REPORT 13 OF THE COUNCIL ON SCIENCE AND PUBLIC HEALTH (A-07)
Use of Serotonin Reuptake Inhibitors in Pregnancy
(Reference Committee E)

EXECUTIVE SUMMARY

Objective: To summarize the current state of knowledge on the use of serotonin reuptake inhibitors (SRIs) during pregnancy.

Methods: English-language reports on studies using human subjects were selected from a MEDLINE search of the literature from 1995 to April 2007 using the terms “serotonin uptake inhibitors/*therapeutic use/*adverse effects,” in combination with “pregnancy,” “pregnancy trimester, first,” “pregnancy complications,” “depression/*drug therapy,” “pregnancy, maternal exposure/*adverse effects,” “infant/newborn,” “abnormalities, drug induced,” “prenatal exposure delayed effects/epidemiology,” and “teratogens.” In addition, the Cochrane Central Controlled Trials Register was searched using the terms “paroxetine,” “fluoxetine,” “sertraline,” “fluvoxamine,” “citalopram,” and “venlafaxine,” and “pregnancy.” Web sites of the American Academy of Pediatrics, Food and Drug Administration, American Psychiatric Association, and American College of Obstetricians and Gynecologists also were searched for documents relevant to the use of SRIs in pregnancy. A total of 268 articles were retrieved for analysis. When high-quality systematic reviews and meta-analyses were identified, they formed the basis for evaluative statements about safety and efficacy. Additional articles were identified by manual review of the references cited in these publications.

Results: Except for paroxetine, prenatal exposure to SRIs in the first trimester is not a risk factor for major congenital malformations. Data are conflicting on whether SRI exposure increases the risk of premature delivery or decreases age-appropriate birth weight. Exposure to paroxetine modestly increases the risk for congenital and certain cardiac malformations, perhaps in a dose dependent fashion. Third trimester exposure to SRIs may increase the risk of persistent pulmonary hypertension of the newborn, and the occurrence of a neonatal behavioral syndrome with central nervous system, respiratory, gastrointestinal, and motor signs. These symptoms may be attributable either to drug withdrawal or serotonin toxicity. Long-term neurobehavioral effects are not apparent.

Conclusion: Untreated depression during pregnancy is associated with obstetrical complications and infant behavioral abnormalities. Use of SRIs in the third trimester is associated with various perinatal complications that generally are self-limiting and resolve with supportive care. Further studies are needed to establish the actual frequency of these complication, whether the symptoms represent excessive serotonergic effects or are a manifestation of drug discontinuation, and whether tapering of the antidepressant late in pregnancy is an appropriate clinical maneuver to protect infants without triggering relapse in the mother or an increase in the incidence of postpartum depression. However, if the mother is treated with SRIs, the neonate should be monitored for possible adverse effects, including during the immediate period after release from the hospital.
REPORT OF THE COUNCIL ON SCIENCE AND PUBLIC HEALTH

CSAPH Report 13-A-07

Subject: Use of Serotonin Reuptake Inhibitors in Pregnancy

Presented by: Mohamed K. Khan, MD, PhD, Chair

Referred to: Reference Committee E
(Paul C. Matson, MD, Chair)

Introduction

Resolution 519 (A-06), introduced by the American Academy of Child and Adolescent Psychiatry, American Academy of Pediatrics (AAP), American Psychiatric Association (APA), and the American Academy of Psychiatry and the Law, and adopted as amended, asks that our American Medical Association (AMA) work with all appropriate specialty societies to prepare a report summarizing the research on the use of selective serotonin reuptake inhibitors (SSRIs) during pregnancy and to promulgate appropriate guidelines concerning the treatment of depression during pregnancy.

During preparation of this report, the Council learned that the APA and the American College of Obstetricians and Gynecologists (ACOG) were collaborating to develop guidance on the use of antidepressants in pregnancy. Therefore, as requested, this report summarizes the research on the use of SSRIs during pregnancy, but defers any action on clinical practice guidelines for the treatment of depression during pregnancy until the APA and ACOG complete their collaborative effort.

Selective serotonin/norepinephrine reuptake inhibitors (SNRIs; e.g., venlafaxine, duloxetine) also may be associated with some of the same effects as SSRIs. Accordingly, “SRI” has been used in some places in this report to refer to the combined class of SSRIs and SNRIs, where appropriate.

Physicians are faced with various scenarios in managing women of childbearing age. They (1) engage in preconception consultations with patients who have depression or other psychiatric disorders (e.g., generalized anxiety, panic, obsessive-compulsive disorder) and are currently being treated with an SRI; (2) advise patients who are taking SRIs in the early weeks of an unplanned pregnancy; (3) must manage pregnant patients who relapse after choosing to discontinue SRI therapy; and (4) treat patients who first experience a depressive episode or other psychiatric disorder when pregnant. Decision-making is complicated by the requirement to estimate risk for the mother and the infant, a task that is further complicated by the fact that depression and anxiety are themselves risk factors for adverse pregnancy outcomes. This report assesses some of the domains relevant to the decision-making process for these patients.

Methods

English-language reports on studies using human subjects were selected from a MEDLINE search of the literature from 1995 to April 2007 using the terms “serotonin uptake inhibitors/*therapeutic use/*adverse effects,” in combination with “pregnancy,” “pregnancy trimester, first,” “pregnancy trimester, second,” “pregnancy trimester, third,” “pregnancy trimester, fourth,” “pa...
complications,” “depression/*drug therapy,” “pregnancy, maternal exposure/*adverse effects,”
“infant/newborn,” “abnormalities, drug induced,” “prenatal exposure delayed
effects/epidemiology,” and “teratogens.” In addition, the Cochrane Central Controlled Trials
Register was searched using the terms “paroxetine,” “fluoxetine,” “sertraline,” “fluvoxamine,”
“citalopram,” and “venlafaxine,” and “pregnancy.” Web sites of the AAP, Food and Drug
Administration (FDA), APA, and ACOG also were searched for documents relevant to the use of
SRIs in pregnancy. A total of 268 articles were retrieved for analysis. When high-quality
systematic reviews and meta-analyses were identified, they formed the basis for evaluative
statements about safety and efficacy. Additional articles were identified by manual review of the
references cited in these publications.

Depression During Pregnancy

Mood disorders are twice as common in women as in men. Estimates of lifetime risk in
community samples have varied from 10% to 25%, with the peak prevalence between 25 and 44
years of age.1,2 Pregnancy does not protect women from depression or other psychiatric disorders
(eg, generalized anxiety, panic disorder, obsessive-compulsive disorder) that may be treated with
SRIs.3-5 Furthermore, women with recurrent major depression who discontinue antidepressant
medications proximate to pregnancy have a 5-fold higher risk of relapse compared with those
who maintain their antidepressant medications.6

The occurrence of (untreated) mood disorders during pregnancy is a significant risk factor for
maternal morbidity and adverse pregnancy outcomes. The effects of depression on the fetus may
be mediated by alteration in feto-maternal physiology, or indirectly by depression-associated
changes in maternal behavior leading to neglect of prenatal care; poor nutritional habits;
emergence of suicidal ideation; and higher rates of smoking, alcohol use, and other substance
abuse. Depression during pregnancy is associated with elevated rates of spontaneous abortion,
preterm delivery, intrauterine growth retardation/lower birth weight, and pre-eclampsia.7-12
Significant and ongoing perinatal maternal stress may “program” aberrant stress responses in
neonates, triggering various neurobehavioral effects that may persist after birth. When maternal
depression extends into, or emerges, in the postpartum period, infants demonstrate lower
cognitive abilities; delayed language development; altered emotional regulation; and impaired
social interactions, including aberrant attachment behaviors.13 The effects of postpartum
depression are relevant to the current discussion because the strongest predictor of postpartum
depression is presence of depression and anxiety during pregnancy.

Developmental Effects of Fetal Exposure to SRIs

Teratogenesis. Prior to 2005, 3 prospective cohort studies, 2 studies utilizing birth registries, and
2 meta-analyses concluded that prenatal SSRI exposure is not a significant risk factor for major
malformations, although one of the cohort studies did find a higher incidence of minor anomaly
clustering among infants with first-trimester fluoxetine exposure.14-20 In contrast to the large
number of studies concluding that early exposure to SSRIs is safe, a recent population-based
cohort study in Denmark found an increased risk of congenital malformations after exposure to
SSRIs in early pregnancy. This study linked prescription records with the Danish Medical Birth
Registry and hospital discharge registries. Specific SSRIs were not analyzed separately, and no
information was provided on the underlying psychiatric or disease status of registrants.21 Two
recent analyses using the Swedish Birth Register of infants born between 1985 and 2004 and the
Canadian (Quebec) Medication and Pregnancy Register of all pregnancies between 1997 and June
2003 confirmed that use of SSRIs (in general) in early pregnancy is not a major risk factor for
infant malformations.22,23
Cardiac Malformations. Although the Swedish and Quebec studies confirmed the overall safety of SSRIs, they found an association between paroxetine use and congenital malformations and/or infant cardiovascular defects, notably ventricular and atrial septum defects.\textsuperscript{22,23} In the Quebec study, this effect was only evident at paroxetine dosages above 25 mg daily.\textsuperscript{23} These findings on paroxetine are in agreement with 2 unpublished reports of company-sponsored studies using a managed care claims database, and a study using Swedish national registry data.\textsuperscript{24-26} In these studies, women who received paroxetine in early pregnancy had approximately a 2-fold increased risk for giving birth to an infant with a cardiac defect compared with all infant registrants, a 1.5-fold increased risk compared with infants of women who received antidepressants other than paroxetine (1.5\% vs 1\%), and a 1.8-fold increased risk for congenital malformations overall compared with infants of women who received other antidepressants in the first trimester. Based on these results, the FDA required that paroxetine be reclassified as Pregnancy Category D and that it carry label warnings about the risk for congenital and cardiac malformations (see below).

Persistent Pulmonary Hypertension. One recent study reported a 6-fold increase in the occurrence of persistent pulmonary hypertension of the newborn (PPHN) in infants exposed to an SSRI after the 20\textsuperscript{th} week of gestation.\textsuperscript{27} The specific SSRI medications that study participants reported using were citalopram, fluoxetine, paroxetine, and sertraline. The incidence of PPHN is low (~1/1000); therefore, even with a 6-fold increased in relative risk, the absolute number of infants affected is small. However, this information also is now included as a class effect in the product labeling of all SRIs.

SSRI Toxicity

Although exposure to SSRIs (except paroxetine) during early gestation does not appear to cause somatic teratogenesis, fetal and brain development continue throughout prenatal life. Thus, other adverse effects associated with SSRI exposure during pregnancy have been reported, including preterm delivery, delayed fetal growth, neonatal toxicity, and neonatal withdrawal symptoms.

Preterm Delivery/Low Birth Weight. Many,\textsuperscript{14,15,18,28,29} but not all,\textsuperscript{14,30,31} studies have found evidence of preterm delivery in SSRI recipients. Virtually none of these studies controlled for the severity of maternal depression, and because the incidence of preterm delivery in these studies closely parallels that of women who are depressed during pregnancy, this effect may represent the effect of maternal depression as much as SSRI exposure.\textsuperscript{7,8}

Similarly, some studies have reported lower birth weights for gestational age in SSRI-exposed infants, particularly at higher doses,\textsuperscript{29,32,33} while others have found no significant effect of SSRI exposure on birth weight.\textsuperscript{14,29,31,34} Most studies did not adequately control for the influence of maternal depression.

Neonatal Toxicity and/or Withdrawal Symptoms

Several case reports have noted the apparent association of late stage pregnancy exposure to SSRIs and symptom clusters in newborns, most commonly tremor/jitteriness, hypertonia, feeding problems, irritability/agitation, and respiratory distress.\textsuperscript{35,36} Databases containing information from spontaneous adverse drug event reports also support an association between SSRI exposure and a cluster of neonatal symptoms and behaviors appearing after delivery, sometime leading to lengthier hospitalization.\textsuperscript{37,39} These symptoms have been variably referred to as SRI withdrawal, SRI toxicity, poor neonatal adaptation, serotonergic excess, or serotonin syndrome. Limitations of case reports and of case series generated from databases of adverse drug event reports on SRI...
toxicity or withdrawal include underreporting, reporting that is biased toward greater symptom severity, limited case information, and inability to determine incidence rates.

Symptoms observed in neonates exposed to SSRIs in utero could be caused by excessive toxic serotonergic effects, abrupt drug withdrawal, or a combination of both. Early-onset symptoms are thought to represent toxicity, while later onset symptoms may be withdrawal reactions. Both a discontinuation syndrome and “serotonin syndrome” reflecting excessive synaptic release of 5-HT have been described in adults. In adults, discontinuation of SSRIs leads to nonspecific symptoms such as disequilibrium (dizziness, ataxia, vertigo), tremor, gastrointestinal symptoms (nausea, vomiting), sensory phenomena (paresthesia, electric shock sensation), sleep disturbances, irritability, and various neuropsychiatric symptoms (anxiety, hypomania, depressed mood, psychomotor impairment). SSRI toxicity manifests as central nervous system (CNS) (irritability, jitteriness, restlessness, anxiety, insomnia), neuromuscular (tremor, dystonia, dyskinesia), and gastrointestinal (nausea, vomiting, diarrhea) signs and symptoms. A more severe “serotonin syndrome” generally requires a combination of drugs that enhance 5-HT function, producing a constellation of CNS (convulsions, disorientation, cognitive impairment) and neuromuscular (hypertonia, rigidity, myoclonus, hyperreflexia, paresthesia) signs and symptoms, as well as autonomic (tachypnea/respiratory distress, tachycardia) and body temperature (chills, diaphoresis, hyperthermia) instability. Some of the symptoms associated with discontinuation (eg, dizziness, nausea, tremor, anxiety/agitation, insomnia) overlap with signs attributable to SRI toxicity. Many similarities exist between symptoms ascribed to “neonatal toxicity” and those described in adults, as well as between symptoms ascribed to “neonatal withdrawal” and adult discontinuation syndromes.

Cohort studies currently provide the highest quality information on perinatal signs and neonatal symptoms associated with prenatal exposure to SSRIs. Limitations of these studies include surveillance bias, sampling bias, and inadequate controls for depression and other birth outcome confounders. A recent, informative systematic review identified 10 cohort studies that had clearly identified maternal SSRI exposure for a minimum of the final trimester of pregnancy through delivery and that assessed neonatal outcomes. The following discussion reflects the findings of this review.

In some of these studies, the control group consisted of women with “early” SSRI use—during first 2 trimesters versus those with third trimester use. Some studies evaluated the presence of a predefined SSRI-related behavioral syndrome, or employed a validated rating scale to evaluate newborn behavior. Results of some studies were complicated by high concomitant use of psychotropic drugs, post-hoc data collection, lack of control for severity of depression or other mental illness, assessments that were not blinded, and obstetrical complications that were inadequately assessed.

One of the earlier prospective controlled cohort studies evaluated the occurrence of “poor neonatal adaptation,” defined as jitteriness, tachypnea, hypoglycemia, hypothermia, hypotonia, mild-moderate respiratory distress, weak or absent cry, suckling problems, or oxygen desaturation on feeding. These symptoms were significantly more frequent among 73 infants exposed to fluoxetine during the third trimester (~32%) versus those with fluoxetine exposure in the first or second trimester (~9%) or those who were unexposed. However, 30% of the women who took fluoxetine in the third trimester also took other psychoactive drugs, and also were more likely to smoke. Additionally, clinicians rating the infant behavior were not blinded, and the severity of depression was not controlled for. Other cohort studies that used similar symptom clusters to define the presence of poor neonatal adaptation found that ~ 22% to 30% of neonates exposed to SSRIs in the third trimester suffered from this syndrome. Neonates exposed to SSRIs also
experienced higher rates of admission to special care nurseries, usually for treatment of respiratory distress.\textsuperscript{28,34,45} When a 5-HT syndrome scale (modeled after adult symptoms of serotonin syndrome) was applied to neonates whose mothers were treated with fluoxetine or citalopram, significantly higher rates of myoclonus, restlessness, tremor, shivering, hyperreflexia, incoordination, rigidity, and nausea were found.\textsuperscript{44}

The overall results of this systematic review indicated that, compared with early gestational exposure or no exposure, late (third term) SSRI exposure carries an overall relative risk of \textasciitilde3 for the appearance of a neonatal behavioral syndrome with CNS, respiratory, motor, and gastrointestinal signs.\textsuperscript{35} Generally, this is a self-limited neonatal behavioral syndrome that is managed with supportive care, although hospital stays may be extended in some cases.

Subsequent to the systematic review, other studies have been reported. A population-based study on women exposed to SSRIs in the third trimester of pregnancy reported that infants exposed to SSRIs had a moderately increased risk of requiring treatment in special or intensive care facilities (15.7\% vs 11.2\%).\textsuperscript{31} Controls had no drug exposure, and were matched according to social status, geographic area, year of birth, and parity, but not severity of maternal depression. Another cohort study comparing 60 infants with SSRI exposure in the third trimester to unexposed infants found evidence of a neonatal abstinence syndrome in 30\% of neonates exposed to SSRIs in utero using a standard rating scale; preterm infants were excluded from analysis.\textsuperscript{49} Another retrospective cohort study confirmed a higher incidence of CNS, respiratory, digestive, and hypoglycemic symptoms in SSRI-exposed infants.\textsuperscript{50} In this study, preterm infants with SSRI exposure during the third trimester had longer hospital stays than preterm infants without SSRI exposure.

Neurobehavioral Effects

Structural organogenesis occurs during the first trimester; however, brain development continues throughout prenatal life. Because SSRIs affect brain neurochemistry, concern has been expressed that exposure during the prenatal period may produce neurobehavioral effects that persist in neonates, infants, and children. For example, pain reactivity in 2-month-old infants is blunted after prenatal SSRI exposure, suggesting possible sustained neurobehavioral effects beyond birth.\textsuperscript{51}

Two prospective cohort studies from the same center compared outcomes of fluoxetine-exposed children, children exposed to tricyclic antidepressants, and infants who were not exposed to antidepressants.\textsuperscript{30,52} No significant differences existed among the 3 groups in cognitive, language, and behavioral development at 16 to 86 months of age, or in IQ, temperament, behavior, reactivity, distractibility, or activity level. However, a longer duration of maternal depression during pregnancy was associated with poorer cognitive function in offspring, and the number of maternal postnatal depressive episodes was associated with diminished language development.\textsuperscript{30}

A small longitudinal study found no difference in internalizing behaviors in children aged 4 to 5 years with in utero exposure to SSRIs compared with unexposed children. The presence of a maternal psychiatric disorder (anxiety) was correlated with the total internalizing score.\textsuperscript{53} One other study that compared children of depressed mothers who were not medicated with children whose depressed mothers took SSRIs found that the latter were slightly delayed in their psychomotor development and displayed subtle changes in motor movement control between the ages of 6 and 40 months.\textsuperscript{54} The presence of maternal depression was based on self-reporting.
Overall, these studies are somewhat reassuring and suggest that “poor neonatal adaptation” or “neonatal withdrawal from SSRIs” does not necessarily translate into significant, persistent behavioral effects.

Current Practice Guidelines and Treatment Recommendations

The APA, AAP, and ACOG have published practice guidelines or opinions on the use of antidepressants during pregnancy. Those offered by the APA and AAP are somewhat dated and were developed prior to the recent findings involving SSRIs, indicating the need for some consensus on how to integrate this new information into contemporary clinical practice.

The current APA Clinical Guideline\textsuperscript{55} indicates that:

\begin{itemize}
  \item Pregnancy, lactation, or the wish to become pregnant may be an indication for psychotherapy as an initial treatment in women with depression.
  \item Women of childbearing potential in psychiatric treatment should be carefully counseled, and “whenever possible, a pregnancy should be planned in consultation with the psychiatrist so that medication may be discontinued before conception, if feasible.”
  \item Antidepressant medications should be considered for pregnant women who have major depressive disorder, as well as for those women who are in remission from major depressive disorder, receiving maintenance medication, and deemed to be at high risk for recurrence if the medication is discontinued.
  \item Consideration should be given to gradually tapering the medication 10 to 14 days before the expected date of delivery.
\end{itemize}

Additionally, the APA’s Committee on Research on Psychiatric Treatments developed a model for treatment decisions on depression during pregnancy.\textsuperscript{56} The model outlines treatment options, and encourages assessing the likelihood of various outcomes, including fetal toxicity, intrauterine death, physical malformations, growth impairment, neonatal toxicity, and persistent neurobehavioral effects. Advice also is provided on patient characteristics (ie, relative values, perception of risk, competence to consent) that may influence decision-making. Optimally, the use of the decision-making model helps to structure and individualize clinical treatment for pregnant women with depression.\textsuperscript{56}

The AAP Practice Parameter on the Use of Psychotropic Medication in Pregnancy\textsuperscript{57}:

\begin{itemize}
  \item Recommends use of the lowest dosage that provides adequate control in order to minimize the risk of fetal and neonatal toxicity.
  \item Recommends that for depression, nortriptyline or desipramine, or possibly fluoxetine, are preferred.
\end{itemize}

Most recently, ACOG’s Committee on Obstetric Practice addressed the controversy regarding use of SSRIs in pregnancy, stating that\textsuperscript{58}:

\begin{itemize}
  \item Potential risks associated with SSRI use throughout pregnancy must be considered in the context of the risk of relapse of depression if maintenance treatment is discontinued.
  \item Treatment with all SSRIs or [SNRIs] or both during pregnancy should be individualized.
  \item Paroxetine use among pregnant women or women planning to become pregnant should be avoided, if possible.
\end{itemize}
Labeling Changes to SSRIs/SNRIs

Following the June 9, 2004, meeting of the FDA’s Pediatric Subcommittee of the Anti-infective Advisory Committee, the Committee strongly endorsed class labeling for the neonatal toxicity/withdrawal syndrome related to in utero exposure to SRIs. Accordingly, class labeling changes were adopted that caution physicians and patients about neonatal complications associated with late pregnancy exposure and note that such complications have required prolonged hospitalization, respiratory support, and tube feeding. The label lists the clinical features of the SRI-related neonatal syndrome; suggests a withdrawal or toxicity mechanism, including serotonin syndrome for these symptom clusters; and states that tapering the medication in the third trimester might be considered an option to reduce or prevent these symptoms. The label also notes that women who discontinued antidepressant medication during pregnancy are more likely to experience a relapse of major depression than those who continue antidepressant medication.

Subsequently, class labeling changes incorporated the emerging data on pulmonary hypertension by noting that infants exposed to SSRIs in late pregnancy may have an increased risk for PPHN. Specific warnings are advanced for paroxetine regarding its association with an increased risk for congenital and cardiac malformations.

Summary and Conclusion

With few exceptions, studies that evaluated the safety of SRIs in early pregnancy have not shown an increased risk of major congenital malformations. These results contributed to the increasing use of these agents during pregnancy. Data are conflicting on whether SRI exposure increases the risk of premature delivery and decreases age-appropriate birth weight. The use of paroxetine appears to be associated with a modest increased risk of major congenital malformations, as well as specific cardiac malformations, perhaps in a dose-dependent fashion.

The use of SRIs in the third trimester is associated with various perinatal complications, most frequently respiratory distress, irritability, and feeding problems. These problems are generally self-limiting and resolve with supportive care, but sometimes require more intensive measures. No deaths have been reported from these syndromes, and data on the possible long-term effects of prenatal SRI exposure on psychomotor and behavioral development, although sparse, are reassuring to date.

Further studies are needed to establish the actual frequency of these complications, whether the symptoms represent excessive serotonergic effects or are a manifestation of drug discontinuation, and whether tapering of the antidepressant late in pregnancy is an appropriate clinical maneuver to protect infants, without triggering relapse in the mother or an increase in the incidence of postpartum depression. Most existing studies have assessed either medication or illness effects without adequately controlling for the other. Consequently, purported adverse effects of SRI exposure may actually represent either direct or indirect effects of maternal depression and vice versa. A clinical study intended to answer many of these questions is ongoing.

The risks of antidepressant treatment during pregnancy cannot be meaningfully determined without a comparison group of depressed women who are untreated during pregnancy. Several studies suggest that untreated depression during pregnancy is associated with obstetrical complications and infant behavioral abnormalities, but studies comparing neonatal outcomes in treated and untreated depressed women during pregnancy are virtually nonexistent. Nevertheless,
there is general agreement that adequate treatment should not be withheld from a depressed pregnant woman in late pregnancy. However, if the mother is treated with SRIs, the neonate should be monitored for possible adverse effects, including during the immediate period after normal delivery and release from the hospital.

Treatment recommendations for perinatal depression should be the product of a thorough risk-benefit assessment that considers the maternal psychiatric history and the potential harmful effects of untreated depression and exposure to antidepressant medications during particular developmental windows. The decision-making process includes informed consent, medication and dose selection, ongoing communication, and eventually, appropriate monitoring of neonates in the immediate postnatal period. The following points are germane:

- Pregnancy does not protect against the occurrence of depression, and the likelihood of relapse is very high in untreated women with recurrent illness.
- Maternal depression adversely affects child development, and prenatal depression may adversely affect birth outcome.
- Transient postnatal behavioral abnormalities in the offspring of treated mothers have not been shown to create long-term problems.
- SRIs carry a small but significant risk for serious medical consequences.

Further research is necessary to better inform treatment decisions in women of childbearing age who suffer from depression.

RECOMMENDATIONS

The Council on Science and Public Health recommends that the following recommendations be adopted and that the remainder of this report be filed:

1. That our American Medical Association encourage further research into the treatment of depression during pregnancy, including the effects of antidepressant drugs, as well as strategies designed to best protect the health and welfare of both the mother and the child. (Directive to Take Action)

2. That the Council on Science and Public Health monitor the activities of relevant medical specialty societies on this issue, including development of practice guidelines or policy statements, and assist as needed in educating the physician community. (Directive to Take Action)

Fiscal Note: Staff costs less than $500 to implement
References


44. Laine K, Heikkinin T, Ekblad U, Kero P. Effects of exposure to selective serotonin reuptake inhibitors during pregnancy on serotonergic symptoms in newborns and cord blood monoamine and prolactin concentrations. *Arch Gen Psychiatry.* 2003;60:720-726.


