# Menstrual Psychosis and the Workup of New-Onset Psychosis in a Teenager

Jonathan T. Heinzman, MD, and E. Taylor Buckingham, MD, MPH

*A 14-year-old female with a history of attention-deficit/hyperactivity disorder (ADHD) and mild intellectual disability presented with 1-3 weeks of paranoid delusions, reduced appetite, decreased psychomotor activity, and a flat affect. After a negative workup for metabolic, endocrine, and toxicity causes she was psychiatrically hospitalized for one week and discharged on risperidone. Although she responded well, she presented again 3 weeks later for social withdraw, agitation, low oral intake, and presumed auditory and visual hallucinations. She had a fever to 102°F, tachycardia, hypertension, urinary incontinence, and had not spoken for 3 days. She stopped risperidone and was switched to lorazepam for concerns for neuroleptic malignant syndrome (NMS). She had little improvement in symptoms on lorazepam, and she had both a normal creatine kinase and no muscle rigidity. Workup for bacterial and viral encephalitis/meningitis was negative and she was presumed to have anti-NMDA receptor encephalitis. She began IVIG and IV methylprednisolone and responded well within 5 days. Antibodies for the NMDAR and voltage-gated potassium channel were then negative. As her symptoms had mostly resolved (except for persistent flat affect) and there was previous concern for NMS, she was discharged without medications. She returned a third-time, three weeks later for social withdrawal, flat affect, agitation, low oral intake, and concern for hallucinations. During the third hospitalization the patient's mother noticed she could predict her daughter's menstruation as these symptoms preceded menstruation for the last three months. Although the patient initially presented approximately 1 year after menarche at age 14, she had previously had monthly, regular menses lasting 5-6 days. She was diagnosed with menstrual psychosis, and her treatment included starting both leuprolide and norethindrone/ethinyl estradiol combined with low-dose haloperidol. Her symptoms significantly improved, and she has had no hospitalizations for nearly 4 years.*

## Psychosis and Early-Onset Schizophrenia

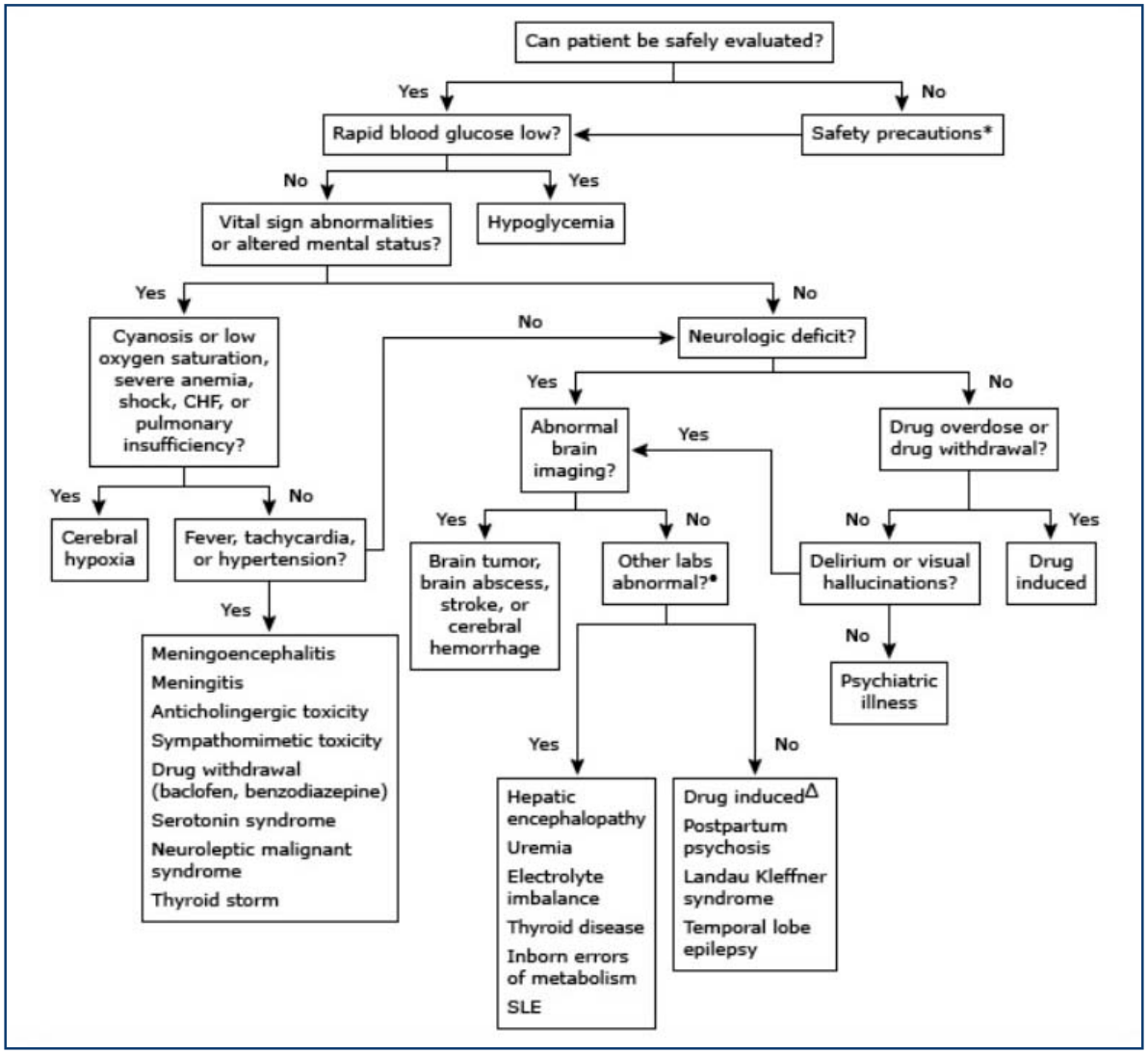
Prevalence estimates for psychotic symptoms in young patients cover a wide range, with a Swedish study estimating that 40% of psychotic symptoms in patients 13-18 years old are caused by early-onset schizophrenia.[1] However, the prevalence of psychosis at 13 years old was one per 10,000 and 17 per 10,000 at 18 years old. Other studies have estimated the prevalence of early-onset schizophrenia (schizophrenia before age 18) at approximately 0.5%.[2] Furthermore, studies of early-onset schizophrenia have found an equal gender ratio, as opposed to the predominantly male diagnosis of schizophrenia in adults.[1]

The clinical manifestations of early-onset schizophrenia can be varied, but the most common findings are prodromal symptoms. These can include developing deficits in attention, reading and language learning, and socialization.[1] While not specific for schizophrenia, studies have also shown that approximately 33% of youth with schizophrenia have a decline in their IQ to below 70 during the prodromal phase. Social withdrawal and worsening academic performance typically occur very gradually and begin over a year before psychotic symptoms. It can be difficult to identify prodromal symptoms, because the decline occurs gradually and the symptoms can mirror many other psychiatric conditions.

## Evaluating Psychosis in Young Patients

The differential diagnosis of psychosis in young patients is broad. Figure 1 shows a suggested approach to evaluating psychosis.[3]

**Figure 1. One Suggested Approach to Evaluating Secondary Psychosis in the Emergency Department Children[3]**




***Note:*** *Reproduced with permission from: Babu KM, Boyer EW. Emergency department evaluation of acute onset psychosis in children. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on July 27, 2018.) Copyright © 2018 UpToDate, Inc. For more information visit* **www.uptodate.com**.

When evaluating psychosis, it is helpful to consider primary versus secondary psychosis. Primary psychosis is due to a psychiatric etiology, such as schizophrenia, and secondary psychosis is due to a medical or substance use etiology. Both are life-threatening and reversible. For acute psychosis one can check blood glucose and vital signs to quickly evaluate for secondary causes, such as hypoglycemia, signs of infection such as fever, serotonin and neuroleptic malignant syndrome with fever, tachycardia, and hypertension. Another common cause of an acute secondary psychosis is substance use or overdose. While a blood alcohol level combined with a urine drug screen can identify many intoxications, cutaneous vasodilation, dry

skin, and pupil dilation can point towards less common intoxications that may not be captured in a drug screen, such as anticholinergics like diphenhydramine.

If the diagnosis is still uncertain, further workup could include CT/MRI brain imaging, to look for tumor, abscess, stroke, or hemorrhage, and an EEG can be obtained if there are concerns for seizures. Further lab testing may be warranted based on clinic presentation. If there is ataxia and macrocytic anemia, then it could be B12 deficiency. If there is peripheral neuropathy and gastroenteritis, then it could be heavy metal toxicity. If there is cerebellar ataxia, chorea, and dysarthria, it could be mercury toxicity. Finally, if there are signs of liver disease or eye findings, it could be Wilson's disease. Other less common etiologies include both steroid- and anticonvulsant-induced psychosis, and the less-known etiology of menstrual psychosis.

## Menstrual Psychosis

Menstrual psychosis was first observed in the 18th century, but since that time it has been described as a "forgotten disorder." A review by Brockington[4] identified 27 confirmed cases, based on detailed case report history on the onset of menses and psychosis. The review also identified 80 likely cases, based on case reports with retrospective history from relatives without optimal dating of menses and psychosis onset. The majority of the cases were reported in the early 1900s.[4,5] It is unclear why the number of cases in the literature decreased, however, it is likely a combination of both historical over diagnosis and current under diagnosis. Although literature on the prevalence is limited, an 1888 study found 1 case in 1,000 admissions,[4] while recent studies estimate a prevalence of 1 in 10,000.[5] No hormonal studies have been conducted and no genetic risk factors have yet been identified,[4] likely due to the "forgotten" nature limiting the number of investigations into the disorder.

Menstrual psychosis is characterized by an acute onset without prodromal symptoms, brief duration with full recovery, psychotic features, and a menstrual/monthly periodicity that has repeated at least once.[4] It appears related to the pituitary-ovarian axis, as has been correlated with anovulatory cycles. To better understand this connection, a brief review of the menstrual cycle is warranted.[6] The menstrual cycle begins with declining estrogen and progesterone inducing menstruation. Follicle-stimulating hormone (FSH) then causes ovarian granulosa cells to secrete estrogen. Estrogen stimulates uterine endometrium proliferation. When estrogen peaks, it induces the LH surge, causing ovulation. The corpus luteum (post-ovulatory follicle) then produces progesterone. Without fertilization, both estrogen and progesterone levels drop and menstruation begins.

Although menstrual psychosis has been classified by both the timing and stage of reproduction life, only the timing classification is prevalent in the literature.[4] *Premenstrual psychosis* is defined as symptoms starting during the second half of the menstrual cycle. *Catamenial psychosis* is defined as symptoms starting with the onset of menstruation. *Paramenstrual psychosis* is defined as symptoms with variable timing to the menstrual cycle. *Epochal menstrual psychosis* is characterized by a bipolar-like psychosis lasting the complete cycle with menstruation linked to switches between depression and mania.[4]

Catamenial psychosis was the subtype diagnosed in the patient case described above. Although the psychotic symptoms may look similar to that of schizophrenia or depression, the return to baseline between episodes, and monthly episodes can help differentiate menstrual psychosis from schizophrenia. Furthermore, there is typically no prodromal phase, as the psychosis begins abruptly—typically soon after menarche.[4] The diagnosis is difficult to make as there are no tests, screens, or associated risk factors.

The treatment of the menstrual psychoses is aimed at the menstrual cycle, which is the underlying cause of the psychosis. Treatment has been focused on both hormone replacement and suppression of the menstrual cycle, along with antipsychotics during the acute psychosis phase. Hormone replacement therapy includes using the GnRH agonist leuprolide with "add-

back" oral contraceptive pills (OCPs) to prevent iatrogenic estrogen deficiency.[4] No formal studies have investigated the proper duration or treatment and therefore all therapy is case-by-case and can potentially continue for many years.

Menstrual psychosis is a rare disorder with a crudely estimated prevalence of 1 in 10,000. Despite the prevalence indicating many women suffer from the disorder, the literature is limited to 80 suspected cases. Further research is needed to describe most aspects of the disorder, including prevalence, pathophysiology, genetic risk, and evidence-based therapies. Education on menstrual psychosis should also be increased as it is likely being missed clinically. Increased identification is important as the treatment is effective, safe, and much different than that of early onset schizophrenia.

### Take Home Summary

Further research and education into menstrual psychosis is important given the "forgotten" nature of the disease. Increased awareness will improve patient care through accurate diagnosis and effective treatment with leuprolide and oral contraceptive pills.

### References


1. Hollis C. Schizophrenia in children and adolescents. *BJPsych Advances*. 2015;21:333-41.
2. Ritsner MS. *Handbook of Schizophrenia Spectrum Disorders*. Dordrecht: Springer. 2011.
3. Babu KM, Boyer EW. Emergency department evaluation of acute onset psychosis in children. *UpToDate*. 2017.
4. Brockington I. Menstrual psychosis. World psychiatry: *Official Journal of the World Psychiatric Association (WPA)*. 2005;4(1):9-17.
5. Brockington I. Menstrual Psychosis: A Bipolar Disorder with a Link to the Hypothalamus. *Curr Psychiatry Rep.* 2011;13:193-7.
6. Kitayama I, Yamaguchi T, Harada M. Periodic psychoses and hypothalamo-pituitary function. *Mie Med J.* 1984(34):127-38.


### About the Authors


**Jonathan T. Heinzman, MD**, is a first-year resident in psychiatry at the University of Iowa Hospitals and Clinics, Iowa City, IA. He is interested in child and adolescent psychiatry and consult-liaison psychiatry

**E. Taylor Buckingham, MD, MPH**, is a clinical child and adolescent psychiatrist at Kaiser Permanente in Aurora, CO. He treats patients with all types of mental illness and particularly enjoys patient education.



The authors extend a special thanks to Dr. Hanna Stevens, MD, PhD, of the University of Iowa, for helpful comments throughout the writing process.

***Disclosure:*** Drs. Heinzman and Buckingham report no biomedical financial interests or potential conflicts of interest.