
Reproductive Mental Health Guideline 5
MENTAL ILLNESS DURING THE PERINATAL PERIOD:
ANXIETY DISORDERS

In contrast to major depressive disorder, less is known about the impact of pregnancy and childbirth on the development and course of anxiety disorders. The most common anxiety disorders include: social anxiety disorder, generalized anxiety disorder, panic disorder, post-traumatic stress disorder, and obsessive-compulsive disorder. Only panic disorder, obsessive – compulsive disorder, and the overlap between anxiety disorder and depression are discussed in this guideline.

ANXIETY DISORDERS

I. PANIC DISORDER

The most distinguishing feature of panic disorder is a sudden and persistent *unreasonable* fear brought on by the presence or anticipation of a specific object or situation. Panic disorder is more common in adult women than in men, and the onset of this disorder is typically during the mid 20s, which coincides with the peak childbearing years. The prevalence of panic disorder in the general adult population has been reported to be around 2%; the prevalence during pregnancy and the postpartum period has not been accurately documented in the literature, due to a lack of longitudinal and epidemiological studies.

The course of this disorder in pregnancy remains unclear. Several case reports of pregnant women with pre-existing panic disorder have suggested a decrease in symptoms during pregnancy.^{1,2} One of the only *prospective* studies however, found no decrease in panic symptoms during pregnancy.³ A recent case series that retrospectively followed 49 women, suggested that patients with milder symptoms of panic may improve during their pregnancies; women with more severe panic disorder however, may constitute a subgroup who are at an increased risk during pregnancy for continuation and exacerbation of the pre-existing illness.⁴ It is possible, therefore, that the conflicting reports in the literature on the impact of pregnancy on panic disorder may be a result of the variability in symptom severity of the patients being described.

Research studies have more consistently shown that the postpartum period is a time of increased susceptibility to both the onset as well as the exacerbation of symptoms of pre-existing panic disorder.^{3,5-7} The pathophysiology of why this worsens postpartum remains unclear. Some researchers have suggested that panic attacks may be the result of rapidly shifting levels of reproductive hormones on the monoaminergic binding sites.⁷ Another possible explanation is that the sharp fall in progesterone levels after delivery results in an increased vulnerability to panic attacks.⁸

II. OBSESSIVE-COMPULSIVE DISORDER

Obsessive-compulsive disorder (OCD) is characterized by persistent, intrusive, and unwanted thoughts that the patient finds difficult to control. In addition, many individuals may experience uncontrollable urges to carry out particular behaviours or rituals in order to alleviate the obsessional thoughts. The prevalence of OCD in the general population is between 1 and 3%; the onset is most commonly in adolescence or early adulthood. Several reports indicate that pregnant and postpartum women may be at an increased risk for the onset of this disorder.⁹⁻¹¹ Women with pre-existing OCD may also be at an increased risk for developing major depression in the postpartum period.¹² Furthermore, there is evidence to suggest that OCD begins and/or worsens more frequently during the postpartum period than at any other time in a woman's life.¹² At the present time, factors that predict the course of OCD in pregnancy and during the postpartum period have yet to be elucidated.

III. OVERLAP BETWEEN ANXIETY DISORDERS AND DEPRESSION

Although depression and anxiety disorders represent discreet clinical syndromes, they do have overlapping symptoms, and may share similar neurobiological mechanisms.^{13,14} The symptoms that most commonly overlap depression and anxiety disorders include sleep and concentration difficulties, tension, excessive worrying, fear, and the onset of panic attacks. Two recent community samples reported that approximately 50% of those who met the criteria for lifetime depression also met the criteria for some type of co-morbid anxiety disorder.^{15,16}

RISK FACTORS FOR AN ANXIETY DISORDER DURING THE PERINATAL PERIOD

Factors associated with a heightened risk for the development of an anxiety disorder during the perinatal period have not been documented as clearly as those for depression. However, clinical experiences indicate that many of the factors that play a role in the development of depression also contribute to panic disorder and/or obsessive-compulsive disorder. This is supported by the fact that there is significant co-morbidity between anxiety disorders and major depressive disorder, as stated earlier, and this overlap likely also extends to the risk factors that contribute to these disorders. These factors include:

I. MAJOR FACTORS

- Previous history of anxiety disorders during pregnancy and/or the postpartum period
- Previous history of anxiety disorders not related to pregnancy or the postpartum period
- Family history (blood relatives) of anxiety disorders during pregnancy and/or the postpartum period

II. CONTRIBUTING FACTORS

- Adverse life events
- Marital instability
- Infants with health problems or perceived difficult temperaments
- Chronic or acute maternal health problems, such as thyroid disease and diabetes
- Relationship to smoking, caffeine intake, exercise

SIGNS AND SYMPTOMS OF ANXIETY DISORDERS DURING THE PERINATAL PERIOD

**TABLE 1: Summary of Criteria for Panic Disorder
(Adapted from DSM-IV, American Psychiatric Association (APA), 1994)¹⁷**

<p>A. The following must both be present:</p> <ol style="list-style-type: none">1. *Recurrent unexpected panic attacks (see description below)2. One or more of these attacks must have been followed by one month or more of any of the following:<ul style="list-style-type: none">-persistent concern about having additional panic attacks-worry about the implications or consequences of the attacks-a significant change in behaviour related to the attacks <p>B. The panic attacks are not due to the direct physiological effects of a substance or a general medical condition</p> <p>C. The panic attacks are not better accounted for by another mental disorder such as Social Phobia, Specific Phobia, Obsessive-Compulsive Disorder, Post-traumatic Stress Disorder, or Separation Anxiety Disorder</p>
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***Panic Attacks**

A panic attack is defined in the DSM-IV as a discrete period in which there is a sudden onset of 4 or more of the following symptoms: pounding heart, sweating, trembling or shaking, shortness of breath, feeling of choking, chest pain or discomfort, nausea, feeling dizzy or lightheaded, derealization or depersonalization, fear of losing control, fear of dying, numbness or tingling sensations, and chills or hot flushes. A panic attack is not a codeable disorder on its own; it is only when several panic attacks occur unexpectedly that a diagnosis of Panic Disorder is made. However, panic attacks that do not occur frequently enough to meet the criteria for panic disorder can occur in the context of other mood disorders, particularly major depression and other anxiety disorders such as obsessive compulsive disorder, social phobia, generalized anxiety disorder, or post-traumatic stress disorder.

In addition, the DSM-IV specifies whether the Panic Disorder is accompanied by Agoraphobia, although agoraphobia is also not considered to be a codeable disorder on its own. Agoraphobia is characterized by anxiety about, and subsequent avoidance of, being in places or situations from which escape might be difficult or in which help may not be available in the event of a panic attack.

**TABLE 2: Summary of Criteria for Obsessive Compulsive Disorder
(Adapted from DSM-IV, American Psychiatric Association (APA), 1994)¹⁷**

A. Either **obsessions** or **compulsions** are present.

Obsessions are defined by:

1. Recurrent and persistent thoughts, impulses, or images that are experienced to be intrusive or inappropriate, and cause marked anxiety or distress.
2. Thoughts, impulses, and images are not simply excessive worrying about real life problems.
3. The person attempts to ignore, suppress, and/or neutralize these thoughts, impulses, and images.
4. The person recognized that these thoughts, impulses, and images are a product of his or her own mind.

Compulsions are defined by:

1. Repetitive behaviours (i.e.: hand washing, checking) or mental acts (i.e.: praying, counting) in response to an obsession.
2. The behaviours and mental acts are aimed at preventing an event or situation, but are not connected in a realistic way to the event or situation.

B. At some point during the course of the disorder, the person recognizes that the obsessions and compulsions are excessive or unreasonable.

C. The obsessions and compulsions cause marked distress, are time consuming, or significantly interfere with a daily, occupational, and/or social functioning.

D. If another clinical psychiatric disorder is present, the obsessions and compulsions must not be limited to it (i.e.: obsessions and compulsions centred on food in the presence of an eating disorder).

E. The obsessions and compulsions are not due to the effects of a substance or due to a general medical condition.

ASSESSMENT TOOLS

There are several screening tools that can be used for early detection and diagnosis of an anxiety disorder during pregnancy and the postpartum period.

I. HAMILTON ANXIETY SCALE (HAM-A)

The HAM-A is a clinician rated scale used to measure the severity of anxiety symptoms, and is the most widely used assessment scale for anxiety.¹⁸ This brief tool consists of 14 items, with each being rated on a scale from 0 to 4. Only one question on this scale deals with “depressed

mood”, thus when the HAM-A is used to assess patients with concomitant major depression, it should be paired with a scale that measures depressive symptoms, such as the HAM-D or MADRS.

II. MINI-INTERNATIONAL NEUROPSYCHIATRIC INTERVIEW (M.I.N.I., Version 5.0.0)

The M.I.N.I. is a short, structured, clinician-rated scale that is based on the criterion for the Axis I psychiatric disorders described in both the DSM-IV (Canada and USA) and the ICD-10 (Europe).¹⁹ Module E of the M.I.N.I. focuses specifically on panic disorder, while module H deals with obsessive-compulsive disorder. The M.I.N.I. is used to *establish* the diagnosis of either of these disorders. The scale has been translated into 30 languages, and both reliability and validity have been demonstrated in several studies.¹⁹ *A copy of the M.I.N.I. can be found in the Journal of Clinical Psychiatry, 1998; 59(Suppl 20): 34-57.*

III. YALE-BROWN OBSESSIVE-COMPULSIVE SCALE (Y-BOCS)

The Y-BOCS is a short questionnaire used to rate the type, severity, and change over time of symptoms in patients who have already been diagnosed with obsessive-compulsive disorder.^{20,21} It consists of 5 questions related to obsessions, and 5 questions related to compulsions, all of which are rated on a 5-point scale. Thus, the total Y-BOCS score yields the range of severity for patients who exhibit both obsessions and compulsions.

MANAGEMENT OF ANXIETY DISORDERS DURING THE PERINATAL PERIOD

The decision of which bio-psychosocial treatment to use depends on the severity of the symptoms (see Table 3).

Table 3: Treatment Modalities for Anxiety Disorders during the Perinatal Period

SYMPTOMS	TREATMENT
Mild to Moderate	I. Psychosocial Therapies A. Cognitive Behavioural Therapy B. Interpersonal Psychotherapy C. Group Therapy D. Family and Marital Therapy E. Psychoeducation F. Supportive Psychotherapy
Moderate to Severe	II. Pharmacotherapy (used in conjunction with Psychosocial Therapies)

I. PSYCHOSOCIAL THERAPIES

A. Cognitive Behavioural Therapy

Cognitive behavioural therapy (CBT) is a drug-free model of treatment that focuses on the interrelationships between thoughts, feelings, behaviour, physical reactions, and the environment. The treatment consists of educational, thought pattern analysis, and behaviour change components. CBT has been found to be highly effective in treating a variety of problems such as depression, anxiety, panic, obsessive-compulsive disorder, and eating disorders,²²⁻²⁴ with a reported success rate of 60-80%.²⁵ Several controlled studies have shown that:

- a) CBT is at least as effective as antidepressant medication for mild to moderate depression
- b) CBT administered in combination with an antidepressant medication yields more enduring results than does either treatment alone, and
- c) long-term CBT treatment has a similar protective effect to long-term medication treatment for recurrent depression and anxiety disorders.²⁶⁻³⁰

A preliminary study examining short-term “cognitive behavioural counseling” for postpartum depression found that women who received 6 sessions of such counseling showed the same degree of improvement in functioning when compared to a group of women receiving the antidepressant medication fluoxetine. Both groups showed significant improvement in functioning when compared to a placebo medication group.³¹ CBT is a very structured form of treatment, and requires motivated individuals to complete weekly homework assignments.

B. Interpersonal Psychotherapy

Interpersonal Psychotherapy (IPT) is a short-term therapy that has been used successfully to treat mild-to-moderate depression and anxiety. The focus of IPT in depressed or anxious patients is on one or more of 4 problem areas: role transitions, interpersonal disputes, interpersonal deficits, and grief.³² In pregnant and postpartum women, the focus of IPT is on role transitions and the acquisition of new skills applicable to motherhood. A technique of IPT that is particularly useful for pregnant and postpartum women is psychoeducation.³² Psychoeducation for these patients involves providing information on the nature and course of mood disorders during or after pregnancy, as well as providing information about child care and child development. Preliminary studies of IPT in pregnant and postpartum women have produced encouraging results.^{32,33} A recent controlled study of 99 women further confirmed that IPT is effective in decreasing depressive symptoms and increasing social adjustment in women with moderate postpartum depression.³⁴

C. Group Psychotherapy

Group psychotherapy for pregnant or postpartum depressed women has been described in two recent pilot studies. In one of these studies,³⁵ therapy consisted of a 10-week program with the following components: 1) social and emotional support from other women who were undergoing similar experiences; 2) education about postpartum depression; 3) a cognitive-behavioural component to target irrational beliefs; 4) exploration of resources within the community; 5) improvement of communication, self-assertion, and problem-solving skills; 6) involvement of

the spouse in group sessions, and; 7) homework tasks in order to reinforce techniques learned in the group sessions. Participants in this group met once a week for 1.5 hours. Results from this pilot study indicate that group therapy is effective in reducing the degree of depression in pregnant and postpartum women.

The other pilot study involved “distressed” women and their partners during the postnatal period.³⁶ These women attended an 8-week long program, with their spouses attending 3 of these sessions. Women who attended this program demonstrated a decrease in maternal distress and an increase in self-esteem over the duration of the 8 weeks.

Specific psychosocial therapies that have been found to be effective for the treatment of mild to moderate mood disorders when administered in a group setting include both cognitive-behavioural therapy and interpersonal psychotherapy.³⁷ The benefits of group psychotherapy for pregnant and postpartum women include: it is cost-effective, it encourages social interaction, and it encourages partner involvement in the treatment plan.

D. Family and Marital Therapy

Marital and family problems are common in the course of mood disorders, and even more common when dealing specifically with perinatal mood disorders. After the birth of the baby, the husband or partner also goes through an adjustment period. In some couples, a baby strengthens their relationship, which leads to a supportive environment for the infant’s growth. The roles of the partner and family become even more crucial if the mother is afflicted with a mood disorder. A stable marital relationship helps new parents adapt to the competing demands of marriage, the infant, and the family. In contrast, a poor marital relationship is the most consistent psychosocial predictor of perinatal depression and anxiety.^{38,39} Many women experience a great deal of stress in attempting to handle both maternal and marital roles.⁴⁰ The presence of a mood disorder in the mother can cause significant complications in both marital and family relationships, and a troubled environment can heighten existing depression or anxiety during the postpartum period.^{41,42}

Techniques for marital and family therapy most often involve behavioural approaches and psychoeducation. Several studies of marital therapy have reported that it is an effective treatment strategy, either as a primary or adjunctive treatment, for reducing symptoms of mood and anxiety disorders, as well as reducing the risk for relapse.^{43,44} The efficacy of marital and family counseling relative to other psychosocial treatments will depend on whether marital and family distresses are actually present in the patient.

E. Psychoeducation

Education for women with mood disorders and their families is a critical component to all treatment programs, regardless of whether they are psychosocial interventions, pharmacological interventions, or a combination. The main goal of psychoeducation is to help the patient and her family to understand the disorder, available treatment options, and strategies to manage the disorder effectively.

F. Supportive Psychotherapy

Supportive psychotherapy involves offering support, reassurance, and psychoeducation to patients and their families. This type of therapy is used to augment other psychosocial interventions and/or pharmacotherapy. Supportive psychotherapy may be the only treatment a woman receives if she is not functioning at a high enough level to engage in Cognitive-Behavioural Therapy or Interpersonal Psychotherapy, or if she refused pharmacotherapy. Supportive group therapy has also been suggested to be effective in the treatment of depression and anxiety disorders.³⁷

II. PHARMACOTHERAPY

When pharmacotherapy is indicated for women who are planning to conceive, pregnant, or postpartum, the risks for harmful drug effects in the baby must be weighed against the risks of untreated depression in the mother. All psychotropic medications cross the placenta and cause *in utero* exposure to the developing fetus. In addition, these medications are found in breast milk in varying amounts, and thus are passed on to the nursing infant. Potential risks to the baby from *in utero* medication exposure may include congenital anomalies, drug toxicity, and neonatal withdrawal syndrome. Potential risks to the baby from exposure to medications through breast milk may include drug toxicity and undetermined effects on neurobehavioural development.

The pharmacological treatment of choice for anxiety disorders is antidepressant medication. However, benzodiazepines may be used in the initial stages, particularly for treatment of acute panic attacks, because antidepressants do not have an immediate onset of symptom relief.⁴⁵ The selective serotonin reuptake inhibitors (SSRIs), are effective in suppressing panic symptoms, although the effective dose ranges are usually higher than those required for the treatment of major depression.

The tricyclic antidepressant (TCA) clomipramine, as well as the SSRIs, can effectively treat obsessive-compulsive disorder by making the obsessions easier to resist, and thereby minimizing the compulsions. In addition, they are effective in decreasing the depressive symptoms in patients who have concomitant major depression.

Combination therapy is most often used for resistant anxiety disorders. For panic disorder, the most commonly used combination is an SSRI with the addition of the benzodiazepine clonazepam. The benzodiazepine is added at the beginning of pharmacotherapy; when the SSRI medication begins to take effect, the benzodiazepine is gradually tapered. For resistant OCD, the most common combination is the use of an SSRI in combination with the TCA clomipramine.

Selection of a psychotropic medication in pregnancy and/or lactation should be based on:

- Patient's prior response to antidepressants⁴⁶
- Anticipated efficacy and response of the individual patient⁴⁵
- Side effect profile in each individual patient⁴⁶
- Concurrent medications and risk of interactions

- Potential adverse effects of the medication for the pregnant woman and her fetus, or for the mother and her nursing infant^{45,47}

Maternal, fetal, and neonatal systems of drug absorption, distribution, metabolism, and elimination are all constantly changing throughout pregnancy and postpartum period. Some of these variations require an increased or decreased dose of a specific medication, thus potentially increasing or decreasing drug exposure to the fetus or nursing infant. In pregnancy, the changes in dosing can be complex depending on the trimester of exposure. The effectiveness of a particular medication should therefore be monitored throughout the entire pregnancy and into the postpartum period in order to achieve the lowest possible dose that provides adequate control of the major depressive disorder.⁴⁵

Table 5 lists dosing information for medications used to treat anxiety disorders, as well as the risks involved with the use of these medications during pregnancy and breastfeeding. Data for many of the newer agents is very limited, and the long-term effects on infants exposed to these agents are undetermined. Strategies to minimize drug exposure during the most sensitive period of gestation and during breastfeeding should be considered. Such strategies may include:

- Use the lowest possible dose of medication that will give a therapeutic response
- When possible, use a medication that is known to result in lower fetal/neonatal exposure, either through lower accumulation in breast milk, and/or through lower documented accumulation in fetal/neonatal serum or one which has a reduced side effect profile in the fetus and newborn
- The use of recently released medications in the perinatal period should be discouraged until more information is available regarding the effects of the medication

The American Food and Drug Administration⁴⁸ has provided 5 categories to classify which medications, when used during gestation, are associated with congenital defects in the developing fetus. Although it doesn't provide information on the effects of the medication during a specific trimester, the FDA classification system is useful for ascertaining possible risks throughout the entire pregnancy, and is widely used.

Table 4a: Food and Drug Administration Pregnancy Risk Categories

A	Adequate, well-controlled studies in pregnant women have failed to demonstrate a risk to the developing fetus.
B	Either animal studies show a risk, but human studies do not; or, if no adequate studies have been conducted in pregnant women, then animal studies have not demonstrated a risk.
C	Human studies are lacking, and animal studies have either produced adverse effects or are also lacking. Therefore, the risk of medication exposure in the fetus cannot be ruled out. Medications should be used in pregnancy only when potential benefits outweigh potential risk.
D	Positive evidence of fetal risk has been demonstrated in humans. However, the potential benefits of use in pregnant women may outweigh the potential risks, thus decisions must be made on an individual basis.
X	The medication is contraindicated in women who are or may become pregnant. The fetal risk of medication exposure clearly outweighs any potential benefits to the mother.

Table 4b: Lactation Risk Categories

L1	The medication has been taken by a large number of breastfeeding mothers without any documented adverse effects in their nursing infants. Controlled studies have been conducted and have not identified an increased risk to infants.
L2	The medication has been studied in a limited number of breastfeeding women, and no adverse effects have been documented in their infants.
L3	No controlled studies of the medication have been conducted in breastfeeding women. The medication should be used only when the potential benefits to the mother outweigh the potential risks of infant exposure.
L4	There is documented evidence of risk to infants exposed to this medication through breast milk. However, the potential benefits of use of the medication in women may outweigh the potential risk to the nursing infants, so the decision must be made on an individual basis.
L5	This medication is contraindicated in mothers who are breastfeeding. Human studies have clearly demonstrated risk to exposed infants, and this risk outweighs any potential benefits.

The lactation risk classification system has been developed by Hale, and is described in detail in his publication *Medications in Mothers' Milk, 9th edition* (2000)⁴⁹. The 5 categories closely follow the pregnancy risk categories of the FDA, and they outline the infants' risk of medication exposure through breast milk.

Table 5: Pharmacologic Treatment of Anxiety Disorders During the Perinatal Period^a

Drug Class	Start Daily Dose at (mg) ^b	Max Daily Dose at (mg)	FDA Pregnancy Risk Category ^c	Fetal Risk ^d	Hale's Lactation Risk Category ^e	Breastfeeding ^f
Tricyclic Antidepressants (TCAs)						
clomipramine (Anafranil®) Ref: 50-52	25-75	300	C	Data analysis has shown that TCA exposure in pregnancy does not increase the incidence of teratogenic effect in humans. Neonatal withdrawal symptoms have been associated with the TCAs. Desipramine may be preferred due to less sedation and GI/cardiac/hypotensive side effects.	L2	All TCAs are excreted into human breast milk, in low concentrations. Larger doses of clomipramine are required for the treatment of OCD than for major depression. This may lead to an increase in the neonatal effects observed with TCAs, particularly dependence and withdrawal.
desipramine (Norpramin®) Ref: 53	25-75	300	C		L2	
imipramine (Tofranil®)	25-75	300	D		L2	
Selective Serotonin Reuptake Inhibitors (SSRIs)						
fluoxetine (Prozac®) Ref: 54-61	10	80	B	Fluoxetine exposure in pregnancy is not associated with increased teratogenic effects in humans, but perinatal effects of 3 rd trimester exposure have been reported. A study of 55 preschool children exposed to fluoxetine <i>in utero</i> reported no long-term adverse effects with respect to IQ, language, or behaviour.	L3 for neonates L2 for older infants	Norfluoxetine, the active metabolite of fluoxetine, has a very long half-life that predisposes to accumulation in the infant, particularly neonates. Adverse effects (colic, fussiness, crying, seizure activity, lower weight gain) have been documented.

- a. Doses adapted from the *Clinical Handbook of Psychotropic Drugs, 10th revised edition (2000)*. Starting doses of medications are lower for pregnant and postpartum women than for the general adult population.
- b. Monograph doses are guidelines only. Doses must be individualised for each patient.
- c. Adapted from the *Food and Drug Administration (FDA, 1979)*. See Table 4a.
- d. Comments adapted from GG Briggs et al., (1998), *Drugs in Pregnancy and Lactation, 5th Edition*, as well as TW Hale (2000), *Medications in Mothers' Milk, 9th edition* Refer to referenced articles for specific details.
- e. Adapted from TW Hale (2000). *Medications in Mothers' Milk, 9th edition*. See Table 4b.
- f. Comments adapted from GG Briggs et al., (1998), *Drugs in Pregnancy and Lactation, 5th Edition*, as well as TW Hale (2000), *Medications in Mothers' Milk, 9th edition* Refer to referenced articles for specific details.

Drug Class Selective Serotonin Reuptake Inhibitors (SSRIs) cont.	Start Daily Dose at (mg)^g	Max Daily Dose at (mg)	FDA Pregnancy Risk Category^h	Fetal Riskⁱ	Hale's Lactation Risk Category^j	Breastfeeding^k
Selective Serotonin Reuptake Inhibitors (SSRIs) cont.						
Fluvoxamine (Luvox) Ref: 62-64	50	300	C	Use of these SSRIs during pregnancy does not appear to have teratogenic effects, but data is limited. One prospective case series reported 26 exposures to fluvoxamine, 97 to paroxetine, and 147 to sertraline in pregnancy. The rates of malformations were similar between all 3 groups, and were not higher than those reported for the control group.	L3 for neonates L2 for older infants	Two small case studies of fluvoxamine exposure through breast milk have reported very low levels in the breast milk, and no adverse events in the infants.
paroxetine (Paxil®) Ref: 62, 65-68	10	60	B		L2	Paroxetine does not have an active metabolite. Paroxetine is excreted into breast milk but with generally undetectable serum levels in infants. No adverse effects were reported.
Citalopram (Celexa) Ref: 73-76	10	60	C	Use of citalopram in pregnancy does not appear to have teratogenic effects, but data is limited. A review of 375 cases of citalopram exposure in early pregnancy found that the rate of congenital anomalies was not higher than that for SSRI exposure or for the general population.	L3	2 case studies of citalopram have reported no adverse effects in nursing infants. 1 study reported uneasy sleep in the infant, and this was correlated to high serum concentration of citalopram. Symptoms were short lasting and disappeared after a dose decrease. Data is limited.

Drug Class Selective Serotonin Reuptake Inhibitors (SSRIs) cont.	Start Daily Dose at (mg) ^g	Max Daily Dose at (mg)	FDA Pregnancy Risk Category ^h	Fetal Risk ⁱ	Hale's Lactation Risk Category ^j	Breastfeeding ^k
Serotonin Reuptake Inhibitors (SSRIs) cont.						
sertraline(Zoloft®) Ref: 62, 69-72	50	225	B		L2	Milk levels have been reported for sertraline and its weak metabolite desmethylsertraline, but with low or undetectable serum levels in the infant. There is one report of a nursing infant with 50% of maternal serum levels, but no adverse effects noted.

g. Monograph doses are guidelines only. Doses must be individualised for each patient.

h. Adapted from the Food and Drug Administration (FDA, 1979). See Table 4a.

i. Comments adapted from GG Briggs et al., (1998), *Drugs in Pregnancy and Lactation*, 5th Edition, as well as TW Hale (2000), *Medications in Mothers' Milk*, 9th edition Refer to referenced articles for specific details.

j. Adapted from TW Hale (2000). *Medications in Mothers' Milk*, 9th edition. See Table 4b.

k. Comments adapted from GG Briggs et al., (1998), *Drugs in Pregnancy and Lactation*, 5th Edition, as well as TW Hale (2000), *Medications in Mothers' Milk*, 9th edition Refer to referenced articles for specific details.

Drug Class Selective Serotonin Reuptake Inhibitors (SSRIs) cont.	Start Daily Dose at (mg)^l	Max Daily Dose at (mg)	FDA Pregnancy Risk Category^m	Fetal Riskⁿ	Hale's Lactation Risk Category^o	Breastfeeding^p
Benzodiazepines						
alprazolam (Xanax®)	0.5	4	D	Exposure to benzodiazepines <i>in utero</i> has been associated with withdrawal symptoms, including irritability and restlessness. Alprazolam has not been associated with congenital anomalies during human pregnancies, however, caution is urged, as data is limited.	L3	Benzodiazepines are excreted into breast milk. These medications are not ideal during breastfeeding due to relatively long half-lives; chronic exposure may therefore be of concern. Monitor infants closely for sedation. Withdrawal symptoms have been reported in infants exposed to alprazolam through breast milk.
clonazepam (Rivotril®) Ref: 77, 78	0.25	8	C	Clonazepam exposure during pregnancy has been associated with symptoms of newborn toxicity, including apnea, cyanosis, lethargy, and hypotonia. No long-term effects have been reported for clonazepam, although data is limited.	L3	Clonazepam has been associated with apnea in nursing infants.
diazepam (Valium®)	5	30	D	Diazepam use in pregnancy has been associated with oral clefts, though the data is conflicting.	L3-acute L4-chronic	Diazepam and its metabolite have long half-lives and tend to accumulate when used for chronic treatment. Diazepam treatment has been associated with withdrawal, lethargy, sedation, and poor suckling in nursing infants.
lorazepam (Ativan®) Ref: 79	1	6	D	Placental transfer of lorazepam is lower than that of other benzodiazepines, but high doses in pregnancy have been associated with "floppy infant syndrome".	L3	When benzodiazepines are indicated, lorazepam may be preferred over the others, due to its shorter half-life and absence of active metabolites.

l. Monograph doses are guidelines only. Doses must be individualized for each patient.

m. Adapted from the Food and Drug Administration (FDA, 1979). See Table 4a.

n. Comments adapted from GG Briggs et al., (1998), Drugs in Pregnancy and Lactation, 5th Edition, as well as TW Hale (2000), Medications in Mothers' Milk, 9th edition Refer to referenced articles for specific details.

o. Adapted from TW Hale (2000). Medications in Mothers' Milk, 9th edition. See Table 4b.

p. Comments adapted from GG Briggs et al., (1998), Drugs in Pregnancy and Lactation, 5th Edition, as well as TW Hale (2000), Medications in Mothers' Milk, 9th edition Refer to referenced articles for specific details.

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