

Stress and preterm delivery: a conceptual framework

Carol J. R. Hogue^a, Susie Hoffman^b and Maureen C. Hatch^c

^aWomen's and Children's Center, Rollins School of Public Health, Emory University, Atlanta, GA, ^bHIV Center for Clinical and Behavioral Studies at New York State Psychiatric Institute and Columbia University, New York, ^cDivision of Epidemiology, Department of Community and Preventive Medicine, Mount Sinai School of Medicine, New York, USA

Summary

Correspondence:

Dr Carol Hogue,
Women's and Children's
Center, Rollins School of
Public Health, Emory
University, 1518 Clifton Road,
N.E., Atlanta, GA 30322, USA.
E-mail:
chogue@sph.emory.edu

Numerous epidemiological studies of various kinds of stress and preterm delivery have produced either negative or weakly positive results. Those inconclusive findings could be either because of the absence of an association or because of recognised methodological problems that may have masked an association. The biological plausibility of the stress hypothesis provides one rationale for continuing stress research, using better study designs. To further this agenda, we propose an epidemiological model, based on the classic 'host, environment, agent' triangle of epidemiological causality. The host is the individual woman, more or less susceptible to stressor-induced pathology. The environment includes the social and cultural conditions that are ongoing stressors as well as social and cultural modifiers of stress e.g. those factors that may influence how a particular stressor is experienced or what the physical response to it may be. The agent is the immediate emotional or physical stressor requiring her response. We draw from recent literature, published principally since 1990, to illustrate this model.

This epidemiological model posits that whether the individual is overwhelmed by stressors depends not only on the strength of the agents but also upon host susceptibility to stress, as well as the background level of acute, environmental and contextual stressors, and the moderating influence of host, environmental and contextual resources for handling stress. Future research needs to be based on stress hypotheses that include all sides of the triangle, data collection instruments that adequately capture relevant stressors and stress responses, and analytical techniques capable of handling complex, multilevel relationships.

Introduction

The question of whether stress increases the risk of preterm delivery has interested epidemiologists for more than a quarter of a century. In one early investigation, Nuckolls and colleagues¹ found that maternal stress during pregnancy was associated with poorer pregnancy outcomes, but only for women who had fewer social supports for buffering stressful events. Subsequent studies of stress, social support, or combinations of stress and social support, conducted in many settings, have not produced consistent results, and when present, positive associations have been of small size.²⁻⁵ If stressful events and lack of social support during pregnancy increase the risk of preterm delivery, then interventions to increase social

support should lengthen gestation. However, many of the randomised trials designed to test this hypothesis have not found interventions to be useful.⁵⁻⁷ The lack of success in these trials could be the result of problems in design or analysis. The trials may have been diluted by inclusion of women in the intervention group who did not need social support. Some have argued that currently available interventions should be offered only to women who both lack intimate support and also are at high risk of preterm delivery.^{5,6,8,9} Yet for women in need, currently available interventions (e.g. nurse home visits once or twice during pregnancy) may not provide an adequate level of intimate support.⁵

It is also possible that the trials were not successful because stress does not increase the rate of preterm

delivery or because social support does not decrease the risk. However, the biological plausibility that stress leads to preterm labour and delivery through one or more biophysical mechanisms¹⁰ would suggest that before concluding that a relationship is unlikely, other reasons for inconsistent results in observational studies and clinical trials should be addressed. These may include incomplete stress exposure assessment or inaccurate delineation of the stress-health causal model, leading to measurement error and failure to account adequately for effect modification.^{4,11}

Three investigations sponsored by the March of Dimes and described in this issue seek to overcome a number of the methodological problems of earlier observational studies of the stress/preterm delivery relationship.¹²⁻¹⁴ Among other strengths, these studies incorporate model-based, multidimensional approaches to the definition and measurement of stress. However, each of the studies is measuring different subsets of potential stressors and responses to stressors. To understand the results of these and future studies, it is useful to determine how they fit within a unified theory of stressors and responses to stressors.¹⁵

Methods: the epidemiological model

The purpose of this paper is to propose a framework for developing a unified theory, using the classic 'host, environment, agent' triangle of epidemiological causality to illustrate the variety of stressors and individual response to stressors as experienced by pregnant women. The host is the individual woman, more or less susceptible to stressor-induced pathology; the environment includes the social and cultural conditions that are ongoing stressors, as well as the social and cultural modifiers of stress, e.g. those factors that may influence how a particular stressor is experienced or what the physical response to it may be; and the agent is the immediate emotional or physical stressor requiring her response. Physiological stress is necessary for growth, development, and maintenance of brain and muscle activity. However, prolonged exposure to a chronic stressor or exposure to an acute stressor that overwhelms the individual's ability to return to physiological homeostasis can result in ill health.¹⁶ The epidemiological model posits that whether or not the individual is overwhelmed depends not only on the strength of the agent but also upon host susceptibility to stress, as well as the background level of acute, environmental and contextual stressors, and

the moderating influence of host, environmental and contextual resources for handling stress.

Our intention is to explore how an elaboration of each component of the agent/host/environment model and of the relationships among these components might lead to research that clarifies for whom and under what conditions exposure to stressors induces preterm delivery. To illustrate this model, we will not provide an exhaustive review of the literature, but will draw from recent literature, principally that published since 1990. Some studies that we will cite suggest a link between an external stressor and a physiological stress response that could lead to preterm delivery. Others examine the relationship between a stressor and preterm delivery *per se*. Our purpose is not to explain how a particular stressor or set of stressors acts within the body to trigger premature labour. In another article in this issue, Wadhwa proposes a theory of the biophysical processes linking stress and early parturition.¹⁰ Rather, it is our goal to explore what constitutes enough of a psychological or physical challenge to elicit a stress response. Together, the two models may be a step towards elucidating a biopsychosocial model of stress and preterm delivery, such as has been proposed for stress and cardiovascular disease.¹⁶

Host susceptibility

Individuals may differ in psychological and physiological responses to the same stressor, reflecting differences in the context within which the stressor occurs (see below) and differences in individual propensity to respond to that type of stressor. One way that differential response to stressors may be measured is by monitoring blood pressure rise in experimental situations. In one small study among pregnant women,¹⁷ elevated blood pressure response to a stressful situation (a mental arithmetic test) was associated with both decreased birthweight and gestational age.

Differential host susceptibility may be specific to the type of stressor. For example, one experimental study showed that among black college students, blood pressure increased in response to racist stimuli but not in response to anger-provoking stimuli.¹⁸ In other experimental studies of African-American and white participants, both cardiovascular activity at rest and after a stressful stimulus were greater in African-Americans.¹⁹ This increased reactivity among

African-Americans does not appear to be associated with familial history of hypertension, suggesting that individuals' exposure history – rather than genetic differences – may explain differentials in host susceptibility.^{19,20} To identify risk factors for increased host susceptibility in African-Americans, further focused research is needed in this population.²⁰

Factors that enhance host susceptibility may include conditions present at birth or personality traits, early life experiences, learned coping resources or strategies, and circumstances of the pregnancy. In this framework, external resources available for coping with stressors, such as levels of social support, are considered part of the environmental context.

Personality traits or early life experiences

Exposure to fetal stressors may affect neural development, predisposing the individual to increased reactivity to stressors in adult life. Physiological stress experienced in the first few years of life may have an impact later in life, owing to an interruption of the normal neural system development at critical points. This leads to reduced 'plasticity' of neurons and lessened ability to 'turn off' the physiological reactions to a stressful situation. Early and continual stressors may also cause 'learned' physiological responses that trigger higher reactivity when similar stressors occur later in life.¹⁶ Chemical odour intolerance, which may be a marker for increased neurological reactivity (including blood pressure reactivity) has been associated with early life experiences, such as poor relationships with the father and with physical abuse, but not with sexual abuse in the absence of physical abuse.²¹ Early and continual personal experiences of individual racism have been hypothesised to sensitise African-American women to increased reactivity.²²

Coping resources or strategies

Buffering coping resources include high self-esteem and having a sense of personal control or mastery over life.²³ Importantly, a sense of control or mastery has been shown to reduce psychological distress and positively affect physical health, as well as to buffer the negative consequences of stressors on mental and physical health (discussed by Thoits²⁴).

Self-esteem has also been shown to buffer against the negative consequences of stressors on mental health, although its role in relation to physical health has been

less well studied (discussed by Thoits²⁴). However, one recent study suggests that low self-esteem may enhance cortisol response to stressors,²⁵ potentially linking it to physical health. Among 20 male participants exposed to psychosocial stressors (public speaking and mental arithmetic in front of an audience), the majority showed rapid diminution of cortisol response over the five days of task repetition. This was not the case for a subgroup of men characterised by low self-esteem, depressed mood and physical symptoms. Among them, an elevated cortisol response to the task continued over the entire period.

These findings suggest that poor personal coping resources may increase the risk of adverse pregnancy outcomes. In studies of pregnancy outcomes to date, only a few have evaluated coping resources. Among low-income pregnant women, Goldenberg *et al.*²⁶ reported an elevated odds of intrauterine growth retardation among women with low scores on scales of mastery and self-esteem. Also, Shiono *et al.*²⁷ found that women with perceptions of helplessness (scoring high on a measure of chance-based locus of control) delivered lighter infants. Similarly, Rini *et al.*²⁸ reported that personal resources (as measured by mastery, self-esteem and optimism) were positively associated with birthweight among 120 Hispanic and 110 white women. Resources also influenced length of gestation indirectly, by means of an influence on reduced anxiety (state and pregnancy anxiety). This last study also evaluated the possibility that resources buffered the negative association between stress and length of gestation. However, there was no evidence of buffering in this population.

An obvious coping resource is financial.²⁴ Lack of financial resources, as defined by poverty status or low socio-economic status, is one of the most consistent risk factors for preterm delivery. Self-esteem and sense of personal control are inversely distributed by social status, suggesting that access to financial resources may be mediated through other coping resources. However, the extent to which lack of financial resources directly affects the individual's ability to cope with stressors has not been well studied.²⁴

Coping strategies, in contrast to coping resources, describe specific behavioural or cognitive attempts to manage stressful demands.²⁹ Strategies have been characterised as problem-focused, in which efforts are directed at the demands themselves, and emotion-focused, in which attention is directed to the emotional reactions to the stressors. Problem-focused coping is

more likely to be used when the stressor is perceived as controllable or modifiable, whereas emotion-focused coping is used more frequently when the stressor is perceived as uncontrollable. To date, research results are inconclusive as to which strategy is the more effective in buffering the health effects of stressors.²⁴

However, in studies of hypertension, an interaction between stressor and type of coping style has been hypothesised to account for the increased prevalence of hypertension among African-Americans. In the face of environmental constraints on achievement resulting from racism (a chronic environmental stressor), an active coping style (termed John Henryism, after the African-American folk hero who pit his strength in driving steel to lay railroad tracks against a steam-powered machine and died in the contest) may lead to chronic elevations in blood pressure. This hypothesis has received some support in epidemiological studies among black men.^{30,31}

Experience of, and means of coping with, anger may mediate such a relationship. Although anger traits have been studied extensively in relation to hypertension and cardiovascular disease (e.g.³²⁻³⁵), their relationship with preterm delivery has yet to be explored. Another important buffer may be spirituality, that is, reliance on a force beyond the individual. (For a discussion, see²⁰) Moderate physical exercise as a coping strategy to reduce the impact of stress probably does not affect gestational age at delivery,^{36,37} heavier exercise has been found to be protective of preterm delivery.³⁸ However, other coping strategies are known to have deleterious effects on pregnancy outcome. These include smoking (with a greater impact on fetal growth than on preterm delivery), alcohol and drug dependence.³

Situational factors

Pregnancy itself can be stressful. Lederman¹¹ identifies four adaptations to pregnancy that can cause anxiety if not easily resolved: ambivalence to the pregnancy and accepting it; identifying and conceptualising a motherhood role; identifying and adapting to changes in intimate relationships; and preparing for the birth event.

Three studies have found that when the pregnant woman expressed anxiety about her pregnancy, she was more likely to experience a low birthweight³⁹ or preterm delivery.^{9,40} However, although these studies collected information on pregnancy anxiety before delivery, it is not possible to ascertain whether subtle

pregnancy complications that may have alerted the woman to impending problems could have triggered pregnancy anxiety and also been the cause of the preterm delivery. If the latter is true, measurement of pregnancy anxiety may be a marker for women at risk of preterm delivery owing to medical problems, but not an independent risk factor for preterm delivery. Future research needs to examine reasons for the pregnancy anxiety as well as provide better information on pre-existing medical risk factors.

Environments or contexts

The social and cultural context of a pregnant woman may add to or alleviate her level of distress. Ameliorating social environmental factors include intimate social support, which has been associated with improved pregnancy outcome in a number of studies,^{5,8,9,40} although attempts to replicate social support in clinical trials to prevent poor pregnancy outcomes have not been effective.⁵⁻⁷ Studies of environmental stressors have included measures of chronic stressors, 'enduring or recurrent difficulties and strains in an area of life'; and hassles, 'smaller, relatively minor, and normally less emotionally arousing events whose effects disperse in a day or two.'^{41,p.2} However, the negative health impact of environmental stressors is not contingent upon an individual's perception of them, because exposed individuals may not view pervasive social, structural factors as stressful. For this reason, measurement of environmental risks must include contextual variables. Illustrations of the types of stressful environmental factors include those associated with gender, with socio-economic status, and with race or ethnicity.

Gender

As only women can be pregnant, there is some evidence that gender-related roles may create stress that could adversely affect pregnancy outcomes. For example, chronic strain in the household role was found to be associated with both preterm delivery and low birthweight in a study conducted in Glasgow.⁴² In the workplace, women are commonly relegated to jobs characterised by low control. Compared with women who exercise greater job control, women with less control over their working conditions may have less self-esteem and greater isolation, with resulting increase in unhappiness and distress.⁴³ Lack of job

control has been associated with increased risk of low birthweight in one study of Norwegian women.⁴⁴ In this study, women in both manual and non-manual jobs experienced higher risks of poor pregnancy outcome if they had less job control. Likewise, gestational hypertension was associated with lower control among women in both high- and low-status jobs in a prospective study of 717 women in New York and Pennsylvania.⁴⁵

The effect of low job control on preterm delivery has not been studied extensively. Among 8711 Danish women, those holding jobs with low control had somewhat higher risk (albeit not statistically significant) of preterm delivery than those in relaxed jobs.⁴⁶ In one case-control study in North Carolina, high job strain (low control coupled with high demand) was associated with preterm delivery only when women worked full-time or throughout their pregnancy. The risk appeared to be greater among African-American than white women. These findings suggest that high job strain may have more impact in the presence of other social stressors, such as racism.⁴⁷ Hard physical work, as distinguished from the emotional stress of high job strain, may constitute an acute stressor, especially during pregnancy (see next section).

Violence against women is a gender-specific stressor that has been associated with risk of unintended pregnancy. However, the association between violence against women and poor pregnancy outcomes is inconclusive, owing in part to lack of validated exposure measures, including severity and chronicity; failure to distinguish among the effects of physical, sexual, and emotional violence; and other methodological problems.⁴⁸

Stress associated with gendered racism has been hypothesised to help explain the excess risk of preterm delivery among African-American women in the US.⁴⁹ Although no study to date has investigated the hypothesis directly, there is evidence that African-American women experience specific environmental stressors unique to discriminated populations.⁴⁹

Poverty

The well-known association between poverty and poor pregnancy outcome has been found consistently across populations, over time, and by various measures of social class and social status. Causal models explaining this association point to the higher exposure to negative life events experienced by poor

individuals, coupled with fewer individual coping resources available to them for adapting to stress, and living within a culture of poverty that encourages hopelessness and resort to unhealthy coping strategies (see above).^{2,3}

Additionally, poor communities are more exposed to environmental hazards such as lead, other toxic agents, and unsafe neighbourhoods, as well as reduced community resources for responding to health and medical emergencies. Including these community-level factors in studies of stress and preterm delivery requires group-level measurement of exposure. These factors have not been used widely in epidemiological research in this area, but a few studies tend to confirm the utility of pursuing contextual causes. In one study of 895 women, neighbourhood poverty was associated with lower maternal warmth towards children.⁵⁰ Another study revealed a high level of prenatal depression among both white and African-American women living in an inner-city neighbourhood. Depression was also related to social factors, such as poor partner and other social supports.⁵¹ Living in a neighbourhood that had a higher mean per capita income than one's own (i.e. positive income incongruity) was associated with better rates of very low birthweight among African-Americans living in Chicago.⁵²

Institutionalised racism

Institutional racism is defined as structural social or cultural patterns that result in the unequal distribution of social benefits or burdens, on the basis of socially constructed racial or ethnic groups. As a consequence of institutional racism, discriminated groups are exposed to increased environmental risks. Institutional racism differs from individualised racial insults, which are interpersonal events that comprise a subset of acute stressors discussed below as agents of stress.

Residential segregation is an example of institutional racism. Among African-American infants, mortality is lower in cities with less residential segregation, a finding that is independent of the effect of household poverty on infant mortality.⁵³ Reduced access to health facilities, increased exposure to random violence, increased exposure to cigarette advertising, and other manifestations of institutionalised racism may have a negative impact on the health of discriminated populations, irrespective of the individual's perception of environmental exposures.

Geronimus^{54,55} has proposed that such environmental as well as individual level stressors may 'weather' discriminated populations, causing them to age more rapidly and become susceptible to pregnancy complications at earlier ages. This weathering may not be amenable to self-report, but may require external assessment of physical, rather than chronological, age.

In addition to the growing evidence that institutionalised racism adversely affects African-American infants' health, there is an emerging literature suggesting that institutional racism in the US may affect Mexican-Americans' reproductive health as well.⁵⁶⁻⁵⁸ The relatively high birthweight of Mexican-American infants has long presented a paradox to reproductive epidemiologists. As a group, Mexican-Americans suffer many socio-economic disadvantages. Paradoxically, their risk of low birthweight is similar to that of whites and much less than that of African-Americans who more closely resemble Mexican-Americans in socio-economic status. Buekens and colleagues⁵⁶ have recently narrowed the paradox to preterm delivery, i.e. compared with non-Hispanic white women, Mexican-American women have a lower risk of preterm delivery.

This advantage in preterm delivery appears to lessen as Mexican-Americans become more exposed to American culture. The mean birthweight for babies of US-born Mexican women was slightly lower (3309 g vs. 3364 g),⁵⁶ possibly owing to a greater risk of preterm delivery among infants of US-born women. Moreover, among foreign-born women the protective effect of Mexican birth may erode with increased exposure to US culture. When compared with recent immigrants (in the US < 5 years), women who had been in the US for 5 years or more before giving birth had an adjusted odds ratio (OR) for preterm delivery of 1.8 [95% CI 1.0-3.2].⁵⁷ The OR was adjusted for confounding variables and for unplanned pregnancy and smoking - negative coping strategies associated with stress. This finding suggests that the stress of acculturation is an independent risk factor for preterm delivery.

Acculturation and increased stress are not synonymous. However, there are intriguing new data to support the hypothesis that the stress associated with acculturation adversely affects pregnancy outcome. In a study of 911 pregnant Mexican-Americans in Los Angeles, investigators used a structural equation model to examine the effects of cultural integration (as measured by a combination of language preference, years in Los Angeles, years of education, and English-speaking) and reduced gestational age.⁵⁸

Increased acculturation of Mexican-American women was associated with increased psychosocial stress, which was associated with shorter gestational age. One important research question is how much stress among Mexican-American women is owing to exposure to institutional racism, individualised racial insults, or the stress of cultural integration *per se*.

Agents

Agents are stressors that provoke immediate individual response to a physical or emotional challenge. Two kinds of stressors have been most extensively studied with respect to their impact on pregnancy outcomes. These are acute, stressful life events and hard, physical work - a type of individual, chronic exposure. A third kind of stressor - individual experiences of racism - holds potential for explaining at least part of the excess preterm delivery rate among African-Americans and the increased preterm delivery rate among Mexican-Americans who have lived in the US for most or all of their lives. Being poor could elicit a fourth type of acute stressor. For example, if a poor person is exposed to personal insult because she is dressed poorly or is begging on the street, then the event would fit into our classification as an agent. However, we are not aware of any studies of poverty viewed from this perspective.

Stressful life events

Stressful life events have been defined as 'exposure to out-of-the-ordinary, demanding events such as job loss, that have the capacity to change the patterns of life or arouse very unpleasant feelings.'^{41, P.2} Stressful life-event scales have been included in many epidemiological studies of poor pregnancy outcomes. One such scale is a part of routine surveillance of pregnancy risk factors in the Centers for Disease Control and Prevention sponsored PRAMS (Pregnancy Risk Assessment Monitoring System).⁵⁹ Some life-event scales also incorporate measures of the individual's response, such as stressfulness rating, which may reflect both event severity and host susceptibility. The evidence that stressful life events adversely affect gestational length or very low birthweight is modest, although recent studies provide more consistent evidence of a small effect.^{8,60-66} Although most studies evaluated only acute events, in three studies that reported associations between

stressors and either preterm delivery⁶⁰ or very low birthweight⁸ both acute and chronic stressors were assessed. This suggests, as our model would predict, that contextual factors may amplify the impact of acute events.

Hard physical work

Hard physical work represents a set of acute stressors not commonly considered within the same framework as stressors that evoke emotional responses. However, biophysical responses to hard physical work are similar to biophysical responses to emotional stress.⁶⁷ Because of this common pathway once the exposure enters the body, we posit that hard physical work must be included in an epidemiological model for stress and preterm delivery. In addition, as working conditions are malleable, reducing physical work-related stress may be an important avenue to reduce stress-related preterm delivery.^{67,68}

In a meta-analysis, Mozurkewich and colleagues⁶⁷ concluded that there is consistent evidence that hard physical work does increase preterm delivery risk, although the ORs are not high, i.e. in the range of 1.2–1.6. The strongest association is between Mamelle's cumulative work fatigue score and preterm delivery. The meta-analysis OR for the Mamelle score was 1.63 [95% CI 1.33, 1.98], which was assessed in six studies with a total of 7719 women.

No intervention trials have been undertaken to determine the effect of modifying work conditions in pregnancy on preterm delivery, but observational studies suggest that public policy to protect pregnant women from hard physical working conditions during pregnancy holds promise for reducing the preterm delivery rate in the US. Papiernik and colleagues⁶⁸ report that improvements in work conditions for pregnant women in France measurably improved preterm delivery rates there. Mozurkewich and colleagues⁶⁷ estimate that one preterm birth might be prevented for each 12–32 pregnant employees in the US who are exposed to cumulative work fatigue. The prevention potential would be even greater among women at higher risk of preterm delivery, such as those who had already experienced a preterm delivery.

Individual experiences of racial insult

The persistent, excess risk of preterm delivery among African-American women has led several investigators

to postulate that stressors differ between African-Americans and non-Hispanic, white Americans. The stressor that is most often mentioned is individual experiences of racial and ethnic discrimination.^{20,22,69–73} One study, directly assessing the association between racism, stress, and gestational age among 147 African-American women, found a racism measure to be associated with negative self-esteem and self-reported stress but not associated with gestational age.⁷⁴

Measures designed to assess individual experiences of racism have been developed for African-American adults^{73,75} and for well-educated, African-American women.⁴⁹ Each measure is based on different assumptions of the way that experiences of racism affect health. The McNeilly *et al.* Perceived Racism Scale⁷³ is based on self-report of life experiences in employment, academic and public settings, and to racist statements in general; the individual's emotional response to each of those experiences; and the person's coping behavioural response to such experiences. Krieger's measure⁷⁵ is similar but much shorter. Behavioural coping response is assessed generally, and there are fewer specific life experiences listed. In studies of hypertension among African-American women, Krieger^{75,76} has hypothesised that the minority of women who state that they have not experienced racism may be more at risk of ill health associated with racist experiences because of denial and the inability to express their feelings. The measure developed by Jackson and colleagues⁴⁹ is based on grounded theory, an inductive anthropological method in which investigators work iteratively to develop measures, in concert with collaborating women from the population of interest. In a validation study of the instrument developed by Jackson and colleagues, 45% of 166 respondents disagreed or strongly disagreed with the statement, 'Racism is a problem in my life.' However, most women agreed or strongly agreed with specific experiences that demand expenditure of energy to cope with racism. For example, 57% agreed with the statement, 'I have to deal with racism directed at African-American children I interact with.'⁴⁹ The investigators caution that measuring the impact of racism on African-American women requires appraisal of how both racial and gender identities shape the experiences of oppression. This finding is mirrored in research by Berger *et al.*⁷⁷ of Mexican-American and Anglo men and women, in which there were significant differences in the association of role strain and self-reported stress by ethnicity and gender.

Discussion: implications for future research

The examples provided above illustrate the value of the agent/host/environment epidemiological model in organising the complex variables of stressors and stress response. This model also helps to identify necessary improvements in epidemiological research. Issues include expanding design and analysis of epidemiological tests of causal models, developing better measures of stressors and stress responses, and selecting appropriate theoretical models.

Designing and analysing epidemiological studies

So far, no specific stressors, such as stressful life events or hard physical work, have been found to affect preterm delivery very much. There is a fairly consistent, low level of effect across studies of various types of stressors. One possible inference is that stress is not an important risk factor. Another interpretation is that studies suffer from common methodological flaws that artificially diminish effect measures, regardless of which stressor they are studying. Implications of the agent/host/environment model support the latter interpretation. This model suggests that limiting stressor assessment to one stressor or to a small number of stressors will underestimate exposure in the study population. It also suggests that measuring objective stressors, without measuring differences in host reactivity and moderating resources, may represent an incorrectly specified model. If acute stressors are harmful only in the presence of socio-environmental stressors or only among susceptible women, then studies that do not account for these possible interactions may fail to show substantial association between stressors and preterm delivery.

Racism is one such ongoing stressor, and this may help to account for the higher rates of preterm delivery among African-Americans. For example, in one study of acute stressors and low birthweight, investigators reported that experiencing a high number of stressful life conditions was associated with an OR of 1.52 [1.33, 1.91] among 1443 African-Americans, but there was no association among 428 white women recruited from the same clinics.³⁹ However, in another study that also included African-American and white women recruited from prenatal clinics,⁶⁴ negative life events were unrelated to preterm delivery in either group. In fact, among white women, experiencing a small

number of positive life events was associated with an increased risk of preterm delivery. To date, too few studies have evaluated the impact of life events among both African-Americans and whites to be able to draw any conclusions on this point.

Three or more agent/host/environment factors may interact to increase or reduce homeostasis. For example, Tesser and Beach⁷⁸ found a curvilinear relationship between the number of negative life events (agent) and judgements of intimate partner relationship quality (social environment); that is, with increasing negative life events, judged relationships got worse then better then worse. At the mid-point, when the correlation between negative life events and intimate relationships was the most negative, the individual's mood (host) was also the most negative. The authors hypothesise that these complex findings result from an ongoing process of stressor and stress response, as experienced by the individual in social context. At first as negative life events increase, the individual's growing negative mood contributes to a more negative view of intimate relationships, without a conscious assessment of the true quality of those relationships. Then, when mood is at the lowest, the individual 'wakes up' to the fact that life events are piling up and makes an independent assessment of the social resources at hand to cope with the stressors. That assessment generally is more favourable towards intimate relationships than was the earlier one (which was unconsciously lowered owing to the person's mood). However, if negative life events continue to increase, and the individual calls upon intimate relationship resources to handle the stress, those resources are strained, resulting in a lesser view of the intimate's ability to help.

This complex finding fits within the sociological study of stress contagion, that has grown from the realisation that stressors often are social and that stress response has a social component. Stress contagion is defined as the 'carry-over' of stressors from one individual to another.⁷⁹ There are three ways that stress is contagious – spillover, crossover, and vulnerability. Spillover is associated with role conflict and overload (social environment). Vulnerability refers to the impact of earlier life experiences on increasing host susceptibility. Crossover happens when one individual assumes the stress of another because of shared fate, role obligations, or commitments (social environment). Perhaps owing to their roles, women have been found to experience higher levels of stress crossover.⁷⁹

Assessing existing stress measures and developing new ones, as necessary

Misclassification may occur when the stressor is not well measured. Previous research has relied on five general categories of stress measures: stressful life-event scales, self-reports of perceived stressfulness and appraisals of threat posed by events, lists of chronic stressors, lists of daily hassles, and environmental or contextual variables. This list may need to be expanded and refined. Depending on the population to be studied, existing measures may not adequately distinguish exposed from unexposed individuals. Model-based research will help to assess how well existing measures may fit proposed new research and identify gaps in measurement that must be filled through the development of new generic or specific measures.

Some studies that have better characterised exposure suggest the merit of a more comprehensive approach. For example, many recent studies have included measures of objective stressor severity^{60,61} and/or subjective ratings of impact.^{61–63,66} In contrast to objective measures of stressor severity, subjective ratings may reflect not only the severity of the event but also host susceptibility. Future studies may be better able to disentangle these two components by including measures of stress vulnerability or responsiveness, rather than including it in the measure of the stressor.

Selecting theoretical models

The agent/host/environment framework does not constitute a comprehensive theory of stress and health (e.g. as discussed in⁷⁹), but rather provides a context to determine the extent to which a given theory may include important and potentially inter-related factors. There is a great need for theoretical development in this area.^{15,24} One comprehensive theory that may prove useful is the biopsychosocial theory,^{16,22,80} which melds individual, social, and cultural variables into an understanding of the biophysical effects of pathological stress. Sociological theories and theoretical perspectives that may help to model parts of the agent/host/environmental framework include social role theory, social ecological theory, the transactional model of stress, the life-event perspective, the life-course perspective, and the feminist perspective.^{24,80}

Conclusion

Numerous epidemiological studies of various kinds of stress and preterm delivery have produced either negative or weakly positive results. Although inconclusive findings may reflect a lack of strong, causal association between stress and gestational length, they could well result from a lack of well-conducted, model-based research. We have proposed an epidemiological model based on the classic agent, host, and environment triangle to explore the necessary components of well-designed epidemiological investigations in this field. While these components do not comprise a comprehensive causal model, they may be of use in evaluating proposed causal models and in designing future, model-based research.

References

- 1 Nuckolls KB, Kaplan BH, Cassel J. Psychosocial assets, life crisis and the prognosis of pregnancy. *American Journal of Epidemiology* 1972; **95**:431–441.
- 2 Williams DR. Socioeconomic differentials in health: a review and redirection. *Social Psychology Quarterly* 1990; **53**:81–99.
- 3 Rutter DR, Quine L. Inequalities in pregnancy outcome: review of psychosocial and behavioural mediators. *Social Science and Medicine* 1990; **30**:553–568.
- 4 Lobel M. Conceptualizations, measurement, and effects of prenatal maternal stress on birth outcomes. *Journal of Behavioral Medicine* 1994; **17**:225–272.
- 5 Hoffman S, Hatch MC. Stress, social support and pregnancy outcome: a reassessment based on recent research. *Paediatric and Perinatal Epidemiology* 1996; **10**:380–405.
- 6 Blondel B. Social and medical support during pregnancy: an overview of the randomized controlled trials. *Prenatal and Neonatal Medicine* 1998; **3**:141–144.
- 7 Hodnett ED. Support during pregnancy for women at increased risk (Cochrane Review). In: *The Cochrane Library* 2000; 2. Oxford: Update Software.
- 8 Edwards CH, Cole OJ, Oyemade UJ, Knight EM, Johnson AA, Westney OE, et al. African-American mothers' perception of their residential environment, stressful life events, and very low birthweight. *Epidemiology* 1998; **9**:286–289.
- 9 Mamelle N, Measson A, Munoz F, Audreas de la Bastie M. Identification of psychosocial factors in preterm birth. *Prenatal and Neonatal Medicine* 1998; **3**:35–38.
- 10 Wadhwa PD, Culhane JF, Rauh V, Barve SS, Hogan V, Sandman CA, et al. Stress, infection and preterm birth: a biobehavioural perspective. *Paediatric and Perinatal Epidemiology* 2000; **15**(Suppl. 2):17–29.
- 11 Ledermen RP. Relationship of anxiety, stress, and psychosocial development to reproductive health. *Behavioral Medicine* 1995; **21**:101–112.
- 12 Holzman C, Bullen B, Fisher R, Paneth N, Reuss L. Pregnancy outcomes and community health: the POUCH study of preterm delivery. *Paediatric and Perinatal Epidemiology* 2001; **15**(Suppl. 2):136–158.
- 13 Kramer M, Goulet L, Lydon J, Séguin L, McNamara H, Dassa

- C, *et al.* Socio-economic disparities in preterm birth: causal pathways and mechanisms. *Paediatric and Perinatal Epidemiology* 2001; **15**(Suppl. 1):104–123.
- 14 Rich-Edwards J, Krieger N, Majzoub J, Zierler S, Liebermann E, Gillman M. Maternal experiences of racism and violence as predictors of preterm birth: rationale and study design. *Paediatric and Perinatal Epidemiology* 2001; **15**(Suppl. 2):124–135.
 - 15 Kogan MD, Alexander GR. Social and behavioral factors in preterm birth. *Prenatal and Neonatal Medicine* 1998; **3**:29–31.
 - 16 Evans RG, Hodge M, Pless JB. If not genetics, then what? Biological pathways and population health. In: *Why Are Some People Healthy and Others Not?* Editors: Evans RG, Barer ML, Marmot TR. New York: de Gruyter, 1994; pp. 133–160.
 - 17 McCubbin JA, Lawson EJ, Cox S, Sherman JJ, Norton JA, Read JA. Prenatal maternal blood pressure response to stress predicts birth weight and gestational age: a preliminary study. *American Journal of Obstetrics and Gynecology* 1996; **175**: 706–712.
 - 18 Armstead CA, Lawler KA, Gorden G, Cross J, Gibbons J. Relationship of racial stressors to blood pressure responses and anger expression in black college students. *Health Psychology* 1989; **8**:541–556.
 - 19 Anderson N, McNeilly M, Myers H. Towards understanding race difference in autonomic reactivity: a proposed contextual model. In: *Individual Differences in Cardiovascular Response to Stress*. Editors: Turner JR, Sherwood A, Light KC. New York: Plenum Press, 1992; pp. 125–146.
 - 20 Harrell JP, Merritt MM, Kalu J. Racism, stress and disease. In: *African American Mental Health*. Editor: Jones RL. Cobb & Henry Publishers, 1998; pp. 247–278.
 - 21 Bell IR, Baldwin CM, Russek LGS, Schwartz GER, Hardin EE. Early life stress, negative paternal relationships, and chemical intolerance in middle-aged women: support for a neural sensitization model. *Journal of Women's Health* 1998; **7**:1135–1147.
 - 22 Hogue CJR. Gender, race, and class: from epidemiologic association to etiologic hypotheses. In: *Women and Health*. Editors: Goldman M, Hatch M. San Diego, CA: Academic Press, 2000; pp. 15–23.
 - 23 Pearlin LI, Schooler C. The structure of coping. *Journal of Health and Social Behavior* 1978; **19**:2–21.
 - 24 Thoits PA. Stress, coping, and social support processes: where are we? What next? *Journal of Health and Social Behavior* 1995; **35** (Extra issue: Forty years of medical sociology: the state of the art and directions for the future):53–79.
 - 25 Kirschbaum C, Pruessner J, Stone AA, Federenko I, Gaab J, Lintz D, *et al.* Persistent high cortisol responses to repeated psychological stress in a sub-population of healthy men. *Psychosomatic Medicine* 1995; **57**:468–474.
 - 26 Goldenberg RL, Cliver SP, Cutter GR, Hoffman HJ, Copper RL, Gotlieb S, *et al.* Maternal psychological characteristics and intrauterine growth retardation. *Pre- and Peri-Natal Psychology Journal* 1991; **6**:129–134.
 - 27 Shiono PH, Rauh VA, Park M, Lederman SA, Zuskar D. Ethnic differences in birth weight: the role of lifestyle and other factors. *American Journal of Public Health* 1997; **87**:787–793.
 - 28 Rini CK, Dunkel-Schetter C, Wadhwa PD, Sandman CA. Psychological adaptation and birth outcomes: the role of personal resources, stress and sociocultural context in pregnancy. *Health Psychology* 1999; **18**:333–345.
 - 29 Lazarus RS, Folkman SM. *Stress, Appraisal, and Coping*. New York: Springer, 1984.
 - 30 James SA, Strogatz DS, Wing SB, Ramsey DL. Socioeconomic status, John Henryism, and hypertension in blacks and whites. *American Journal of Epidemiology* 1987; **126**:664–673.
 - 31 James SA, Keenan NL, Strogatz DS, Browning SR, Garrett JM. Socioeconomic status, John Henryism, and blood pressure in black adults. The Pitt County Study. *American Journal of Epidemiology* 1992; **135**:59–67.
 - 32 Theorell T, Alredsson L, Westerholm P, Falck B. Coping with unfair treatment at work – what is the relationship between coping and hypertension in middle-aged men and women? An epidemiological study of working men and women in Stockholm (the WOLF study). *Psychotherapy and Psychosomatics* 2000; **69**:86–94.
 - 33 Harenstam A, Theorell T, Kaijser L. Coping with anger-provoking situations, psychosocial working conditions, and ECG-detected signs of coronary heart disease. *Journal of Occupational Health Psychology* 2000; **5**:191–203.
 - 34 Horsten M, Ericson M, Perski A, Wamala SP, Schenck-Gustafsson K, Orth-Gomer K. Psychosocial factors and heart rate variability in healthy women. *Psychosomatic Medicine* 1999; **61**:49–57.
 - 35 Williams RB, Barefoot JC, Blumenthal JA, Helms MJ, Luecken L, Pieper CF, *et al.* Psychosocial correlates of job strain in a sample of working women. *Archives of General Psychiatry* 1997; **54**:543–548.
 - 36 Kramer MS. Regular aerobic exercise during pregnancy. *Cochrane Database of Systematic Reviews* [computer file]: 2: CD000180, 2000.
 - 37 Riemann MK, Kanstrup HIL. Effects on the foetus of exercise in pregnancy. *Scandinavian Journal of Medicine and Science in Sports* 2000; **10**:12–19.
 - 38 Hatch M, Levin B, Shu X-O, Susser M. Maternal leisure-time exercise and timely delivery. *American Journal of Public Health* 1998; **88**:1528–1533.
 - 39 Orr ST, James SA, Miller CA, Barakat B, Daikoku N, Pupkin M, *et al.* Psychosocial stressors and low birth weight in an urban population. *American Journal of Preventive Medicine* 1996; **12**:459–466.
 - 40 Dunkel-Schetter C. Maternal stress and preterm delivery. *Prenatal and Neonatal Medicine* 1998; **3**:39–42.
 - 41 Wethington E, Almeida D, Brown GW, Frank E, Kessler RC. The assessment of stressor exposure. Ithaca, NY: Cornell University, Bronfenbrenner Life Course Center, 1998; BLCC Working Paper 98–21, pp. 1–41.
 - 42 Pritchard CW, Teo Mfphm PYK. Preterm birth, low birthweight and the stressfulness of the household role for pregnant women. *Social Science and Medicine* 1994; **38**:89–96.
 - 43 Pugliesi K. Work and well-being: gender differences in the psychological consequences of employment. *Journal of Health and Social Behavior* 1995; **36**:57–71.
 - 44 Wergeland E, Strand K. Work pace control and pregnancy health in a population-based sample of employed women in Norway. *Scandinavian Journal of Work and Environmental Health* 1998; **24**:206–212.
 - 45 Landsbergis PA, Hatch MC. Psychosocial work stress and pregnancy-induced hypertension. *Epidemiology* 1996; **7**: 346–351.
 - 46 Henriksen TB, Hedegaard M, Secher NJ. The relations between psychosocial job strain, and preterm delivery and low birthweight for gestational age. *International Journal of Epidemiology* 1994; **23**: 764–774.

- 47 Brett KM, Strogatz DS, Savitz DA. Employment, job strain, and preterm delivery among women in North Carolina. *American Journal of Public Health* 1997; **87**:199–204.
- 48 Gazmararian JA, Petersen R, Spitz AM, Goodwin MM, Saltzman LE, Marks JS. Violence and reproductive health: current knowledge and future research directions. *Maternal and Child Health Journal* 2000; **4**:79–84.
- 49 Jackson FM, Phillips MT, Hogue CJR, Curry-Owens TY. Examining the burdens of gendered racism: implications for pregnancy outcomes among college-educated African American women. *Maternal and Child Health Journal* 2001; **5**:95–107.
- 50 Klebanov PK, Brooks-Gunn J, Duncan GJ. Does neighborhood and family poverty affect mothers' parenting, mental health, and social support? *Journal of Marriage and the Family* 1994; **56**:441–445.
- 51 Hobfoll SE, Ritter C, Lavin J, Hulsizer MR, Cameron RP. Depression prevalence and incidence among inner-city pregnant and postpartum women. *Journal of Consulting and Clinical Psychology* 1995; **63**:445–453.
- 52 Collins JW Jr, Herman AA, David RJ. Very-low-birthweight infants and income incongruity among African American and white parents in Chicago. *American Journal of Public Health* 1997; **87**:414–417.
- 53 Polednak AP. *Segregation, Poverty, and Mortality in Urban African Americans*. New York: Oxford University Press, 1997; pp. 1–184.
- 54 Geronimus AT. The effects of race, residence, and prenatal care on the relationship of maternal age to neonatal mortality. *American Journal of Public Health* 1986; **76**:1416–1421.
- 55 Geronimus AT. The weathering hypothesis and the health of African-American women and infants: evidence and speculations. *Ethnicity and Disease* 1992; **2**:207–221.
- 56 Buekens P, Notzon F, Kotelchuck M, Wilcox A. Why do Mexican Americans give birth to few low-birth-weight infants? *American Journal of Epidemiology* 2000; **152**:347–351.
- 57 Guendelman S, English PB. Effect of United States residence on birth outcomes among Mexican immigrants: an exploratory study. *American Journal of Epidemiology* 1995; **142**(Suppl. 9):S30–S38.
- 58 Zambrana R, Scrimshaw S, Collins N, Dunkel-Schetter C. Prenatal health behaviors and psychosocial risk factors in pregnant women of Mexican origin: the role of acculturation. *American Journal of Public Health* 1997; **87**:1022–1026.
- 59 Centers for Disease Control and Prevention. *PRAMS 1996 Surveillance Report*. Atlanta, Georgia: Division of Reproductive Health, National Center for Chronic Disease Control and Prevention, Centers for Disease Control and Prevention, 1999.
- 60 Mutale T, Creed F, Maresh M, Hunt L. Life events and low birthweight – analysis by infants preterm and small for gestational age. *British Journal of Obstetrics and Gynaecology* 1991; **98**:166–172.
- 61 Hedegaard M, Henriksen TB, Secher NJ, Hatch M, Sabroe S. Do stressful life events affect duration of gestation and risk of preterm delivery? *American Journal of Epidemiology* 1996; **86**: 347–354.
- 62 Lobel M, Dunkel-Schetter C, Scrimshaw S. Prenatal maternal stress and prematurity: a prospective study of socioeconomically disadvantaged women. *Health Psychology* 1992; **11**:32–40.
- 63 Nordentoft M, Lou HC, Hansen D, Nim J, Pryds O, Rubin P, et al. Intrauterine growth retardation and premature delivery: the influence of maternal smoking and psychosocial factors. *American Journal of Public Health* 1996; **86**:347–354.
- 64 Goldenberg RL, Cliver SP, Mulvihill FX, Hickey CA, Hoffman HJ, Klerman KV, et al. Medical, psychosocial, and behavioral risk factors do not explain the increased risk for low birth weight among black women. *American Journal of Obstetrics and Gynecology* 1996; **175**:1317–1324.
- 65 Zambrana RE, Dunkel-Schetter C, Collins NL, Scrimshaw SC. Mediators of ethnic-associated differences in infant birth weight. *Journal of Urban Health: Bulletin of the New York Academy of Medicine* 1999; **76**:102–116.
- 66 Honner MJ, Zubrick SR, Stanley FJ. The role of life events in different categories of preterm birth in a group of women with previous poor pregnancy outcome. *European Journal of Epidemiology* 1994; **10**:181–188.
- 67 Mozurkewich EL, Luke B, Avni M, Wolf FM. Working conditions and adverse pregnancy outcome: a meta-analysis. *Obstetrics and Gynecology* 2000; **95**:623–635.
- 68 Papiernik E, Keith LG, Bouyer J, Dreyfus J, Lazar P (eds.). *Effective Prevention of Preterm Births: The French Experience Measured at Haguenau*. In: *Birth Defects Original Article Series, Vol. 25, Number 1*. West Plains, New York: March of Dimes Birth Defects Foundation, 1989.
- 69 Williams DR. Racism and health: a research agenda. *Ethnicity and Disease* 1996; **6**:1–6.
- 70 Clark R, Anderson NB, Clark VR, Williams DR. Racism as a stressor for African Americans. *American Psychologist* 1999; **54**: 805–816.
- 71 Hogue CJ, Hargraves MA. Preterm birth in the African-American community. *Seminars in Perinatology* 1995; **19**:255–262.
- 72 Krieger N. Embodying inequality: a review of concepts, measures, and methods for studying health consequences of discrimination. *International Journal of Health Services* 1999; **29**: 295–352.
- 73 McNeilly MD, Anderson NB, Armstead CA, Clark R, Corbett M, Robinson EL, et al. The perceived racism scale: a multidimensional assessment of the experience of white racism among African Americans. *Ethnicity and Disease* 1996; **6**:154–166.
- 74 Murrell NL. Stress, self-esteem, and racism: relationships with low birth weight and preterm delivery in African American women. *Journal of National Black Nurses Association* 1996; **8**:45–53.
- 75 Krieger N. Racial and gender discrimination: risk factors for high blood pressure? *Social Science and Medicine* 1990; **30**: 1273–1281.
- 76 Krieger N, Sidney S. Racial discrimination and blood pressure: the CARDIA study of young black and white adults. *American Journal of Public Health* 1996; **86**:1370–1378.
- 77 Berger PS, Cook AS, DelCampo RL, Herrera RS, Weigel RR. Family/work roles' relation to perceived stress: do gender and ethnicity matter? *Journal of Family and Economic Issues* 1994; **15**:223–242.
- 78 Tesser A, Beach SRH. Life events, relationship quality, and depression: an investigation of judgment discontinuity in vivo. *Journal of Personality and Social Psychology* 1998; **74**:36–52.
- 79 Wethington E. *Contagion of Stress*. Ithaca, New York: Cornell Careers Institute, 1999; BLCC Working Paper 99–18, pp. 1–45.
- 80 Iams JD. Atherosclerosis: a model for spontaneous preterm birth. *Prenatal and Neonatal Medicine* 1998; **3**:138–140.