

# First-Trimester Stress May Prompt Early Delivery

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RANCHO MIRAGE, CALIF. — Mothers who experience high levels of stress during early pregnancy appear to convey distress signals to their fetuses, prompting their fetuses to eventually produce high levels of hormones that speed delivery.

The phenomenon suggests the presence of a "placental clock" for parturition that may be set months before the onset of labor, said Curt A. Sandman, Ph.D., professor and vice chair of psychiatry at the University of California, Irvine.

The pattern was seen in a prospective evaluation of pregnant California women who happened to be enrolled in a comprehensive study of pregnancy outcomes when the magnitude 6.7 Northridge earthquake struck early the morning of Jan. 17, 1994, killing dozens of people and leveling thousands of homes.

Those subjects who were in their first trimester showed highly elevated levels of stress hormones, but those in their third trimester had much lower levels of stress hormones, Dr. Sandman said at a conference on sleep in infancy and childhood sponsored by the Annenberg Center for Health Sciences.

Months later, women who had been exposed to the stress of the earthquake early in pregnancy were significantly more likely than other mothers to deliver early.

"An early maternal message that it's a hostile world primes the placental clock for a CRH [corticotropin-releasing hormone] response later," he said.

Subsequent studies in 550 consecutive pregnant subjects confirmed a consistent link between high levels of maternal cortisol early in pregnancy and elevated levels of placenta-derived CRH in the third trimester. Every 1 U of cortisol (g/dL) measured at weeks 14-16 predicted 34 U of CRH (pg/dL) at 30-32 weeks' gestation.

Elevated CRH not only seems to speed delivery, but also appears to have profound consequences on the fetal response to stimuli and, later, a child's response to stress.

The complex interaction between maternal stress, fetal CRH, pregnancy outcomes, and infant and childhood behavior has been the target of studies conducted over more than 12 years as part of the women and children's health and well-being project at UCI, Dr. Sandman explained.

More than 1,000 women and 600-700 infants have been enrolled thus far in studies that begin with extensive prenatal assessment beginning at about 10 weeks' gestation. Neuroendocrine profiles assess the maternal stress axis, while ultrasound examinations and studies of fetal behavior continue throughout pregnancy.

Infant stress examinations begin with the routine first heel-stick test received in the nursery, when researchers take advantage of a naturally occurring opportunity to evaluate salivary cortisol. Babies' responses to the stress of immunizations are also measured and temperament analyses conducted at 6-8 weeks.

The children continue to be followed. Beginning at aged 5-7 years, they are assessed with cognitive tests and structural MRI.

A number of intriguing observations have emerged from the UCI studies, including evidence that suggests stress in the womb may have far-reaching consequences on health and behavior.

The metabolic story begins early in pregnancy, with an increase in neuropeptides from the maternal hypothalamic-pituitary-adrenal stress axis. Apparently in response, the placenta produces circulating CRH, which in turn downregulates the maternal stress system, blocking communication

between the hypothalamus and pituitary. Both the quantity and the timing of stress hormone production is important.

"Women, as pregnancy advances, become immunized to the effects of stress," explained Dr. Sandman, who said the finding explains why stress hormones were not as high in subjects who experienced the earthquake late in pregnancy. "When stress happens, matters," he said.

Further research by the UCI group suggests that the fetus is very much influenced

by stress signals. Fetuses exposed to high levels of stress hormones show a diminished ability to respond to new and familiar auditory stimuli. After birth, babies exposed early to high levels of stress hormones exhibit altered fear responses.

It may be that human fetuses exposed early to very high levels of stress hormones begin adapting very early to a perceived hostile environment by setting the scene for an early escape from the womb and altered fight-flight responses to new stimuli. ■

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