



## **Primary Psychotic Disorders**

### **Women with Schizophrenia**

#### *Self-Study*

#### **Contributors**

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#### **Learning Objectives**

1. To understand the relationship between female reproductive hormones and the clinical course of women with Schizophrenia.
2. To recognize sex-linked differences in the phenomenology of Schizophrenia.
3. To describe sexual health considerations in the treatment of women with Schizophrenia.
4. To identify general guidelines for care of women with Schizophrenia in the perinatal period.

#### **Demographics**

- The incidence of schizophrenia is slightly lower in women (male:female ratio of 1.4:1).
- Women tend to present at an older age.
  - Average onset of illness approximately 4 years later for women than for men.
  - Women show a more bimodal distribution in age of onset, with a unique second peak in the late 40's (around perimenopause).

#### **Hormones**

- Estrogen has a relatively neuroprotective effect on dopamine receptor sensitivity.
- Symptoms may fluctuate with the menstrual cycle: classically worsening at times when estradiol/progesterone levels are lower (e.g. follicular phase). This may correspond to more frequent hospitalizations during lower estrogen periods.
- Women with schizophrenia may have lower levels of estradiol throughout the menstrual cycle. This is not related to antipsychotic-induced hyperprolactinemia.
- Studies are ongoing to determine the role of progesterone and its metabolites such as allopregnanolone.
- Dehydroepiandrosterone Sulphate (DHEA-S) and testosterone may be elevated in first episode psychosis.

#### **Symptom Profile and Prognosis**

- Women tend to have better functioning in social relationships, academic work, and conduct. This could occur because women demonstrate overall better pre-morbid functioning, and/or due to later age of onset.
- There are no significant sex differences in rates of symptomatic and functional remission.
- Women have fewer negative symptoms.
- Men have more comorbid alcohol use.
- Medication considerations:



- Pre-menopausal women can usually achieve effects with lower medication doses in comparison with men, due to absorption, metabolism and the presence of estrogen at the dopamine receptor site.
- Women are at greater risk for torsades de pointes.
- Women are more susceptible to tardive dyskinesia.

### **Risk to Offspring**

- Schizophrenia has a strong genetic component. There are numerous genes involved, and the illness occurs due to a combination of genetic risk and environmental factors.
  - If one parent carries a diagnosis of schizophrenia, the probability that it will be passed down to the offspring is 13%.
  - If both parents have the diagnosis, the risk is 30-50%.
  - Children of parents with schizophrenia are also at higher risk for other mental health conditions (e.g. bipolar disorder).
- Risk may be greater for infants delivered during late winter or early spring.
- Maintaining adequate nutrition, vitamin D and folic acid supplements, immunizations, and avoiding substance use can reduce risk in offspring.

### **Conception, Fertility, and Family Planning**

- In the early to mid 1900's women with schizophrenia were believed to be subfertile. During this time period, women with schizophrenia were institutionalized, sexual activity was restricted, and opportunities for sexual encounters were limited.
- As deinstitutionalization began in the 1950s, women with schizophrenia returned to living in the community. Rates of conception have increased since this time, likely related to both increased opportunities for sexual encounters and advances in psychopharmacology (e.g. prolactin-sparing antipsychotics).
- Women with schizophrenia may experience sexual dysfunction related to the disease itself, physical health, psychotropic medications, and psychosocial factors.
  - Positive, negative, and cognitive symptoms of schizophrenia can impair the development of stable sexual relationships.
  - Treatment of women with Schizophrenia should include regular inquiry into sexual health and family planning. While many women with Schizophrenia successfully parent, severe and treatment-refractory disease may present a contraindication to parenting. In this case, concerns about symptoms of Schizophrenia impairing the patient's ability to parent should be communicated to the patient, and if appropriate, her partner and family.
- First-generation antipsychotics often cause hyperprolactinemia. Symptoms include amenorrhea, galactorrhea, gynecomastia, orgasmic dysfunction, decreased libido and decreased fertility in some women.
- If a woman desires pregnancy and is experiencing difficulty with conception due to antipsychotic-induced hyperprolactinemia, consider
  - 1) reducing the dose and/or
  - 2) switching to a prolactin-sparing antipsychotic.

### **Contraception and Sexual Health**

- Intimacy, sex, sexually transmitted infections, conception, and contraception should be discussed with all women of childbearing age, including women with schizophrenia.



- Many do not use contraception, including barrier methods, even when they do not wish to become pregnant. They experience higher rates of sexual assault, coerced sex, high-risk sexual behavior, and more lifetime sexual partners. As a result,
  - They have higher exposure to sexually transmitted infections.
  - Women with schizophrenia have high rates of unplanned, unwanted pregnancies. Emergency contraception may be helpful for women in this situation.
- Contraceptive counseling is critical to prevent unplanned, unwanted pregnancies and should be offered to any woman not desiring pregnancy. In particular, long-acting reversible contraceptives are the most effective form of birth control.
- Women receiving long acting injectable psychiatric medications may prefer the Depo-Provera injection; this can easily be given in conjunction with psychiatric LAIs to help with adherence.

### **Intimate Partner Violence**

- Women with schizophrenia have increased rates of intimate partner violence during pregnancy which may result in pregnancy complications and/or custody issues.
- Women with severe mental illness in both inpatient and outpatient settings have up to a 50% rate of IPV victimization and up to a 20% rate of IPV perpetration.
- Women may have difficulty determining the line between intimacy and assaultive behavior with physical closeness.
- Symptom burden can be higher in women who experience IPV and result in increased risk of hospitalization and suicidal ideation.

### **Pregnancy**

- Pregnancy is not protective against psychotic symptoms and severity of illness prior to pregnancy correlates with severity of illness during pregnancy. Women who discontinue psychiatric medications during pregnancy are at increased risk of relapse, impacting the woman and fetus. Half of women with schizophrenia who do not maintain psychiatric medication during pregnancy will relapse. The psychiatric provider should work with the OB provider to ensure the woman is not mistakenly advised to discontinue medication.
- Women with schizophrenia are less likely to receive prenatal care. Mental health providers should work closely with the OB provider to ensure patient is connected with prenatal care
- Regular follow up appointments with both mental health and OB providers are essential to assess for physical well-being and exacerbation in mental health symptoms.
- Women with schizophrenia have high risk of pregnancy complications including malformations, prematurity, low birth weight, small for gestational age infants, and stillbirth.
  - This may be confounded by reduced utilization of prenatal care, higher risk of poor nutrition, and higher rates of tobacco, alcohol, and illicit drug use.
- Pregnancy can impact the metabolism, excretion, absorption, and distribution of psychotropic medications so more frequent monitoring is needed. Rapid physiologic changes related to pregnancy may influence psychotic symptoms.
- Active psychotic symptoms can adversely affect nutrition, prenatal care and stress levels.
- If psychiatric symptoms require inpatient hospitalization during pregnancy, it is often difficult to find inpatient hospitalization opportunities as few can accommodate late stage pregnancy and active psychosis.
- Prenatal classes can be helpful to prepare for childbirth.
- Assessment of the support system of the woman and her capacity to care for children should be started during pregnancy.
- Psychiatric Advance Directives may be useful to prepare for possible psychiatric crisis.



## Postpartum

- Childbirth is a significant stressor and can trigger psychotic symptoms in women with schizophrenia.
- Discontinuation of psychotropic medications increases risk for relapse of mental illness in the postpartum period.
- Breastfeeding is possible while taking antipsychotics and should be discussed on a case by case basis in regards to effect on the infant.
- In bipolar disorder, increased vulnerability to symptom exacerbation is usually within the first month postpartum. In schizophrenia, increased vulnerability to symptom exacerbation can continue through the first postpartum year and frequent monitoring should continue during this time.
- Illness exacerbations during this time can include delusions about the birth, the baby, or hallucinations to harm mother or baby and result in difficulty bonding, poor infant care, infanticide, and suicide.
- Psychotic symptoms in the postpartum setting are often similar to pre-pregnancy symptoms.
- Additional support may be needed with housing, parenting, and child care.
- If parenting, sedating antipsychotics may make it difficult to care for the baby during the night
- About half of women with schizophrenia will temporarily or permanently lose custody of their children.

## Perimenopause

- Approximately 37% of women with schizophrenia develop the disorder after age 45, with some indications that their illness is more severe than in men who first develop schizophrenia around the same age.
- As mentioned above, the leading theory for the second epidemiologic peak in diagnosis is that estrogen serves as a protective factor.
- Currently there is no consensus on the role of estrogen replacement in treatment of schizophrenia, though one study has demonstrated decreased positive symptoms with in patients on a transdermal estrogen patch.
- Antipsychotic induced hyperprolactinemia can lead to loss of bone density, which can then be worsened by menopausal decreases in estrogen. Consider early screening for osteoporosis and cardiovascular disease in patients taking typical antipsychotics, risperidone, or paliperidone.

## References

Austin, J. C., Hippman, C., & Honer, W. G. (2012). Descriptive and numeric estimation of risk for psychotic disorders among affected individuals and relatives: Implications for clinical practice. *Psychiatry Research*, 196, 52–56

Bergemann, N., Mundt, C., Parzer, P., Jannakos, I., Nagl I., Salbach, B. ... Resch, F. (2005). Plasma concentrations of estradiol in women suffering from schizophrenia treated with conventional versus atypical antipsychotics. *Schizophrenia Research*, 73(2-3) 357-366.

Bergemann, N., Parzer, P., Nagl, I., Salbach, B., Runnebaum, B., Mundt, C., & Resch, F. (2002). Acute psychiatric admission and menstrual cycle phase in women with schizophrenia. *Archives of Women's Mental Health*, 5(3): 119-126.



Crawford, M.B., & DeLisi, L. E. (2016). Issues related to sex differences in antipsychotic treatment. *Current Opinion in Psychiatry*, 29, 211-217.

de Boer, M. K., Castelein, S., Wiersma, D., Schoevers, R. A., & Knegtering, H. (2015). The facts about sexual (dys)function in schizophrenia: An overview of clinically relevant findings. *Schizophrenia Bulletin*, 41(3), 674-686. DOI: 10:1093/schbul/sbv001

Frieder, A., Dunlop, A. L., Culpepper, L., & Bernstein, P. S. (2008). The clinical content of preconception care: Women with psychiatric conditions. *American Journal of Obstetrics & Gynecology*, supplement, S328-S332.

Galderisi, S., Bucci, P., Ucock, A., & Peuskens, J. (2012). No gender differences in social outcome in patients suffering from schizophrenia. *European Psychiatry*, 27(6), 406-408.

Grossman, L.S., Harrow, M., Rosen, C., Faull, R., & Strauss, G.P. (2008). Sex differences in schizophrenia and other psychotic disorders: A 20-year longitudinal study of psychosis and recovery. *Comprehensive Psychiatry* 49(6), 523-529.

Hafner, H. (2003). Gender differences in schizophrenia. *Psychoneuroendocrinology*, 28, 17-54.

Hatters Friedman, S., Loue, S. (2008). Intimate partner violence among women with severe mental illness. *Psychiatric Times*, 25(4), 52-53.

Howard, L. M. (2005). Fertility and pregnancy in women with psychotic disorders. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 119, 3-10.

Lange, B., Mueller, J.K., Leweke, F.M., & Bumb, J.M. (2017). How gender affects the pharmacotherapeutic approach to treating psychosis: A systematic review. *Expert Opinion on Pharmacotherapy*, 18, 351-362.

Miller, L. J. (1997). Sexuality, reproduction, and family planning in women with schizophrenia. *Schizophrenia Bulletin*, 23(4), 623-635.

Misiak, B., Frydecka, D., Loska, O., Moustafa, A.A., Samochowiec, J., Kasznia, J., & Stanczykiewicz, B. (2018). Testosterone, DHEA and DHEA-S in patients with schizophrenia: A systematic review and meta-analysis. *Psychoneuroendocrinology*, 89, 92-102.

Nau, M. L., & Peterson, A. L. (2014). Chronic mental illness in pregnancy and postpartum. In D. L. Barnes (Eds.), *Women's reproductive health across the lifespan* (pp.123-140). Switzerland: Springer.

Rasic, D., Hajek, T., Alda, M., & Uher, R. (2014). Risk of mental illness in offspring of parents with schizophrenia, bipolar disorder, and major depressive disorder: A meta-analysis of family high-risk studies. *Schizophrenia Bulletin*, 40(1), 28-38.

Robinson, G. E. (2012). Treatment of schizophrenia in pregnancy and postpartum. *Journal of Population Therapeutics and Clinical Pharmacology*, 19(3), e380-e386.

Seeman, M. V. (2013). Clinical interventions for women with schizophrenia: Pregnancy. *Acta Psychiatrica Scandinavica*, 127, 12-22. DOI: 10.1111/j.1600-0447.2012.01897.x



Sun, J., Walker, A.J., Dean, B., van den Buuse, M., & Gogos, A. (2016). Progesterone: The neglected hormone in schizophrenia? A focus on progesterone-dopamine interactions. *Psychoneuroendocrinology*, 74, 126-140.

Vigod, S. N., & Ross, L. E. (2010). Epidemiology of psychotic symptoms during pregnancy and postpartum in women with schizophrenia. *Current Women's Health Reviews*, 6, 17-21.