

Perinatal and Postpartum Mood Disorders

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Perinatal and Postpartum Mood Disorders

*Perspectives and Treatment Guide for
the Health Care Practitioner*

SUSAN DOWD STONE, MSW, LCSW

ALEXIS E. MENKEN, PhD

Editors

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Ian Brockington, PhD, FRCPsych, has a distinguished career in maternal mental health that has spanned decades and has mightily contributed to our body of knowledge in this field. He was a Professor of Psychiatry, University of Birmingham (1983–2001, now emeritus), a Visiting Professor at The University of Chicago (1980–1981), Washington University in St. Louis (1981), Nagoya University (2002), and Kumamoto University (2003). Dr. Brockington is the Founder and First President of the Marcé Society. He was also the Founder and 1st Chairman, Section on Women's Mental Health, World Psychiatric Association. Dr. Brockington has written extensively on the subject. Notable contributions include "Motherhood and Mental Health" (1996) and "Eileithyia's Mischief: the Organic Psychoses of Pregnancy, Parturition and the Puerperium" (2006).

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Jane Israel Honikman, MS, co-founded Postpartum Education for Parents (PEP) in 1977 and became the Executive Director of the Santa Barbara Birth Resource Center in 1984. She founded Postpartum Support International in 1987 and was elected as PSI's first president in 1989. She has authored many articles and educational materials on postpartum depression, including her books "Step by Step" (2000) and "I'm listening" (2002). She lectures extensively on the role of social support and the emotional health of families during the perinatal period.

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Foreword

Motherhood is skilled, emotionally demanding, and exhausting work. In most families, the mother is the main source of comfort, care, and counsel: all members benefit from her devotion, enthusiasm, and resourcefulness, and all—especially the children—suffer from her discouragement. Every effort we make to improve mothers' well-being and morale is a contribution to family life, and the health of the next generation. Helping mothers is the responsibility of many professionals and professions—clinical and scientific psychology, psychiatry, social work, midwifery, academic nursing, general medical practice, obstetrics, pediatrics, pharmacology, pathology, and law. In addition, laity in many countries have organized their own networks of support, which play a vital role.

Our knowledge of the mental disorders that afflict mothers has made strides in recent times, with a deluge of publications from all over the world. In my book, *Motherhood and Mental Health* (1996), I reviewed about 4,000 works that had appeared up to that time, dating back to Hippocrates. Much of the best literature was German, French, and Scandinavian, with, of course, contributions from other Western European nations and North America. But since then—within 12 years—at least as many more papers have been published, with many other nations contributing—Chile, Hong Kong, India, Japan, Nigeria, Singapore, and Turkey, to name a few. These countries represent those parts of our world where most of the infants are born, so it is appropriate that we are now hearing how their women experience motherhood.

The science of maternal mental illness has become more detailed. When I entered this field of clinical work and science in 1975, it was usual to speak of three postpartum psychiatric entities—the maternity blues, postpartum psychosis, and postnatal depression. The *blues* (strictly defined) is a transient, subclinical disturbance, and concern has

been displaced to more severe and persistent disorders. Postpartum psychoses, we now know, are of many distinct kinds. At least a dozen forms of organic (neuropsychiatric) psychoses can complicate pregnancy, parturition, or the puerperium; these are now rare, but they used to account for at least one-quarter of cases, and certain forms (eclamptic psychosis, infective delirium, Wernicke-Korsakov psychosis, and cerebral venous thrombosis) may still be prevalent in the Third World. That form of psychosis that is still relatively common in Europe and North America (rather less than 1/1,000 births) is considered to be a variant of bipolar (manic depressive) disorder, but sometimes the illness is atypical, with *cycloid* or *acute polymorphic* features. (These terms are not used in the United States, where *schizophreniform* is perhaps equivalent.) As for *postnatal depression*, this is also heterogeneous. In some mothers, the main disorder is not depression, but anxiety. There are anxious themes specific to pregnancy—for example, *tocophobia* (the fear of delivery). In the puerperium, the main themes are infant-focused anxiety, which can reach the severity of a phobia, or agonizing foreboding about the child's health and safety, especially the fear of crib death (SIDS). In addition, a particular variant of obsessive compulsive disorder—obsessions of infanticide—is quite common. In other mothers, depression is a mask for a completely different disorder. A large modern literature has been concerned with the consequences of severe or traumatic labor, which can be followed by persistent stress symptoms or pathological complaining. Unwanted pregnancy is another source of extreme stress. It is still common in nations with ready access to termination, and surely much more common in those that forbid or strongly discourage abortion: it carries an increased risk of several forms of psychopathology. It may lead to denial of pregnancy (conscious or hysterical), which has obstetric risks and occasionally ends in neonaticide (the killing of the newborn). Another disorder, described and explored by American academic nurses, is a disturbance of the mother-fetus relationship (affiliation), which in extreme degree can lead to fetal abuse. After delivery, severe disorders of the mother-infant relationship are seen; often these are combined with depression, but not always. Thus we now confront an array of different pre- and postpartum disorders that challenge the diagnostic skills of mental health professionals, but also lead in to an arsenal of specific therapies.

The present compendium is focused on perinatal mood disorders. Appropriately, the authors come from many professions, including social work, psychology, law, psychiatry, nursing, health education, neurobiology,

pediatrics, and obstetrics. Lay organizations are represented by both the founder and current president of Postpartum Support International and the What to Expect Foundation. The purpose is education, targeted at health care professionals of all kinds, and students in all those professions. The importance of recognizing, assessing, and treating perinatal mood disorders cannot be too strongly emphasized. This volume will summarize what is now known and serve as a primer for clinical reference. It will broadcast an optimistic message. Ignorance and pessimism are no longer justified. We are in a much stronger position to understand what is wrong with these troubled mothers and to intervene effectively. A great deal can now be done to restore mothers to full mental health.

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Finally, my love, pride, and admiration are endlessly extended to my precious daughter, Julia Michelle Rish, whose ever-watchful curiosity and support of her mother's journey brings joy at every turn. This is for you Julia, and beloved children everywhere who have endured with their mothers and found the loving strength to understand. By your sound rejection of stigma and ignorance, you offer hope to future generations of mother and child and bear witness to triumph over tragedy.

Susan Dowd Stone

Having immersed myself in the world of maternal mental health for the past 15 years, I have found the opportunity to think deeply about the meaning of motherhood, with all its challenges, risks, demands, and rewards, to be tremendously valuable. Many thanks to our editor, Sheri W. Sussman, for her faith in this book and Katherine Tengco for her tireless editorial assistance. The development of my career path has been deeply influenced by Mary D'Alton, MD; Catherine Monk, PhD; and Governor Richard Codey and Mary Jo Codey. I am fortunate to be surrounded by a wonderful study group, and teachers such as Gary Kose, PhD; Ivan Bresgi, PhD; Dorothy Cantor, PsyD; and others too numerous to mention. My greatest teachers have been my parents, Drs. Etta and Milton Ehrlich, both of whom are psychologists and have generously shared their wisdom. More important, both have taught me mindful and nurturing mothering. I am grateful to my brothers, Dimitri and Gregor Ehrlich, for their vast compassion and endless humor. My life and work has been deeply influenced by Virginia Brown and Melissa Neubauer, dear friends who have taught me so much about the meaning of motherhood by surviving extraordinary and unspeakable loss. There is no greater model for maternal love than the following friends, all of whom have shown me that they know how to live with profound intention and kindness: Lisa Tuttle, Mark Burrell, Karen D'Avanzo, Cynthia Green, Michelle Phillips, Melissa Katz, and, of course, my much-loved Mariana Castaneda. I am especially grateful to Peg Rosen for her lucid thinking and bottomless friendship. I am indebted to Bruce Menken, love of my

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Alexis E. Menken

Introduction

Our nation is finally awakening to acknowledge the full spectrum of maternal experience. Medical, neurobiological, and psychiatric research are merging and sharing their growing knowledge base with clinical, social, and legislative communities. Some states, such as New Jersey and Illinois, already have laws encouraging screening, detection, treatment delivery, and additional research for the long-ignored public health crisis of perinatal mood disorders. As we have become better equipped and more motivated to carefully assess the mental health of childbearing mothers, the incidence of such illnesses has appeared to increase, but perhaps we are simply illuminating long existent facts.

One major task of this growing interdisciplinary initiative is the education of our health care providers. As professional caregivers from many disciplines provide services to women anticipating pregnancy, who are currently pregnant, or who are in the postpartum, the need for consistent evaluative awareness to the full spectrum of perinatal mental health outcomes requires organization and attention.

Perinatal and Postpartum Mood Disorders: Perspectives and Treatment Guide for the Health Care Practitioner is meant to offer an overview and classic text responsive to the need for multidisciplinary education specific to the perinatal period. Such disciplines include obstetrics, gynecology, psychiatry, medicine, social work, psychology, nursing, social support, law, and literacy, professions that acknowledge and accept their responsibility to attend to the full spectrum of maternal experience, including mental health. While ambitious in reach, the authors who contributed time and thought to this project are well recognized leaders, thinkers, clinicians, and advocates within this practice specialty. We, therefore, wish to begin this introduction by offering our respectful appreciation of each contributing author who has honored this text and its readers with his or her considerable knowledge. Please take a moment

to read of their significant contributions to the issue and this text. Many authors have additional and more extensive writings also worthy of your pursuit. We hope this overview will encourage further in-depth exploration of the subject matter.

The enormous impact of compromised maternal mental health on child development, social stability, and family health has offered indisputable evidence demanding less vertical and broader, more inclusive research and study. This text is an effort to bring perspective to the issue and help practice evolve toward current dictates of evidence-based science and research in perinatal mental health.

The textbook begins by establishing the importance of maternal mental health. Vivette Glover, Kristin Bergman, and Thomas G. O'Connor have written a chapter on groundbreaking research explaining the effects of maternal stress, anxiety, and depression during pregnancy on the neurodevelopment of the child. These authors present compelling evidence for the importance of assessing and treating maternal anxiety and stress during pregnancy to prevent neurodevelopmental sequelae in the fetus.

Ian Brockington, who has studied maternal child attachments across the decades and has researched the topic for major studies and diagnostic evaluations, shares his wisdom and current view of the diagnostic spectrum of attachment disorders. Julia Chase-Brand, a psychiatrist with a background in biology, brings both disciplines to bear in evaluation of maternal mental illness as it affects children and adolescents. Her work with this population brings rich perspective to her findings and evaluative overview.

Shaila Misri and Karen Joe's chapter offering an in-depth exploration of diagnostic etiology and should be required reading for many professionals developing perinatal specialties. Dr. Misri's prolific written and research contributions to our current body of knowledge offer readers further opportunities for learning.

The second part of this textbook addresses different perspectives on risk factors, screening, and diagnosis. Linda Klempner has written a summary overview of the history of postpartum depression and how screening tools have been developed. Dr. Klempner's chapter will provide the reader with necessary tools to begin screening patients. Kathleen Kendall-Tackett is a health psychologist and researcher who presents the reader with an overview of alternative treatments. As many women make inquiries about alternate roads to recovery, this chapter will help prepare the clinician for those questions.

Sandra N. Jolley and Tricia Spach have provided health care professionals with psychobiological underpinning to understand Perinatal Mood Disorders. While many clinicians feel that there is a biological basis for perinatal mood disorders, Jolley and Spach elucidate brain physiology and how this contributes to the perinatal period. Andrea Braverman gives voice to the role of assisted reproductive technology in perinatal mood disorders. Dr. Braverman's chapter is one of the first published works to tackle this severely neglected area.

The third part of this text addresses perinatal mood disorders from the perspective of four different professionals. Alexandra Spadola speaks to the experience of the obstetrician. She acknowledges the special role that an obstetrician can play in the life of the patient and how this relationship can be pivotal to helping women get the treatment they need. Mary Ann LoFrumento provides the pediatrician's perspective with an all-inclusive guideline for pediatric practice. Dr. LoFrumento's chapter should serve as a template for pediatric practice guidelines for helping with perinatal mood disorders. Cheryl T. Beck describes the nurses' vantage point. Dr. Beck provides concrete and manageable steps, not only for nurses, but for all professionals working with new mothers. George Parnham is our nation's foremost leading legal expert on the evolution of appropriate recourse and defense for the small percentage of women whose undetected, untreated, and severe maternal mental illness has led them into the justice system. Mr. Parnham challenges our nation's response to such cases, and offers current status and perspective on the insanity defense as applied to this population.

The fourth section of this volume offers an overview of various treatment options. Catherine Birndorf and Alexandra Sacks grapple with the complicated decision-making process that couples must face when considering psychotropic medication during pregnancy and lactation. This is never a simple evaluative process and the authors provide a meticulous explanation of how to explore the decision tree with your patient. This is not a one-size-fits-all approach, and they clarify essential issues that must be explored when helping couples make these difficult decisions. Co-editor Susan Dowd Stone emphasizes the need for research and treatment that includes focus on common comorbidities presenting across the perinatal period, suggesting this could lead to better treatment outcomes. Dowd Stone also proposes consideration of Dialectical Behavior Therapy for treatment of complex cases as its theory appears to be well aligned with the presumed etiology of perinatal mood disorders. Margaret Spinelli makes the case for Interpersonal Psychotherapy

as an efficacious treatment for perinatal depression. IPT has consistently demonstrated reduction in depressive symptoms, attends to the profound role changes of parenthood, helps with grief responses, and targets more skillful management of interpersonal transactions. Co-editor Alexis Menken has written about the psychodynamic approach to working with postpartum depression. Her focus is on the development of maternal identity and the dynamics that need to be addressed to help a woman find her own voice as a mother. Lisa Bernstein, Executive Director of the What to Expect Foundation, addresses, with Eve Weiss, the issues of literacy and effective disbursements of needed information to often-underserved populations. Finally, Jane Honikman, founder of Postpartum Support International, the world's leading network devoted to perinatal mental health, gives us a history of grassroots efforts to connect women to appropriate services, and, most important, to each other.

The Importance of Maternal Mental Health

PART
I

1

The Effects of Maternal Stress, Anxiety, and Depression During Pregnancy on the Neurodevelopment of the Child

VIVETTE GLOVER, KRISTIN BERGMAN, AND
THOMAS G. O'CONNOR

Symptoms of anxiety and depression are frequent during pregnancy. Indeed, they are more common in late pregnancy than in the postpartum period (Heron, O'Connor, Evans, Golding, & Glover, 2004). Pregnancy is also a period in which major life events cluster, as women, and their partners, begin to adjust to a major life transition. Several studies show that domestic violence in pregnancy is common (Chhabra, 2007; Macy, Martin, Kupper, Casanueva, & Guo, 2007). It is now apparent that it is important to recognize and reduce all this, both for the woman herself, and also for the sake of her future child. There is evidence that maternal anxiety and stress during pregnancy can affect the neurodevelopment of the fetus.

It is a commonly held belief in many societies that the mood of a mother during pregnancy can affect the development of the child she is bearing. In 400 B.C., Hippocrates was already aware of the importance of emotional attitudes for the outcome of pregnancy. In China, more than a thousand years ago, recognition of the importance of prenatal attitudes led to the institution of the first antenatal clinic (Ferreira, 1965). However, it is only recently that this idea has been investigated scientifically in both animal and human research.

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There is very strong evidence from animal studies that maternal stress in pregnancy has a long-term effect on the behavior of the offspring (Weinstock, 2001). With animals, it is possible to cross foster the prenatally stressed pups to control mothers after birth, and thus clarify the timing of the exposure. Prenatal stress in animal models has been linked with a wide range of outcomes, including altered cerebral laterality and abnormal sexual behavior. However, the most widely reproduced effects are on cognition, including reduced memory and attention, and increased anxiety and emotional dysregulation. Work with nonhuman primates has identified some brain bases of the prenatal stress effects. For example, Coe et al. have shown that exposure to unpredictable noise, either early or late in pregnancy, resulted in reduced volume of the hippocampus in the offspring (Coe et al., 2003). This is a part of the brain that is important for memory. The responsiveness of the hypothalamic-pituitary-adrenal axis (HPA), which produces the stress hormone called cortisol, was also increased in the offspring. Other experiments have shown the effects of prenatal stress may be moderated and even reversed by positive postnatal rearing, suggesting that, although there may be persisting effects of prenatal stress, it is not inevitable (Maccari et al., 1995).

STUDIES SHOWING A LINK BETWEEN ANTENATAL STRESS AND ANXIETY AND THE NEURODEVELOPMENT OF THE CHILD

There is now good evidence in humans also that if a mother is stressed or anxious while pregnant, her child is substantially more likely to have emotional or cognitive problems, including an increased risk of symptoms of attention deficit/hyperactivity, anxiety, or language delay (for reviews, see Talge, Neal, & Glover, 2007; Van den Bergh, Mulder, Mennes, & Glover, 2005). These findings are independent of effects due to maternal postnatal depression and anxiety.

A pioneering study linking antenatal stress with effects on the child was published by D. H. Stott in 1973 (Stott, 1973). Information was collected from 200 women in Scotland in 1965–1966, at the end of their pregnancy. The questions asked of the mother concerned her physical and mental health, the course of the pregnancy, and her social circumstances. The health, development, and behavior of the child were followed for the next 4 years. Stott's major conclusion was that stresses

during pregnancy involving severe and continuing personal tensions, in particular marital discord, were closely associated with child morbidity in the form of ill health, neurological dysfunction, developmental delays, and behavior disturbance.

In a study carried out in Washington, D.C., with predominantly primiparous African American women, it was found that several psychosocial variables, including stress, anxiety, and partner interaction, were associated with reduced behavioral scores on the Brazelton Neonatal Behavior Assessment Scale (NBAS) when the newborns were 2 days of age (Oyemade et al., 1994). An Israeli study examined the outcome for two cohorts of boys, one group consisting of those born in the year of the Six-Day War and a second group born 2 years later. The children from the “war exposed pregnancies” had significant developmental delays and evinced regressive behavior (Meijer, 1985), although antenatal and postnatal stress effects were not distinguished in the analyses. A retrospective study by McIntosh et al. (McIntosh, Mulkins, & Dean, 1995) showed that if the mother experienced moderate emotional stress, or smoked cigarettes during pregnancy, her child was more likely to be diagnosed with an attention deficit disorder. These studies laid the important groundwork and provided a springboard for the better-controlled more recent studies described below.

The Effects on the Child

There is now good evidence from many independent prospective studies that antenatal stress predicts adverse social/emotional and cognitive outcomes during childhood. In the last 5 years several prospective studies have been published. Even though these studies used a wide range of different methods, both for measuring antenatal stress or anxiety and for assessing the child, they all found links in a way that revealed an effect on the development of the fetal brain. These studies are mainly European with two conducted in North America (Field et al., 2003; Laplante et al., 2004); none are from developing countries or countries at war, where one might predict that the effects would be even more marked.

It is clear that a wide range of different outcomes can be affected by prenatal stress. One set of studies shows an effect of prenatal stress or anxiety on the cognitive development of the child as assessed by scores on the Bayley Mental Developmental Index (MDI) (Bergman, Sarkar, O'Connor, Modi, & Glover, 2007; Huizink, Robles de Medina, Mulder, Visser, & Buitelaar, 2003) or language development (Laplante et al.,

2004). The MDI is a widely used standardized tool for the assessment of cognitive development in infants and young children. Other studies have shown links between antenatal stress/anxiety and behavioral/emotional problems in the child. The most consistent adverse outcome is in symptoms of Attention Deficit Hyperactivity Disorder (ADHD) (O'Connor, Heron, Golding, Beveridge, & Glover, 2002; Rodriguez & Bohlin, 2005; Van den Bergh & Marcoen, 2004). However, other effects have been observed also, such as an increase in anxiety (O'Connor et al., 2002; Van den Bergh & Marcoen, 2004) and in externalizing problems (Van den Bergh & Marcoen, 2004). It is likely that the particular outcome affected depends on the specific genetic vulnerabilities of the child. There is now good evidence for gene/environment interactions with respect to the postnatal development of psychopathology (Caspi et al., 2003); it is probable that the same occurs prenatally.

The studies have examined children at a wide range of ages, from the newborn to 17 years, and it is clear that the effects of prenatal stress can be long lasting. Two studies found impairment in the newborn using the Brazelton NBAS (Brouwers, van Baar, & Pop, 2001; Field et al., 2002) and one study used the Prechtl neurological assessment (Lou et al., 1994). Field et al. (2003) reported that the newborns of mothers with high anxiety had greater relative right frontal brain activation (as measured by EEG) and lower vagal tone. The babies also spent more time in deep sleep and less time in quiet and active alert states, and showed more state changes and less optimal performance on the NBAS (motor maturity, autonomic stability, and withdrawal). Lou et al. (1994) proposed that there may be a "fetal stress syndrome" analogous to the "fetal alcohol syndrome," on the basis of their study showing that antenatal life events resulted in a smaller head circumference, lower birthweight, and lower neurological scores on the Prechtl scale.

O'Connor, Heron, Golding, and Glover (2003) showed a continuity of effects from 4 to 7 years old and Van den Bergh and colleagues have found links between antenatal anxiety and child depression in adolescence (Van den Bergh, Van Calster, Smits, Van Huffel, & Lagae, 2007).

Another effect of prenatal stress appears to be on laterality. Glover, O'Connor, Heron, and Golding (2004) used the large community ALSPAC cohort to test the hypothesis that antenatal maternal anxiety is associated with altered lateralization in humans, as demonstrated by mixed handedness. Maternal anxiety at 18 weeks of pregnancy predicted an increased likelihood of mixed handedness in the child, independent of

parental handedness, obstetrical and other antenatal risks, and postnatal anxiety. For this outcome measure, unlike with late ADHD symptoms or anxiety, there was no link with anxiety at 32 weeks. Obel, Hedegaard, Henriksen, Secher, and Olsen (2003) have also shown that antenatal life events are associated with a higher prevalence of mixed handedness in the child. Both studies found that this effect was stronger with antenatal anxiety/stress than with antenatal depression.

Atypical laterality has been found in children with autism, learning disabilities, and other psychiatric conditions, including problems with attention as well as in adult schizophrenia (Glover et al., 2004). There is anecdotal evidence for a link between antenatal maternal stress and both autism and dyslexia, in addition to the evidence discussed already for ADHD. It is an interesting possibility that many of these symptoms or disorders, which are associated with mixed handedness, share some neurodevelopmental components in common, which may be exacerbated by antenatal maternal stress or anxiety.

More needs to be understood about the exact period of gestation that is most important for all the effects described here. Different studies have found different periods of vulnerability. What is clear is that the effects are not confined to the first trimester. Although the basic body structures are formed early, the brain continues to develop, with neurons making new connections, throughout gestation. In the study of O'Connor et al. (2002) anxiety was measured only at 18 and 32 weeks gestation, and the associations were stronger with the latter time point. It remains possible that the effects were actually maximal at midgestation, for example, about 24 weeks. It is also likely that the gestational age of sensitivity is different for different outcomes. Brain systems underlying different aspects of cognition or behavior mature at different stages.

What Causes Risk to the Child?

The evidence shows that the effect is not specific to one type of stress or anxiety. It also seems that many neurodevelopmental effects can be observed with relatively low levels of anxiety or stress (O'Connor, Heron, & Glover, 2002). Most of the studies have used maternal self-rating questionnaires, some used anxiety questionnaires, and others measures of stress (O'Connor et al., 2002; Van den Bergh & Marcoen, 2004). Some studies assessed daily hassles (Huizink et al., 2003), whereas others focused on life events (Bergman et al., 2007; Lou et al., 1994), perceived stress (Rodriguez & Bohlin, 2005), or pregnancy specific worries. Others

have used exposure to an external trauma, such as a severe Canadian ice storm (Laplante et al., 2004) or the Chernobyl disaster.

However, it is also of interest that one study has found, in a cohort of financially and emotionally stable women, that there was a small but significant positive association between antenatal stress and both the mental and physical development of the child (DiPietro, Novak, Costigan, Atella, & Reusing, 2006). The authors suggest that a small to medium amount of antenatal stress may actually be helpful for the development of the child, although this remains to be confirmed.

None of the published studies have used clinical interviews, and, consequently, none can demonstrate if there are differences among these disorders with respect to the effect on the fetus and child. Many subtypes of anxiety disorder are recognized, including generalized anxiety, panic, specific phobia, posttraumatic stress, acute stress, and obsessive-compulsive disorders. These disorders may involve quite different physiological processes (Tsigos & Chrousos, 2002). It is interesting that the actual life events found in one study to be most linked with both low scores on the Bayley Mental Developmental Index and increased fear reactivity were “separation/divorce” and “cruelty by the partner” (Bergman et al., 2007). This finding is similar to the conclusion by Stott (1973) that continuing personal tensions (in particular, marital discord) were a particular risk factor for later “neurological dysfunction, developmental delays and behavior disturbance in the child” (p. 785).

The high co-occurrence of symptoms of anxiety and depression raises questions about the specific predictions from maternal anxiety. However, there is some evidence that the effect on the child derives more from prenatal anxiety rather than depression. O'Connor et al. (2002) found that, although antenatal depression was associated with child behavioral problems in a similar way to prenatal anxiety, the effect was smaller; furthermore, when prenatal anxiety was covaried, the association with depression was not significant. In contrast, the prediction from prenatal anxiety to child behavioral problems was substantial and not reduced when prenatal depression was covaried. The authors also found that the link between antenatal anxiety and child behavioral problems was separate and additive to the effects of postnatal depression (O'Connor, Heron, & Glover, 2002).

There have been no studies that have addressed the important question of whether stress due to the mother working during pregnancy has adverse effects on neurodevelopment of the child. There have been several such studies in relation to preterm delivery and these suggest that

work per se is not damaging; it only becomes harmful when the woman is working when she does not want to, or feels out of control (Homer, James, & Siegel, 1990).

In summary, there is growing evidence that the risk most closely linked with adverse child outcomes is maternal anxiety/stress. There is also evidence that the effects on the child are not restricted to extreme anxiety or stress in the mother, but can occur across quite a wide range (O'Connor et al., 2002). On the other hand, more research is needed into what types of anxiety/stress are most predictive of later developmental and health problems. The consistent findings across studies, despite different measures of anxiety and stress, may indicate that the risk derives from a broad range of negative emotions that occur in stressed and anxious individuals.

Magnitude of Effect

The size of the effects found in many of these studies is considerable, although it is important to emphasize that most children are not affected. In the general population study of O'Connor et al. (2002), it was found that women in the top 15% for symptoms of anxiety at 32 weeks gestation had double the risk of having children with behavioral problems at 4 and 7 years of age, even after allowing for multiple covariates. It raised the risk for a child of this group of women having symptoms of ADHD, anxiety or depression, or conduct disorder, from 5% to 10%. Thus 90% were not affected. However these results imply that the attributable load in behavioral problems due to antenatal anxiety is of the order of 15%.

Van den Bergh and Marcoen (2004) found that maternal anxiety during pregnancy accounted for 22% of the variance in symptoms of ADHD in 8–9-year-old children. LaPlante et al. (2004) showed that the level of prenatal stress exposure accounted for 11.4% and 12.1% of the variance in the toddlers' Bayley MDI and productive language abilities, respectively, and accounted for 17.3% of the variance of their receptive language abilities. Bergman et al. (2007) also observed an effect of antenatal life events at 18 months of age, accounting for 22% of the variance in Bayley's MDI scores.

Most of these are substantial effects, but there remains considerable variation across children. Bergman et al. (2007), for example, have found that, although antenatal maternal stress increases the risk for both cognitive delay and raised anxiety, these do not necessarily occur in the same children.

Possible Mechanisms

The mechanisms underlying the effects of prenatal stress in women on the development of the fetus and child are far from clear. In animal models, the central role of the stress hormone cortisol in mediating prenatal stress effects in both mother and offspring is well established (Schneider, Moore, Kraemer, Roberts, & DeJesus, 2002; Weinstock, 2001), although many other systems, such as those involving dopamine and serotonin have also been shown to be involved.

In humans, presumably stress or anxiety changes the maternal physiology, including her hormonal levels, and these in turn affect the development of the fetus. Stress and anxiety are generally associated with elevated activity in both the HPA axis and the sympathetic system, although the relationships are complex. However, the maternal HPA axis becomes desensitized to stress during pregnancy, as gestation increases (Kammerer, Adams, Castelberg Bv, & Glover, 2002; Sarkar, Bergman, Fisk, & Glover, 2006). Even though we know that there is a strong correlation between maternal and fetal levels of cortisol (Sarkar, Bergman, Fisk, O'Connor, & Glover, 2007), and that this correlation is increased with higher maternal anxiety (unpublished observations), suggesting that the placenta becomes more permeable to cortisol with increased stressor anxiety, much remains to be understood.

Maternal anxiety during pregnancy has also been associated with reduced blood flow to the baby through the uterine arteries (Teixeira, Fisk, & Glover, 1999), but we do not know whether this is of clinical significance.

CLINICAL IMPLICATIONS AND OPPORTUNITY FOR INTERVENTIONS

The implications of the research described above is that anxiety and stress during pregnancy should receive more attention, both for the sake of the woman herself and for the development of her future child.

Effective interventions to reduce maternal stress and/or anxiety during pregnancy should help to decrease the incidence of cognitive and behavioral problems in children. The evidence suggests that it is not only extreme levels of stress and anxiety that need attention, but possibly, the most affected 15% of the population. Also, it is not only

clinically diagnosed mental illness that is important here, but stress due to other factors too, especially the relationship with the partner.

However, there have been few studies that have directly evaluated nonpharmacological, psychological, or social support interventions in pregnancy, and only one research program that has followed up with the child. This is the program that has been conducted by Olds and co-workers over many years, the nurse family partnership (Olds, 2002; Olds et al., 2002; Olds et al., 2004). Although this program was not specifically targeted to help the mental health or emotional state of the mother, it provides considerable social support to vulnerable mothers, starting in pregnancy. The subjects were asked about, and helped with, both support networks and domestic violence. The participants were especially deprived groups of mostly teenage, first-time mothers. Specially trained nurses completed an average of 6.5 home visits during pregnancy and 21 visits from birth to the children's second birthdays, with a focus on health care, development and education of the mother, and teaching parenting skills. The outcomes were compared with standard care. The nurse visitations produced significant effects on a wide range of maternal and child outcomes. Nurse-visited mothers and children interacted with one another more responsively, and 6-month-old infants were less likely to exhibit emotional distress in response to fear stimuli. At 21 months, nurse-visited children born to women with low psychological resources were less likely to exhibit language delays, and, at 24 months, they exhibited superior mental development on the MDI. The children have been followed up for 15 years, and findings include fewer long-term behavioral problems and fewer convictions (Olds et al., 1998). There is no direct evidence that a reduction of maternal stress during pregnancy contributed to the positive gains in the intervention group, but that is a very plausible hypothesis. It is well established that lack of social support or confiding relationships are strong risk factors for antenatal mood disturbance (Bowen & Muhajarine, 2006). Additional studies to evaluate the efficacy of similar types of interventions starting during pregnancy, with a special focus on mental illness, social support, and help with partner relationships, should be part of the agenda for new public health research.

One small randomized, controlled trial of 16 sessions of interpersonal psychotherapy for antenatal depression has been conducted (Spinelli & Endicott, 2003). It was found to be effective in reducing the depression, and the authors recommend it as a first line of antidepressant treatment during pregnancy. There has been a meta-analysis of treatments

for depression in both pregnancy and postpartum (Bledsoe & Grote, 2006). The authors conclude that a range of treatments have been found to be effective, with cognitive behavioral therapy producing the largest effect sizes.

Teixeira, Martin, Prendiville, and Glover (2005) assessed whether a short period of directed or passive relaxation would reduce maternal self-rated anxiety, heart rate, plasma catecholamines, cortisol and uterine artery blood flow in pregnant women. Both methods reduced maternal state anxiety and heart rate, the directed therapy more so. Passive relaxation while sitting on a chair had a greater effect in reducing cortisol and norepinephrine. There was a striking lack of correlation between the psychological effects and all the biological indices measured. We have to be aware that it is possible that in order to reduce the physiological effects of anxiety during pregnancy, different methods may be needed from those that are effective at ameliorating subjective anxiety.

CONCLUSION

There is now good evidence that maternal anxiety and stress during pregnancy substantially increase the risk for adverse long-term effects on the neurodevelopment of her child, even though most children are not affected. These effects are not limited to mothers experiencing extreme distress, but occur across the range. Neither are they limited to mothers suffering from a diagnosed mental illness. Relationship strain with the partner is a strong risk factor for adverse child outcome. Different children can be affected in different ways, probably depending on their genetic vulnerabilities and timing of the exposure. We do not know the critical gestational ages of sensitivity, and they are likely to vary for different outcomes. Independent studies have found effects from early to late gestation, suggesting that it is important to recognize and treat emotional problems from early in pregnancy, but that it is not too late to provide benefit later on. There have been few studies that have studied psychological interventions during pregnancy, and only one support study that has subsequently followed up with the child. However, it is reasonable to assume that interventions for which there is evidence of efficacy outside pregnancy, to treat anxiety, depression, or partner relationship problems, will be of benefit to the mother, and that they should be tailored to meet each woman's particular problems. They may well be of benefit to her child also.

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