force. (2013). *Bringing light to motherhood: Community provider perinatal mental health toolkit* (2nd ed.). Los Angeles, CA: Los Angeles County Perinatal Mental Health Task Force.
- Luberto, C. M., White, C., Sears, R. W., & Cotton, S. (2013). Integrative medicine for treating depression: An update on the latest evidence. *Current Psychiatry Reports*, 15(9), 391. doi:10.1007/s11920-031-0391-2.
- Lucas, M., Asselin, G., Merette, C., et al. (2009). Effects of ethyl-eicosapentaenoic acid omega-3 fatty acid supplementation on hot flashes and quality of life among middle-aged women: A double-blind, placebo-controlled, randomized clinical trial. *Menopause*, 16(2), 357–366.
- Malm, H., Artama, M., Gissler, M., & Ritvanen, A. (2011). Selective serotonin reuptake inhibitors and risk for major congenital abnormalities. *Obstetrics & Gynecology*, 118(1), 111–120.
- Maschi, S., Clavenna, A., Campi, R., Schiavetti, B., Bernat, M., & Bonati, M. (2008). Neonatal outcome following pregnancy exposure to antidepressants: A prospective controlled cohort study. *British Journal of Obstetrics & Gynecology*, 115, 283–289.
- Massart, R., Mongeau, R., & Lanfumey, L. (2012). Beyond the monoaminergic hypothesis: Neuroplasticity and epigenetic changes in a transgenic mouse model of depression. *Philosophical Transactions of the Royal Society B*, 367, 2485–2494.
- McCloughen, A., & Foster, K. (2011). Weight gain associated with taking psychotropic medication: An integrative review. *International Journal of Mental Health Nursing*, 20(3), 202–222.
- Milgrom, J., Gemmill, A. W., Bilszta, J. L., Hayes, B., Barnett, B., ... Buist, A. (2008). Antenatal risk factors for postpartum depression: A large prospective study. *Journal of Affective Disorders*, 108, 147–157.
- Moses-Kolko, E. L., Berga, S. L., Kairo, B., Sit, D. K., & Wisner, K. L. (2009). Transdermal estradiol for postpartum depression: A promising treatment option. *Clinical Obstetrics & Gynecology*, 52(3), 516–529.
- National Centre for Health and Clinical Excellence. (2007). *Antenatal and postnatal mental health: Clinical management and service guidance (CG)*. London: NICE.
- O'Mahen, H., Himle, J. A., Gedock, G., Henshaw, E., & Flynn, H. (2013). A pilot randomized controlled trial of cognitive behavioral therapy for perinatal depression adapted for women with low incomes. *Depression and Anxiety*, 30, 679–687.
- Oats, M. P. (2003). Perinatal psychiatric disorders: A leading cause of maternal morbidity and mortality. *British Medical Bulletin*, 67, 219–229.
- Osborne, L. M., & Monk, C. (2013). Perinatal depression - The fourth inflammatory morbidity of pregnancy?: Theory and literature review. *Psychoneuroendocrinology*, 38(10), 1929–1952. doi:10.1016/j.psychneuen.2013.03.019.
- Palmsten, K., & Hernandez-Diaz, S. (2012). Can non-randomized studies on the safety of antidepressants during pregnancy convincingly beat confounding, chance, and prior beliefs? *Epidemiology*, 23(5), 686–688.
- Papakostas, G. I., Shelton, R. C., Zajecka, J. M., Etamad, B., Rickels, K., Clain, A., ... Bottiglieri, T. (2012). L-Methylfolate as adjunctive therapy for SSRI-resistant major depression: Results of two randomized, double-blind, parallel-sequential trials. *American Journal of Psychiatry*, 169, 1267–1274.
- Parry, B. L., Mahan, A. M., Mostofi, N., Lew, G. S., & Gillin, J. C. (1993). Light therapy of late luteal phase dysphoric disorder: An extended study. *American Journal of Psychiatry*, 150(9), 1417–1419.
- Pearson, R. M., Fernyhough, C., Bentall, R., Evans, J., Heron, J., & Joinson, C. (2013). Association between maternal depressogenic cognitive style during pregnancy and offspring cognitive style 18 years later. *American Journal of Psychiatry*, 170(4), 434–441.

- Pettinati, H. M., O'Brien, C. P., & Dundon, W. D. (2013). Current status of co-occurring mood and substance use disorders: A new therapeutic target. *American Journal of Psychiatry*, *170*, 23–30.
- Pramyothin, P., & Khaodhiar, L. (2010). Metabolic syndrome with the atypical antipsychotics. *Current Opinions in Endocrinology, Diabetes & Obesity*, *17*(5), 460–466.
- Pratt, L. A., Brody, D. J., & Gu, Q. (2011). *Antidepressant use in persons aged 12 and over: United States, 2005–2008. NCHS data brief, no 76*. Hyattsville, MD: National Center for Health Statistics.
- Rai, D., Lee, B. K., Dalman, C., Golding, J., Lewis, G., & Manusson, C. (2013). Parental depression, paternal antidepressant use during pregnancy, and risk of autism spectrum disorders. *British Medical Journal*, *346*, f2059.
- Rapkin, A. J., & Winer, S. A. (2008). The pharmacologic management of premenstrual dysphoric disorder. *Expert Opinions in Pharmacotherapy*, *9*(3), 429–445.
- Ross, L. E., Grigoriadis, S., Mamishashvili, L., Vonderporten, E. H., Roerecke, M., Rehm, J., ... Chueng, A. (2013) Selected pregnancy and delivery outcomes after exposure to antidepressant medication: A systematic review and metaanalysis. *Journal of the American Medical Association Psychiatry*, *70*(4), 436–443.
- Sandman, C. A., Davis, E. P., Buss, C., & Glynn, L. M. (2012). Exposure to prenatal psychobiological stress exerts programming influences on the mother and her fetus. *Neuroendocrinology*, *95*, 8–21.
- Sidebottom, A. C., Harrison, P. A., Godecker, A., & Kim, H. (2012). Validation of the Patient Health Questionnaire (PHQ)-9 for prenatal depression screening. *Archives of Women's Mental Health*, *15*(5), 367–374.
- Soares, C. N. (2013). Depression in peri- and postmenopausal women: Prevalence, pathophysiology and pharmacological management. *Drugs & Aging*, *30*(9), 677–685.
- Sockol, L. E., Epperson, C. N., & Barber, J. P. (2011). A meta-analysis of treatment for perinatal depression. *Clinical Psychology Review*, *31*(5), 839–849.
- Spinelli, M. G. (2009). Postpartum psychosis: Detection of risk and management. *American Journal of Psychiatry*, *166*(4), 405–408.
- Stahl, S. M. (2000). *Essential psychopharmacology: Neuroscientific basis and practical applications* (2nd ed.). Cambridge: Cambridge University Press.
- Sternfeld, B., Guthrie, K. A., Ensrud, K. E., Lacroix, A. Z., Larson, J. C., Dunn, A. L., ... Caan, B. J. (2014). Efficacy of exercise of menopausal symptoms: A randomized controlled trial. *Menopause*, *21*(4), 330–338.
- Straub, H., Adams, M., Kim, J. J., & Silver, R. K. (2012). Antenatal depressive symptoms increase the likelihood of preterm birth. *American Journal of Obstetrics & Gynecology*, *207*(329), e1–e4.
- Suri, R., Helleman, G., Stowe, Z. N., Cohen, L. S., Aquino, A., & Altschuler, L. L. (2011). A prospective, naturalistic, blinded study of early neurobehavioral outcomes for infant following prenatal antidepressant exposure. *Journal of Clinical Psychiatry*, *72*(7), 1002–1007.
- Swalm, D., Brooks, J., Doherty, D., Nathan, E., & Jacques, A. (2010). Using the Edinburgh postnatal depression scale to screen for perinatal anxiety. *Archives of Women's Mental Health*, *13*, 515–522.
- Topiwala, A., Hothi, G., & Ebmeier, K. P. (2012). Identifying patients at risk of perinatal mood disorders. *Practitioner*, *256*(1751), 15–18. 2.
- United States Food and Drug Administration. (2013). Use of selective serotonin reuptake inhibitors in pregnancy and cardiac malformations: A propensity-score matched cohort in CPRD. *Pharmacoepidemiology and Drug Safety*, *22*(9), 942–951.
- USA Preventive Services Task Force. (2009). Screening for depression in adults: U.S. Preventive Services Task Force Recommendations Statement. *Annals of Internal Medicine*, *151*, 784–792.
- van der Wal, M. F., van Eijsden, M., & Bonsel, J. G. (2007). Stress and emotional programs during pregnancy and excessive infant crying. *Journal of Developmental Behavioral Pediatrics*, *28*(6), 431–437.
- Wisner, K. L., Sit, K. K., Hanusa, B. H., Moses-Kolko, E. L., Bogen, D. L., Hunker, D. F., ... Singer, L. T. (2009). Major depression and antidepressant treatment: Impact on pregnancy and neonatal outcomes. *American Journal of Psychiatry*, *166*, 557–566.

- Wisner, K. L., Sit, D. K. Y., & Moses-Kolko, E. L. (2006). Antipsychotic treatment during pregnancy: A model for decision-making. *Advances in Schizophrenia and Clinical Psychiatry*, 3(1), 48–55.
- Wisner, K. L., Zarin, D. A., Holmboe, E. S., Appelbaum, P. S., Gelenberg, A. J., Leonard, H. L., & Frank, E. (2000). Risk-benefit decision making for treatment of depression during pregnancy. *American Journal of Psychiatry*, 157(12), 1933–1940.
- World Health Organization. (2009). *Mental health aspects of women's reproductive health: A review of the literature*. Geneva: WHO Press.
- Yawn, B. P., Dietrich, A. J., Wollan, P., Bertram, S., Graham, D., Huff, J., ... Pace, W. D. (2012). TRIPPD: A practice-based network effectiveness study of postpartum depression screening and management. *Annals of Family Medicine*, 10, 320–329.
- Yonkers, K. A., Norwitz, E. R., Smith, M. V., Lockwood, C. J., Gotman, N., Luchansky, E., ... Belanger, K. (2012). Depression and serotonin reuptake inhibitor treatment as risk factors for preterm birth. *Epidemiology*, 23(5), 677–685.
- Yonkers, K. A., Pearlstein, T. B., & Gotman, N. (2013). A pilot study to compare fluoxetine, calcium, and placebo in the treatment of premenstrual syndrome. *Journal of Clinical Psychopharmacology*, 33(5), 614–620.
- Yonkers, K. A., Wisner, K. L., Stewart, D. E., Oberlander, T. F., Dell, D. L., Stotland, N., ... Lockwood, C. (2009). The management of depression during pregnancy: A report from the American Psychiatric Association and the American College of Obstetrics and Gynecology. *General Hospital Psychiatry*, 31(5), 403–413.
- Ystrom, E. (2012). Breastfeeding cessation and symptoms of anxiety and depression: A longitudinal cohort study. *BMC Pregnancy Childbirth*, 12(1), 36.
- Zhang, X., Liu, K., Sun, J., & Zheng, Z. (2010). Safety and feasibility of repetitive transcranial magnetic stimulation (rTMS) as a treatment for major depression during pregnancy. *Archives of Women's Mental Health*, 13(4), 369–370.