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Onset and Exacerbation of Obsessive-Compulsive Disorder in Pregnancy and the Postpartum Period

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Abstract: ONSET AND EXACERBATION OF OBSESSIVE-COMPULSIVE DISORDER IN PREGNANCY AND THE POSTPARTUM PERIOD.
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The overarching goal of this study was two-fold; to determine the prevalence of perinatal onset or worsening of OCD symptoms in women attending a university-based research program, and to determine whether there is a continuity between perinatal onset or worsening of OCD and premenstrual exacerbation of such symptoms.

Women ages 18 to 69 years old that were enrolled in the Yale OCD Research Program between 1990 and 1995 were interviewed by phone or in person regarding demographics, onset and course of OCD, types of primary OCD symptoms, treatment history, comorbid diagnoses including substance use/abuse, and the impact of pregnancy and menstruation on OCD onset and symptoms. Those who had at least one pregnancy were placed into the Preg group and those who had never been pregnant into the NPreg group. The Preg group was further subdivided; those who reported onset of OCD during pregnancy or the puerperium were assigned to the Puerperal Related (PR) group while those that denied onset of OCD related to pregnancy were assigned to the Non-Puerperal (NP) group. For our secondary aim addressing premenstrual worsening, those women who were in the PR group were combined with women with pre-existing OCD that worsened during pregnancy or the postnatal period.

All data were summarized using descriptive statistics (means, SDs, frequencies). Continuous measures were compared between groups using a Student's t-test and categorical variables were assessed using the chi-square test. All analyses were considered statistically significant at $P < 0.05$ and performed using SAS, version 9.1.

Of the Preg group, 24 (30.8%) fell into the PR subgroup; 11 (14.1%) reported onset during pregnancy, 1 (1.3%) had onset after a miscarriage, and 12 (15.4%) had onset during the postpartum period. Out of 132 total pregnancies, 29 (22.0%) involved an improvement in OCD symptoms, 45 (34.1%) involved an exacerbation of symptoms, and 58 (43.9%) did not change symptom severity in women with pre-existing illness. Although worsening of symptoms prior to menses was reported by the same proportion of women in the Preg group as in the NPreg group, women in the PR group and those with perinatal exacerbation were more likely to report premenstrual worsening of OCD symptoms compared to all others.

Findings from this study provide additional evidence that pregnancy and childbirth are frequently associated with the onset of OCD or worsening of symptoms in those with pre-existing disorder. In addition, there appears to be continuity between OCD onset and/or exacerbation across the reproductive life cycle, at least with menstruation and pregnancy. These data can not address the impact of menopause on OCD symptoms. Our findings are consistent with those from other groups, but all need to be confirmed in prospective studies.

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Table of Contents

I. Background and Rationale

Pregnancy and the puerperium (postpartum) are stages of life traditionally associated with emotions such as happiness, joy, and excitement for a new mother and her family. However, there are accounts of puerperal mental illness since the time of Hippocrates. Primitive theories of the etiology of these childbirth-related disturbances involved uterine vapors, toxins, and deposits of milk in the brain. Recent speculations about the causes of puerperal mental illness highlight the importance of psychodynamic issues, alterations in the neuroendocrine milieu and psychosocial/interpersonal stressors both specific and nonspecific to childbearing (1). It is now well known that the puerperium represents a time of increased vulnerability to psychiatric disorders, particularly depression, psychosis, and the largely understudied obsessive-compulsive disorder. OCD in the postpartum period often goes undiagnosed and thus untreated, resulting in devastating consequences for the patient, her family, and the newborn.

1.a. Phenomenology and Natural History of OCD

Obsessive-compulsive disorder is an anxiety disorder characterized by recurrent, intrusive thoughts or ideas that are recognized as being senseless, yet give rise to anxiety and distress. In addition, the individual feels urges to perform excessive rituals to neutralize or suppress these disturbing feelings. Avoidance of situations related to obsessional concerns is common and contributes to decline in the individual's ability to

function at home, work and/or in the social/familial realm. The specific content of obsessions and compulsions is highly variable and patient-dependent, but a common theme concerns uncertainty over responsibility for harm or mistakes. Common themes for obsessional thoughts include: fears of contamination, aggression or violence, inappropriate sexual activity, need for symmetry, and concerns about making mistakes. Compulsive behaviors may involve ritualistic checking, washing, counting, or repeating routine activities. The onset of OCD is typically gradual, occurring over months to years (2).

OCD is one of the most common psychiatric disorders in the world, with an estimated lifetime prevalence rate of 2-3% in the general adult population (3). Unlike depression, which has a female predominance, OCD affects male and female adults roughly equally (4, 5). Without effective treatment, the course of the illness is usually chronic and deteriorating, with symptoms interfering significantly with daily functioning in multiple aspects of life.

1.b. Phenomenology and Prevalence of OCD During Pregnancy

Many studies in recent years have focused on postpartum depression or psychoses, but little effort has been devoted to studying OCD in the perinatal context. Interpretation of findings from early studies is complicated by antiquated diagnostic methods and/or relatively small sample sizes, in addition to being primarily case series and retrospective reports. To date, no studies have confirmed subject reports of perinatal or premenstrual worsening of OCD with prospective ratings. Thus the exact incidence or

prevalence rates of pregnancy or postpartum onset OCD or exacerbation of OCD are unknown (6). The wide range of percentages reported in the following studies may be a result of the differing methods of data collection, lack of uniform diagnostic criteria, and the innate differences in patient populations.

In 1957, Pollitt found that pregnancy and childbirth were associated with the onset of obsessive symptoms in 11% of 93 patients with OCD (7). Ingram (1961) noted in his retrospective review of 89 inpatients with "obsessional states" that for 16.9% of the group, the onset had occurred in association with pregnancy, making it the most common precipitating event (8). However, Lo (1967) reported such an association in only 5% of 56 OCD patients (9).

More recently, Buttolph and Holland (1990), using a questionnaire limited by a 33% response rate, reported that OCD began during pregnancy in 15% of 39 women and during the postpartum period in 21% (10). Neziroglu and colleagues found that approximately 40% of the 64 women with OCD (professionally diagnosed according to DSM-IIIR criteria) in their study who had been pregnant experienced initial symptom onset during one of their pregnancies (11). In a related case series, Sichel et al. (1993) reported on fifteen non-depressed patients with new-onset OCD beginning early in the postpartum period. Eight women had no previous psychiatric history, and all the patients responded well to treatment with a serotonergic reuptake blocker (12). On the other hand, Williams and Koran (1997) reported that only 13% of women in their series who had been pregnant associated the onset of their OCD (according to DSM-IV criteria) with pregnancy (13). Maina et al. (1999) reported the onset of OCD at postpartum in 50% of women who had been pregnant, but no onsets at pregnancy (14). A more recent study by

Labad (2005) and colleagues of 46 female OCD patients found that OCD onset occurred at pregnancy in 2% and at postpartum in 7% of the subjects (15).

In addition to these examples of initial symptom onset occurring during the perinatal period, available research also yields some evidence of exacerbation of pre-existing OCD during this time. In 1987, the first report of a case of OCD exacerbation during pregnancy was published, describing a 26-year-old woman with a fluctuating course of the illness who experienced a severe and prolonged decompensation during her second pregnancy (16). Buttolph and Holland (1990) reported that 69% of the 39 female OCD patients in their study described a relationship between the onset or an exacerbation of OCD and some aspect of pregnancy, birth, or care of their children. OCD worsened during pregnancy in 8% of the women, and during the postpartum period in 15%. Triggering events included infertility, miscarriage, pregnancy, birth and care of the first child, and birth and care of subsequent children (10).

In another study, miscarriage was a significant risk factor for the recurrence of OCD in women with pre-existing illness (17). In Labad's study, worsening of pre-existing OCD was reported by 8% of patients at pregnancy and 50% at postpartum (15). Overall, however, the data on OCD exacerbation during pregnancy is limited and somewhat equivocal. For example, in the study described above by Williams and Koran, 69% of the 29 women with pre-existing OCD described no change in symptoms during pregnancy. 17% described worsening, and 14% described improvement. However, postpartum exacerbation of OCD symptoms was noted by 29% of the patients (13). Altshuler et al. noted that exacerbation of pre-existing OCD is common in women after delivery, even when medication discontinuation is successful during pregnancy (18).

OCD is a heterogeneous disorder in that it can present with a wide variety of obsessions and compulsions. Despite this diversity of symptoms, previous studies appear to show a consistent pattern during the puerperium with regard to content of the obsessions and compulsions. For example, it appears that contamination obsessions and washing or cleaning rituals are prevalent during pregnancy, while postpartum OCD tends to be manifested as ego-dystonic intrusive obsessional thoughts of harming the infant, accompanied by avoidance behaviors or checking rituals (11, 13, 14, 19, 20). In contrast to the gradual onset of typical OCD, postpartum OCD appears to be characterized by the rapid onset of obsessional symptoms after the birth. As an example, in the case series mentioned above by Sichel's group, the mean time to onset of OCD symptoms was 2.2 weeks after delivery. These symptoms presented primarily as intrusive obsessional thoughts of harming their babies. Although no associated compulsive rituals developed, as would be expected in the course of classical OCD, all the women exhibited some degree of avoidance behavior toward their infants as a response to these obsessions which they found to be extremely frightening and disturbing (19). In another case series, the mean time of onset of OCD symptoms was 3.7 weeks following delivery, with onset as early as the second postpartum day reported (21).

1.c. Neurobiology - Evidence Linking Serotonin, Gonadal Hormones, and OCD

In the past, research on neuropsychiatric disorders has often attempted to associate each disorder with either a deficiency or an excess within a single neurotransmitter system. For example, the serotonin hypothesis of OCD was initially

developed as a result of the finding that serotonin reuptake inhibitors (SRIs) are the most effective treatment for OCD. However, further studies gave no definitive evidence that a dysregulation of serotonin function was the primary or only neurochemical disturbance in OCD. Moreover, only 40-60% of OCD patients respond to SRI monotherapy, and even these patients may only have a partial response. Thus it must be acknowledged that SRIs also act via other neurotransmitter systems, and it is likely that OCD is a result of a disturbance in several of these neurochemical pathways (22). In a comparison of four studies of various SRIs in OCD patients via meta-analysis, it appeared that greater improvement in OCD symptoms was actually associated with *less* selectivity for serotonin (23). Both serotonergic and dopaminergic systems appear to have a modulating effect on elements of the basal ganglia circuit that are implicated in OCD, suggesting that certain cases of OCD (for example, with tics) may respond best to an SRI-neuroleptic combination (24, 25). Reviewers have also hypothesized that a relative excess of basal ganglia dopaminergic activity underlies compulsive behaviors (26).

A limited number of imaging studies investigating anatomic brain regions involved in OCD have been published to date. Although the studies are small and have varied results, there is some convergence of the data indicating involvement of the orbitofrontal cortex, the caudate, and the anterior cingulate cortex (27, 28). As further evidence of involvement of the caudate nucleus, a number of disorders associated with abnormalities in the caudate including Tourette's syndrome, Sydenham's chorea, Parkinson's disease, and Huntington's disease, are frequently accompanied by obsessive compulsive behaviors (24).

Since pregnancy and/or childbirth appear to exacerbate or contribute to the onset of OCD in a sizable portion of women, investigators have theorized that pregnancy-specific psychosocial stresses, parenting responsibilities, and/or changes in the neuroendocrine milieu are the most likely contributors to this phenomenon. During pregnancy, there is a profound increase in gonadal steroid (estrogen and progesterone) levels over 9 months of gestation, only to be followed by a precipitous drop in both estradiol and progesterone to hypogonadal levels within 48 hours (29). It has been hypothesized that the extreme fluctuations in these hormones may have an adverse impact on serotonergic function, producing the notably acute onset of symptoms early in the postpartum period (12). Few studies have actually tested this hypothesis, but results from studies in postpartum rats indicate that serotonin receptor changes in the limbic area are negatively correlated with progesterone levels (30). While between estradiol, progesterone, and its neurosteroid derivative allopregnanolone (ALLO), multiple neurotransmitter systems are modulated, the relationship between these steroids and serotonin have seemed most relevant in the context of OCD in the perinatal period.

The effects of gonadal steroids on serotonin are complex and region specific, but it is clear that serotonergic neurotransmission (i.e., synthesis, metabolism, uptake, and receptor sites) is at least partially modulated by changes in estrogen and progesterone (31-33). Estrogens were found to exert a biphasic effect on the density of serotonin receptors in the female rat brain: an acute reduction in serotonin receptor density throughout the brain is followed 48 to 72 hours later by a selective increase in those brain regions known to contain estrogen receptors--hypothalamus, preoptic area, and amygdala (34). Iancu et al. presented the case of a woman who developed OCD during a pregnancy

and recovered completely after giving birth, suggesting a strong biological influence on the development of the illness; after the hormonal changes abated, the symptoms disappeared as well (20). It should be noted, however, that this case differs from most reports of OCD onset during pregnancy, in which the symptoms continued or recurred after birth.

As further evidence for a temporal relationship between manipulation of gonadal hormones and a change in OCD symptoms, there have been several case reports documenting the onset or exacerbation of OCD associated with administration of oral contraceptives, which alter the individual's neuroendocrine milieu. In two of these cases, discontinuation of the exogenous hormones led to clinical improvement (35, 36).

Although all studies have been based on retrospective reports, it appears that a sizable proportion of women with OCD experience an exacerbation of their primary symptoms during the premenstruum, thus lending further evidence that ovarian hormones may contribute to the pathogenesis of OCD in such cases, if not in general (4, 37). In the Williams and Koran study previously discussed, 42% of the women surveyed reported regular premenstrual worsening of their OCD (13). Similarly, the Labad study found that OCD onset occurred in the same year as menarche in 22% of their subjects, and worsening of preexisting OCD during the premenstruum was reported by 20%. In addition, the number of premenstrual mood symptoms (including anxiety, irritability, mood lability, and depressed mood) was associated with both premenstrual worsening of primary OCD symptoms, and onset or worsening of OCD during the puerperium. Patients with an onset or exacerbation of OCD during the puerperium also more frequently reported premenstrual worsening of symptoms and a previous history of major

depressive disorder, including postpartum depression (15). Premenstrual dysphoria and high rates of postpartum depression have also been described in female OCD patients in general (12, 13). Likewise, women with a history of premenstrual syndrome are at higher risk for postpartum depression and psychosis (38). To link all of these observations, it has been proposed that a common dysregulation of serotonergic neurotransmission, which can be accentuated by ovarian steroid fluctuations, may be involved in the pathophysiology of OCD, postpartum depression, and premenstrual syndrome (24, 39).

1.d. Evidence For Oxytocin Involvement in the Pathogenesis of OCD

While serotonin was the initial and has been the primary neurotransmitter investigated in the pathophysiology of OCD, poor treatment response to SRIs in up to 40% of OCD patients has made it critical to shift focus to other possible contributors. Most recently, the hormone oxytocin (40) and neurotransmitters dopamine (41) and glutamate (42) have been of considerable interest. Given the role of oxytocin in parturition and lactation, this overview will be limited to discussion of studies examining oxytocin's role in OCD. Oxytocin is a nonapeptide synthesized primarily in the paraventricular and supraoptic nuclei of the hypothalamus, which project to the posterior pituitary gland (43). Pituitary release of oxytocin into the bloodstream increases in late pregnancy and the postpartum period, where it stimulates uterine contractions and milk ejection. Notably, oxytocin has also been implicated as a centrally active neuropeptide responsible for stimulating sexual, maternal, grooming, and affiliative behaviors in animals (44-46). Interestingly, it is through the initiation of these "normal" behaviors

that oxytocin has been purported to play a role in the pathogenesis of OCD. It has been suggested that the increase in autogrooming observed with oxytocin administration in rodents (47), for example, may be similar to the repetitive hand washing and cleaning present in many patients with OCD (40). It is equally conceivable that obsessions regarding the infant's safety and compulsions such as checking are pathological correlates of normal maternal behavior; most new mothers are understandably vigilant about their baby's health and welfare.

These central effects may be mediated by projections of oxytocinergic neurons to extrahypothalamic brain areas, including regions of the brainstem and forebrain (48). For example, it has been shown that oxytocin fibers from the paraventricular nucleus project to structures of the limbic system (49), one of the prime candidates for a possible anatomic site of dysfunction in OCD (22). To further support the association between oxytocin and OCD, in a 1994 study, Leckman et al. found correlations between cerebrospinal fluid oxytocin levels and OCD severity among untreated patients (50).

Interestingly, ovarian steroids (namely estrogen) influence both neurosecretory and intracerebrally projecting oxytocinergic neurons. The concentration of oxytocin and its receptor in the CNS are responsive to circulating steroid levels (51). For example, estrogen treatment stimulates the release of oxytocin into the peripheral circulation (52) and induces oxytocin binding sites in the brain (53). It is unknown how estrogen mediates these changes, although apparently a subpopulation of oxytocinergic neurons have binding sites for estradiol (54). In addition, in examination of female rats undergoing puberty and ovariectomy, Miller et al. showed that ovarian steroids modulate

neuronal oxytocin mRNA; they observed a significant increase in oxytocin mRNA concomitant with puberty and reversible with ovariectomy (48).

Thus the brain, in addition to mammary and uterine tissue, appears to be a target organ for oxytocin in the postpartum period. As further support of this hypothesis, Insel demonstrated an increase in oxytocin binding in the bed nucleus of stria terminalis (BNST) of rats during the postpartum period (55). Oxytocin is elevated in the third trimester of pregnancy and early postpartum period, which coincides with the time that many women report onset of obsessive-compulsive symptoms. Vaginocervical stimulation, which occurs with a miscarriage or abortion, has also been shown to increase oxytocin levels (56), which gives a plausible explanation for the occurrence of these symptoms after a fetal loss.

However, in contrast to Leckman's finding of increased CSF oxytocin levels in patients with OCD, two other studies reported no correlation between OCD symptoms and CSF oxytocin levels (57, 58). In addition, several investigators attempting to treat OCD with intranasal oxytocin have reported inconsistent results (59, 60). Most recently, Epperson et al. found that intranasal oxytocin, even at 3 and 6 times the dosages previously tested, had no effect on obsessive-compulsive symptoms (61). Given the difficulty in getting peripherally administered oxytocin across the blood-brain barrier and into the CNS, it is difficult to conclude that a negative finding indicates no association between oxytocin and OCD; thus methods must be developed to investigate central oxytocin function in this disorder.

Still, there are problems with assuming a purely biological (neurohormonal) etiology of pregnancy related OCD. Importantly, there is no direct evidence that

hormonal “imbalances” play a causal role. Gonadal hormone influences on CNS serotonin function vary with length of exposure, dose, and species. In general, the precise neurobiological mechanisms of OCD remain unclear, and research in this area is still preliminary. Moreover, biological theories alone do not account for the evident specificity in symptom presentation among women with puerperial onset OCD. Abramowitz et al. (2001) also reported an interesting finding of an onset or exacerbation in OCD symptoms among new fathers, which is inconsistent with a purely biological model and suggests that the transition to parenthood may entail other factors which unmask the vulnerability to OCD in these individuals (62).

1.e. Genetic Predisposition to Illness

Although many women with postpartum psychiatric illness have no prior psychiatric history, there is often a strong family history of affective disorders, particularly depression and postpartum depression (38). Since the dramatic hormonal changes described above occur as part of the reproductive cycle in all women, it seems that the development and exacerbation of mood disorders and OCD at these vulnerable periods requires more than just fluctuating hormone levels, but also a genetic predisposition. These currently unidentified genetic “defects” probably relate to subtle alterations in the number and function of certain receptors and enzymes, as well as minor structural and anatomical differences in the CNS (39).

There appears to be a definite familial concentration of OCD (63-65). Interestingly, a study by Lochner, et al. (2004) of a relatively genetically homogenous

population of subjects revealed that a sexually dimorphic pattern of genetic susceptibility to OCD may be present (37). These findings were consistent with several earlier studies of genetics in OCD (63, 66, 67).

Comorbidity data and family genetic studies indicate that 10-20% of OCD cases probably have a biological relationship to Tourette's syndrome (TS). Evidence indicates that OCD and TS may be transmitted together as an autosomal dominant trait with mixed expressivity, influenced in part by gender – for example, a woman carrying the diathesis will likely express it as OCD and not TS (24). Clearly, future research focusing on the role of pregnancy and childbirth in triggering the onset of OCD would benefit from the inclusion of relevant genetic factors.

1.f. Social Factors Which May Contribute to OCD During Pregnancy

Several studies have reported an earlier onset of obsessive-compulsive disorder more commonly in men (age 5-15 yrs.), with a later onset (age 23-35 yrs.) more common in women (68, 69). This may be evidence of gender-divergent etiological factors in OCD, including certain "triggering" life events for women during this time period, namely the birth of a child. To further support the concept that the incidence of OCD in women is highest during childbearing years, it has been reported that the age of onset of OCD in women has a bimodal distribution, with peak incidences occurring at 13-16 and 22-32 years of age (11). In an investigation of the occurrence of stressful or potentially triggering events in the recent history of patients with OCD, Maina et al. (1999) discovered that OCD female individuals were more likely than normal female subjects to

report exposure to peripartum events. This was the only significant difference found between OCD and control subjects in terms of number and type of life events. In addition, it was observed that postpartum OCD was much more frequent in primiparae (75%), that it frequently follows a pre- and post-term pregnancy (62.5%) and that it is often associated with delivery by caesarean section (62.5%) (14). Although there was no control group for comparison, these observations suggest that certain situations associated with increased stress to the mother (i.e., first child, obstetric complications) may increase the risk for development of postpartum OCD.

In new mothers with pre-existing OCD or who are otherwise vulnerable (i.e., genetic or characterlogic predisposition), the responsibility of looking after a helpless, totally dependent infant combined with other environmental and family changes after the birth may be a source of significant psychological stress causing exacerbation or new onset of the disorder (13). Situations such as being a single mother, an unplanned pregnancy, and having a poor relationship with one's own mother may be additional risk factors (70). In his study, Lo reported that 30% of his postpartum OCD patients exhibited a fluctuating disease course with exacerbations corresponding to environmental stress (9).

Interestingly, it appears that pregnancy and the postpartum are also vulnerable periods for the development of OCD in expecting fathers. Abramowitz et al. described four males who presented with rapid-onset OCD symptoms associated with their spouse's pregnancy or the birth of their child. All the fathers reported unwanted obsessional thoughts of harming their newborn or unborn child, similar in character to those reported consistently by pregnant or postpartum women (62). Clearly, this phenomenon further

highlights the need to look beyond purely biological models to explain puerperial OCD, and perhaps OCD in general.

1.g. Psychology – primary parental preoccupations and other adaptive behaviors

From an evolutionary perspective on psychopathology, it has been proposed that highly conserved maternal behavior, while adaptive and crucial for reproductive success, also leaves women vulnerable to certain forms of mental illness, notably OCD (71). Maternal behavior includes creating a safe environment for the infant, cleaning, checking, and nursing, all of which normally become intense parental preoccupations during pregnancy and the postpartum period. For both parents, the perinatal period often involves an altered mental state characterized by excitement and heightened sensitivity to environmental and emotive cues; it has been described as “almost an illness” that a parent must experience and recover from in order to create and sustain an environment that can meet the needs of the newborn (72, 73). The infant becomes an increasingly exclusive focus of thought and action. The intrusive worries that develop concerning parental adequacy and the infant’s safety, as well as the resultant harm avoidant behavior or compulsions, resemble thoughts and behaviors encountered in OCD. Thus, it logically follows that some forms of OCD (i.e., perinatal) may be the result of an inappropriate activation or lack of down-regulation of the neural circuits normally active during the initial phases of parental behavior (74).

While it is difficult to imagine the presence of aggressive thoughts toward the infant as being evolutionarily adaptive, these thoughts appear to be highly correlated with

checking compulsions, especially in women with postpartum onset major depression (75); checking may be viewed as maternal vigilance about the infant, and thus potentially adaptive maternal behavior. In her study of obsessions and compulsions in women with major depression (postpartum onset vs. non-postpartum onset), Wisner (1999) found that women with postpartum onset depression experienced a higher frequency of these aggressive obsessional thoughts (mostly involving harming the infant) than women with non-postpartum onset (75). Moreover, Jennings et al. found the prevalence of "passing" aggressive thoughts among postpartum women without depression to be 6.5%, suggesting that unwanted thoughts concerning harm to the newborn occur fairly frequently even among healthy women (1 in every 15 childbearing females) (76).

A cognitive-behavioral model has also been proposed as an explanation for pregnancy or postpartum onset OCD. According to this theory, certain individuals have a tendency to think and behave in a certain pathological way as a result of prior experiences. In the case of OCD, vulnerable individuals misappraise common and benign intrusive, ego-dystonic thoughts as threatening, leading to increased preoccupation with the thoughts and attempts to neutralize them via compulsive rituals or avoidance behaviors (77, 78). Essentially, the thought is interpreted as equivalent to the action (i.e., thinking about violent behavior is the same as committing a violent act). In this explanation, pregnancy and the postpartum period would be considered especially vulnerable times for the development of obsessional problems in anyone sharing responsibility for the infant; the more responsible one feels in a given situation, the worse it will seem to have violent or negative thoughts (62). In support of this model, it would account for the development of OCD symptoms in both genders, as well as the success of

cognitive behavioral therapy as a treatment strategy. However, it cannot be assumed that these irrational beliefs are the cause of OCD, as empirical studies have primarily been correlational. In addition, it is difficult to completely ignore the neurobiological evidence, including the success of SSRIs as a treatment strategy.

One possibility that has been proposed to explain the observed exacerbation of OCD during pregnancy and the postpartum period involves an overwhelming of one's psychological coping mechanisms during these times. Stern and Cobb (1978) reported that the most common underlying theme in OCD is fear of harming oneself or others (79). While it may be possible for someone with these obsessions to cope with them by physically avoiding other people or harmful objects/situations, the physical unity a pregnant woman has with the fetus may overwhelm her avoidance strategies and lead to an acute decompensation (16).

1.h. Relationship of OCD with postpartum depression and other co-morbidities

In the nongravid population, major depressive disorder is the most common comorbid diagnosis in patients with OCD, with lifetime prevalence rates varying from 35-80% (80-82). A similar relationship seems to exist between postpartum OCD and depression. It is unknown, however, whether OCD symptoms represent a cause or effect of postpartum depression. It is also possible that OCD and depression could simultaneously occur as a result of an independent variable, such as neurobiological changes or increased social/psychological stress in the postpartum period. Whatever the nature of the relationship, it is clear that the presence of obsessional thoughts regarding

harming the infant is common among women with postpartum depression – up to 41% of mothers with depression may have thoughts of harming their infants (76). In addition, the group of women with pre-existing OCD studied by Williams and Koran experienced postpartum depression at a rate of 37%, in comparison with the estimated annual prevalence of postpartum depression of 10%-13% in the general population (13). In another study, 9 out of 15 women who presented with new onset OCD in the postpartum period developed a secondary major depression about 2-3 weeks after onset of the primary obsessive illness (19).

Although these prior studies called the recurrent, ego-dystonic thoughts of infanticide an obsession consistent with postpartum OCD, the accuracy of this classification is unclear given the number of women who developed depression, in addition to the lack of compulsions or other obsessions more typical of OCD. Isolated obsessions of infanticide occurring in late pregnancy and the postpartum period have also been reported in the literature as a central psychopathologic feature of women diagnosed with schizophrenia and depression as well as OCD (83). Future studies are needed to determine whether intrusive thoughts of infanticide alone represent true OCD, depressive ruminations, or some other disorder all together.

OCD patients may also have a high lifetime prevalence of panic disorder as well as other anxiety disorders (84). In Sichel's case series described above, seven of the patients had a history of panic disorder, suggesting a similar relationship between pregnancy-related OCD and other anxiety disorders, and a potential heightened vulnerability in patients with these illnesses to onset of OCD in the puerperium (19).

II. Hypothesis and Study Aims

The primary goal of this study was to examine the impact of pregnancy, childbirth and menstruation on the onset and/or exacerbation of OCD according to DSM-IIIR criteria in women attending a university-based OCD Clinic between 1990 and 1995. In addition, we sought to examine the relationship between reports of menstrual cycle exacerbation in OCD symptoms and onset or exacerbation of OCD during pregnancy and the puerperium. We hypothesized that:

1. Within female OCD, there is a subset of patients whose symptoms are caused or exacerbated by fluctuations in female sex hormones that take place in the menstrual cycle and in the course of pregnancy and delivery. Thus women with OCD who reported perinatal onset or exacerbation of their symptoms would be more likely to experience premenstrual exacerbation of their OCD symptoms than those women with OCD who have experienced at least one previous pregnancy but deny perinatal onset or exacerbation of their disorder.

2. Compared with women with a history of pregnancy but no OCD exacerbations, the hormonally sensitive subgroup will:

(a) Report specific OCD symptoms that correspond with oxytocin-related rodent postpartum behavior, or that are related to typical human postpartum behavior, including contamination concerns, checking and cleaning, and aggressive obsessions (related to harming the infant), which have been frequently reported in the literature.

(b) Report a more acute onset of symptoms, (versus a gradual onset, which is more typically seen in OCD) corresponding to the rapid changes in hormonal levels.

(c) Report high rates of co-morbid affective disorders, as well as a strong family history of OCD and/or postpartum affective disorder. This is based on the existing literature regarding the significant influence of gonadal hormones on affective disorders, the relationship of these disorders with OCD, and contributing genetic factors.

III. Method

IIIa. Subjects and Recruitment

The data for this study were drawn from the medical records and verbal reports of individuals referred to the Yale OCD Clinic on the Clinical Neuroscience Research Unit at Connecticut Mental Health Center in New Haven, CT between 1990 and 1995. While men enrolled in the Clinic were also interviewed, this project focused on data obtained from women between age 18 and 69 years who met DSM-IIIR criteria for OCD according to a Structured Clinical Interview for Diagnosis (85) and had no lifetime history of an Axis I psychotic disorder or substance dependence disorder within the previous year. All participants were fluent in English. According to consenting procedures of the day, women who were already discharged from the OCD Clinic were sent a letter notifying them that a staff member would be contacting them to conduct an interview of approximately 30 minutes duration. Women were informed that the purpose of the interview was to obtain information about the onset and type of OCD symptoms they experience and how various treatments, substance use, and/or life events may have impacted their symptoms. Those who wished not to participate could indicate so by return mail or by phone. If such a request was not received, individuals were contacted by phone to conduct the interview. Individuals who were actively enrolled in the OCD Clinic were interviewed when they presented for a scheduled appointment. None of the active subjects refused to complete the interview.

For the purposes of this study, women were placed into one of two groups; Ever Pregnant (Preg) and Never Pregnant (NPreg) by virtue of self-report of their obstetrical history. Those women who were in the Preg group were further subdivided according to the following parameters: those who reported onset of OCD during pregnancy or the puerperium were assigned to the Puerperal Related (PR) group while those that denied onset of OCD related to pregnancy were assigned to the Non-Puerperal (NP) group.

IIIb. Database and Assessments

During the course of their treatment in the Yale OCD Clinic, patients were administered a number of clinical interviews including OCD severity ratings and depression inventories via the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) and the Yale Depression Inventory (YDI), respectively (86). This information was obtained from each participants Clinic record. The primary goal of the interview, from which data for this study was extracted, was to develop a complete database of all the patients (both male and female) who had been or were enrolled in the OCD Clinic. The database includes information regarding the following areas:

a. *Demographic data*: age, sex, marital status (single, married, divorced, widowed), race, level of education, and occupation.

b. *Clinical features of OCD*: age at onset of minor and major obsessive-compulsive symptoms and age of onset of the major syndrome. Patients were asked to characterize their obsessions and compulsions from a list of target symptoms, as well as describe the onset (acute vs. gradual) and course of

the disease over their lifetime (episodic vs. chronic). In order to investigate the relationship of their OCD symptoms to reproductive events (in women only), questions were asked regarding changes in symptoms prior to menses, during pregnancy, and in the postpartum period.

c. *Other variables*: history of substance use, medical history, prior psychiatric history (including co-morbid psychiatric illness), family history, and physical or psychological trauma.

IIIc. Statistical analysis

All data were summarized using descriptive statistics (means, SDs, frequencies). Continuous measures were compared between groups using a Student's t-test and categorical variables were assessed using the chi-square test. All analyses were considered statistically significant at $p < .05$ and performed using SAS, version 9.1.

IV. Results

IVa. Subjects - Pregnant versus Never Pregnant Group Comparisons

Of 140 potential subjects, sufficient data on OCD symptoms in relation to pregnancy was obtained in 126 women. Since this was the primary focus of our study, data from the remaining 14 subjects were not included in any analyses. Seventy-eight women reported having had at least one pregnancy (Preg Group), while 48 women reported never having been pregnant (NPreg Group).

Descriptive information for the Preg and NPreg groups is presented in Table 1. Mean age ± SD at presentation to the Yale OCD Clinic was significantly younger in the NPreg Group (32.6 ± 13 years) than the Preg Group (40.8 ± 10.8 years) ($t=3.82$, $df=123$, $p<0.0002$). However, there was no significant difference in age at onset of OCD in the Preg Group (26 ± 9 years) compared to the NPreg Group (23.8 ± 10.6 years) ($t=1.22$, $df=120$, $p=0.70$). The Preg group is comprised of 92.0% Caucasian women, 6.7% Hispanic women, and 1.3% other, while the NPreg group is comprised of 98% Caucasian and 2% Hispanic women. Compared to women in the NPreg Group, women in the Preg Group were more likely to be married ($X^2= 40.5$, $df =2$, $p<0.0001$) and less educated ($X^2=6.4$, $df=2$, $p=0.04$). Finally, there were no significant differences regarding comorbid diagnoses or family psychiatric history (including only professionally diagnosed illness). The majority of women in both groups reported a personal and family history of depression, substance abuse, and/or other anxiety disorder. Of the women who reported having co-morbid psychiatric diagnoses, the majority (in all groups) said that OCD presented first. A minority of subjects reported onset of depression or trichotillomania before OCD, and one subject who reported OCD onset related to pregnancy presented with new onset OCD and postpartum depression simultaneously.

Pregnancy Related Onset versus Onset Unrelated to Pregnancy Subgroup Comparisons

Of the Preg group, 24 (30.8%) fell into the PR subgroup by virtue of having reported the onset of OCD to be related to either pregnancy, fetal loss, or the postpartum period. Eleven of the Preg group (14.1%) reported onset during pregnancy, 1 (1.3%) had

onset after a miscarriage, and 12 (15.4%) had onset during the postpartum period. Thus, roughly half of the PR subgroup experienced onset during pregnancy while the other half experienced onset during the puerperium. Table 2 provides descriptive information for the PR and NP subgroups. Mean age ± SD on admission for the PR (39.3 ± 8.2 years) and NP (41.5 ±11.8) groups was similar, as was age at onset of OCD (PR subgroup 27 ± 7.1; NP subgroup 25.6 ± 9.8). There were no significant differences in any between subgroup comparisons with the exception that more women in the NP (22.2%) than in the PR subgroup (4.2%) carried a comorbid diagnosis which fell into our category of "other" (X^2=3.9, df=1, p=0.05). This category included diagnoses such as trichotillomania, eating disorders, and Tourette's syndrome. In addition, women in the NP subgroup (22.2%) were more likely to report a family history of substance abuse than women in the PR subgroup (4.2%) (X^2=3.9, df=1, p=0.05). While Yale Brown Obsessive Compulsive Scale (YBOCS) Scores obtained on admission to the OCD Clinic were available on roughly half of the women in each subgroup, there was a trend for women in the PR (29.5 ± 7.0) to have higher YBOCS Scores than women in the NP subgroup (25.7 ± 4.9) (t=1.93, df=35, p=0.06). YBOCS Scores in this range are consistent with moderate to severe illness. This is reflected in the baseline global assessment of function (GAF) scores which were lower in the PR subgroup (51.6 ± 7.1) but not significantly different from that in the NP (56.3 ± 14.0).

IVb. Course and Characteristics of OCD:

Preg and NPreg Group Comparisons

As mentioned, there was no significant difference found between the Preg and NPreg groups in the age of onset of OCD, and the vast majority (greater than 95%) described their course of illness as chronic rather than episodic. A greater proportion of women who had been pregnant reported acute onset of symptoms (47.8%), but this did not differ statistically from women who had never been pregnant (31.4%) (X^2=2.56, df=1, p=0.11).

The frequency of specific types of OCD symptoms in the Preg and NPreg groups is depicted in Table 6. Significant differences in specific types of symptoms were present only for religious/scrupulosity obsessions (X^2=6.01, df=1, p=0.01), ordering/arranging compulsions (X^2=5.51, df=1, p=0.02), and miscellaneous compulsions (X^2=6.633, df=1, p=0.01). There was also a trend for women in the NPreg Group to report having sexual obsessions (X^2=3.25, df=1, p=0.07) and a greater number of symptoms overall (t=1.8, df=123, p=0.07). Approximately 21% of women with OCD who had been pregnant experienced obsessions regarding harming their infant.

PR and NP Subgroup Comparisons

Women with pregnancy-related onset of OCD had a similar number of pregnancies as those with OCD onset unrelated to pregnancy, although onset of OCD with pregnancy was most likely to occur during or after the first pregnancy (Table 4). As was expected with any index event serving as a trigger for symptom onset, 62% of women in the PR subgroup reported acute onset of OCD symptoms compared to 42% in the NP subgroup. However, this difference was not statistically significant (X^2=2.4, df=1, p=0.12). Of the 12 women who reported postpartum onset of OCD, 10 answered

the question of how long after delivery their symptoms began. Seven out of the 10 reported that the onset of their OCD occurred "right away," while the remainder reported onset of symptoms within the first 6 months after delivery.

Type of obsessions and compulsions reported as primary symptoms by the PR and NP subgroups is described in Table 7. Only obsessions regarding contamination were significantly greater in the PR subgroup (66.7%) versus the NP subgroup (35.9%) (X^2=6.33, df=1, p=0.01). Interestingly, aggressive obsessions regarding the infant did not differ statistically.

IVc. Changes in Existing OCD During Pregnancy and the Premenstruum: Group and Subgroup Comparisons

Women in the Preg group who had onset of OCD prior to becoming pregnant reported worsening of symptoms with pregnancy in 45 (34.1%) cases, no change in 58 (43.9%), and improvement in 29 (22.0%). These results are reported in terms of pregnancies (rather than percentage of women) since nine women reported an exacerbation of OCD symptoms during one pregnancy, yet an improvement or no change during another. Women in the Preg and NPreg groups experienced worsening of symptoms prior to menses at approximately the same rate (48.4% of Preg, 51.6% of NPreg – see Table 3). As shown in Table 5, when women in the PR group were combined with those who reported any pregnancy-related worsening, there was a significant association with premenstrual worsening of OCD symptoms (X^2=3.93, df=1, P=.047).

V. Conclusion/Discussion

Main Findings:

Pregnancy and childbirth are characterized by enormous physiologic and psychological demands for the woman. The findings from our study add to the growing literature suggesting that pregnancy and childbirth can trigger the onset of OCD or the exacerbation of the ongoing disorder in a substantial number of women. Our discovery that roughly 30% of women experienced a perinatal related onset of the disorder is similar to that reported by others (10, 11). The predicted relationship between pregnancy-related symptoms and PMS related symptoms was confirmed, suggesting that there is a "hormone related" subtype of OCD in women. Women with pregnancy-related onset of OCD or perinatal worsening of pre-existing OCD are more likely to experience premenstrual exacerbation of their OCD symptoms when compared to those women with previous pregnancies but onset of OCD outside the perinatal period or no perinatal worsening. This latter finding is similar to what has been observed in affective disorders such as PMDD and PPD (87). In terms of changes in preexisting OCD, our results about changes during pregnancy are in agreement with previous studies, which reported both improvement and worsening of symptoms at this reproductive event.

In terms of specific symptoms present among our subjects, although there was a significantly greater amount of contamination obsessions reported by the PR group (which is consistent with prior research), we were surprised to find no significant difference between the groups in obsessions or compulsions related to typical postpartum behaviors (i.e., checking, cleaning, ordering/arranging). We hypothesized that women

with postpartum OCD would be more likely to have these types of symptoms as abnormal manifestations of normal maternal behavior. In addition, there was no significant difference found between the PR and NP groups in terms of having aggressive obsessions (including related to harming the infant), and there was a lower than expected proportion of women in the PR group (25%) reporting worries about aggression or harm to the infant. These findings are likely due to the stigma surrounding having these thoughts, and the resulting fear of admitting their presence in an interview format.

Although, as described above, a majority of women in the PR subgroup reported acute onset of OCD symptoms, our hypothesis that this would differ significantly from that reported by women with onset unrelated to pregnancy was not supported.

The comorbidity rate of about 65% of mood disorders (primarily major depression) in both groups of women is consistent with the results of previous research. However, our hypothesis that this percentage would be higher in the PR group versus the NP group was not supported. Moreover, in this sample and with the measures available, we did not find a significant difference between the groups in terms of family history of OCD or postpartum OCD/affective disorders.

Study Limitations:

Based on the retrospective studies that have been done, as many as 11% to 47% of women have their first onset of OCD in the peripartum period (13, 14, 92). Our results also suggest that both pregnancy and the postpartum may be periods of risk for the initiation of OCD, with the two periods conferring relatively equal risk. However, the results of prior research, including our study, are limited by their reliance on retrospective

recall. As discussed, there are no prospective studies analyzing the course of OCD during different reproductive events. Future prospective studies are necessary to further clarify the prevalence of OCD during pregnancy and the postpartum period, as well as to identify subgroups of women who may be particularly vulnerable to the development of this disorder. Another limitation of our study is the relatively small sample size, which reduces statistical power and makes it difficult to obtain definitive conclusions. If the sample size was increased, some of our negative results may have achieved significance. In addition, this study did not investigate changes in symptom severity specifically in the postpartum period; this is a definite weakness, as some women may have not been able to distinguish between pregnancy and the postpartum period when asked to recall changes in their symptoms at that time. Again, prospective assessments could address this weakness in the present research.

Future Directions:

In reviewing the literature, several suggestions can be made for future studies. Based on the results of Maina's study, which showed that postpartum OCD was much more frequent in the context of certain pregnancy complications or characteristics (14), future studies should include an assessment of obstetric complications in women with peripartum OCD symptoms. In addition, more studies need to consider the role of breastfeeding, as this extends and contributes to the period of hormonal fluctuations and often delays the return of the ovarian cycle. Regarding obsessions of harming the infant, future studies should assess these thoughts in more detail, including their frequency, the

level of distress induced, and the mother's assessment of the likelihood that she would carry out such thoughts.

Likewise, in future studies, greater emphasis should be placed on determining comorbid psychiatric diagnoses, as there is a high rate of comorbidity between OCD and major depression, even when related to pregnancy. In terms of treatment, the efficacy of high-potency dopaminergic antagonists in the treatment of certain OCD patients, as well as evidence linking dopamine excess to compulsive behaviors, argue for further exploration of the dopaminergic system.

Conclusions:

Even if no physical harm is done to the infant as a result of a mother's obsessional thoughts, these thoughts may negatively affect the infant's development in a variety of ways. For example, mothers who fear harming their infants may avoid them as a result, preventing the development of a secure mother-child relationship and affecting proper infant care. In addition, these obsessional thoughts likely affect a mother's confidence in her abilities, and may further hinder the development of a close relationship with her child (76). Increasing data shows that a poor early interaction between the parent and the infant may have detrimental long-term effects on the child, including increased vulnerability to stress and an increased risk for developing psychiatric disorders later in life (88, 89). Animal studies have also highlighted the importance of early mothering in determining the future maternal behavior of the adult offspring (90, 91).

OCD in the peripartum period is probably an underdiagnosed entity. It is thus crucial for healthcare providers to inquire about these problems and be aware of their

potential consequences, so that early intervention may take place. Women should be reassured that the occurrence of intrusive ego-dystonic thoughts is common, so that they may receive appropriate care without having to suffer in silence. Also, the extent to which peripartum OCD predicts increased likelihood of recurrence of the disorder during or after future pregnancies needs to be investigated, and if possible, prophylactic efforts should be made. Given current theories on the etiology of puerperal mental illness, it may be helpful for physicians to inquire about the severity of PMS symptoms, as well as personal and family psychiatric history, when attempting to perform risk assessment for a patient.

That approximately half (46-56%) of all of the women in this study, regardless of pregnancy history, reported a worsening of OCD symptoms during the premenstruum suggests that clinicians should consider the premenstruum as a trigger for symptom exacerbation and make decisions regarding treatment accordingly. Women with OCD who feel that their symptoms worsen in the premenstruum should keep a daily diary of symptom severity similar to that which is done by women undergoing evaluation for premenstrual dysphoric disorder. As a goal for future research, it would be interesting to prospectively assess the premenstruum and the puerperium in the same group of patients to determine if worsening of OCD during the premenstruum could act as a predictor of worsening or onset related to pregnancy.

Despite the limitations acknowledged above, our findings provide additional evidence that pregnancy and childbirth are frequently associated with the onset of OCD or worsening of symptoms in those with pre-existing disorder. In addition, the results of our research point to the relatively significant role of gonadal hormones in this

phenomenon; there appears to be continuity between OCD onset and/or exacerbation across the reproductive life cycle, at least with menstruation and pregnancy. Although the premenstruum, pregnancy, and postpartum periods all have differing hormonal shifts, they can all be characterized as hormonally unstable periods relative to other times in a woman's life cycle. Appreciating and understanding the role these hormones play in influencing the course of OCD may help to elucidate potential neurobiological mechanisms of this psychopathology, and will hopefully lead to the development of new concepts in treatment. However, concurrent with these hormonal fluctuations are dramatic and potentially stressful changes in the mother's psychosocial and interpersonal situation. Future studies will need to be designed in such a manner to begin to tease apart the relative contributions incorporated in the biopsychosocial model of the pathogenesis of OCD in the perinatal context.

Table 1. Demographic and Clinical Information - Preg vs. NPreg

	Pregnant (N=78)		Never Pregnant (N=48)		Statistics
	N	Mean±SD or (%)	N	Mean±SD or (%)	
Age on Admission	77	40.8±10.8	48	32.6±13.0	**t=3.82, df=123, P=.0002**
Race					
Caucasian	69	(92)	47	(98)	X^2=2.01, df=2, P=.37
Hispanic	5	(6.7)	1	(2)	
Other	1	(1.3)	0	(0)	
Marital					
Single	8	(10.4)	31	(64.6)	**X^2=40.5, df=2, P=.0001**
Married	54	(70.1)	14	(29.2)	
Divorced	15	(19.5)	3	(6.3)	
Education					
H.S. or less	31	(40.8)	10	(21.3)	**X^2=6.4, df=2, P=.04**
Technical school/partial college	15	(19.7)	17	(36.2)	
College or professional school	30	(39.5)	20	(42.3)	
Baseline Y-BOCS	37	27.0±5.9	26	25.1±5.9	t=1.27, df=61, P=.21
Baseline GAF	58	54.8±12.3	40	55.4±10.9	t=0.24, df=96, P=.81
Age onset of OCD	76	26.0±9.0	46	23.8±10.6	t=1.22, df=120, P=.23
Number prior psych hospitalizations	78	1.0±1.7	47	0.9±1.5	t=0.39, df=123, P=.70
Co-morbid diagnoses					
Any	48	(61.5)	34	(70.8)	X^2=1.13, df=1, P=.29
Substance abuse	0	(0)	1	(2.1)	X^2=1.64, df=1, P=.20
Affective disorder	41	(52.6)	25	(52.1)	X^2=0.003, df=1,

					P=.96
Other anxiety disorder	10	(12.8)	7	(14.6)	X^2=0.08, df=1, P=.78
Other	13	(16.7)	11	(22.9)	X^2=0.75, df=1, P=.39
Family history					
Any	69	(90.8)	39	(81.3)	X^2=2.38, df=1, P=.12
Substance abuse	13	(16.7)	9	(18.8)	X^2=0.09, df=1, P=.76
Affective disorder	18	(23.1)	12	(25.0)	X^2=0.06, df=1, P=.81
OCD	9	(11.5)	3	(6.3)	X^2=0.96, df=1, P=.33
Other anxiety disorder	3	(3.9)	0	(0)	X^2=1.89, df=1, P=.17
Other	8	(10.3)	2	(4.2)	X^2=1.51, df=1, P=.22

Table 2. Demographic and Clinical Information - PR vs. NP

	Pregnancy Related Onset (N=24)		Onset Unrelated to Pregnancy (N=53)		Statistics
	N	Mean±SD or (%)	N	Mean±SD or (%)	
Age on Admission	24	39.3±8.2	53	41.5±11.8	t=0.81, df=75, P=.42
Race					
Caucasian	21	(91.3)	48	(92.3)	X^2=2.53, df=2, P=.28
Hispanic	1	(4.4)	4	(7.7)	
Other	1	(4.3)	0	(0)	
Marital					
Single	4	(16.7)	4	(7.6)	X^2=1.52, df=2, P=.47
Married	16	(66.7)	38	(71.7)	
Divorced	4	(16.7)	11	(20.7)	
Education					
H.S. or less	8	(33.3)	23	(44.2)	X^2=1.01, df=2, P=.60
Technical school/partial college	6	(25.0)	9	(17.3)	
College or professional school	10	(41.7)	20	(38.5)	
Baseline Y-BOCS	13	29.5±7.0	24	25.74.9	t=1.93, df=35, P=.06
Baseline GAF	19	51.6±7.1	39	56.314.0	t=1.36, df=56, P=.18
Age onset of OCD	24	27.0±7.1	52	25.59.8	t=0.70, df=74, P=.49
Number prior psych hospitalizations	24	1.2±2.0	54	0.91.6	t=0.67, df=76, P=.51
Co-morbid diagnoses					
Any	13	(54.2)	35	(64.8)	X^2=0.80, df=1, P=.37
Substance abuse	0	(0)	0	(0)	N/A
Affective disorder	12	(50)	29	(53.7)	X^2=0.09, df=1,

					P=.76
Other anxiety disorder	4	(16.7)	6	(11.1)	X^2=0.46, df=1, P=.50
Other	1	(4.2)	12	(22.2)	**X^2=3.9, df=1, P=.05**
Family history					
Any	20	(87.0)	49	(92.5)	X^2=0.58, df=1, P=.45
Substance abuse	1	(4.2)	12	(22.2)	**X^2=3.90, df=1, P=.05**
Affective disorder	5	(20.8)	13	(24.1)	X^2=0.10, df=1, P=.75
OCD	2	(8.3)	7	(13.0)	X^2=0.35, df=1, P=.55
Other anxiety disorder	1	(4.2)	2	(3.7)	X^2=0.10, df=1, P=.92
Other	2	(8.3)	6	(11.1)	X^2=0.14, df=1, P=.71

Table 3. OCD and Reproductive Events - Preg vs. NPreg

	Pregnant (N=78)		Never Pregnant (N=48)		Statistics
	N	Mean±SD or (%)	N	Mean±SD or (%)	
Number of pregnancies	68	2.5±1.5		N/A	N/A
Number of abortions/miscarriages	66	0.5±0.8		N/A	N/A
Lifetime course of OCD					
Episodic	3	(4.2)	0	(0)	X^2=1.84, df=1, P=.18
Chronic	69	(95.8)	43	(100)	
Initial onset of major syndrome					
Acute	33	(47.8)	11	(31.4)	X^2=2.56, df=1, P=.11
Gradual	36	(52.2)	24	(68.6)	
Symptom changes prior to menses					
No change	27	(43.5)	14	(45.2)	
Worse	30	(48.4)	16	(51.6)	X^2=0.81, df=2, P=.67
Uncertain	5	(8.1)	1	(3.2)	
Onset - pregnancy					
No	66	(84.6)		N/A	N/A
Yes	12	(15.4)			
Onset - post loss					
No	18	(94.7)		N/A	N/A
Yes	1	(5.3)			

Onset - postpartum				
No	66	(84.6)	N/A	N/A
Yes	12	(15.4)		

Table 4. OCD and Reproductive Events - PR vs. NP

	Pregnancy-related Onset (N=24)		Onset unrelated to Pregnancy (N=54)		Statistics
	N	Mean±SD or (%)	N	Mean±SD or (%)	
Number of pregnancies	24	2.6±1.5	44	2.45±1.5	t=-0.46, df=66, P=.65
Number of abortions/miscarriages	24	0.6±0.9	42	0.6±0.79	N/A
Lifetime course of OCD					
Episodic	1	(4.8)	2	(3.9)	X^2=0.03, df=1, P=.87
Chronic	20	(95.2)	49	(96.1)	
Initial onset of major syndrome					
Acute	13	(61.9)	20	(41.7)	X^2=2.40, df=1, P=.12
Gradual	8	(38.1)	28	(58.3)	
Symptom changes prior to menses					
No change	6	(37.5)	21	(45.7)	X^2=0.54, df=2, P=.76
Worse	9	(56.3)	21	(45.7)	
Uncertain	1	(6.2)	4	(8.7)	
Onset - pregnancy					

No	12	(50.0)	N/A	N/A
Yes	12	(50.0)		
Onset - post loss				
No	7	(87.5)	N/A	N/A
Yes	1	(12.5)		
Onset - postpartum				
No	12	(50.0)	N/A	N/A
Yes	12	(50.0)		

Table 5. OCD and Reproductive Events - Combined Analysis

	Onset Related OR worsening Sx during Pregnancy		Onset Unrelated to Pregnancy		Statistics
	N	Mean±SD or (%)	N	Mean±SD or (%)	
Symptom changes prior to menses					
No change	10	(34.5)	17	(60.7)	
Worse	19	(65.5)	11	(39.3)	**X^2=3.93, df=1, P=.047**

Table 6. Major OCD Symptoms - Preg vs. NPreg

	Pregnant (N=77)	Never Pregnant (N=48)	Statistics
	N (%)	N (%)	
Major OCD Symptoms			
Aggressive	22 (28.6)	18 (37.5)	X^2=1.08, df=1, P=.30
Contamination	35 (45.5)	23 (47.9)	X^2=0.07, df=1, P=.79
Sexual	4 (5.2)	7 (14.6)	X^2=3.25, df=1, P=.07
Hoarding/saving	5 (6.5)	6 (12.5)	X^2=1.33, df=1, P=.25
Religious/scrupulosity	3 (3.9)	8 (16.7)	**X^2=6.01, df=1, P=.01**
Symmetry/exactness	17 (22.1)	13 (27.1)	X^2=0.41, df=1, P=.52
Somatic/illness	5 (6.5)	4 (8.3)	X^2=0.15, df=1, P=.70
Misc. obsessions	23 (30)	15 (31)	X^2=0.03, df=1, P=.87
Cleaning/washing	45 (58.4)	23 (47.9)	X^2=1.32, df=1, P=.25
Checking	38 (49.4)	27 (56.3)	X^2=0.56, df=1, P=.45
Repeating	24 (31.2)	18 (37.5)	X^2=0.53, df=1, P=.47
Counting	12 (15.6)	11 (22.9)	X^2=1.06, df=1, P=.30
Ordering/arranging	17 (22.1)	3 (6.3)	**X^2=5.51, df=1, P=.02**
Collecting	5 (6.5)	8 (16.7)	X^2=3.28, df=1, P=.07
Misc. compulsions	11 (14.3)	16 (33.3)	**X^2=6.33, df=1, P=.01**
Worry - aggression/harm to babies	16 (20.8)	n/a	
Total number of major symptoms	3.7±1.4 (n=77)	4.2±2.0 (n=48)	t=1.8, df=123, P=.07

Note: One woman in the Pregnant Group had missing data thus the sample size for this table was n=77

Table 7. Major OCD Symptoms - PR vs. NP

	Pregnancy-related Onset (N=24)	Onset unrelated to Pregnancy (N=53)	Statistics
	N (%)	N (%)	
Major OCD Symptoms			
Aggressive	5 (20.8)	17 (32.1)	X^2=1.02, df=1, P=.31
Contamination	16 (66.7)	19 (35.9)	**X^2=6.33, df=1, P=.01**
Sexual	1 (4.2)	3 (5.7)	X^2=0.07, df=1, P=.78
Hoarding/saving	0 (0)	5 (9.4)	X^2=2.42, df=1, P=.12
Religious/scrupulosity	1 (4.2)	2 (3.8)	X^2=0.01, df=1, P=.93
Symmetry/exactness	6 (25.0)	11 (20.8)	X^2=0.17, df=1, P=.68
Somatic/illness	2 (8.3)	3 (5.7)	X^2=0.19, df=1, P=.66
Misc. obsessions	6 (25.0)	17 (32.1)	X^2=0.39, df=1, P=.53
Cleaning/washing	17 (10.8)	28 (52.8)	X^2=2.20, df=1, P=.14
Checking	12 (50.0)	26 (49.1)	X^2=0.01, df=1, P=.94
Repeating	8 (33.3)	16 (30.2)	X^2=0.08, df=1, P=.78
Counting	1 (4.2)	11 (20.8)	X^2=3.46, df=1, P=.06
Ordering/arranging	6 (25.0)	11 (20.8)	X^2=0.17, df=1, P=.68
Collecting	0 (0)	5 (9.4)	X^2=2.42, df=1, P=.12
Misc. compulsions	2 (8.3)	9 (17.0)	X^2=1.01, df=1, P=.32
Worry - aggression/harm to babies	6 (25.0)	10 (18.9)	X^2=0.38, df=1, P=.54
Total number of major symptoms	3.7±1.3 (n=24)	3.6±1.5 (n=53)	t=0.19, df=75, P=.85

Note: One woman in the Onset Unrelated to Pregnancy Group did not have this information thus sample size for this table is N=53

References

1. Turnbull JM. Mental illness in the puerperium. Canadian Psychiatric Association Journal 14(5):525-6, 1969 Oct.
2. First MB, ed. Diagnostic and Statistical Manual - Text Revision (DSM-IV-TR™, 2000). IV-TR ed. Washington, DC: American Psychiatric Association; 2000.
3. Karno M, Golding JM, Sorenson SB, Burnam MA. The epidemiology of obsessive-compulsive disorder in five US communities. Archives of General Psychiatry 45(12):1094-9, 1988 Dec.
4. Rasmussen SA, Eisen JL. Epidemiology of obsessive compulsive disorder. [Review] [22 refs]. Journal of Clinical Psychiatry 51 Suppl:10-3; discussion 14, 1990 Feb.
5. Bebbington PE. Epidemiology of obsessive-compulsive disorder. Br J Psychiatry;Suppl (35):2-6, 1998.
6. Brandes M, Soares CN, Cohen LS. Postpartum onset obsessive-compulsive disorder: diagnosis and management. [Review] [152 refs]. Archives of Women's Mental Health 7(2):99-110, 2004 Apr.
7. Pollitt J. Natural history of obsessional states. British Medical Journal 1957;9:133-40.
8. Ingram IM. Obsessional illness in mental hospital patients. Journal of Mental Science 1961;107:382-402.
9. Lo WH. A follow-up study of obsessional neurotics in Hong Kong Chinese. Br J Psychiatry 1967;113(501):823-32.
10. Buttolph ML, & Holland, A.D. Obsessive-compulsive disorders in pregnancy and childbirth. In: M. Jenike LB, & W. Minichiello, ed. Obsessive-compulsive disorders: theory and management. Chicago: Year Book Medical; 1990:89-97.
11. Neziroglu F, Anemone R, Yaryura-Tobias JA. Onset of obsessive-compulsive disorder in pregnancy.[see comment]. Am J Psychiatry 1992;149(7):947-50.
12. Sichel DA, Cohen LS, Rosenbaum JF, Driscoll J. Postpartum onset of obsessive-compulsive disorder. Psychosomatics 34(3):277-9, 1993 May-Jun.
13. Williams KE, Koran LM. Obsessive-compulsive disorder in pregnancy, the puerperium, and the premenstruum. Journal of Clinical Psychiatry 58(7):330-4; quiz 335-6, 1997 Jul.
14. Maina G, Albert U, Bogetto F, Vaschetto P, Ravizza L. Recent life events and obsessive-compulsive disorder (OCD): the role of pregnancy/delivery. Psychiatry Research 89(1):49-58, 1999 Dec 13.
15. Labad J, Menchon JM, Alonso P, Segalas C, Jimenez S, Vallejo J. Female reproductive cycle and obsessive-compulsive disorder. Journal of Clinical Psychiatry 66(4):428-35; quiz 546, 2005 Apr.
16. Brandt KR, Mackenzie TB. Obsessive-compulsive disorder exacerbated during pregnancy: a case report. International Journal of Psychiatry in Medicine 17(4):361-6, 1987.
17. Geller PA, Klier CM, Neugebauer R. Anxiety disorders following miscarriage. Journal of Clinical Psychiatry 62(6):432-8, 2001 Jun.

18. Altshuler LL, Hendrick V, Cohen LS. Course of mood and anxiety disorders during pregnancy and the postpartum period. [Review] [68 refs]. Journal of Clinical Psychiatry 59 Suppl 2:29-33, 1998.
19. Sichel DA, Cohen LS, Dimmock JA, Rosenbaum JF. Postpartum obsessive compulsive disorder: a case series. Journal of Clinical Psychiatry 54(4):156-9, 1993 Apr.
20. Iancu I, Lepkifker E, Dannon P, Kotler M. Obsessive-compulsive disorder limited to pregnancy. Psychotherapy & Psychosomatics 64(2):109-12, 1995.
21. Arnold L. A case series of women with postpartum-onset obsessive-compulsive disorder. J Clin Psychiatry 1999;1:103-8.
22. Rauch SL, Jenike MA. Neurobiological models of obsessive-compulsive disorder. [Review] [106 refs]. Psychosomatics 34(1):20-32, 1993 Jan-Feb.
23. Jenike MA, Hyman S, Baer L, et al. A controlled trial of fluvoxamine in obsessive-compulsive disorder: implications for a serotonergic theory.[see comment]. American Journal of Psychiatry 147(9):1209-15, 1990 Sep.
24. Jenike MA, Rauch SL, Cummings JL, Savage CR, Goodman WK. Recent developments in neurobiology of obsessive-compulsive disorder. Journal of Clinical Psychiatry 57(10):492-503, 1996 Oct.
25. McDougle CJ, Goodman WK, Price LH, et al. Neuroleptic addition in fluvoxamine-refractory obsessive-compulsive disorder. American Journal of Psychiatry 147(5):652-4, 1990 May.
26. Pitman RK. Animal models of compulsive behavior. [Review] [66 refs]. Biological Psychiatry 26(2):189-98, 1989 Jun.
27. Insel TR. Toward a neuroanatomy of obsessive-compulsive disorder.[see comment]. [Review] [57 refs]. Archives of General Psychiatry 49(9):739-44, 1992 Sep.
28. Whiteside SP, Port JD, Abramowitz JS. A meta-analysis of functional neuroimaging in obsessive-compulsive disorder. Psychiatry Research 132(1):69-79, 2004 Nov 15.
29. Speroff L, Fritz M, eds. Clinical Gynecologic Endocrinology & Infertility. 7th Edition ed. Philadelphia: Lippincott Williams & Wilkins; 2005.
30. Glaser J, Russell VA, de Villiers AS, Searson JA, Taljaard JJ. Rat brain monoamine and Serotonin S2 receptor changes during pregnancy. Neurochemical Research 15(10):949-56, 1990 Oct.
31. Pecins-Thompson M, Brown NA, Kohama SG, Bethea CL. Ovarian Steroid Regulation of Tryptophan Hydroxylase mRNA Expression in Rhesus Macaques. J Neurosci 1996;16(21):7021-9.
32. Sumner BEH, Fink G. The density of 5-hydoxytryptamine2A receptors in forebrain is increased at pro-oestrus in intact female rats. Neuroscience Letters 1997;234(1):7-10.
33. Ehrenkranz JR. Effects of sex steroids on serotonin uptake in blood platelets. Acta Endocrinologica 83(2):420-8, 1976 Oct.
34. Biegon A, McEwen BS. Modulation by estradiol of serotonin receptors in brain. Journal of Neuroscience 2(2):199-205, 1982 Feb.
35. Moskovitz RA, Lingao A. Binge eating associated with oral contraceptives. American Journal of Psychiatry 136(5):721-2, 1979 May.
36. Calanchini C. [Development of a compulsive syndrome by ovulation inhibitors]. [German]. Schweizer Archiv fur Neurologie und Psychiatrie 137(4):25-31, 1986.

37. Lochner C, Hemmings SM, Kinnear CJ, et al. Corrigendum to "gender in obsessive-compulsive disorder: clinical and genetic findings" [Eur. Neuropsychopharmacol. 14 (2004) 105-113].[republished from Eur Neuropsychopharmacol. 2004 Mar;14(2):105-13; PMID: 15013025]. European Neuropsychopharmacology 14(5):437-45, 2004 Oct.
38. Dalton K. Prospective study into puerperal depression. British Journal of Psychiatry 118(547):689-92, 1971 Jun.
39. Steiner M, Dunn E, Born L. Hormones and mood: from menarche to menopause and beyond. [Review] [183 refs]. Journal of Affective Disorders 74(1):67-83, 2003 Mar.
40. Leckman JF, Goodman WK, North WG, et al. The role of central oxytocin in obsessive compulsive disorder and related normal behavior. [Review] [230 refs]. Psychoneuroendocrinology 19(8):723-49, 1994.
41. Denys D, Zohar J, Westenberg HG. The role of dopamine in obsessive-compulsive disorder: preclinical and clinical evidence. Journal of Clinical Psychiatry 65 Suppl 14:11-7, 2004.
42. Chakrabarty K, Bhattacharyya S, Christopher R, Khanna S. Glutamatergic dysfunction in OCD. Neuropsychopharmacology 30(9):1735-40, 2005 Sep.
43. Silverman AJ, Zimmerman EA. Magnocellular neurosecretory system. Annual Review of Neuroscience 6:357-80, 1983.
44. Insel TR. Oxytocin--a neuropeptide for affiliation: evidence from behavioral, receptor autoradiographic, and comparative studies. [Review] [144 refs]. Psychoneuroendocrinology 17(1):3-35, 1992.
45. Pedersen CA, Prange AJ, Jr. Induction of maternal behavior in virgin rats after intracerebroventricular administration of oxytocin. Proceedings of the National Academy of Sciences of the United States of America 76(12):6661-5, 1979 Dec.
46. McCarthy MM. Oxytocin inhibits infanticide in female house mice (Mus domesticus). Hormones & Behavior 24(3):365-75, 1990 Sep.
47. Kaltwasser MT, Crawley JN. Oxytocin and cholecystokinin induce grooming behavior in the ventral tegmentum of the rat. Brain Research 426(1):1-7, 1987 Nov 17.
48. Miller FD, Ozimek G, Milner RJ, Bloom FE. Regulation of neuronal oxytocin mRNA by ovarian steroids in the mature and developing hypothalamus. Proceedings of the National Academy of Sciences of the United States of America 86(7):2468-72, 1989 Apr.
49. Sofroniew MV WA. Central nervous system distribution of vasopressin, oxytocin, and neurophysin. In: Martinez JL JR, Mesin RB, Rigter H, McGraugh JL, ed. Endogenous Peptides and Learning and Memory Processes. New York: Academic Press; 1981:327-69.
50. Leckman JF, Goodman WK, North WG, et al. Elevated cerebrospinal fluid levels of oxytocin in obsessive-compulsive disorder. Comparison with Tourette's syndrome and healthy controls. Archives of General Psychiatry 51(10):782-92, 1994 Oct.
51. Greer ER, Caldwell JD, Johnson MF, Prange AJ, Jr., Pedersen CA. Variations in concentration of oxytocin and vasopressin in the paraventricular nucleus of the hypothalamus during the estrous cycle in rats. Life Sciences 38(25):2311-8, 1986 Jun 23.
52. Yamaguchi K, Akaishi T, Negoro H. Effect of estrogen treatment on plasma oxytocin and vasopressin in ovariectomized rats. Endocrinologia Japonica 26(2):197-205, 1979 Apr.

53. De Kloet ER, Rotteveel F, Voorhuis TA, Terlou M. Topography of binding sites for neurohypophyseal hormones in rat brain. European Journal of Pharmacology 110(1):113-9, 1985 Mar 26.
54. Rhodes CH, Morrell JI, Pfaff DW. Estrogen-concentrating neurophysin-containing hypothalamic magnocellular neurons in the vasopressin-deficient (Brattleboro) rat: a study combining steroid autoradiography and immunocytochemistry. Journal of Neuroscience 2(12):1718-24, 1982 Dec.
55. Insel TR. Postpartum increases in brain oxytocin binding. Neuroendocrinology 44(4):515-8, 1986.
56. Kendrick KM, Keverne EB, Hinton MR, Goode JA. Cerebrospinal fluid and plasma concentrations of oxytocin and vasopressin during parturition and vaginocervical stimulation in the sheep. Brain Research Bulletin 26(5):803-7, 1991 May.
57. Altemus M, Jacobson KR, Debellis M, et al. Normal CSF oxytocin and NPY levels in OCD. Biological Psychiatry 45(7):931-3, 1999 Apr 1.
58. Swedo SE, Leonard HL, Kruesi MJ, et al. Cerebrospinal fluid neurochemistry in children and adolescents with obsessive-compulsive disorder. Archives of General Psychiatry 49(1):29-36, 1992 Jan.
59. Ansseau M, Legros JJ, Mormont C, et al. Intranasal oxytocin in obsessive-compulsive disorder. Psychoneuroendocrinology 12(3):231-6, 1987.
60. den Boer JA, Westenberg HG. Oxytocin in obsessive compulsive disorder. Peptides 13(6):1083-5, 1992 Nov-Dec.
61. Epperson CN, McDougle CJ, Price LH. Intranasal oxytocin in obsessive-compulsive disorder. Biological Psychiatry 40(6):547-9, 1996 Sep 15.
62. Abramowitz J, Moore K, Carmin C, Wiegartz PS, Purdon C. Acute onset of obsessive-compulsive disorder in males following childbirth. Psychosomatics 42(5):429-31, 2001 Sep-Oct.
63. Nestadt G, Samuels J, Riddle M, et al. A family study of obsessive-compulsive disorder. Archives of General Psychiatry 57(4):358-63, 2000 Apr.
64. Pauls DL, Alsobrook JP, 2nd, Goodman W, Rasmussen S, Leckman JF. A family study of obsessive-compulsive disorder. American Journal of Psychiatry 152(1):76-84, 1995 Jan.
65. Sciuto G, Pasquale L, Bellodi L. Obsessive compulsive disorder and mood disorders: a family study. American Journal of Medical Genetics 60(6):475-9, 1995 Dec 18.
66. Camarena B, Rinetti G, Cruz C, Gomez A, de La Fuente JR, Nicolini H. Additional evidence that genetic variation of MAO-A gene supports a gender subtype in obsessive-compulsive disorder. American Journal of Medical Genetics 105(3):279-82, 2001 Apr 8.
67. Cavallini MC, Pasquale L, Bellodi L, Smeraldi E. Complex segregation analysis for obsessive compulsive disorder and related disorders. American Journal of Medical Genetics 88(1):38-43, 1999 Feb 5.
68. Noshirvani HF, Kasvikis Y, Marks IM, Tsakiris F, Monteiro WO. Gender-divergent aetiological factors in obsessive-compulsive disorder. British Journal of Psychiatry 158:260-3, 1991 Feb.

69. Rasmussen SA, Tsuang MT. Clinical characteristics and family history in DSM-III obsessive-compulsive disorder. American Journal of Psychiatry 143(3):317-22, 1986 Mar.
70. Paykel ES, Emms EM, Fletcher J, Rassaby ES. Life events and social support in puerperal depression. British Journal of Psychiatry 136:339-46, 1980 Apr.
71. Leckman JF, Herman AE. Maternal behavior and developmental psychopathology. Biological Psychiatry 51(1):27-43, 2002 Jan 1.
72. Leckman JF, Feldman R, Swain JE, Eicher V, Thompson N, Mayes LC. Primary parental preoccupation: circuits, genes, and the crucial role of the environment. [Review] [120 refs]. Journal of Neural Transmission 111(7):753-71, 2004 Jul.
73. Winnicott D. Primary maternal preoccupation. In: Collected Papers: Through Paediatrics to Psycho-Analysis. New York: Basic Books; 1956.
74. Leckman JF, Mayes LC, Feldman R, Evans DW, King RA, Cohen DJ. Early parental preoccupations and behaviors and their possible relationship to the symptoms of obsessive-compulsive disorder. Acta Psychiatrica Scandinavica, Supplementum 396:1-26, 1999.
75. Wisner KL, Peindl KS, Gigliotti T, Hanusa BH. Obsessions and compulsions in women with postpartum depression. Journal of Clinical Psychiatry 60(3):176-80, 1999 Mar.
76. Jennings KD, Ross S, Popper S, Elmore M. Thoughts of harming infants in depressed and nondepressed mothers. Journal of Affective Disorders 54(1-2):21-8, 1999 Jul.
77. Salkovskis PM. Understanding and treating obsessive-compulsive disorder. [Review] [55 refs]. Behaviour Research & Therapy 37 Suppl 1:S29-52, 1999 Jul.
78. Rachman S, de Silva P. Abnormal and normal obsessions. Behaviour Research & Therapy 16(4):233-48, 1978.
79. Stern RS, Cobb JP. Phenomenology of obsessive-compulsive neurosis. Br J Psychiatry 1978;132:233-9.
80. Bellodi L, Sciuto G, Diaferia G, Ronchi P, Smeraldi E. Psychiatric disorders in the families of patients with obsessive-compulsive disorder. Psychiatry Research 42(2):111-20, 1992 May.
81. Barlow D. Obsessive compulsive disorder. In: DH B, ed. Anxiety and Its Disorders. New York: The Guilford Press; 1989:598-635.
82. Rasmussen SA, Eisen JL. The epidemiology and differential diagnosis of obsessive compulsive disorder. [Review] [35 refs]. Journal of Clinical Psychiatry 55 Suppl:5-10; discussion 11-4, 1994 Oct.
83. Button JH, Reivich RS. Obsessions of infanticide. A review of 42 cases. Archives of General Psychiatry 27(2):235-40, 1972 Aug.
84. Robins LN, Helzer JE, Weissman MM, et al. Lifetime prevalence of specific psychiatric disorders in three sites. Archives of General Psychiatry 41(10):949-58, 1984 Oct.
85. First MB, Spitzer RL, Gibbon M, Williams JB. Structured Clinical Interview for DSM-IV Axis I Disorders- Patient Edition SCID-I/P. New York: New York State Psychiatric Institute; 1995.

86. Goodman WK, Price LH, Rasmussen SA, et al. The Yale-Brown Obsessive Compulsive Scale. I. Development, use, and reliability. Archives of General Psychiatry 46(11):1006-11, 1989 Nov.
87. Bloch M, Rotenberg N, Koren D, Klein E. Risk factors associated with the development of postpartum mood disorders. Journal of Affective Disorders 88(1):9-18, 2005 Sep.
88. Sroufe LA, Carlson EA, Levy AK, Egeland B. Implications of attachment theory for developmental psychopathology. [Review] [60 refs]. Development & Psychopathology 11(1):1-13, 1999.
89. Kendler KS, Kessler RC, Neale MC, Heath AC, Eaves LJ. The prediction of major depression in women: toward an integrated etiologic model. American Journal of Psychiatry 150(8):1139-48, 1993 Aug.
90. Francis D, Diorio J, Liu D, Meaney MJ. Nongenomic transmission across generations of maternal behavior and stress responses in the rat. Science 286(5442):1155-8, 1999 Nov 5.
91. Suomi SJ RC. A history of motherless mothering at the University of Wisconsin Primate Laboratory. In: Reite M CN, ed. Child abuse: the non-human data. New York: Alan R Liss; 1983:49-78.
92. Leckman JF, Mayes LC. Preoccupations and behaviors associated with romantic and parental love. Perspectives on the origin of obsessive-compulsive disorder. [Review] [152 refs]. Child & Adolescent Psychiatric Clinics of North America 8(3):635-65, 1999 Jul.