Bipolar disorder in women: Contraception and preconception assessment and counseling

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INTRODUCTION

Prepregnancy counseling is relevant to all female patients with bipolar disorder who are of reproductive age, regardless of their plans regarding pregnancy [1]. Unplanned pregnancies are common in the general population, and the risk of unplanned pregnancies appears to be greater in women with bipolar disorder than in healthy controls [2]. Contraception should be encouraged for patients who wish to avoid pregnancy, and patients who consider becoming pregnant should receive preconception counseling about the risks to the patient and her child.

This topic reviews contraception and the preconception assessment and counseling of women with bipolar disorder. Indications for maintenance pharmacotherapy during pregnancy, selecting preconception and prenatal maintenance treatment for bipolar patients, and the teratogenic and postnatal effects of medications used for bipolar disorder are discussed separately. (See "Bipolar disorder in women: Indications for preconception and prenatal maintenance pharmacotherapy" and "Bipolar disorder in women: Preconception and prenatal maintenance pharmacotherapy" and "Teratogenicity, pregnancy complications, and postnatal risks of antipsychotics, benzodiazepines, lithium, and electroconvulsive therapy".)

DEFINITION OF BIPOLAR DISORDER

Bipolar disorder is characterized by episodes of mania (table 1), hypomania (table 2), and major depression (table 3) [3]. The subtypes of bipolar disorder include bipolar I and bipolar II. Patients with bipolar I disorder experience manic episodes, and nearly always experience major depressive and hypomanic episodes. Bipolar II disorder is marked by at least one hypomanic episode, at least one major depressive episode, and the absence of manic episodes. Additional information about the clinical features and diagnosis of bipolar disorder is discussed separately. (See "Bipolar disorder in adults: Clinical features" and "Bipolar disorder in adults: Assessment and diagnosis", section on 'Diagnosis'.)

CONTRACEPTION

We discuss family planning desires and contraceptive need with all women of reproductive potential. Information to guide the selection of contraception in women with mood and other medical disorders is available through the World Health Organization Medical Eligibility Criteria and the United States Centers for Disease Control US Medical Eligibility Criteria for Contraceptive Use. While the guidelines are generally similar, the clinician should use the one that best matches the population.

Unmet contraceptive need — Small studies suggest that women with bipolar disorder are characterized by suboptimal use of contraception, lower levels of family planning, and higher rates of unintended pregnancy:

- In a survey of 136 female patients receiving maintenance pharmacotherapy (including drugs that appear to be teratogenic), 41 percent did not use birth control [4].
- Studies comparing euthymic, reproductive-age women with bipolar disorder to matched healthy control women reported women with bipolar disorder were three times more likely to have an unintended pregnancy or be ambivalent about pregnancy [2,5].

Approach to contraceptive selection — While the patient ultimately selects her contraceptive method, we take the following approach to thinking about contraception in women with bipolar disorder:

- For women who desire the most effective contraception or durable contraception, we discuss long-acting reversible contraceptives (LARCs), including the copper intrauterine device (IUD), levonorgestrel-releasing IUDs, and the etonogestrel implant (figure 1). These methods require minimal user action, have failure rates of less than 1 percent, have high continuation rates in this population, and last from 3 to 12 years, depending on the device. In particular, the copper IUD contains no hormones, does not interfere with

concurrent medications, and maintains efficacy for up to 12 years, although it may make menstrual bleeding heavier. While data regarding progestin-releasing IUDs or implants in women with bipolar disorder are limited, use of these products does not appear to worsen mood or increase the risk of hospitalization, and both generally lessen menstrual flow [6,7]. (See 'Impact of hormonal contraception on mood' below.)

LARC methods are similar in efficacy to sterilization but have no surgical risk. However, for women who do not desire future fertility, surgical sterilization (male or female) is a reasonable option. General principles of contraceptive selection and the attributes of various contraceptive methods are presented separately:

- (See "Contraception: Counseling and selection".)
- (See "Intrauterine contraception: Background and device types".)
- (See "Intrauterine contraception: Candidates and device selection".)
- (See "Contraception: Etonogestrel implant".)
- (See "Overview of female permanent contraception".)
- (See "Vasectomy".)

- For women who do not find LARC methods acceptable or desire contraception for a only short timeframe, we discuss hormonal contraception, including combined estrogen-progestin products (oral pills, transdermal patch, and vaginal rings) and progestin-only methods (depot medroxyprogesterone acetate [DMPA] injections and progestin-only oral pills). These methods are effective when used correctly and consistently, although they are not as effective as LARC (figure 1). Concerns for these methods include need for regular action on the part of the user and higher discontinuation rates in this population [7]. Mood and medication interactions are reviewed below. (See 'Impact of hormonal contraception on mood' below and 'Potential drug interactions' below.)

  More information on each contraceptive method is reviewed in detail separately.

  - (See "Combined estrogen-progestin oral contraceptives: Patient selection, counseling, and use".)
  - (See "Depot medroxyprogesterone acetate (DMPA): Formulations, patient selection and drug administration".)
  - (See "Depot medroxyprogesterone acetate (DMPA): Efficacy, side effects, metabolic impact, and benefits".)
  - (See "Contraception: Progestin-only pills (POPs)".)

- For women who desire contraception only at the time of vaginal intercourse, we discuss pericoital and barrier contraceptives. Pericoital contraception includes the single-size

diaphragm (commercial name Caya) with spermicide, cervical cap (where available) with spermicide, and the spermicide-containing contraceptive sponge. Barrier methods include male and female condoms. Major limitations of these methods include lower efficacy compared with the above methods and need for patient-directed use with every act of intercourse (figure 1).

- (See "Pericoital (on demand) contraception: Diaphragm, cervical cap, spermicides, and sponge".)
- (See "External (formerly male) condoms".)
- (See "Internal (formerly female) condoms".)

- Women who require emergency contraception are candidates for any of the available options [8]. The copper IUD is the most effective method, does not impact mood, and provides ongoing contraception. While not specifically studied in women with bipolar disorder, the hormone-based emergency contraceptives (ulipristal acetate and levonorgestrel) are short-acting, and complications with use in this population have not been reported. (See "Emergency contraception".)

- Women at risk of sexually transmitted infection are advised about consistent condom use (male or female) even if other contraceptive methods are being used. (See "External (formerly male) condoms" and "Internal (formerly female) condoms".)

Impact of hormonal contraception on mood — Although supporting data are limited, hormonal methods of contraception do not appear to increase the risk of hospitalization for mood exacerbations in women with bipolar disorder, and one small study reported mood stabilization in women treated with DMPA [6,7,9]. However, studies of progestins in other populations have reported possible negative effects on mood, so we advise women who desire hormonal contraceptives to track their symptoms and have close follow-up [10].

Of note, use of the estrogen receptor antagonist tamoxifen can be effective for mania [11]; this antimanic effect is discussed separately. (See "Bipolar mania and hypomania in adults: Choosing pharmacotherapy", section on 'Other options'.)

Potential drug interactions — Anticonvulsant medications, including carbamazepine, induce hepatic enzymes and increase the metabolism of hormonal contraceptives, which in turn decreases contraceptive efficacy [12]. Thus, we, along with other experts, advise women with bipolar disorder who are treated with carbamazepine to avoid combined estrogen-progestin contraception (oral pills, transdermal patch, and vaginal ring) and progestin-only pills, and instead choose an IUD, etonogestrel implant, or DMPA injection [8,12]. Carbamazepine use does not appear to lessen DMPA and etonogestrel implant efficacy because these methods

provide continuous hormone exposure above the threshold required for ovulation suppression, although supporting data are limited. The hormone effect of the levonorgestrel-releasing IUDs is mainly local within the uterus and not impacted by alterations in hepatic enzymes. Additional information about the interaction of carbamazepine and hormonal contraception is discussed separately. (See "Overview of the management of epilepsy in adults", section on 'Contraception'.)

However, hormonal contraception may be acceptable for some women who also require carbamazepine. For situations where a LARC method is not appropriate or declined, or the patient has other medical indications for hormonal contraceptive use (eg, heavy menstrual bleeding), the use of a combined hormonal or progestin-only method affords better protection from unintended pregnancy than no contraception at all. Women who desire oral estrogen-progestin pills may benefit from 24/4 dosing regimens rather than the traditional 21/7 approach because 24/4 products have fewer hormone-free days, although supporting data are not available. Women who elect to use hormonal contraception and carbamazepine are also counseled on the regular use of condoms (male or female) to provide additional contraception. Detailed information about carbamazepine and hormonal contraception failure is discussed separately. (See "Overview of the management of epilepsy in adults", section on 'Contraception'.)

Women who require lamotrigine are also advised to avoid estrogen-containing contraceptives because estrogen increases lamotrigine clearance, and thus reduces its efficacy for treating bipolar disorder [13]. However, for women who desire combined estrogen-progestin methods either for contraception or treatment of other medical disorders, a reasonable alternative approach is to prescribe higher doses of lamotrigine. Additional information about drug-drug interactions between lamotrigine and combined hormonal contraception is discussed separately. (See "Antiseizure medications: Mechanism of action, pharmacology, and adverse effects", section on 'Lamotrigine'.)

PRECONCEPTION ASSESSMENT

The clinical assessment of bipolar patients who consider becoming pregnant includes a psychiatric and general medical history, mental status and physical examination, and focused laboratory tests [14-16]. The general preconception evaluation for all patients is discussed separately. (See "The preconception office visit", section on 'Risk assessment at the preconception office visit'.)

The psychiatric history for bipolar patients should emphasize the following:

- **Age** – Women should be aware that fertility declines and the risk of fetal chromosomal abnormalities rises with increasing age, especially after the mid-30s.

- **Weight** – Many female bipolar patients are obese, which increases the risk of pregnancy complications (eg, gestational diabetes, preeclampsia, cesarean delivery, and fetal neural tube defects) [17] (see "Obesity in pregnancy: Complications and maternal management"). Clinicians should encourage patients to conceive at a normal body mass index (BMI), which is calculated from height and weight (calculator 1). Weight loss for overweight patients with dietary therapy, exercise, and other treatments is discussed separately. (See "Obesity in adults: Overview of management".)

- **Current status of bipolar disorder and course of illness** – Clinicians should assess current symptoms of mania (table 1), hypomania (table 2), and major depression (table 3); number of prior mood episodes, particularly during the previous two to five years; and history of psychotic features (delusions and/or hallucinations) and suicidal and homicidal ideation and behavior. Bipolar patients are encouraged to delay pregnancy until their illness is stable, and a long (eg, ≥2 years) duration of euthymia prior to conception is preferred.

- **Medications** – Several medications used to treat bipolar disorder appear to be teratogenic, including valproate and carbamazepine, and to a lesser extent lithium. (See "Teratogenicity, pregnancy complications, and postnatal risks of antipsychotics, benzodiazepines, lithium, and electroconvulsive therapy".)

- **Supplements** – Many patients do not realize that herbal supplements are potentially harmful to the fetus.

- **Substance abuse** – Drug, alcohol, and nicotine abuse is widespread among bipolar patients. Women with bipolar disorder should be screened for substance use disorders, educated about the potential impact on the baby, and offered substance abuse treatment; these issues are discussed separately.

  - (See "Bipolar disorder in adults: Clinical features", section on 'Substance use disorders'.)
  - (See "Substance use during pregnancy: Screening and prenatal care".)
  - (See "Substance use disorders: Clinical assessment".)
  - (See "Alcohol use disorder: Psychosocial management".)
  - (See "Cannabis use disorder: Clinical features, screening, diagnosis, and treatment".)
  - (See "Opioid use disorder: Pharmacologic management".)
  - (See "Stimulant use disorder: Treatment overview".)
    (See "Stimulant use disorder: Psychosocial management".)

- (See "Bipolar disorder in adults: Clinical features".)

- **Psychosocial functioning** – Psychosocial stressors (eg, domestic violence, marital conflict, inadequate social support, and financial problems) are likely to disrupt the patient's stability and should be addressed before pregnancy

The general medical history should emphasize the metabolic syndrome and diabetes, which commonly occur in bipolar patients and should be stabilized prior to attempting conception [17]. (See "Metabolic syndrome (insulin resistance syndrome or syndrome X)" and "Overview of general medical care in nonpregnant adults with diabetes mellitus".)

FERTILITY

Bipolar patients may have more difficulty conceiving than individuals without the disorder, but this is not established [18]. One review found that fertility rates are lower among patients with bipolar disorder than individuals without the disorder [19].

It is not known if ovulatory function in bipolar patients is impaired, as reflected by menstrual difficulties, due to conflicting results across studies. A retrospective study found that patients who had yet to start pharmacotherapy (n = 295) were more likely to report menstrual cycle irregularities than controls (n = 619; 34 versus 22 percent) [13]. However, another study that assessed patients with bipolar disorder (n = 103) and controls (n = 36) found that the rates of menstrual abnormalities were comparable [20].

Menstrual cycle irregularities in some bipolar patients are due to medications, including:

- **Antipsychotics** – Antipsychotics can increase prolactin levels, which can result in oligomenorrhea or amenorrhea and galactorrhea. Although hyperprolactinemia is more likely to occur with either risperidone or first-generation antipsychotics, it has also been reported with other second-generation antipsychotics, such as olanzapine and ziprasidone [13,21-23]. (See "Clinical manifestations and evaluation of hyperprolactinemia".)

- **Valproate** – Valproate use has been linked with polycystic ovarian syndrome (menstrual irregularities and hyperandrogenism) in bipolar patients [13,24]. (See "Clinical manifestations of polycystic ovary syndrome in adults".)

Assessing menstrual cycle patterns before starting antipsychotics or valproate can help determine if medications are causing menstrual abnormalities that are observed after starting the drugs. Additional information about the evaluation, causes, and treatment of infertility is discussed separately. (See "Overview of infertility".)

PRECONCEPTION AND PRENATAL PHARMACOTHERAPY

For bipolar patients who plan to or do become pregnant, we suggest maintenance pharmacotherapy. (See "Bipolar disorder in women: Indications for preconception and prenatal maintenance pharmacotherapy" and "Bipolar disorder in women: Preconception and prenatal maintenance pharmacotherapy".)

RISKS ASSOCIATED WITH PREGNANCY

Although pregnancy in bipolar patients is associated with several risks, bipolar disorder is not a contraindication for pregnancy [25]. We encourage clinicians to include the spouse when discussing these risks with the patient, as well as other family members who may be called upon to support the patient during and after the pregnancy.

Risk of maternal mood episodes — Clinicians should describe the risk of suffering bipolar mood episodes during pregnancy. As an example, a retrospective study in parous women with bipolar I disorder (n = 980) found that perinatal mood episodes had occurred in 56 percent, and among parous bipolar II patients, 40 percent [26]. Clinicians should also explain that pharmacotherapy may reduce this risk. In addition, clinicians, patients, and family members are encouraged to develop prespecified contingency plans for treating mood episodes that occur during pregnancy [25].

Relapse during pregnancy — Although bipolar patients often suffer mood episodes during pregnancy, it is not known if pregnancy changes the risk of recurrence. Some patients may experience fewer recurrences during pregnancy [27], whereas the course of illness in other pregnant patients remains unchanged or worsens [28,29].

In two retrospective studies of pregnant bipolar patients, recurrent mood episodes occurred in 5 and 23 percent:

- One study in pregnant patients (n = 436) found that recurrent mood episodes occurred in 5 percent [30].
- In another study (n = 1120), recurrences during pregnancy were observed in 23 percent of patients [31].

For pregnant bipolar patients, the risk of recurrence appears to be greatest during the first trimester. In a prospective observational study of 63 patients who suffered a mood episode, the timing was as follows [28]:

- First trimester – 66.6 percent of patients
- Second trimester – 23.8 percent
- Third trimester – 9.5 percent

The most common morbidity in pregnant bipolar patients is major depression [31,32]. In a prospective observational study of 81 mood episodes, the polarity was [28]:

- Major depression – 42 percent of episodes
- Mixed (concurrent symptoms of major depression and mania/hypomania) – 32 percent
- Mania or hypomania – 26 percent

This finding is consistent with the observation that depression is the predominant mood state for bipolar patients in general [33,34].

Clinical factors that may be associated with relapse during pregnancy include [28,32]:

- Shorter period of clinical stability prior to conception
- Discontinuing pharmacotherapy between six months prior to conception and 12 weeks after conception
- Unplanned pregnancy
- Current psychiatric comorbidity
- Lifetime duration of bipolar disorder ≥5 years
- History of at least one recurrent mood episode per year following onset of bipolar disorder

Relapse after discontinuing pharmacotherapy — Maintenance treatment during pregnancy may protect bipolar patients against recurrent mood episodes [32]. In a prospective observational study, euthymic pregnant patients who either continued (n = 27) or discontinued (n = 62) pharmacotherapy were followed through the end of pregnancy [28]. Maintenance medications included lithium, valproate, lamotrigine, carbamazepine, olanzapine, quetiapine, and antidepressants, with some patients taking more than one drug. Among the results:

- Relapse occurred in fewer patients who continued pharmacotherapy than patients who stopped pharmacotherapy (37 versus 86 percent)

- The proportion of time spent ill with a mood episode during pregnancy was less in patients who continued pharmacotherapy than patients who stopped pharmacotherapy (9 versus 43 percent of weeks)

Indications for maintenance pharmacotherapy during pregnancy, and selecting preconception and prenatal maintenance treatment for bipolar patients are discussed separately. (See "Bipolar

disorder in women: Indications for preconception and prenatal maintenance pharmacotherapy" and "Bipolar disorder in women: Preconception and prenatal maintenance pharmacotherapy".)

Recurrence of bipolar mood episodes in pregnant patients appears to be greater if medications are quickly discontinued [29]. In a prospective observational study of 62 patients who discontinued pharmacotherapy, the median time to recurrence was shorter if medications were discontinued in less than 15 days, compared with tapering and stopping medications over 15 or more days (2 versus 22 weeks) [28]. This finding is consistent with other studies that have found that recurrence is more likely if stable maintenance pharmacotherapy for bipolar disorder is terminated over 1 to 14 days, compared with a more gradual taper [35-37].

Postpartum mood episodes — The risk of bipolar mood episodes appears to be greater in the postpartum period than during pregnancy. A retrospective study of 1120 pregnancies in bipolar patients found that mood episodes occurred more than twice as often in the postpartum period (six months following live births) than during pregnancy [31]. A second retrospective study of 700 perinatal events in bipolar I patients found that more than 90 percent occurred in the postpartum period [26]. Additional information about the risk of postpartum mood episodes is discussed separately. (See "Bipolar disorder in postpartum women: Epidemiology, clinical features, assessment, and diagnosis", section on 'Epidemiology'.)

Congenital defects in offspring — The base rate for congenital defects in the offspring of patients with bipolar disorder appears to be no different than that of the general population, which is 2 to 5 percent [38-42]. Although one study found that bipolar disorder was associated with congenital anomalies, the study did not account for the use of psychotropic drugs [43]. Some medications that are used to treat bipolar disorder appear to be teratogenic, including valproate and carbamazepine, and to a lesser extent lithium.

The increased risk of malformations and adverse postnatal developmental effects due to treatment of bipolar disorder during pregnancy is discussed separately, as are the general principles of teratology.

- (See "Teratogenicity, pregnancy complications, and postnatal risks of antipsychotics, benzodiazepines, lithium, and electroconvulsive therapy".)
- (See "Antenatal use of antidepressants and the potential risk of teratogenicity and adverse pregnancy outcomes: Selective serotonin reuptake inhibitors".)
- (See "Antenatal use of antidepressants and risks of teratogenicity and adverse pregnancy outcomes: Drugs other than selective serotonin reuptake inhibitors".)
- (See "Congenital anomalies: Approach to evaluation".)

Risk of pregnancy complications — Adverse pregnancy and birth outcomes may occur more often in women with bipolar disorder regardless of treatment status, compared to women without bipolar disorder. A national registry study compared outcomes in pregnant bipolar patients who were treated with antipsychotics, carbamazepine, lamotrigine, lithium, and/or valproate (n = 320), pregnant bipolar patients who were not treated with these drugs (n = 554), and pregnant women without bipolar disorder who did not receive these drugs (n = 331,263) [42]. The analyses, which controlled for potential confounders such as maternal age and substance use disorders, found that:

- Induced or planned caesarean delivery occurred in more treated and untreated bipolar patients than women without bipolar disorder (38 and 31 versus 21 percent)
- Preterm birth occurred in more treated and untreated bipolar patients than women without bipolar disorder (8 and 8 versus 5 percent)
- Adverse pregnancy and birth outcomes were comparable for treated and untreated bipolar patients

In addition, a study of an administrative dataset included pregnant women with bipolar disorder (n >1800) and pregnant women with no mental illness (n >432,000), and found that bipolar disorder was associated with preterm birth (odds ratio 2.0, 95% CI 1.7-2.3) and severe large for gestational age birthweight (>97th percentile; odds ratio 1.3, 95% CI 1.1-1.5) [43]. Although the analyses controlled for several potential confounds (eg, maternal age and gestational hypertension and diabetes), the study did not control for other factors (eg, psychotropic drug use).

Prenatal infections and bipolar disorder in offspring — It is not known if in utero exposure to infectious agents is a risk factor for developing bipolar disorder, due to conflicting results across observational studies:

- ***Toxoplasma gondii*** – Three studies suggest that prenatal exposure to *Toxoplasma gondii* is associated with bipolar disorder in the offspring, whereas a fourth study found no association:
  - One study found that seropositivity to *Toxoplasma gondii* antibodies was higher in bipolar patients (n = 110) than healthy controls (n = 106; 77 versus 48 percent) [44], and a second study also found elevated antibodies in bipolar patients (n = 54) compared with controls (n = 314; odds ratio 2) [45]. In a third study that identified bipolar individuals (n = 41) in a nationally representative sample from the United States,

Toxoplasma gondii seroprevalence was associated with bipolar disorder (odds ratio 2) [46].

- However, one study compared 127 bipolar patients and 127 matched controls for antibodies to *Toxoplasma gondii* in blood drawn within one week of birth, and found no association between neonatal seropositivity and an increased risk of bipolar disorder [47].

- **Influenza** – A study compared 92 adult bipolar patients and 722 matched controls for in utero exposure to influenza (based upon clinical diagnoses of mothers), and found that gestational exposure to influenza at any time during pregnancy was four times greater in offspring with bipolar disorder, compared with controls [48]. In a subsequent study that used the same dataset, exposure to influenza was based upon maternal serologies; the second study found no increase in risk of bipolar disorder among offspring of mothers with serologic documentation of influenza exposure [49]. However, both studies found that in utero exposure to influenza was associated with a five- to sixfold greater risk of bipolar disorder with psychotic features.

- **Other** – Onset of bipolar disorder does not appear to be associated with exposure to cytomegalovirus [45,47] or to herpes simplex virus type 1 and 2 [47].

Obstetric complications and bipolar disorder in offspring — Obstetrical complications do not appear to play a role in the pathogenesis of bipolar disorder:

- A meta-analysis of eight observational studies found that exposure to obstetric complications (eg, maternal anemia, rubella, prematurity, prolonged labor, and neonatal respiratory problems) was comparable for bipolar patients (n = 272) and healthy controls (n = 331; 31 versus 29 percent) [50].

- In a subsequent retrospective study that compared 120 bipolar patients with 98 healthy controls, difficulties during delivery (eg, breech delivery, cesarean section, cord around the neck, and labor >24 hours) were comparable for patients and controls (66 and 57 percent) [51].

- A national registry study found that in bipolar patients (n = 724) and matched controls without bipolar disorder or psychotic disorder (n = 1419), exposure to obstetric complications (uterine bleeding, maternal hypertension, breech presentation, forceps delivery, emergency cesarean section, induced labor, and neonatal monitoring or intensive care) was comparable, after adjusting for maternal factors such as age, education, number of previous births, psychiatric history, and smoking [52].

However, a national registry study found an association between preterm birth and increased risk of hospitalization in adulthood for bipolar disorder, which occurred in a monotonic manner [53]. Compared to adults with term births:

- Adults born at 32 to 36 weeks were three times more likely to have bipolar disorder (hazard ratio 3, 95% CI 2-5)
- Adults born at less than 32 weeks gestation were seven times more likely to have bipolar disorder (hazard ratio 7, 95% CI 3-21)

Risk of child inheriting psychopathology

Bipolar disorder — Bipolar patients who consider having children typically want information about the risk that offspring will inherit bipolar disorder. Suggestions for prenatal psychiatric genetic counseling are discussed in the tables (table 4 and table 5). Although patients may benefit from specialist psychiatric genetic counseling [54], this service is often not available.

The genetics of bipolar disorder are discussed separately. (See "Bipolar disorder in adults: Epidemiology and pathogenesis", section on 'Genetics'.)

Other disorders — The offspring of bipolar parents typically inherit psychopathology other than bipolar disorder, including [55-65]:

- Schizophrenia
- Schizoaffective disorder
- Unipolar major depression
- Substance use disorders
- Oppositional defiant disorder and conduct disorder
- Disruptive mood dysregulation disorder
- Attention deficit hyperactivity disorder
- Anxiety disorders

As an example, an observational study followed 108 offspring with at least one bipolar parent for up to 12 years, from adolescence (mean age at study intake 17 years) to adulthood [66]. Among the offspring, the lifetime prevalence of at least one psychiatric diagnosis was 72 percent. However, a diagnosis of bipolar I disorder, bipolar II disorder, or cyclothymic disorder was made in only 13 percent. By contrast, the lifetime prevalence of anxiety disorders, substance use disorders, and unipolar major depression was 25, 23, and 17 percent.

Risk of developmental disorders in offspring — Maternal bipolar disorder may not be associated with developmental disorders in the offspring. A prospective observational study

included offspring of women with prenatal bipolar disorder who were not treated with psychotropic medications (n = 27), and offspring of women who did not have bipolar disorder and were not treated with psychotropic medications (n = 116) [67]. Assessments of the infants at age one year found that neuromotor, cognitive, and behavioral functioning were comparable for the two groups.

Reducing risks — Pregnancy outcomes may be improved in bipolar patients who:

- **Achieve clinical stability prior to conception** – For bipolar patients who want to conceive, we suggest that they wait until they are clinically stable for at least 6 to 24 months [25]. A prospective observational study of 89 pregnant bipolar patients found that a short period of clinical stability between the most recent mood episode and conception was associated with recurrent mood episodes during pregnancy [28].

- **Use folic acid** – Folic acid is recommended for all women planning to conceive and is discussed separately. (See "Preconception and prenatal folic acid supplementation" and "Nutrition in pregnancy: Dietary requirements and supplements", section on 'Folate/folic acid' and "Management of epilepsy during preconception, pregnancy, and the postpartum period", section on 'Folic acid supplementation'.)

Other preconception interventions that can reduce risks to a woman's pregnancy are discussed separately. (See "The preconception office visit", section on 'Interventions'.)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (See "Patient education: Bipolar disorder (The Basics)" and "Patient education: Coping with high drug prices (The Basics)".)

- Beyond the Basics topics (See "Patient education: Bipolar disorder (Beyond the Basics)" and "Patient education: Coping with high prescription drug prices in the United States (Beyond the Basics)".)

These educational materials can be used as part of psychoeducational psychotherapy. (See "Bipolar disorder in adults: Psychoeducation and other adjunctive maintenance psychotherapies", section on 'Group psychoeducation'.)

The National Institute of Mental Health also has educational material explaining the symptoms, course of illness, and treatment of bipolar disorder in a booklet entitled "Bipolar Disorder," which is available online at the website or through a toll-free number, 866-615-6464. The web site also provides references, summaries of study results in language intended for the lay public, and information about clinical trials currently recruiting patients.

More comprehensive information is provided in many books written for patients and family members, including The Bipolar Disorder Survival Guide: What You and Your Family Need to Know, written by David J. Miklowitz, PhD (published by The Guilford Press, 2002); An Unquiet Mind: A Memoir of Moods and Madness, written by Kay Jamison, PhD (published by Random House, 1995); and Treatment of Bipolar Illness: A Casebook for Clinicians and Patients, by RM Post, MD, and GS Leverich, LCSW (published by Norton Press, 2008).

The Depression and Bipolar Support Alliance (available at the website or 800-826-3632) is a national organization that educates members about bipolar disorder and how to cope with it. Other functions include increasing public awareness of the illness and advocating for more research and services. The organization is administered and maintained by patients and family members, and has local chapters.

The National Alliance on Mental Illness (available at the website or 800-950-6264) is a similarly structured organization devoted to education, support, and advocacy for patients with any mental illness. Bipolar disorder is one of their priorities.

SUMMARY

- Bipolar disorder is characterized by episodes of mania (table 1), hypomania (table 2), and major depression (table 3). (See 'Definition of bipolar disorder' above and "Bipolar disorder in adults: Assessment and diagnosis", section on 'Diagnosis'.)

- Bipolar patients who want to avoid pregnancy should receive information about contraception, especially long-acting reversible contraceptives. Antiepileptics that are used to treat bipolar disorder may interact with hormonal contraception. Carbamazepine may render oral contraceptives ineffective, and conversely, oral contraceptives that include estrogen may reduce the effectiveness of lamotrigine. (See 'Contraception' above.)

- The clinical assessment of bipolar patients who consider becoming pregnant includes a psychiatric and general medical history, mental status and physical examination, and focused laboratory tests. The psychiatric history should emphasize age, body mass index (calculator 1), current clinical status of bipolar disorder and course of illness, medications, supplements, substance abuse, and psychosocial functioning. (See 'Preconception assessment' above.)

- Bipolar patients may have more difficulty conceiving than individuals without the disorder, but this is not established. Antipsychotics and valproate can cause ovulatory dysfunction. (See 'Fertility' above.)

- Euthymic bipolar patients often receive maintenance pharmacotherapy prior to conception and during pregnancy. (See "Bipolar disorder in women: Preconception and prenatal maintenance pharmacotherapy".)

- Up to 70 percent of pregnant bipolar patients suffer at least one mood episode during pregnancy, but it is not known if pregnancy changes the risk of recurrence. The risk of recurrence appears to be greatest during the first trimester, and the most common morbidity is major depression. Risk factors for recurrence include a shorter period of clinical stability prior to conception, discontinuing pharmacotherapy (especially if medications are tapered and stopped in less than 15 days), unplanned pregnancy, current psychiatric comorbidity, lifetime duration of bipolar disorder ≥5 years, and history of at least one recurrent mood episode per year following onset of bipolar disorder. (See 'Relapse during pregnancy' above.)

- Adverse pregnancy and birth outcomes appear to be more common in women with bipolar disorder regardless of treatment status, compared to women without bipolar disorder. (See 'Risk of pregnancy complications' above.)

- The base rate for congenital defects in the offspring of patients with bipolar disorder appears to be no different than that of the general population, which is two to five percent. However, some medications used to treat bipolar disorder appear to be teratogenic, including valproate and carbamazepine, and to a lesser extent lithium. (See

"Teratogenicity, pregnancy complications, and postnatal risks of antipsychotics, benzodiazepines, lithium, and electroconvulsive therapy".)

- Bipolar disorder aggregates within families and there is evidence that genes are involved in the pathogenesis of the disorder. The estimated prevalence of bipolar disorder in children of families with one bipolar parent is 9 percent, whereas the rate in the general population is 1 to 2 percent. (See 'Bipolar disorder' above.)

- In addition, the offspring of bipolar parents may inherit schizophrenia, schizoaffective disorder, unipolar major depressive disorder, substance use disorders, oppositional defiant disorder, conduct disorder, attention deficit hyperactivity disorder, and anxiety disorders. (See 'Other disorders' above.)

- Pregnancy outcomes may be improved in bipolar patients who achieve clinical stability prior to conception and use folic acid. (See 'Reducing risks' above.)

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