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Recognizing and Managing Postpartum Psychosis: A Clinical Guide for Obstetric Providers

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Introduction

Postpartum psychosis is at once the most dangerous and the least understood of perinatal psychiatric disorders. It affects 1-2 per 1,000 women and constitutes a true psychiatric emergency, one that requires immediate hospitalization and treatment.[1, 2] The lack of knowledge about what it is, how to recognize it, and how to treat it – combined with stigma about perinatal psychiatric disorders in general and the lack of appropriate treatment venues – mean that it is often missed, by both obstetricians and psychiatrists, with sometimes tragic consequences.

Postpartum psychosis has been noted since antiquity. Hippocrates described the first case known to the medical literature, in 400 BC; his patient was delusional, confused, and insomniac within six days of a twin birth[3]. A medieval gynecologist attributed the disorder to “too much moisture in the womb, causing the brain to fill with water.” [4] By the late eighteenth century, German and French obstetricians and neurologists were beginning to write more frequently about the disease. In 1858, French psychiatrist Louis Victor Marcé published his “Treatise on the Madness of Women who are Pregnant, Recently Delivered, or Nursing.” [5] Marcé’s carefully observed treatise, while suggesting treatments that today seem woefully barbaric (applying leeches to the vulva, for example), nevertheless is a model of observation – and Marcé saw in his postpartum mothers the same symptoms that doctors struggle to control today. His observations led him to conjecture about the role of the immune response and the endocrine system, two systems that today are widely acknowledged to contribute to postpartum mental illness.

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Clinical Presentation

The name “postpartum psychosis” is not, perhaps, the best moniker for an illness that is at least as much an affective, or mood, disorder as it is a psychotic disorder. Many clinicians mistakenly believe that the term can be applied to any psychotic symptoms in the postpartum period, or that its clinical features will be identical to those of schizophrenia or other primary psychotic disorders. In fact, the symptoms of postpartum psychosis are distinctive and unique. The onset is typically sudden, and occurs within the first two weeks postpartum.[6-8] The literature has frequently described the distinctive clinical features (See Box 1), which include a delirium-like waxing and waning of consciousness, disorganization and confusion, depersonalization, and bizarre delusions (often concerning the child or childbirth). Early warning symptoms include insomnia, anxiety, irritability, or mood fluctuation. While the psychotic symptoms are often the most dramatic manifestation, women also present with mood symptoms – mania (can be irritable or elevated), depressive symptoms, or mixed symptoms. A recent clinical cohort study tracked the phenotypic characteristics of 130 consecutive cases of PPP, and used latent class analysis to describe three separate symptom profiles:

1. cases characterized by mania and/or agitation, with irritability much more common than elevated mood (34%)
2. cases characterized by depression and/or anxiety (41%)
3. cases showing an atypical or mixed profile (25%). [9]

Across all cases, 25% of patients were disorganized, 20% disoriented, 10% had disturbed consciousness, and 5% developed catatonia. Seventy-two percent had abnormal thought content, which most often consisted of persecutory delusions, and a minority had frank hallucinations. See Boxes 2 3 4 for representative clinical case presentations.

Etiology and Risk Factors

Postpartum psychosis is one of the few psychiatric disorders with a clear biological trigger: childbirth. The nineteenth-century psychiatrists who first described it (Esquirol, Marcé) noted that symptoms were often associated with pregnancies that had gone awry, due to infection, preeclampsia, hypertension, or other medical problems, [5] but more recent studies have been inconclusive about whether medical factors in pregnancy consistently predict risk for the disorder, with several studies finding that no pregnancy-related or obstetrical factors offer heightened risk for PPP [10-13] and others finding some specific risks, as outlined below (Box 5).[14-16]

Parity

Numerous studies have found a higher risk for PPP in primiparous women. [12, 14, 16-18] While some of that risk may exist because some women who experience PPP do not have further children (in one recent study, only 45% went on to have subsequent pregnancies)[15] that fact does not entirely explain the risk, for even those that restrict analysis to women who have had more than one pregnancy find a consistent risk for primiparous women.[14] Some of this risk may be due to the increased psychosocial stress of a first child, but some may

also be due to unknown biological factors. Research has not yet illuminated whether time between pregnancies, pregnancies with different fathers, or sex of the fetus may affect a woman's risk, but these would be interesting areas to explore given the emerging literature on these areas for other pregnancy morbidities.[19-21]

Personal history of bipolar disorder

The strongest single risk factor for PPP is a personal history of bipolar disorder, with 20-30% of parous women with known bipolar disorder experiencing PPP. [22] Yet in a recent large study only 33% of women presenting with PPP had a prior psychiatric history, and of those only one-third had been diagnosed with bipolar disorder.[15] While there is increasing evidence that some women with PPP will experience only puerperal episodes, most women who present with PPP as their first psychiatric episode will eventually meet criteria for bipolar disorder, with one comprehensive study showing a risk of a subsequent non-puerperal episode of 69%. A presentation of PPP should therefore be considered bipolar disorder – and treated as such – until proved otherwise.

Family history/genetic factors

While no specific genes that contribute to risk have been identified, there is strong evidence that puerperal psychotic episodes run in families. [23] [24, 25]

Pre-eclampsia

The clinical features and risk factors for pre-eclampsia overlap with those of PPP, including the strong risk of primiparity and the high risk of subsequent episodes. Evidence so far is inconclusive, however, with some studies finding no increased risk for PE in women with PPP.[26] One recent registry-based study did find a strong relationship between PE and first-onset postpartum psychiatric episodes, with an odds ratio approaching 5 in primiparous women – but did not distinguish between PPP and other types of postpartum psychiatric disturbance.[27] This remains an intriguing area for further research.

Sleep disturbance

Sleep loss has long been recognized as a trigger for mania, and in fact sleep deprivation can be used as an effective, if drastic, treatment for depression.[28, 29] [30-34] There has been very little research specifically on sleep deprivation and puerperal manic or psychotic episodes, though there has been an association noted between women who have longer labours or give birth in the middle of the night and the subsequent development of PPP.[35, 36] A recent study found that women with known bipolar disorder who report that sleep disturbance is a common trigger for their manias are at heightened risk for episodes of PPP. [37] This finding was specific to PPP (as opposed to postpartum depression, PPD), and indicates that future research in this area is warranted.

Immune dysregulation

Perhaps the most intriguing recent evidence about the biological origins of PPP is the evidence for immune system dysregulation. Bergink and colleagues have explored several areas of immune dysfunction in PPP,[38, 39] and found evidence for increased rates of

autoimmune thyroiditis (present in 19% of subjects with PPP and only 5% of controls)[40] as well as failure of normal T cell elevation, increased monocyte to non-monocyte ratio, and significant up-regulation of immune-related genes in subjects with PPP. [38, 39] Kumar and colleagues examined immune cell types by flow cytometry and found significant alterations in number and type of T cells and Natural Killer cells in women with PPP.[41] This is one of the most active areas of biological research on PPP.

Hormonal change

While the precipitous drop in estrogen and progesterone in the 24 hours following childbirth is a tempting candidate for the etiology of postpartum psychiatric disorders, most studies have shown little difference in absolute levels of reproductive hormones between healthy women and those experiencing psychiatric symptoms. [42, 43] Instead, certain women seem to have a vulnerability to hormonal fluctuation. [44] There has been very little research on hormonal contributors to postpartum psychosis specifically. There have been case reports of women with PPP who have hypoparathyroidism[45] and Sheehan's syndrome[46] and on the role of melatonin. [47] Some small trials and case reports have examined estrogen and progesterone for prevention or treatment of PPP, with mixed results for estrogen and no good evidence to support the use of progesterone (as summarized by Doucet 2011).[48] While further research is clearly needed, at this time the evidence does not support the use of hormones either to treat or to prevent PPP.

Screening and Assessment

There is no standardized set of questions or screening tool for postpartum psychosis, and the diversity of presentation makes it difficult to create an algorithm for screening. The widely used Edinburgh Postnatal Depression Scale,[49] a 10-item self-report screen for PPD, will pick up symptoms of depression or anxiety, but it cannot distinguish between unipolar and bipolar depression, nor can it assess symptoms of psychosis. There is also no completely standard set of laboratory tests, due to the rarity of the disorder – but evidence about the biological etiology has grown enough at this point to suggest a likely set of laboratory tests. Box 6 and Box 7 outline the most important screening questions and laboratory tools.

Differential Diagnosis

Postpartum psychosis is one of three affective (mood) syndromes that can affect women in the postpartum. The baby blues affect 85-90% of women.[50, 51] [52] This is a self-limited syndrome of mood lability (up or down), tearfulness, and feeling overwhelmed, but without serious effects on the woman's functioning. It occurs within days of birth and is generally resolved within two weeks. It is unrelated to psychiatric history, and requires no intervention other than support. Postpartum depression (PPD) is a more serious disorder that can include low mood, anhedonia, and sometimes suicidality. It affects 10-20% of postpartum women. [53] The Diagnostic and Statistical Manual defines it as a depressive episode "with peripartum onset," beginning in the third trimester or within four weeks postpartum. Symptoms must last at least two weeks to qualify as a depressive episode, but any woman whose symptoms are severe and affect functioning, and/or is suicidal is unable to function or exhibits suicidality should be suspected of likely depression even if that time criterion has

not been met. Although it often begins within the DSM-specified time period, many women will not present until later in the postpartum course. Women with postpartum depression are often anxious,[54] and postpartum women can also present with generalized anxiety disorder, a condition in which patients worry excessively about things across many domains of life.

Perhaps the most difficult psychiatric condition to distinguish from postpartum psychosis is postpartum obsessive-compulsive disorder (OCD). There is evidence of an increased risk of onset and flare of OCD during times of reproductive transition,[55, 56] and it is important to distinguish between the frightening intrusive thoughts common in OCD (obsessions) and the delusions that characterize PPP. See Table 1 for a description of these differences.

In addition to these psychiatric conditions, there are a number of medical conditions that must be considered in suspected cases of postpartum psychosis. The waxing and waning of consciousness that is often seen is reminiscent of delirium, and delirium for medical causes (most commonly infection surrounding parturition) should be at the top of any clinician's differential. Tests of attention and cognitive function, such as the Mini Mental State Exam (MMSE) and the Montreal Cognitive Assessment (MoCA), can help to determine whether delirium is present, as can lab tests including urinalysis and complete blood count. There have been a number of cases of autoimmune encephalitis presenting as postpartum psychosis, and postpartum abnormalities such as Sheehan's Syndrome or flares of autoimmune diseases (such as lupus) can also have neuropsychiatric presentations.[57] See Box 8 for a complete differential list.

Management

Treatment Setting

Postpartum psychosis is a psychiatric emergency that requires inpatient hospitalization. In much of the developed world, that hospitalization can take place in a dedicated mother-baby psychiatric unit, the type of facility that is deemed best practice in many countries.[58] These units, which were first established in the 1950s in the UK and in the 1970s and 1980s in Europe and Australia, promote mother-baby attachment during the period of treatment for severe mental illness in the postpartum. Unfortunately, this is a concept that has yet to take hold in the United States, where there are no psychiatric units that permit babies to stay with their mothers. Many clinicians, whether obstetricians or psychiatrists, and many patients and families, are therefore reluctant to seek hospitalization when it means a disruption of the mother-child bond and a disruption of breastfeeding. The severity of postpartum psychosis, however, means that in the U.S. treatment setting such separation is usually warranted. Postpartum psychosis is associated with high rates of both suicide and infanticide,[59] and treatment can occur most safely and rapidly in the context of inpatient hospitalization. Any obstetrician encountering a suspected case of postpartum psychosis should therefore seek immediate psychiatric consultation (if inpatient) or refer the patient to the emergency room (if outpatient).

Pharmacological Treatment

The rarity of postpartum psychosis, and the ethical difficulty of randomizing postpartum patients experiencing a psychiatric emergency, means that the evidence about treatments relies on data from small observational studies only. A 2011 review identified 10 studies of pharmacological interventions to prevent postpartum psychosis and 17 to treat it.[48] Approaches studied included antipsychotics, mood stabilizers, hormones, propranolol, and electroconvulsive therapy (ECT), all in either case reports or small observational studies. Some evidence of efficacy was found for all approaches except hormone therapy. The strongest evidence was found for ECT, for which three small studies reported improvement for all women undergoing ECT for postpartum psychosis.

Since that time, the group of Bergink et al., in the Netherlands, has published numerous larger studies on both the etiology and treatment of postpartum psychosis. In the largest treatment trial to date, this group followed 64 women from admission for postpartum psychosis through 9 months postpartum, following a 3-step treatment algorithm.[60] Step 1 was lorazepam at bedtime for 3 days; 4 out of 64 subjects remitted at this stage. Step 2 was the addition of an antipsychotic (usually haloperidol 2-6 mg daily) on day 4; 12 of the remaining 60 subjects remitted at this stage. Step 3 was the addition of Lithium after two weeks of non-response to steps 1 and 2, to a targeted Lithium serum level between 0.8 and 1.2 mmol/L; 47 of the remaining 48 subjects remitted at this stage (with the remaining patient discharged against medical advice prior to remission). Step 4 was ECT after 12 weeks of non-response to steps 1, 2, and 3, and no subjects advanced to this stage. The investigators tapered off benzodiazepines and antipsychotics after symptom remission, and continued Lithium (or antipsychotics if the patient responded without Lithium) for nine months, with nearly 80% of patient retaining full remission at 9 months postpartum.

This timetable for treatment is unrealistic in U.S. treatment settings, where the average acute psychiatric hospitalization lasts only 10 days.[61] Because 98% of subjects in Bergink's study responded to Lithium, most perinatal psychiatrists recommend the early addition of Lithium. Because there is a high rate of recurrence (over 54% recurrence of PPP in one recent study),[15] prophylaxis with Lithium is recommended for subsequent postpartum episodes. This recommendation is based on the treatment algorithm of Bergink et al.,[60] as described above – in that study, only 10% of those maintained on Lithium throughout the follow-up period relapsed. Another study of women maintained on Lithium throughout pregnancy found a relapse rate of 11% during pregnancy and 29% in the postpartum for any mood episode, including PPP. [62] (We do not yet have a study, however, that has examined the efficacy of prophylaxis specifically for subsequent pregnancies in women who have experienced PPP.) While there are risks to using Lithium in both pregnancy and breastfeeding,[63, 64] those risks are much lower than was once thought and for many women will be outweighed by the risks of PPP (which include suicide, infanticide, poor mother-child bonding, and subsequent PPD with consequences for child development). See Box 9 for a recommended treatment algorithm.

Psychosocial Supports

Given the severity of symptoms, pharmacological treatment is always necessary in postpartum psychosis. Low socioeconomic status and acute stressors increase women's risk for postpartum depression,[10] but do not affect the risk for postpartum psychosis – and evidence concerning psychosocial treatments is weak. Yet family and other psychosocial support is crucial for recovery in postpartum psychosis. Regardless of the type of mood symptoms involved (manic or depressive or both), insomnia is a prominent feature of the illness, and sleep hygiene interventions are crucial. Support for the other parent, if any, is also important, as is specific feedback designed to improve the mother-baby interaction. Some groups have used video feedback, individual interventions by nursing staff, or baby massage.[60, 65]

Patient and Child Safety

Perhaps the scariest aspect of PPP for the practicing obstetrician is how to determine whether the patient is a danger to herself or the child. Because rates of suicide and infanticide are high,[59] it is important to assess this, and to remember that it is always better to err on the side of extra caution. Women with psychiatric illness can and do make excellent mothers – but those with acute postpartum psychosis may be in danger of harming their children either deliberately or through neglect in the throes of illness. Involve psychiatry if at all possible in making this determination – it is easy for non-specialists to misinterpret intrusive, obsessional thoughts for psychotic thoughts.

Summary and Discussion

Postpartum psychosis is a devastating complication of childbirth that carries high risks for both mother and child. Any suspected case requires a thorough psychiatric evaluation as soon as possible. The rarity of the disorder makes it difficult to study, and the amount we do not know about risk factors, prevention, and treatment is large. Nevertheless, there are certain key clinical features and risk factors of which the practicing obstetrician can and should be aware:

- Remember that women with known bipolar disorder are at greatest risk – but that only 1/3 of women who present with PPP will have a prior psychiatric history.
- Remember to ask all patients about personal and family history of bipolar disorder.
- Remember that primiparous women are at highest risk.
- Always ask about sleep disturbance – while all new mothers will have disrupted sleep, those who are not able to sleep when they have the opportunity should raise a red flag.
- Always ask, in a neutral and non-judgmental way, about the woman's thoughts of harming herself or the child – and remember that the important distinction is whether a woman is disturbed or horrified by these thoughts (indicating that they may be obsessions).

- Remember that PPP is a psychiatric emergency; if you suspect it, the patient must have a psychiatric evaluation as soon as possible (in the emergency room if necessary).

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Synopsis:

Postpartum psychosis is a psychiatric emergency that affects 1-2 of 1,000 women. Key clinical features include mood fluctuation, abnormal thoughts or behaviors, and confusion. Women with a history of bipolar disorder are at heightened risk, as are first-time mothers, and current research on the causes focuses on biological triggers such as immune dysregulation. Women with postpartum psychosis require inpatient hospitalization, and should be treated with Lithium, antipsychotics, and benzodiazepines.

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Key Points

- Postpartum psychosis (PPP) is a rare psychiatric emergency that can danger the lives of mother and child.
- It most often arises within 10 days of childbirth, and is characterized by bizarre thoughts and/or behavior, alterations of consciousness, and mood fluctuation.
- The single biggest risk factor is a personal history of bipolar disorder, and most women with PPP will go on to develop bipolar disorder.
- It occurs more often in first-time mothers.
- It carries high rates of suicide and infanticide and suspected cases require psychiatric evaluation as soon as possible.
- Treatment requires hospitalization and aggressive pharmacological management.

Box 1:**Clinical Features of Postpartum Psychosis**

- Disorganization
- Confusion
- Depersonalization
- Insomnia
- Irritability
- Abnormal thought content (delusions and/or hallucinations)
- Abnormal mood (mania or agitation; depression; mixed)

Clinical Case Presentation #1**Postpartum Psychosis with Manic Features**

Ms. A was a high-achieving professional with no prior psychiatric history who had a twin birth twelve days prior to her psychiatric presentation. Her babies had been born at term by a planned C-section due to chorioamnionitis; antibiotic therapy was successful and she left the hospital on time four days after the birth. She slept very little in the hospital and was noted by the nurses to be extremely vigilant about the babies and mildly anxious. Her family reported that she did not sleep at all for six days following her hospital discharge. She expressed great anxiety about arrangements at home (worrying about clothes, diapers, and the like), and about the ability of other family members to manage the twins. She was exclusively breastfeeding until two days prior to presentation, when her family dissuaded her from breastfeeding in the hope that she would be able to sleep more; the intervention did not help. On the day of presentation, she began to be suspicious of several family members, accusing them of poisoning the babies' bottles, and began to hide the bottles in secret locations around the house. When her mother suggested that they drive to the hospital, the patient bolted from the car into traffic and was found several hours later by a police officer, who drove her to the emergency room. Upon arrival, the patient was oriented to her name and the date, but was unsure where she was, spoke very quickly and was uninterruptable, and talked loudly about the cameras she was sure were watching her in the emergency room and about the physicians, whom she felt were in league with her family to poison the infants.

Clinical Case Presentation #2**Postpartum Psychosis with Depressed Features**

Ms. B was a sheltered young woman from an insular immigrant community. She had experienced childhood trauma and had a known history of depression and anxiety, successfully treated with antidepressants in the past. She had been well throughout her pregnancy, on no medication, but within five days of an uncomplicated spontaneous vaginal birth she became disoriented at home and was unable to find her way from her bedroom to the living room. Over the next several days, her family reported that she moved very slowly and seemed confused; she had poor appetite, did not seem to understand how to hold or care for the baby, and spent much of the day lying in bed but did not seem able to sleep. She began to make worrisome statements such as “I’m not here” and “I didn’t have a baby.” The patient’s general practitioner prescribed an antidepressant, which did not help her symptoms, and the patient became increasingly confused and unable to complete daily activities such as showering and eating. The family took over the care of the baby and assigned a family member to care for the patient at home. Several weeks later, the situation had not improved, and the family presented to a psychiatrist. The patient was oriented to her name only; she could not name the season, nor what type of building she was in; she clung to her sister’s hand and was unable to find the door of the room she was in. When she was asked about her baby, the patient stated “I don’t have a baby, I’m not married.”

Clinical Case Presentation #3**Postpartum Psychosis with Mixed Features**

Ms. C was an elementary school teacher who was quite knowledgeable about mental health. She had no prior psychiatric history, but had two first-degree relatives with bipolar 1 disorder, one of whom had had multiple hospitalizations and was eventually stabilized on Lithium. Her pregnancy was uneventful, but labor lasted over 36 hours and ended in an emergency C-section, which the patient found traumatic. Two days after discharge, she represented to the hospital stating she had had a panic attack in the middle of the night and was unable to sleep; this was her first panic attack. The overnight resident deemed her anxious but stable, treated her with lorazepam, and discharged her. She represented several hours later complaining of continued insomnia and anxiety. The consulting psychiatrist could elicit no symptoms of frank mania or psychosis, but was concerned about her anxiety, insomnia, and family history of bipolar disorder. She was discharged with lorazepam three times daily to close, twice weekly follow-up with a perinatal psychiatrist. At her second outpatient visit, the patient reported that she was now sleeping six hours nightly but continued to feel anxious. The psychiatrist started sertraline at 25 mg. Two days later, the patient's partner called the psychiatrist, stating that the patient was writhing on the floor, complaining of bugs crawling over her skin, and had been agitated and pacing just before. By the time the patient arrived in the emergency room for evaluation, she was mute and catatonic.

Box 5:**Known Risk Factors for Postpartum Psychosis**

- Personal history of bipolar disorder
- Family history of bipolar disorder
- Prior episode of postpartum psychosis
- Primiparity
- Sleep loss

Box 6**– Important Screening Questions for Patient and/or Family**

- Is this the patient's first psychiatric presentation?
- If she has a psychiatric history, is it of depression, mania, or both?
- Is there any family history of bipolar disorder?
- Has the patient been using any substances?
- Does the patient have thoughts of harming herself or the child? *Important to ask this in a non-judgmental fashion, for example: "It can be very overwhelming to be a new mother. Sometimes women have scary thoughts; they might think about hurting themselves, or hurting their babies. Has that ever happened to you?"*

Box 7**– Important Assessment Tools**

- Complete physical examination
- Neurological examination
- Comprehensive metabolic panel
- Complete blood count
- Urinalysis
- Urine toxicology screen
- Thyroid stimulating hormone, free T4, and TPO antibodies
- Ammonia level
- If neurological symptoms present, brain imaging and testing for limbic encephalitis

Box 8:**Differential Diagnosis for Postpartum Psychosis**

- Baby blues
- Postpartum depression
- Generalized anxiety disorder
- Obsessive-compulsive disorder
- Delirium
- Autoimmune encephalitis (i.e., NMDA receptor)
- Sheehan's syndrome
- Autoimmune flare (i.e., neuropsychiatric symptoms of lupus)
- Intoxication
- Medication reaction (i.e., steroid-induced mania)

Box 9.**Treatment Recommendations for Acute Postpartum Psychosis**

- Benzodiazepine (lorazepam 0.5-1.5 mg TID)
- Antipsychotic (high potency preferred, haloperidol 2-6 mg or olanzapine 10-15 mg)
- Lithium (to achieve serum level of 0.8-1.2 mmol/L)
- Taper benzodiazepine and antipsychotic once symptom remission achieved
- Continue Lithium monotherapy for 9 months (can lower to achieve serum level of 0.6-0.8 after symptom remission if severe side effects)
- For future pregnancies, begin prophylactic Lithium monotherapy during pregnancy or immediately postpartum

Table 1:

Obsessions vs. Delusions

Obsessions	Delusions
<ul style="list-style-type: none">• Intrusive thoughts that are unwanted and horrifying to patient• Can be sexual, religious or violent• Patient has no desire to act on these thoughts• Thoughts cause considerable distress and patient may avoid things or engage in compulsive behavior (checking, seeking reassurance) to ease that distress• <i>Example: Mother has an intrusive thought about molesting her child while changing diapers; this horrifies her and she insists that her husband change all diapers</i>	<ul style="list-style-type: none">• Fixed false belief• Content often bizarre or unusual; can also be sexual, religious, or violent• Patient may want to act on these thoughts or feel compelled to do so• Thoughts may not cause significant distress• <i>Example: Mother believes her child has been cursed by the Devil and that she must throw him out the window</i>