Provided for non-commercial research and education use.
Not for reproduction, distribution or commercial use.

This article appeared in a journal published by Elsevier. The attached copy is furnished to the author for internal non-commercial research and education use, including for instruction at the authors institution and sharing with colleagues.

Other uses, including reproduction and distribution, or selling or licensing copies, or posting to personal, institutional or third party websites are prohibited.

In most cases authors are permitted to post their version of the article (e.g. in Word or Tex form) to their personal website or institutional repository. Authors requiring further information regarding Elsevier's archiving and manuscript policies are encouraged to visit:

http://www.elsevier.com/copyright

Author's personal copy

Brain, Behavior, and Immunity 23 (2009) 750–754

Contents lists available at ScienceDirect

Brain, Behavior, and Immunity

journal homepage: www.elsevier.com/locate/ybrbi

Short Communication

Depressive symptoms are associated with elevated serum proinflammatory cytokines among pregnant women ☆

Lisa M. Christian [a,b,*], Albert Franco [c], Ronald Glaser [b,d], Jay D. Iams [e]

[a] Department of Psychiatry, The Ohio State University Medical Center, 1670 Upham Drive, Columbus, OH 43210, USA
[b] Institute for Behavioral Medicine Research, The Ohio State University Medical Center, USA
[c] Carolinas Medical Center, Department of Obstetrics and Gynecology, 1000 Blythe Blvd., Charlotte NC 28203, USA
[d] The Ohio State University Medical Center, 2175 Graves Hall, 333 W. 10th Avenue, Columbus, Ohio 43210, USA
[e] The Ohio State University Medical Center, Department of Obstetrics and Gynecology, 395 West 12th Ave., Fifth Floor, Columbus, Ohio 43210, USA

ARTICLE INFO

Article history:
Received 11 December 2008
Received in revised form 10 February 2009
Accepted 18 February 2009
Available online 1 March 2009

Keywords:
Inflammation
Cytokines
Interleukin-6
Psychoneuroimmunology
Pregnancy
Depressive symptoms
Depression
Stress
Socioeconomic status
Psychosocial

ABSTRACT

Psychosocial stress and depressive symptoms are associated with increased risk of negative perinatal outcomes including preterm delivery and gestational hypertension. Inflammation is a likely mechanism by which distress may promote these outcomes. It is well-established that stress and depressive symptoms are associated with elevated serum inflammatory markers in nonpregnant populations. However, the immune system exhibits significant changes during pregnancy. Thus, the extent to which these findings extend to pregnancy is largely unknown. The current study examined associations among perceived stress, depressive symptoms, and serum inflammatory markers in a sample of 60 pregnant women. Fifty seven percent were African-American, 82% had completed high school or less education, and 63% reported an annual family income below $15,000. Participants completed the Perceived Stress Scale (PSS) and the Center for Epidemiologic Studies Depression Scale (CES-D). Serum levels of interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) were determined using high sensitivity immunoassays. Regression analyses demonstrated that after controlling for pre-pregnancy Body Mass Index (BMI), higher scores on the CES-D were related to significantly higher levels of IL-6 ($\beta = .23$, $p = .05$) and marginally higher TNF-α ($\beta = .24$, $p = .06$). Perceived stress was not significantly related to serum levels of IL-6 or TNF-α. In sum, these results indicate that depressive symptoms are associated with higher levels of maternal serum inflammatory markers during pregnancy. These data are consistent with the contention that depressive symptoms may contribute to negative perinatal outcomes via inflammatory pathways.

© 2009 Elsevier Inc. All rights reserved.

1. Introduction

Preterm birth affects 12–13% of births in the U.S. and is a leading cause of infant mortality (Goldenberg et al., 2008). Greater stress and depressive symptoms have been related to increased risk of spontaneous preterm birth and preeclampsia, a leading cause of medically indicated preterm birth (Hobel et al., 2008; Kurki et al., 2000). Relationships of stress and depressive symptoms with negative perinatal outcomes remain after controlling for behavioral and demographic explanations, suggesting a role for more direct physiological pathways.

A likely mechanism linking psychological distress with negative perinatal outcomes is inflammation. Earlier literature described successful pregnancy as an antiinflammatory phenomenon; this was presumed to prevent rejection of the fetus by the maternal immune system (Wegmann et al., 1993). Later literature indicates that inflammatory processes are critical during the peri-implantation period and that immune adaptations during ongoing pregnancy are more complex than initially described (Chaouat et al., 2004; Raghupathy, 2001). However, consistent evidence indicates that excessive inflammation is incompatible with healthy pregnancy; elevations in maternal serum inflammatory cytokines, including interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and interleukin-1β (IL-1β), are causally associated with increased risk negative perinatal outcomes including gestational hypertension and risk of preterm delivery (Raghupathy and Kalinka, 2008).

It is well-established that stress and depressive symptoms predict elevations in circulating inflammatory cytokines in

☆ This project was supported by NIH training grant T32AI55411, APA Division 38 (Health Psychology) Graduate Student Research Award, the American Psychological Foundation/Council of Graduate Departments of Psychology (APF/COGDOP) Scholarship Program, the OSU Department of Women's Studies and the Coca-Cola Critical Difference for Women Grant Program, the American Psychological Association Dissertation Research Award, and the OSU Alumni Grants for Graduate Research and Scholarship (LMC) as well as the OSU General Clinical Research Center (MO1-RR-00034).

* Corresponding author. Address: Department of Psychiatry, The Ohio State University Medical Center, 1670 Upham Drive, Columbus, OH 43210, USA. Fax: +1 614 293 4200.
E-mail address: Lisa.Christian@osumc.edu (L.M. Christian).

0889-1591/$ - see front matter © 2009 Elsevier Inc. All rights reserved.
doi:10.1016/j.bbi.2009.02.012

Author's personal copy

nonpregnant humans and animals (Raison et al., 2006; Zorrilla et al., 2001). Limited research has examined whether these associations generalize to pregnancy. Available data indicate that perceived stress is associated with elevated maternal serum proinflammatory cytokines, lower antiinflammatory cytokines, and exaggerated production of the proinflammatory cytokines by lymphocytes stimulated *in vitro* (Coussons-Read et al., 2007, 2005). To our knowledge no studies have demonstrated a relationship between proinflammatory cytokines and current depressive symptomatology during pregnancy. It is estimated that 3–5% of women meet criteria for major depression during pregnancy, with an approximately equivalent number experiencing subclinical depressive symptoms (Gaynes et al., 2005). Women who lack social support or experience greater social conflict are likely to experience more depressive symptoms during pregnancy (Rhodes and Woods, 1995). Moreover, rates of both depression (Seguin et al., 1995) and preterm delivery (Goldenberg et al., 2008) are substantially higher among women from lower versus higher socioeconomic backgrounds.

Addressing gaps in the literature, the current study examined associations among perceived stress, current depressive symptoms, and serum inflammatory markers among women from primarily lower socioeconomic backgrounds. We hypothesized that greater perceived stress and depressive symptoms would be associated with higher maternal serum levels of IL-6 and TNF-α. It was expected that rates of clinically significant depressive symptoms would be relatively high among this sample of women due to chronic stress associated with low socioeconomic status. Finally, we hypothesized that greater social support and less social conflict would be reflected by lower rates of perceived stress and depressive symptomatology.

2. Method

2.1. Participants

Sixty pregnant women were recruited from the Ohio State University (OSU) Prenatal Clinic. The mean age of participants was 25 years (SD = 4.8). Women completed the study visit at an average of 15 weeks (SD = 7.8) gestation. Women were excluded from participation if they reported recent acute illness or if fetal anomaly was indicated per medical records. Though rare in the study population, women were excluded if they had chronic health conditions with implications for immune function including rheumatoid arthritis, multiple sclerosis, or infection with human immunodeficiency virus. Each participant was compensated $10 and provided a parking pass. The study was approved by the OSU Biomedical Institutional Review Board. Data were collected from October 2005 to June 2007.

2.2. Demographic and psychosocial measures

Each participant provided demographic information regarding her age, race, education level, marital status, income, and employment status. Women also reported their height and pre-pregnancy weight. Data about health behaviors were recorded, including alcohol consumption in the past 48 h, participation in regular physical activity (defined as $\geqslant$1 h per week of vigorous activity), the number of hours of sleep in the previous night and previous three nights, and frequency of prenatal vitamin use.

The Center for Epidemiologic Studies Depression Scale (CES-D) was used to measure depressive symptomatology (Basco et al., 1997; Radloff, 1977). Higher scores on the CES-D have been associated with greater risk of negative perinatal outcomes including preterm delivery (Orr et al., 2002). The 4-item version of the Perceived Stress Scale (PSS) was used to measure the subjective experiences of stress and coping with stress using the past month as timeframe. The PSS measures a construct that is independent of depressive symptomatology (Cohen et al., 1983).

Social support was measured using the 12-item Interpersonal Support Evaluation List (ISEL) (Cohen and Hoberman, 1983). The hostility/impatience and insensitivity subscales of the Test of Negative Social Exchange (TENSE) were used to assess frequency of negative social experiences (Ruehlman and Karoly, 1991). To provide additional descriptive information, participants completed two questions rating their own and their partner's happiness about pregnancy on a scale from 1 to 10 (Brown and Eisenbert, 1995). Scores between 1 and 3 indicate unhappiness, 4–7 indicate ambivalence, and 8–10 indicate happiness.

2.3. Cytokine measurements

Whole blood was collected into vacutainer tubes between 9:30 am and 1:30 pm. Samples were immediately centrifuged, aliquoted, and placed in −80 °C degree freezer storage until analysis. Serum levels of cytokines were assayed in duplicate using ultra sensitive multiplex kits from Meso Scale Discovery (MSD) per kit instructions. Sensitivity for both IL-6 and TNF-α was .3 pg/ml. The intra-and inter-assay coefficients of variation were 4.1% and 8.7% for IL-6 and 2.7% and 10.4% for TNF-α.

2.4. Analytic strategy

Cytokine values were log transformed to normalize the data distribution prior to statistical analyses. IL-6 and TNF-α refer to the log transformed value for these markers throughout. Data points $\geqslant$3 standard deviations from the mean were considered to be outliers. Using this cut-off, four samples of IL-6 and one sample of TNF-α were excluded from analyses.

Descriptive statistics were calculated for demographic, psychosocial, and health behavior variables. To identify potential confounding factors, relationships between demographic factors and inflammatory markers were examined. Next, regression analyses including previously identified covariates were utilized to test the primary hypotheses related to relationships between perceived stress, depression, and inflammatory markers. Further analyses were conducted to examine the effects of social support and social conflict within this model. Data analyses were performed using SPSS statistical software (SPSS 16.0).

Table 1
Demographic characteristics.

Age (years)	Range: 18–37 Mean: 25.24 (SD = 4.89)
Race	African-American = 34 Caucasian = 19 Asian = 1 Bi-racial = 6
Marital status	Unmarried = 46 Married = 14
Education	Less than high school = 19 High school = 30 Greater than high school = 11
Employment Status	Employed = 25 Unemployed = 35
Income	<$15,000 = 38 15,000–29,999 = 14 >30,000 = 6
Body Mass Index (kg/m^2)	
Pre-pregnancy	27.78 (SD = 6.08)
Per scale	28.54 (SD = 6.72)
Weeks gestation	15 (SD = 7.8)
Gravidity	3.1 (SD = 1.8)
Parity	2.4 (SD = 1.2)

Author's personal copy

Table 2
Scores on psychosocial measures.

	Range	Mean (SD)
CES-D	1–41	17.05 (10.14)
PSS	0-13	6.65 (2.82)
TENSE		
Hostility	0–3	0.65 (0.73)
Insensitivity	0–3	0.78 (0.95)
ISEL	16–48	38.75 (7.25)
Parental happiness		
Mother	1–10	6.93 (3.13)
Father	1–10	7.87 (2.59)

Abbreviations: CES-D, Center for Epidemiologic Studies Depression Scale; PSS, Perceived Stress Scale; TENSE, Test of Negative Social Exchange; ISEL, Interpersonal Support Evaluation List; Parental Happiness, mother's ratings of her own and her partner's happiness about pregnancy.

3. Results

3.1. Demographic characteristics

Sixty women participated in the study. Demographic and descriptive data are presented in Table 1. The majority of participants were African-American (57%), unmarried (76%), had completed high school or less education (82%), and reported a total annual family income below $15,000 (63%). Pre-pregnancy BMI based on self-report was highly correlated with BMI as measured at the study visit ($r = .94$, $p < .001$), suggesting adequate accuracy. Because the accuracy of BMI at the study visit was affected by pregnancy-related weight gain, pre-pregnancy BMI was utilized for statistical analyses.

3.2. Descriptive statistics

Descriptive statistics related to the psychosocial characteristics are presented in Table 2. The average score on the CES-D was 17 (SD = 10); 31 women (52%) scored at or above a clinical cut-off of 16. Scores on the Perceived Stress Scale (PSS) ranged from 0 to 13 with an average of 6.65 (SD = 2.82). Based on the two-item measure assessing maternal and perceived paternal happiness about pregnancy, 32 women were classified as happy, 16 were ambivalent, and 12 were unhappy. Overall, 27 women (45%) rated both themselves and their partner as happy about the pregnancy.

3.3. Demographic factors and inflammation

To identify potential confounding factors to be included as covariates in subsequent analyses, associations between inflammatory markers and demographic variables were examined. There was no association between IL-6 or TNF-α with age, marital status (married versus unmarried), employment status (employed versus unemployed), income or education (*ps* > .05). Further, neither gestational age at the time of participation nor timing of the blood draw was significantly related to levels of either inflammatory marker (*ps* > .05). There were no significant differences in serum IL-6 or TNF-α between Caucasian versus African-American women (*ps* > .05). Finally, as expected, BMI prior to pregnancy was significantly correlated with IL-6 ($r = .54$, $p < .01$), and TNF-α ($r = .34$, $p < .01$). Based on these analyses, pre-pregnancy BMI was included as a covariate in subsequent analyses of psychosocial correlates of inflammation.

3.4. Primary analyses: stress, depressive symptoms, and serum proinflammatory cytokines

Regression analyses were conducted to test the main hypothesis that perceived stress and depressive symptoms would predict higher levels of serum proinflammatory cytokines. Controlling for pre-pregnancy BMI, higher CES-D scores were associated with significantly higher IL-6 ($\beta = .23$, $t(2,55) = 1.98$, $p = .05$; See Table 3). Similarly, the relationship between higher CES-D scores and higher TNF-α was marginally significant ($\beta = .24$, $t(2,58)$, $p = .06$). Perceived stress as measured by the Perceived Stress Scale (PSS) was not associated with levels of IL-6 ($\beta = 0.03$, $t(2,55) = 0.22$, $p = .83$) or TNF-α ($\beta = -0.10$, $t(2,58) = -0.76$, $p = .45$).

Table 3
Regression analyses – relationships between depressive symptoms and maternal serum levels of IL-6 ($n = 56$) and TNF-α ($n = 59$).

Step	Predictor	Estimate β	ΔR^2	ΔF	p
IL-6 (lg pg/ml)					
1	Pre-pregnancy BMI	.61	.29	22.14	<.01
2	CES-D	.23	.05	3.93	.05
TNF-α (lg pg/ml)					
1	Pre-pregnancy BMI	.39	.12	7.61	<.01
2	CES-D	.24	.05	3.63	.06

To determine whether differences in health behaviors may mediate the relationship between depressive symptoms and inflammatory markers, relationships between each health behavior and each inflammatory marker were examined. Descriptive information regarding health behaviors is presented in Table 4. No health behaviors (sleep in previous night, sleep in previous three nights, prenatal vitamin use, cigarette smoking or regular vigorous activity) were significantly associated with serum levels of IL-6 or TNF-α (*ps* > .05). No woman reported alcohol consumption in the previous 48 h. Thus, none of the health behaviors measured accounted for the relationship between depressive symptoms and inflammatory markers.

3.5. Psychosocial correlates of depressive symptoms

Analyses were conducted to identify psychosocial correlates of depressive symptoms. As expected, depressive symptoms were positively correlated with perceived stress ($r = .50$, $p < .01$). Univariate ANOVA analyses demonstrated that women who were classified as unhappy about their pregnancies had significantly greater depressive symptoms (mean CES-D = 22, SD = 10) as compared to women who were classified as happy about their pregnancies (mean CES-D = 16, SD = 10; $p = .04$). Women who reported less social support as measured by the ISEL reported greater depressive symptoms ($r = -.54$, $p < .01$). Moreover, more frequent hostile and insensitive social interactions as measured by the TENSE were associated with greater depressive symptoms (*rs* = .51 and .48, *ps* < .01).

Additional analyses were conducted to examine whether social support and social conflict were unique predictors of depressive symptoms. After controlling for ISEL scores, TENSE hostility scores remained significantly associated with depressive symptoms ($\beta = .32$, $t(1,59) = 2.67$, $p = .01$), indicating that these measures of social support and social conflict provided unique information. Together, the ISEL and the TENSE hostility subscale accounted for 42%

Table 4
Health behaviors.

Current smoker	Yes: 15 No: 45
Prenatal vitamin use	5–7 days/week: 46 None: 13
Regular exercise	Yes: 24 No: 28
Sleep	
Hours (past day)	6.65 (SD = 1.8)
Hours (past 3 days)	21.10 (SD = 6.7)

Note: No woman reported alcohol use in the 48 h prior to her study participation.

Author's personal copy

of the variance in depressive symptoms. After controlling for ISEL scores, the TENSE insensitivity subscale was no longer associated with depressive symptoms ($\beta = .17$, $t(1,59) = 1.25$, $p = .21$), indicating that these measures provided overlapping predictive value.

4. Discussion

This study provides evidence that current depressive symptoms are associated with elevations in circulating proinflammatory cytokines during human pregnancy. The relationship between symptom severity and both IL-6 and TNF-α was equivalent to a small effect size, which is comparable to data from nonpregnant populations (Miller et al., 2002).

Contrary to previous studies (Coussons-Read et al., 2007, 2005), perceived stress was not significantly related to inflammation. As compared to previous studies, women in the current study were from significantly lower socioeconomic backgrounds. Thus, the lack of effect of perceived stress may reflect that under conditions of sufficient stress the experience of depressive symptoms is a better predictor of physiological effects than is perceived stress. In addition the measure of perceived stress utilized and/or gestational age at the time of measurement may account for the lack of effect of perceived stress in the current study.

Although it is often a happy time, the experience of pregnancy itself can be a stressor, particularly for women with unplanned pregnancies (Yali and Lobel, 2002). In the current sample, 47% of women were classified as ambivalent or unhappy about their pregnancies. Women classified as unhappy about their pregnancies ($n = 12$) had significantly greater depressive symptoms than did women who were happy about their pregnancies ($n = 33$), suggesting that unplanned pregnancy may contribute to depressive symptomatology.

As expected, lower social support and more frequent negative social interactions were associated with greater depressive symptoms. Together, social support and hostile social interactions accounted for 42% of the variance in depressive symptoms. These data are consistent with previous findings that social support and social conflict are unique and robust predictors of risk of depressive symptoms (Westdahl et al., 2007).

Low socioeconomic status (SES) has been associated with higher levels of inflammatory markers (Koster et al., 2006; Steptoe et al., 2002). In the current study neither income nor education was associated with IL-6 or TNF-α levels. Relatedly, neither income nor education was significantly predictive of perceived stress or depressive symptoms. This is likely attributable to the restricted range of socioeconomic status included. The ability to detect effects of socioeconomic status would be greater in a sample which included more women of moderate to high socioeconomic status.

In addition to socioeconomic status, potential differences based on race were of interest. It has been proposed that, via inflammatory pathways, both genetic and environmental factors contribute to the 2- to 3-fold greater risk of preterm delivery seen in African-American as compared to Caucasian women (Giscombe and Lobel, 2005). In the current investigation, IL-6 and TNF-α levels did not differ statistically between African-American and Caucasian women. However, African-American women exhibited non-significantly higher level of IL-6. Specifically, mean IL-6 was 1.15 (SD = .52) pg/ml among Caucasian women and 1.43 (SD = .90) pg/ml among African-American women. The ability to detect a difference of this magnitude, which is equivalent to a small to medium effect, was limited by the sample size.

The current study assessed parameters of interest at only one timepoint which was at an average of 15 weeks gestation. A relatively early timepoint was selected because early identification of women who may be at risk of negative perinatal outcome will allow greater time for intervention. However, longitudinal studies in which women are followed throughout pregnancy and delivery would provide much needed information regarding the effects of depressive symptoms at different stages of pregnancy.

This study provides novel data linking depressive symptoms to elevated maternal serum proinflammatory cytokines during pregnancy. Due to the relatively low base rate of preterm delivery and preeclampsia, the current investigation did not allow adequate statistical power to examine effects of depressive symptoms and inflammation on negative perinatal outcomes. Further research is needed to demonstrate that distress affects perinatal health via inflammatory pathways. To that end, this investigation is ongoing; accrual of an adequate number of study participants will allow for examination of the health consequences of the associations reported. The prevalence of depressive symptoms during pregnancy, particularly among women from disadvantaged backgrounds, highlights the importance of continued investigation.

Acknowledgements

These data were collected as part of the first author's doctoral dissertation. I would like to thank my advisor, Janice Kiecolt-Glaser for her support of this project, my dissertation committee members for their helpful input, and my undergraduate research assistants for their efforts. Portions of this study were previously presented at the 2008 annual meeting of the Psychoneuroimmunology Research Society in Madison, Wisconsin.

References

Basco, M.R., Krebaum, S.R., Rush, A.J., 1997. Outcome measures of depression. In: Strupp, H.H., Horowitz, L.M., Lambert, M.J. (Eds.), Measuring Patient Changes in Mood, Anxiety, and Personality Disorders. American Psychological Association, Washington, DC, pp. 207–245.

Brown, S., Eisenbert, L., 1995. The Best Intentions: Unintended Pregnancy and the Well-Being of Children and Families. National Academy Press, Washington, DC.

Chaouat, G., Ledee-Bataille, N., Dubanchet, S., Zourbas, S., Sandra, O., Martal, J., 2004. Reproductive immunology 2003: reassessing the Th1/Th2 paradigm? Immunol. Lett. 92, 207–214.

Cohen, S., Hoberman, H.M., 1983. Positive events and social supports as buffers of life change stress. J. Appl. Soc. Psychol. 13, 99–125.

Cohen, S., Kamarck, T., Mermelstein, R., 1983. A global measure of perceived stress. J. Health Soc. Behav. 24, 385–396.

Coussons-Read, M.E., Okun, M.L., Nettles, C.D., 2007. Psychosocial stress increases inflammatory markers and alters cytokine production across pregnancy. Brain Behav. Immun. 21, 343–350.

Coussons-Read, M.E., Okun, M.L., Schmitt, M.P., Giese, S., 2005. Prenatal stress alters cytokine levels in a manner that may endanger human pregnancy. Psychosom. Med. 67, 625–631.

Gaynes, B.N., Gavin, N., Meltzer-Brody, S., Lohr, K.N., Swinson, T., Gartlehner, G., Brody, S., Miller, W.C., 2005. Perinatal Depression: Prevalence, Screening Accuracy, and Screening Outcomes. Evidence Report/Technology Assessment No. 119. AHRQ Publication No. 05-E006-2. Rockville, MD: Agency for Healthcare Research and Quality.

Giscombe, C.L., Lobel, M., 2005. Explaining disproportionately high rates of adverse birth outcomes among African Americans: the impact of stress, racism, and related factors in pregnancy. Psychol. Bull. 131, 662–683.

Goldenberg, R.L., Culhane, J.F., Iams, J.D., Romero, R., 2008. Epidemiology and causes of preterm birth. Lancet 371, 75–84.

Hobel, C.J., Goldstein, A., Barrett, E.S., 2008. Psychosocial stress and pregnancy outcome. Clin. Obstet. Gynecol. 51, 333–348.

Koster, A., Bosma, H., Penninx, B., Newman, A., Harris, T.B., van Eijk, J., Kempen, G., Simonsick, E.M., Johnson, K.C., Rooks, R.N., Ayonayon, H.N., Rubin, S.M., Kritchevsky, S.B., 2006. Association of inflammatory markers with socioeconomic status. J. Gerontol. A, 284–290.

Kurki, T., Hiilesmaa, V., Raitasalo, R., Mattila, H., Ylikorkala, O., 2000. Depression and anxiety in early pregnancy and risk for preeclampsia. Obstet. Gynecol. 95, 487–490.

Miller, G.E., Stetler, C.A., Carney, R.M., Freedland, K.E., Banks, W.A., 2002. Clinical depression and inflammatory risk markers for coronary heart disease. Am. J. Cardiol. 90, 1279–1283.

Orr, S.T., James, S.A., Blackmore Prince, C., 2002. Maternal prenatal depressive symptoms and spontaneous preterm births among African-American women in Baltimore, Maryland. Am. J. Epidemiol. 156, 797–802.

Radloff, L.S., 1977. The CES-D scale: A self-report depression scale for research in the general population. Appl. Psychol. Meas. 1, 385–401.

Raghupathy, R., 2001. Pregnancy: success and failure within the Th1/Th2/Th3 paradigm. Semin. Immunol. 13, 219–227.

Raghupathy, R., Kalinka, J., 2008. Cytokine imbalance in pregnancy complications and its modulation. Front. Biosci. 13, 985–994.

Author's personal copy

Raison, C.L., Capuron, L., Miller, A.H., 2006. Cytokines sing the blues: inflammation and the pathogenesis of depression. Trends Immunol. 27, 24–31.
Rhodes, J.E., Woods, M., 1995. Comfort and conflict in the relationship of pregnant, minority adolescents: Social support as a moderator of social strain. J. Community Psychol. 23, 74–84.
Ruehlman, L.S., Karoly, P., 1991. With a little flak from my friends: development and preliminary validation of the Test of Negative Social Exchange (TENSE). Psychol. Assess. J. Consult. Clin. Psychol. 3, 97–104.
Seguin, L., Potvin, L., St-Denis, M., Loiselle, J., 1995. Chronic stressors, social support, and depression during pregnancy. Obstet. Gynecol. 85, 583–589.
Steptoe, A., Owen, N., Kunz-Ebrecht, S., Mohamed-Ali, V., 2002. Inflammatory cytokines, socioeconomic status, and acute stress responsivity. Brain Behav. Immun. 16, 774–784.
Wegmann, T.G., Line, H., Guilbert, L., Mosmann, T.R., 1993. Bidirectional cytokine interactions in the maternal–fetal relationship: is successful pregnancy a Th2 phenomenon? Immunol. Today 14, 353–356.
Westdahl, C., Milan, S., Magriples, U., Kershaw, T., Rising, S.S., Ickovics, J.R., 2007. Social support and social conflict as predictors of prenatal depression. Obstet. Gynecol. 110, 134–140.
Yali, A.M., Lobel, M., 2002. Stress–resistance resources and coping in pregnancy. Anxiety Stress Coping 15, 289–309.
Zorrilla, E.P., Luborsky, L., McKay, J.R., Rosenthal, R., Houldin, A., Tax, A., McCorkle, R., Seligman, D.A., Schmidt, K., 2001. The relationship of depression and stressors to immunological assays: a meta-analytic review. Brain Behav. Immun. 15, 199–226.