Antenatal depression: Risks of cognitive impairment and psychopathology in the offspring

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INTRODUCTION

The offspring of pregnant women who are depressed are at greater risk of delays in acquiring language skills, compared with the offspring of nondepressed pregnant women. In addition, antenatal depression is associated with psychopathology in the children, including aggressive behavior, anxiety, depression, and hyperactivity.

This topic reviews the association between antenatal depression and cognitive impairment and psychopathology in the children. The association between antenatal depression and pregnancy and neonatal outcomes, as well as abnormal infant and child development, is discussed separately, as are the risks of prenatal antidepressants, and the clinical features, assessment, diagnosis, and treatment of antenatal depression:

- (See "Antenatal depression: Pregnancy and neonatal outcomes".)
- (See "Antenatal depression: Risks of abnormal infant and child development".)
- (See "Antenatal use of antidepressants and the potential risk of teratogenicity and adverse pregnancy outcomes: Selective serotonin reuptake inhibitors".)
- (See "Antenatal use of antidepressants and risks of teratogenicity and adverse pregnancy outcomes: Drugs other than selective serotonin reuptake inhibitors".)
- (See "Antenatal exposure to selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs): Neonatal outcomes".)

- (See "Unipolar major depression during pregnancy: Epidemiology, clinical features, assessment, and diagnosis".)
- (See "Mild to moderate episodes of antenatal unipolar major depression: Choosing treatment".)
- (See "Severe antenatal unipolar major depression: Choosing treatment".)

QUALITY OF EVIDENCE

Information about the association between antenatal depression and adverse pregnancy outcomes and adverse outcomes in the offspring comes from low to moderate quality studies. (See "Antenatal depression: Risks of abnormal infant and child development", section on 'Quality of evidence'.)

POTENTIAL MECHANISMS

There are several possible direct and indirect mechanisms by which antenatal maternal depression may adversely affect pregnancy outcomes and outcomes in the offspring. (See "Antenatal depression: Risks of abnormal infant and child development", section on 'Potential mechanisms'.)

COGNITION

It is not known if antenatal depression is associated with impairments in general cognitive functioning in the offspring. However, it appears that antenatal depression is associated with delays in acquiring language skills.

General cognitive functioning — The association between antenatal depression and general cognitive performance in the offspring is not clear, due to contradictory findings across studies.

One review found that prenatal depression is associated with diminished general cognitive performance in the children [1]. As an example, a prospective study enrolled pregnant women (n = 223); after controlling for potential confounding factors (eg, maternal age, gestational age, and maternal postnatal depression), the analyses found that high levels of antenatal depressive symptoms were associated with decreased cognitive performance in children at age 18 months [2].

However, other studies suggest that antenatal depression is not associated with diminished cognition in the offspring:

- One prospective study included offspring (n = 27) of women with antenatal major depression who were not treated with antidepressants, and offspring (n = 98) of women without antenatal depression or exposure to antidepressants [3]. During follow-up lasting 18 months postpartum, infant and child cognition in the two groups were comparable.

- A prospective study included children of mothers with antenatal depression (n = 42) and children of mothers without antenatal depression (controls, n = 33); none of the mothers were treated with selective serotonin reuptake inhibitors (SSRIs), and the children were assessed at age five to six years [4]. General cognition was comparable in the children of mothers with antenatal depression and the controls.

Whether antenatal depression is associated with cognitive performance in the offspring may depend upon the severity of the depressive syndrome. As an example, mild to moderate antenatal depression, which is often not treated with pharmacotherapy, may not be associated with cognitive impairment.

Specific cognitive functions

Language — Maternal antenatal depression may predict delays in acquiring language skills.

- A prospective study tested language acquisition in infants of mothers who were depressed during pregnancy and not treated with pharmacotherapy (n = 21), and in control infants whose mothers were not depressed during pregnancy (n = 32). Testing occurred at 6 and 10 months of age. Whereas controls performed as expected, performance was altered in infants of depressed mothers [5].

- A prospective study found that maternal antenatal symptoms of anxiety and depression, lasting for approximately 30 weeks, were associated with language delay in children age three years (n >50,000) (relative risk 1.8, 95% CI 1.4-2.4) [6]. The effect was independent of exposure to SSRIs during pregnancy and other potential confounders.

- A prospective study included children of women who screened positive for antenatal depression but not postnatal depression (use of antidepressant drugs not specified, n >1500), and children of women who screened negative for antenatal and postnatal symptoms (n >8000). The children were screened for developmental delays, including language skills, at age 18 months [7]. Developmental delays were more likely to be

observed in offspring of mothers with antenatal depressive symptoms than controls (odds ratio 1.5, 95% CI 1.2-2.0).

Intelligence — Multiple prospective studies suggest that prenatal depression is not associated with adverse effects upon intelligence in the offspring [4]:

- One observational study compared the intelligence of children (age three to six years) born to women with antenatal depression who were not treated with antidepressants (n = 54) and children of women who were healthy during pregnancy (n = 62) [8]. The full scale intelligence quotients in children of depressed mothers and healthy mothers were comparable (108 and 112); verbal and performance intelligence quotients were also comparable.

- A study evaluated children of women with antenatal depressive symptoms (presumably not treated with antidepressants, n = 81), and children (n = 949) of women without antenatal depression; the children were tested at age three years [9]. Vocabulary (strongly correlated with verbal and full scale intelligence quotient) in the two groups was comparable.

- A study of mother-child dyads (n = 121) found that prenatal maternal depression did not predict full scale intelligence quotients in the offspring at age 16 years [10].

One prospective study of mother-offspring pairs (nearly 7000) found that prenatal depressive symptoms were associated with lower full scale intelligence quotients in children at age eight years, controlling for postnatal depressive symptoms and other potential confounds (none of the pregnant women used antidepressants [11]) [12]. However, the effect appeared to be mediated at least in part by unhealthy diets before and after delivery. In addition, another study using the same dataset found that antenatal depression was not associated with lower intelligence in the offspring [13].

PSYCHOPATHOLOGY

Emotional and behavioral dysfunction — Emotional and behavioral dysfunction is a composite variable that includes such elements as anxiety, attention deficit hyperactivity disorder (ADHD), conduct disorder, depression, and oppositional defiant disorder. Several studies suggest that emotional and behavioral dysfunction is greater in the offspring of depressed pregnant women, compared with the offspring of nondepressed pregnant women [1,4,7,14,15]. As an example:

- A prospective study followed a community cohort of mother-child dyads (nearly 8000) for up to 14 years, and controlled for potential confounding factors (such as obstetric outcomes [eg, birth weight and gestational age], parenting behavior, and postnatal depression) in the analyses [16]. Prenatal depression was associated with emotional problems (anxiety and/or depression) and behavioral problems (eg, ADHD, conduct disorder, and/or oppositional defiant disorder) in the children at age four years. In addition, the adverse effects persisted at age 13 years. However, the use of medications was not reported.

- A prospective study comprised pregnant women (n >2200) and their children, aged two to six years [17]. After adjusting for potential confounding factors (eg, maternal history of depression, use of psychotropics during pregnancy, and maternal and paternal postpartum depression), the analyses found that antenatal maternal depressive symptoms were associated with emotional and behavioral problems. This effect was most pronounced in women with consistently high depressive symptoms across pregnancy.

- One prospective study included children (n = 98) of women with prenatal depressive symptoms who were not treated with antidepressants, and children (n = 723) of women who did not have depressive symptoms and were not treated with antidepressants; the children were assessed at age four or five years [18]. After adjusting for potential confounding factors (eg, maternal age, smoking, and use of alcohol), the analyses found that behavioral problems were greater in the children exposed to prenatal depressive symptoms.

Although antenatal depression appears to be associated with impairment of general emotional and behavioral functioning, the observed effect is sometimes small:

- A prospective observational study compared children born to women with antenatal depressive symptoms who were not treated with antidepressants (n = 231) and children of women who were healthy during pregnancy (n >48,000); the children were assessed at age seven years [19]. Emotional and behavioral problems (eg, conduct and peer problems, and hyperactivity and inattention) were present in more children of women with antennal depressive symptoms than controls (4 versus 3 percent).

- A prospective study included pregnant women with prenatal depressive symptoms (n = 376) and pregnant women without clinically significant depression (n >5500); none of the women were treated with selective serotonin reuptake inhibitors [20]. After controlling for potential confounding factors (eg, maternal age, education, and postnatal depressive symptoms), affective problems were more common in children of mothers with depressive

symptoms, compared with children of mothers without depression (odds ratio 1.4, 95% CI 1.2-1.8).

Both genetics and environmental influences (eg, the quality of parenting and effects of living in a household with depressed individuals) are probably involved in the association between antenatal depression and psychopathology in the offspring [1]. The role of genetics in the pathophysiology of depression is discussed separately. (See "Unipolar depression: Genetics".)

The subsections below describe the evidence regarding the association between antenatal depression and more specific behaviors and disorders.

Aggressive and antisocial behavior — Prospective observational studies suggest that antenatal depression is associated with aggressive and antisocial behavior in the offspring [21,22]:

- One study assessed pregnant women (n = 271, including 39 with major depression) and subsequently examined the offspring at age one year [23]. Aggressive behavior in the children was determined by laboratory observations and parental reports, and the analyses controlled for potential confounding factors (eg, socioeconomic status and maternal antisocial behavior). The results showed that prenatal maternal depression was associated with aggressive behavior.

- A prospective study assessed pregnant women (n >2800) for depressive symptoms, and the children were assessed at age 11 years [24]. After controlling for potential confounding factors (eg, maternal use of tobacco and alcohol during pregnancy, and maternal depression during the postnatal period and afterwards), prenatal depressive symptoms were modestly associated with conduct problems.

In addition, other prospective studies have found that prenatal depression is associated with a diagnosis of conduct disorder and/or oppositional defiant disorder:

- A study included children born to women with prenatal depression (n = 38; treatment not reported) and women who were not depressed (n = 82); the children were assessed at age 16 years [25]. The analyses controlled for potential confounds (eg, parental antisocial behavior, socioeconomic status, and postnatal depression), and found that antisocial behavior (diagnosis of conduct disorder and/or having been arrested) occurred more often in the offspring of depressed than nondepressed mothers (47 versus 27 percent).

- Another prospective study of mother-offspring pairs (n >3000) found that prenatal maternal depression was associated with small increase in conduct disorder, oppositional

defiant disorder, and/or ADHD (externalizing disorders) in children at ages seven to eight years [26].

Anxiety — Prospective studies suggest that prenatal depression is associated with anxiety disorders in the offspring, but the observed effect may be small:

- One study included pregnant women who were assessed for depressive symptoms (use of antidepressant drugs not reported), and their children who were assessed for anxiety disorders at age 18 years [27]. After controlling for potential confounding variables (eg, maternal age, maternal smoking or use of alcohol during pregnancy, and postnatal maternal and paternal depression and anxiety), the analyses found that anxiety disorders occurred in more children of women with depressive symptoms than children of nondepressed women (11 versus 6 percent).

- A study of mother-child dyads (n = 121) found that antenatal depression (use of antidepressant drugs not reported) was associated with subsequent anxiety in the children [10]. However, exposure to postpartum maternal depressive episodes may have accounted for this effect.

Autism — It is not clear if prenatal depression is associated with an elevated risk of autism in the offspring, due to inconsistent results across different studies.

Evidence that suggests prenatal depression is not associated with an elevated risk of autism in the children includes the following:

- A registry study ascertained cases of autism (n >1600), and age and sex matched controls without autism (n >16,000); neither cases nor controls were exposed in utero to antidepressants [28]. In analyses that were adjusted for several potential confounding factors (eg, parental ages at birth of child and socioeconomic status), a lifetime history of depression prior to the birth of the child participating in the study was comparable for mothers of offspring with autism and mothers of controls.

- A study of a healthcare organization database identified children with autism (n = 298 cases) and age and sex matched children without autism (n = 1507 controls) [29]. After adjusting the analyses for selective serotonin reuptake inhibitor (SSRI) use during pregnancy, depression was not associated with an increased risk of autism.

- A national registry study included pregnant women (n >4000) with a lifetime history of unipolar depression or bipolar disorder, and pregnant women without depression or bipolar disorder (n >600,000); none of the women used antidepressants [30]. After

adjusting for potential confounding factors (eg, parental age at conception, gestational age, and child's sex), the analysis found that the risk of autism in the two groups was comparable.

The following studies suggest that prenatal depression is associated with an elevated risk of autism in the children:

- A prospective study included pregnant women with prenatal depressive symptoms (n = 376) and pregnant women without clinically significant depression (n >5500); none of the women were treated with SSRIs [20]. The analyses controlled for potential confounding factors (eg, maternal age, education, and postnatal depressive symptoms), and found that autistic symptoms were more common in children of mothers with depressive symptoms, compared with children of mothers without depression (odds ratio 1.4, 95% CI 1.1-1.9).

- A national registry study of live births (n >600,000) included children born to mothers with a lifetime history of depression (n >3000) [31]. The risk of autism was greater in the offspring of mothers with depression than mothers without depression (relative risk 1.8, 95% CI 1.3-2.5); however, the analysis did not account for antenatal use of SSRIs.

- A national registry study included children with autism (n = 22), and age and sex matched children without autism (n >30,000) [32]. A history of depression was more common in mothers of children with autism, compared with mothers of children without autism (odds ratio 1.7, 95% CI 1.0-2.6). However, the analyses did not account for use of antidepressants.

- A retrospective study recruited parents (n = 48) of families with two autistic children and parents (n = 60) of families with a Down syndrome child [33]. The lifetime prevalence of unipolar major depression was greater in the parents of children with autism than parents of children with Down syndrome (33 versus 12 percent). In addition, the rate of depression was higher in grandparents, as well as aunts and uncles, of children with autism. However, the study did not report the use of antenatal antidepressants.

The studies that suggest prenatal maternal depression is associated with autism support the hypothesis that the association between antenatal exposure to SSRIs and autism in some observational studies is due to confounding by indication. If women with depression or other indications for SSRIs are more likely to have children with autism spectrum disorder, a false association between SSRI use and autism may be found in observational studies [31]. (See "Antenatal exposure to selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs): Risk of autism in the offspring".)

Genetic factors are apparently involved in the pathogenesis of autism, and studies have found that genes putatively involved in the pathogenesis of unipolar major depression may also confer risk for autism [34]. Additional information about the pathogenesis of autism is discussed separately. (See "Autism spectrum disorder in children and adolescents: Terminology, epidemiology, and pathogenesis", section on 'Pathogenesis'.)

Depression — Prospective observational studies indicate that antenatal depression is associated with depression in the offspring, such that the elevated risk for depression in children extends into late adolescence [1]:

- A study included pregnant women (n >2800) who were assessed for antenatal depressive symptoms, and their offspring who were assessed for depression at age 18 years [35]. Depression was more likely to occur in offspring of women with antenatal depression than offspring of women without antenatal depression (odds ratio 1.5, 95% CI 1.0-2.2). The association was independent of maternal depression following the postpartum period. However, antenatal use of antidepressant drugs was not reported.

- Another study of mother-child dyads included mothers with antenatal depression (n = 38, use of antidepressant drugs not reported) and mothers without antenatal depression (n = 83) [10]. When the children were assessed at age 16 years, emotional disorders (eg, unipolar major depression or persistent depressive disorder [dysthymia]) were present in more children of mothers with antenatal depression than nondepressed mothers (42 versus 20 percent). However, exposure to postpartum maternal depressive episodes may have accounted for this effect.

- One study enrolled pregnant women and followed the mother-child dyads (n >800) for up to 22 to 25 years after birth [36]. The analyses suggested that antenatal maternal depressive symptoms were associated with offspring physical health problems, which in turn were associated with offspring depressive symptoms during young adulthood. However, maternal use of antenatal antidepressants was not reported, nor is it clear to what extent the effect of antenatal maternal depression was confounded by postnatal maternal depression.

Hyperactivity — Prenatal depression appears to be associated with hyperactivity in the offspring:

- A prospective study assessed pregnant women (n >2800) for depressive symptoms, and the children were assessed at age 11 years [24]. After controlling for potential confounding factors (eg, maternal use of tobacco and alcohol during pregnancy, and

maternal depression during the postnatal period and afterwards), prenatal depressive symptoms were modestly associated with hyperactivity.

- A prospective study included pregnant women with consistently high levels of depression throughout pregnancy (n >500) and pregnant women with consistently low levels of depression throughout pregnancy (controls, n >1200); the children were assessed at age three to six years [37]. After controlling for potential confounding variables (eg, maternal use of psychotropic medications, maternal ADHD, and maternal postpartum depression), the analyses found that ADHD symptoms occurred in more children of mothers with antenatal depression than controls (32 versus 15 percent).

PREGNANCY AND NEONATAL OUTCOMES

Antenatal depression may be associated with adverse pregnancy and neonatal outcomes. (See "Antenatal depression: Pregnancy and neonatal outcomes".)

ABNORMAL INFANT AND CHILD DEVELOPMENT

Antenatal depression may be associated with abnormal infant and child development. (See "Antenatal depression: Risks of abnormal infant and child development".)

TREATING ANTENATAL DEPRESSION

Several options are available for treating antenatal depression. (See "Mild to moderate episodes of antenatal unipolar major depression: Choosing treatment" and "Severe antenatal unipolar major depression: Choosing treatment".)

RISKS OF ANTIDEPRESSANTS

The risks of maternal antidepressant medication with regard to fetal and infant development are discussed separately.

- (See "Antenatal use of antidepressants and the potential risk of teratogenicity and adverse pregnancy outcomes: Selective serotonin reuptake inhibitors" and "Antenatal use of antidepressants and risks of teratogenicity and adverse pregnancy outcomes: Drugs other than selective serotonin reuptake inhibitors" and "Antenatal exposure to selective

serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs): Neonatal outcomes".)

- (See "Antenatal use of antidepressants and the potential risk of teratogenicity and adverse pregnancy outcomes: Selective serotonin reuptake inhibitors" and "Antenatal use of antidepressants and risks of teratogenicity and adverse pregnancy outcomes: Drugs other than selective serotonin reuptake inhibitors" and "Antenatal exposure to selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs): Neonatal outcomes".)
- (See "Antenatal use of antidepressants and the potential risk of teratogenicity and adverse pregnancy outcomes: Selective serotonin reuptake inhibitors" and "Antenatal use of antidepressants and risks of teratogenicity and adverse pregnancy outcomes: Drugs other than selective serotonin reuptake inhibitors" and "Antenatal exposure to selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs): Neonatal outcomes".)

POSTPARTUM DEPRESSION

Antenatal depression is a risk factor for postpartum depression, which in turn is associated with abnormal child development as well as cognitive impairment and psychopathology. (See "Postpartum depression: Adverse consequences in mothers and their children".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, “The Basics” and “Beyond the Basics.” The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on “patient info” and the keyword(s) of interest.)

- Basics topics (see "Patient education: Depression in adults (The Basics)")

- Beyond the Basics topics (see "Patient education: Depression in adults (Beyond the Basics)")

SUMMARY

- The association between antenatal depression and general cognitive performance in the offspring is not clear, due to contradictory findings across studies. However, antenatal depression appears to be associated with delays in acquiring language skills. (See 'Cognition' above.)
- Emotional and behavioral dysfunction is a composite variable that includes such elements as anxiety, attention deficit hyperactivity disorder, conduct disorder, depression, and oppositional defiant disorder. Several studies suggest that emotional and behavioral dysfunction is greater in the offspring of depressed mothers, compared with offspring of nondepressed mothers. However, the observed effect may be small. (See 'Emotional and behavioral dysfunction' above.)
- Antenatal depression is associated with specific behaviors and disorders, including aggressive and antisocial behavior, anxiety disorders, depressive disorders, and hyperactivity in the offspring. (See 'Aggressive and antisocial behavior' above and 'Anxiety' above and 'Depression' above and 'Hyperactivity' above.)
- It is not clear if prenatal depression is associated with an elevated risk of autism in the offspring. (See 'Autism' above.)
- Several options are available for treating antenatal depression. (See "Mild to moderate episodes of antenatal unipolar major depression: Choosing treatment" and "Severe antenatal unipolar major depression: Choosing treatment".)

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