Psychoneuroimmunoendocrinology
Review and Commentary
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Pregnancy and Women's Health

Psychoneuroimmunoendocrinology describes the unity of mental, neurological, hormonal, and immunological functions, addressing the impact of cognitive images of the mind (whatever its elusive definition) on the central nervous, endocrine, and immune systems. It encompasses biofeedback and voluntary controls, impacts on physiology of thought and belief, past/present stress, placebos, social relationships, and "energy medicine." This column highlights clinical applications of cogent studies from these arenas of holistic medicine in the new millennium.

Breast Milk and Laughter

Patients with atopic eczema often complain of sleep disturbance; levels of blood melatonin in eczema patients are low compared to healthy subjects. Laughter has been shown to increase natural killer cell activity in blood and free radical-scavenging capacity in saliva in healthy subjects. Forty-eight infants, aged five to six months, with eczema and allergies to latex and house dust mites were studied along with their mothers. Half of the nursing mothers of these infants had eczema, while another 24 mothers were healthy. The mothers viewed either an 87-minute humorous DVD featuring Charlie Chaplin or an 87-minute non-humorous weather information DVD at 8 PM. After viewing, melatonin in breast milk was checked sequentially in samples from 10 and 12 PM and 2, 4, and 6 AM, and skin wheal responses to dust mites and histamine were checked in the infants. Laughter from viewing the humorous DVD increased the levels of breast-milk melatonin in both mothers with eczema and healthy mothers, compared to those watching the non-humorous weather information DVD. Allergic skin responses to latex and dust mites of infants were reduced after feeding with breast milk from mothers with or without eczema after their laughter sessions, but not in those whose mothers watched the non-humorous DVD.


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Prematurity and Stress

In this study of 1,860 consecutive white women anticipating delivery, 1,513 were included after exclusions for multiple pregnancy, diabetes, refusals, and loss to follow-up. Gestational age was determined by ultrasound and maternal dates; preterm birth was defined as less than 37 completed weeks. Independent variables included smoking, alcohol and caffeine consumption, and a range of indicators of socioeconomic status and psychological stress. Unifactorial analyses showed that lower social class, less education, single marital status, low income, trouble with "nerves" and depression, a need for help from professional agencies, and little contact with neighbors were all significantly associated with an increased risk of preterm birth. There were no apparent effects of smoking, alcohol, or caffeine on the length of gestation overall, although there was an association between smoking and delivery before 32 weeks. Cluster analysis found women delivering preterm infants belonged either to a lower social status group or to a higher social status group of older women.

COMMENT: Adverse social circumstances were associated with preterm birth: lower social class, being unmarried, having a low income, being less educated, and experiencing a poor social support system were prominent factors. All of these, of course, spell added stress. Persons in adverse social circumstances also have a lower reservoir of skills with which to deal with the stress. In the press of the pregnancy itself, there may be little time for upgrading stress management skills with counseling sessions or cognitive education. Even one training session, however, could wield enormous influence. Such a session might introduce the rudiments of meditation, involve biofeedback, or be purely cognitive in pointing out attitude shifts that address the sources of stress. Many persons in adverse circumstances do not appreciate or love themselves, a skill that requires help to learn if the family of origin lacked the appropriate parental support.

Pregnancy and Stress

One hundred and seventy pregnant women completed the Holmes-Rahe schedule of recent experiences as part of their prenatal care. Complications of the gestation included premature birth, need for cesarean section, preeclampsia, birth trauma, and low birth weight. The odds ratio for complications was threefold higher for women whose Schedule of Recent Experiences score was in the high range both prior to and during pregnancy vs. women who had neither elevation (2p=.05).


COMMENT: This older study using the time-tested Holmes-Rahe Schedule of Recent Events found that high scores in pregnant women predicted higher complication rates. The authors do not conclude what mechanisms are involved. A reasonable partial explanation can be seen in the comment of the following study.

Prematurity and Attitudes

Seven hundred and eighty-six pregnant, employed women were selected from a nationally representative sample of 12,686 adults. Data concerning work status, job title, and other factors affecting pregnancy outcome were obtained from the National Longitudinal Survey of Labor Market Experience. Assessment of job experience was based on job title, using an established catalogue of occupation characteristics. After accounting for the physical exertion entailed in a job, occupational psychological stress as measured by job title was not associated with preterm, low birthweight delivery for the sample as a whole (relative risk = 1.16 [NS]). However, for those women who did not want to remain in the work force, work-related stress increased their risk of experiencing preterm delivery 8.1-fold (95% CI 1.5 - 50.2).


COMMENT: Personal motivation toward work, as well as the physical effort of work, should be considered in evaluating the impact of a job's psychological characteristics on pregnancy outcome. In this study, work-related physical exertion proved unrelated to pre-term low birth weight at delivery. Highly significantly related, however, was the relative risk of 8.1 for premature delivery and low birth weight in the group who did not want to be working compared to the group whose members wanted to be working. The specter of attitude again enters the picture. Attitudes may be considered to be the state-of-mind factors that determine the quality of our perceptions. More positive attitudes allow us to attune to more positive perceptions and negative attitudes the opposite. Since our thinking only relates to our perceptions, attitudes rest astride the major pathway leading to our thinking. Best we should pay careful attention to them.

Preeclampsia and Stress

Preeclampsia occurred in 180 of 3,321 working, pregnant Norwegian women who completed a questionnaire sorting them into a cohort reporting a highly stressful and hectic work pace vs. those who never or rarely worked at a hectic pace. Relative risk for preeclampsia in those working at a stressful and hectic pace was 1.4 vs. those who had jobs in which they did not face hectic stress (p<.05). Those lifting loads of 22-44 pounds were almost twice as likely to develop preeclampsia vs. women who never or rarely lifted these amounts.


COMMENT: Knowing that stress raises catecholamine levels and that catecholamines metabolites raise free radical levels, and that preeclampsia is at least in part a free-radical related problem, this stress/eclampsia relationship makes sense. No multifactorial analysis is presented in the study, which might have compared the heavy-lifting factor with the hectic-pace factor. This study, in contrast to the study above, infers that heavy lifting does contribute to risk of premature delivery.

Spontaneous Abortion and Stress

Using 970 subjects in an emergency department to measure stress with a life event inventory and drawing from subjects in an early pregnancy study, the odds ratio for spontaneous abortion at ≥ 11 weeks was 2.9
for association with more life-event stress (95% CI 1.4-6.2) vs. those with little life-event stress. Women experiencing more than one stressful life event used more alcohol and public assistance. Spontaneous abortion at any gestational age was not associated, implying that life-event stress increases the risk of chromosomally normal spontaneous abortion. Tobacco use was also associated with an increased risk of spontaneous abortion, whereas lack of prenatal care was only associated with fetal loss at ≥11 weeks.


COMMENT: Early miscarriage in this study was significantly associated with higher levels of stressful life events. Natal questionnaires are rarely comprehensive enough to include questions regarding stressful events in the life of the patient. Were they included and were attending physicians to pay attention to the stress and help patients develop skills to manage it, the results might be altered. This, however, is not commonly part of the accepted purview of the obstetrician or attending physician. If we look at the whole person and accept the concept of a holistic approach to medical care, the purview broadens from biomedicine to bio-psycho-social-spiritual medicine.

Hypnosis and Breech Conversion in Late Pregnancy
One hundred pregnant women with fetuses in breech position at 37-40 weeks of gestation had more than one session of hypnotherapy with suggestions for general relaxation and release of anxiety and fear. They were also asked in the hypnotic state why their fetus was in breech presentation. Hypnosis was repeated as regularly as possible until delivery or until conversion to vertex presentation. Eighty-one percent of the fetuses of mothers in the intervention group converted spontaneously or as a result of successful external cephalic version to vertex presentation. They were compared with 100 carefully matched control women who had not experienced hypnosis, whose success rate with external cephalic version was 48%.


COMMENT: The difference was obviously statistically significant, but no statistical data were presented. How can we explain this huge disparity? Was it the placebo effect of additional attention? The belief of the patient that this uncommonly used hypnotic process would work? In either case, how would the placebo effect of extra attention or belief in hypnosis lead to the mechanical or physiological changes necessary to keep the fetus in cephalic presentation? For now, we can only speculate about the continued mysteries of some of the improbable, yet nonetheless demonstrated, mind-body effects.

Infertility and Psychological Factors
In this review of 53 studies, negative psychological factors tended to be positively correlated with infertility. The two generally related areas were chronic psychosocial stresses and maladaptive behavioral responses in coping with these stresses.


COMMENT: In this review, psychosocial stress and resulting maladaptive behaviors played major roles in infertility studies. It may be reasonably argued that endocrinological factors can easily be altered by stress,
which in turn affects adrenal hormone levels and the feedback loop to the hypothalamus and pituitary. Whatever the eventual completed picture reveals, it will undoubtedly be multifactorial.

Infertility, Depression, and Anxiety

This study included 107 women with primary infertility and 63 healthy women in the control group. The Hospital Anxiety Depression Scale was completed by both groups and repeated once more after three months to the infertility group. The severity of psychological symptoms was greater in those in the infertility group who had attempted nonmedical solutions, who were under pressure from their husbands’ families because of their infertility, and who reported “bad” relations with their husbands. At the end of the three months, the patients who achieved pregnancy showed significantly lower levels of anxiety and depression scores than the group of patients who did not. Age, attempts at nonmedical solutions, pressure from the husband’s family because of infertility, and anxiety level at the start of the study were variables that predicted poor results.

COMMENT: It can be useful and even essential to take cultural factors into account in evaluating the mental health of infertile women. This study was done in the nation of Turkey, where the pressure of husbands’ families for offspring is culturally deeply ingrained. Even within that framework, higher anxiety levels at the outset predicted higher rates of infertility even with appropriate treatment.

Low Birthweight and Stress

Social stress was assessed in 92 women with low-birthweight babies and 92 controls using the detailed Life Events and Difficulties Schedule (LEDS) measure of life events and severe chronic difficulties. The low-birthweight group was divided into preterm delivery (n = 40), small for gestational age (SGA)(n = 40), and mixed groups. Adjusted analysis showed that three factors were significantly associated with pre-term delivery: a previous low-birthweight baby, severe life event/difficulty, and bleeding during pregnancy. For SGA babies, the factors were previous low-birthweight baby, low social support, and smoking.

COMMENT: By using a reliable measure of life events and adequate numbers of low-birthweight babies, this study overcame the potential inaccuracies of previous studies and indicates a more specific and potent relation between social stress and low birthweight. The three contributing factors were not analyzed in a multifactorial design to relate the strength of each. The psychosocial factor of stress is the least likely to gain the attention of the health professional – not because it is less important, but because the professional has not been trained to understand its importance or has not been trained in the treatment approaches that will make a difference. We health professionals tend to subtly and even unconsciously avoid diagnosing conditions for which we have poor solutions or answers. What a great opportunity for learning and expanding horizons!

Early Miscarriage and Stress

In this case-control study, 603 women, aged 18-55, whose most recent pregnancy had ended in first trimester miscarriage (<13 weeks of gestation) were compared to 6,116 women, aged 18-55, whose most recent pregnancy had progressed beyond 13 weeks. After adjustment for multiple confounders, increased risk for first trimester miscarriage was independently associated with high maternal age; previous miscarriage; assisted conception; low pre-pregnancy body mass index; regular or high alcohol consumption; feelings of stress and the experience of higher numbers of stressful or traumatic events; high paternal age; and a change in partners. Previous live birth, nausea, vitamin supplementation, a daily diet of fresh fruits and vegetables, and the ability to feel well enough to fly or to have sex were all associated with reduced risk. Caffeine consumption, smoking, moderate or occasional alcohol consumption, educational level, socio-economic circumstances, or work during pregnancy – after adjustment for nausea – were likewise not associated with risk for early miscarriage.


COMMENT: The results confirm that advice to encourage a healthy diet, reduce stress, and promote emotional well-being might help women in early pregnancy (or planning a pregnancy) reduce their risk of miscarriage. Findings of increased risk associated with previous termination, stress, change of partner, and low pre-pregnancy weight are noteworthy. Addressing all the above-mentioned factors is important. It’s been said, “we are what we eat.” It seems valid to also say “we are how we identify and handle stress.”

Robert Anderson is a retired family physician who has authored five major books: Stress Power!, Wellness Medicine, The Complete Self-Care Guide to Holistic Medicine (co-author), Clinician’s Guide to Holistic Medicine (McGraw Hill, 2001), and The Scientific Basis for Holistic Medicine, (6th edition, 2004), available from American Health Press, holos@charter.net. Anderson was the founding president of the American Board of Holistic Medicine, past president of the AHMA, and former Assistant Clinical Professor of Family Medicine at the University of Washington; he is currently an Adjunct Instructor in Family Medicine at Bastyr University.