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## The impact of stress in pregnancy

Vivette Glover and Jane Barlow review the evidence for the lasting effects of stress and anxiety during pregnancy

### Introduction

**Adapted with kind permission from the Journal of Children's Services.**

**Original publication: Glover V, Barlow J.**

**Psychological adversity in pregnancy: what works to improve outcomes? *J Children's Services*, 2014;9(2):96-108.**

**Available from: [dx.doi.org/10.1108/JCS-01-2014-0003](https://doi.org/10.1108/JCS-01-2014-0003)**

A happy and trouble-free pregnancy is something that all parents and practitioners might hope for, but for many couples this is not the reality and many women can experience anxiety and/or depression at some point during their pregnancy. This article outlines the immediate and long-term effects that may be experienced by some but not all babies as a result of such problems, and highlights the need for interventions aimed at reducing anxiety and depression before and during the transition to parenthood.

Anxiety – a state of fearfulness about what may happen in the future – is relatively common in pregnancy, affecting 12 - 20% of women.<sup>1</sup> Depression – a set of symptoms including negative thoughts and feelings

about the present – can affect a similar number of women both in the antenatal and postnatal period.<sup>2</sup> Both anxiety and depression in pregnancy are associated with postnatal depression.<sup>2</sup> Many women also experience other problems in pregnancy that are strongly associated with both anxiety and depression. For example, around 30% of domestic abuse starts during pregnancy,<sup>3</sup> and around 9% of women are being abused during pregnancy or after giving birth.<sup>4</sup> Around 1% of pregnancies in the UK (20,000 women per year) involve a drug dependent mother,<sup>5</sup> and such drug dependency co-exists with a range of other difficulties including mental health problems.<sup>6,7</sup>

### Types of stress in pregnancy that can affect the developing baby

A range of stress-inducing circumstances may adversely affect the future health of the baby. These can vary from very severe stress caused, for example, by the death of an older child or other bereavement (Khashan et al., 2008), to quite mild stresses, such as daily hassles.<sup>8</sup> Other types of stresses that have been found to have an impact on the baby include relationship problems

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with the partner,<sup>9</sup> as well as exposure to acute external disasters such as 9/11,<sup>10</sup> Chernobyl,<sup>11</sup> a Louisiana hurricane,<sup>12</sup> and war.<sup>13</sup> Both anxiety<sup>14,15,16,17,18</sup> and depression<sup>14,19</sup> have also been found to have an impact on the developing fetus and baby.

### Impact of adverse mental health

Adverse prenatal mental health of the type described above is associated with a wide range of outcomes both in the short (i.e. immediately following birth) and longer term (i.e. through to adolescence and adulthood). Very severe stress in the first trimester such as the death of an older child has been shown to be associated with an increase in congenital malformations.<sup>20</sup> Less severe forms of stress are associated with somewhat lower birthweight and reduced gestational age<sup>21,22</sup> and an altered sex ratio, with fewer males to females being born than in an unstressed population.<sup>23,24</sup>

Beyond these immediately obvious effects at birth, other longer-term consequences for the baby have also been identified in a number of studies. Examples in young children include the neurodevelopmental functioning of newborns;<sup>25</sup> and the behaviour of infants and toddlers (e.g. difficult temperament,<sup>15,26</sup> sleep problems,<sup>27</sup> and lower cognitive performance and increased fearfulness.<sup>9</sup>

Studies on older children, aged 3 to 16, have shown an association between prenatal stress and neurodevelopmental outcomes, including an increased risk (usually about double) of child emotional problems, especially anxiety and depression, and symptoms of ADHD and conduct disorder.<sup>14,21,28,29,30,31</sup> Other studies have shown a reduction in cognitive performance.<sup>17,32</sup>

Two studies have found an increased risk of schizophrenia in adults born to mothers who experienced stress during pregnancy including the death of a relative,<sup>33</sup> and exposure to the invasion of the Netherlands in 1940.<sup>13</sup>

A further set of studies on both animals and humans have shown associations between prenatal stress and a range of altered physical and physiological outcomes. These include reductions in brain grey matter density,<sup>34</sup> which may be associated with neurodevelopmental and psychiatric disorders as well as cognitive and intellectual impairment. Several studies have shown that prenatal stress is associated with an altered diurnal pattern or altered function of the HPA axis, although the pattern of alteration is quite complex.<sup>35</sup>

### Critical periods of sensitivity in pregnancy

There is little consistency in the literature regarding the most critical time in pregnancy for the influence of prenatal stress, and there are different times of sensitivity dependent on the outcome studied, and the stage of development of the relevant brain or other structures. The two studies of schizophrenia, for example, found the most critical period to be the first trimester, when neuronal cells are migrating to their eventual site in brain, a process previously suggested to be disrupted in schizophrenia.<sup>13,33</sup> In contrast, two studies of conduct disorder, or antisocial behaviour, found the greatest associations with stress in later pregnancy.<sup>21,36</sup>

### Mechanisms involved

The mechanisms by which prenatal stress affects the developing baby are not fully understood, but seem to involve changes in the environment in utero during specific critical periods, which may then alter key processes in the baby's development, with long-term consequences. One of the key mechanisms identified in humans is the overexposure of the fetus to glucocorticoids (i.e. the stress hormone cortisol) as a result of the impact of stress on placental functioning.<sup>37</sup> Stress appears to affect the barrier enzyme, which converts cortisol to the inactive cortisone. Increased maternal stress or anxiety reduces the level of this enzyme in the placenta, thus potentially allowing more cortisol to pass through to the fetus.<sup>37</sup>

The neurotransmitter serotonin is another possible mediator of prenatal stress-induced effects on the baby's neurocognitive and behavioural development. During gestation serotonin regulates cell division, differentiation and synaptogenesis. Animal studies have shown that increased serotonin exposure during gestation is associated with alterations in many neuronal processes and subsequent changes in offspring behavior. Recent work has identified an endogenous serotonin biosynthetic pathway in the human placenta,<sup>38</sup> suggesting a possible role for alterations in placental serotonin in human fetal programming.

Prenatal stress has also been shown to cause changes to the DNA of experimental animals – known as epigenetic changes – for example, in the DNA that codes for the receptor for cortisol<sup>39</sup> In humans, stress during pregnancy caused by violence from the partner has been shown to cause epigenetic changes in the DNA for this same receptor, in the blood of their adolescent children.<sup>40</sup>

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### The importance of improving maternal psychological wellbeing in pregnancy

The studies outlined here provide a strong indication of the importance of intervening during pregnancy to reduce the risk of adverse maternal mental health and its impact on child development.

The newly updated National Institute for Health and Care Excellence (2014) guideline on ante and postnatal mental health<sup>41</sup> provides clear guidance about screening for common mental health problems in pregnancy such as anxiety and depression, using the two Whooley questions (i.e. 'During the past month, have you often been bothered by feeling down, depressed or hopeless?'; 'How often have you often been bothered by having little interest or pleasure in doing things?'), and the two-item Generalised Anxiety Disorder scale (GAD-2) (i.e. 'During the past month, have you been feeling nervous, anxious or on edge?'; 'Have you not been able to stop or control worrying?').

The guidelines recommend that if a woman responds positively to either of the depression identification questions or is at risk of developing a mental health problem, or there is clinical concern, the practitioner should consider: using the Edinburgh Postnatal Depression Scale (EPDS) or the Patient Health Questionnaire (PHQ-9) as part of a full assessment or referring the woman to her GP or, if a severe mental health problem is suspected, to a mental health professional. They also recommend that if a woman scores three or more on the GAD-2 scale, consider using the GAD-7 scale for further assessment or referring the woman to her GP or, if a severe mental health problem is suspected, to a mental health professional. If a woman scores less than 3 on the GAD-2 scale, but you are still

concerned she may have an anxiety disorder, you should ask the following question: 'Do you find yourself avoiding places or activities and does this cause you problems?' If she responds positively, you should consider using the GAD-7 scale for further assessment or referring the woman to her GP or, if a severe mental health problem is suspected, to a mental health professional. It is also important to find out if the woman is experiencing any other form of major stress, such as domestic abuse, and if so to institute appropriate help.

Evidence-based methods of intervening to support women experiencing moderate problems include Guided self-help; computerized CBT or exercise; non-directive counselling (e.g. listening visits); brief CBT or IPT (Interpersonal Psychotherapy). Women experiencing more severe problems will require specialist support from a psychiatrist and possibly medication.

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### Free online course

Babies in Mind: Why the Parent's Mind Matters, The University of Warwick.

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### Summary of implications for policy and practice

- The psychological wellbeing of women in pregnancy can have long-term effects on the child, especially in terms of their later emotional and behavioural adjustment.
- This evidence points to the importance of intervening during pregnancy to provide support that is aimed at reducing stress, anxiety and depression, and promoting reflective function.
- A number of evidence-based methods of working to promote the mental wellbeing of women during pregnancy are currently available, and should be implemented.
- More still needs to be done to ensure that the treatment of common mental health problems in pregnancy is routinely addressed.



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## References

1. Heron J, O'Connor TG, Evans J et al. The course of anxiety and depression through pregnancy and the postpartum in a community sample, *J Affect Disord* 2004;80(1):65-73.
2. Marcus SM, Flynn HA, Blow FC and Barry KL. Depressive symptoms among pregnant women screened in obstetrics settings, *J Women's Health* 2003;12(4):373-80.
3. Department of Health. *Improving Services for Women and Child Victims of Violence: Action Plan* Department of Health, London 2010.
4. Taft A. *Violence against women in pregnancy and after childbirth: current knowledge and issues in healthcare responses*. Australian Domestic and Family Violence Clearinghouse Issues. Paper No. 6, University of New South Wales, Sydney 2002.
5. Home Office. *Hidden harm*. Executive summary of the report of an inquiry by the Advisory Council on the Misuse of Drugs, Home Office, London 2003.
6. Frischer M, Crome I, Macleod J, et al Substance misuse and psychiatric illness: prospective observational study using the general practice research database. *J Epidemiol Community Health* 2005;59:847-50.
7. Hans SL, Victor JB and Linda G H. The role of psychopathology in the parenting of drug dependent women. *Dev Psychopathol* 1999;11:957-77.
8. Huizink AC, Robles de Medina PG, Mulder EJ et al. Stress during pregnancy is associated with developmental outcome in infancy, *J Child Psychol Psychiatry* 2003;44(6):810-8.
9. Bergman K, Sarkar P, O'Connor TG, et al. Maternal stress during pregnancy predicts cognitive ability and fearfulness in infancy", *J Am Acad Child Adolesc Psychiatry* 2007;46(11):1454-63.
10. Yehuda R, Engel SM, Brand SR, et al. Transgenerational effects of posttraumatic stress disorder in babies of mothers exposed to the world trade center attacks during pregnancy. *J Clin Endocrinol Metab* 2005;90(7):4115-8.
11. Huizink AC, Bartels M, Rose RJ, et al. Chernobyl exposure as stressor during pregnancy and hormone levels in adolescent offspring, *J Epidemiol Community Health* 2008;62: e5.
12. Kinney DK, Miller AM, Crowley DJ, et al. Autism prevalence following prenatal exposure to hurricanes and tropical storms in Louisiana. *J autism dev disorders* 2008;38(3):481-8.
13. van Os J and Selten JP. Prenatal exposure to maternal stress and subsequent schizophrenia. The May 1940 invasion of the Netherlands. *Br J Psychiatry* 1998;172:324-6.
14. O'Connor TG, Heron J, Golding J, et al. Maternal antenatal anxiety and children's behavioural/emotional problems at 4 years. Report from the avon longitudinal study of parents and children. *Br J Psychiatry* 2002;180:502-8.
15. Austin MP, Hadzi-Pavlovic D, Leader L, et al. Maternal trait anxiety, depression and life event stress in pregnancy: relationships with infant temperament. *Early Hum Dev* 2005;81(2):183-90.
16. Obel C, Hedegaard M, Henriksen TB, Secher NJ and Olsen J. Psychological factors in pregnancy and mixed-handedness in the offspring. *Dev Med Child Neurol* 2003;45(8):557-61.
17. Mennes M, Stiers P, Lagae L and Van den Bergh B. Long-term cognitive sequelae of antenatal maternal anxiety: involvement of the orbitofrontal cortex. *Neurosci Biobehav Rev* 2006;30(8):1078-86.
18. McMahon CA, Boivin J, Gibson FL, et al. Pregnancy-specific anxiety, ART conception and infant temperament at 4 months post-partum. *Hum Reprod* 2013;28(4):997-1005.
19. Pawlby S, Hay D, Sharp D, et al. Antenatal depression and offspring psychopathology: the influence of childhood maltreatment. *Br J Psychiatry* 2011;199(2):106-12.
20. Hansen D, Lou HC and Olsen J. Serious life events and congenital malformations: a national study with complete follow-up. *Lancet* 2000;356(9233):875-80.
21. Rice F, Harold GT, Boivin J, et al. The links between prenatal stress and offspring development and psychopathology: disentangling environmental and inherited influences. *Psych Med* 2010;40(2):335-45.
22. Wadhwa PD, Sandman CA, Porto M, et al. The association between prenatal stress and infant birth weight and gestational age at birth: a prospective investigation. *Am J Obstet Gynecol* 1993;169(4):858-65.
23. Obel C, Henriksen TB, Secher NJ, Eskenazi B and Hedegaard M. Psychological distress during early gestation and offspring sex ratio. *Hum Reprod* 2007;22(11):3009-12.
24. Peterka M, Peterkova R and Likovsky Z. Chernobyl: prenatal loss of four hundred male fetuses in the Czech Republic. *Reprod Toxicol* 2004;18(1):75-9.
25. Diego MA, Field T, Hernandez-Reif M, et al. Prepartum, postpartum, and chronic depression effects on newborns. *Psychiatry* 2004;67(1):63-80.
26. Buitelaar JK, Huizink AC, Mulder EJ, et al. Prenatal stress and cognitive development and temperament in infants. *Neurobiol Aging* 2003;24(S1):S53-S60 discussion S7-8.
27. O'Connor TG, Capriello P, Blackmore, ER, et al. Prenatal mood disturbance predicts sleep problems in infancy and toddlerhood. *Early Hum Dev* 2007;83(7):451-8.
28. Kleinhaus K, Harlap S, Perrin M, et al. Prenatal stress and affective disorders in a population birth cohort. *Bipolar Disord* 2013;15(1):92-9.
29. Van Den Bergh BR and Marcoen A. "High antenatal maternal anxiety is related to ADHD symptoms, externalizing problems, and anxiety in 8- and 9-year-olds. *Child Dev* 2004;75(4):1085-97.
30. Rodriguez A and Bohlin G. Are maternal smoking and stress during pregnancy related to ADHD symptoms in children? *J Child Psychol Psych* 2005;46(3):246-54.
31. Beversdorf DQ, Manning SE, Hillier A, et al. Timing of prenatal stressors and autism", *J Autism Dev Disord* 2005;35(4):471-8.
32. Laplante DP, Brunet A, Schmitz N, et al. Project ice storm: prenatal maternal stress affects cognitive and linguistic functioning in 5 1/2-year-old children. *J Am Acad Child Adolesc Psych* 2008;47(9):1063-72.
33. Khashan AS, Abel KM, McNamee R, et al. Higher risk of offspring schizophrenia following antenatal maternal exposure to severe adverse life events. *Arch Gen Psychiatry* 2008;65(2):146-52.
34. Buss C, Davis EP, Muftuler LT, et al. High pregnancy anxiety during mid-gestation is associated with decreased gray matter density in 6-9-year-old children. *Psychoneuroendocrinology* 2010;35(1):141-53.
35. Glover V, O'Connor TG and O'Donnell K. Prenatal stress and the programming of the HPA axis. *Neurosci Biobehav Rev* 2010;35(1):17-22.
36. O'Connor TG, Heron J, Golding J and Glover V. Maternal antenatal anxiety and behavioural/emotional problems in children: a test of a programming hypothesis.. *J Child Psychol Psych Allied Disc* 2003;44(7):1025-36.
37. O'Donnell KJ, Bugge Jensen A, Freeman L, et al. Maternal prenatal anxiety and downregulation of placental 11beta-HSD2. *Psychoneuroendocrinology* 2012;37(6):818-26.
38. Bonnin A, Goeden N, Chen K, et al. A transient placental source of serotonin for the fetal forebrain, *Nature* 2011;472(7343):347-50.
39. Mueller BR and Bale TL. Sex-specific programming of offspring emotionality after stress early in pregnancy. *J Neurosci* 2008;28(36):9055-65.
40. Radtke KM, Ruf M, Gunter HM, et al. Transgenerational impact of intimate partner violence on methylation in the promoter of the glucocorticoid receptor. *Transl Psychiatry* 2011;1(e21):1-6.
41. National Institute for Health and Care Excellence. Antenatal and postnatal mental health: clinical management and service guidance. Clinical guideline 192. London: NICE; 2014. Available from: [www.nice.org.uk/Guidance/CG192](http://www.nice.org.uk/Guidance/CG192) Accessed 16 April 2015.