

First-Trimester Stress May Prompt Early Delivery

BY BETSY BATES
Los Angeles Bureau

RANCHO MIRAGE, CALIF. — Mothers who experience high levels of stress during early pregnancy appear to convey distress signals to their fetuses, prompting them to 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 on 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 ($\mu\text{g}/\text{dL}$) 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 neuroep-

ptides 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.

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.

Dr. Sandman said these preliminary findings are not altogether surprising. Animal studies show that drought or famine produces smaller offspring, born early. This represents adaptation, since those animals that survive are small, requiring less food than usual in an environment of scarce resources.

Preterm birth may be an attempt to escape an inhospitable environment, identified as such by an exquisitely sensitive placenta measuring signals suggesting malnourishment or high levels of stress. ■

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

GYNECARE TVT*

Tension-free Support for Incontinence

GYNECARE TVT* with abdominal guides

Tension-free Support for Incontinence

GYNECARE TVT* Obturator System

Tension-free Support for Incontinence

SUMMARY OF PACKAGE INSERT

INDICATIONS

GYNECARE TVT, GYNECARE TVT with abdominal guides and GYNECARE TVT Obturator System are intended to be used in women as suburethral slings for the treatment of stress urinary incontinence (SUI) resulting from urethral hypermobility and/or intrinsic sphincter deficiency.

CONTRAINDICATIONS

As with any suspension surgery, these procedures should not be performed in pregnant patients. Additionally, because the PROLENE® polypropylene mesh will not stretch significantly, it should not be performed in patients with future growth potential including women with plans for future pregnancy.

WARNINGS AND PRECAUTIONS

- Do not use these devices for patients who are on anti-coagulation therapy.
- Do not use these devices for patients who have a urinary tract infection.
- Users should be familiar with surgical technique for urethral suspensions and should be adequately trained in these procedures before employing these devices.
- Acceptable surgical practice should be followed for these procedures as well as for the management of contaminated or infected wounds.
- These procedures should be performed with care to avoid large vessels, nerves, bladder and bowel. Attention to patient anatomy and correct passage of the device will minimize risks.
- Bleeding may occur postoperatively. Observe for any symptoms or signs before releasing the patient from hospital.
- Do not remove the plastic sheaths until the tape has been properly positioned.
- Ensure that the tape is placed with no tension under the midurethra.
- PROLENE mesh in contaminated areas should be used with the understanding that subsequent infection may require removal of the material.
- Do not perform these procedures if you think the surgical site may be infected or contaminated.
- Since no clinical information is available about pregnancy following a suburethral sling procedure with these devices, the patient should be counseled that future pregnancies may negate the effects of the surgical procedure and the patient may again become incontinent.
- Since no clinical information is available about vaginal delivery following these procedures, in case of pregnancy delivery via cesarean section should be considered.
- Postoperatively, the patient should be advised to refrain from heavy lifting and/or exercise (e.g., cycling, jogging) for at least three to four weeks and intercourse for one month. The patient can usually return to other normal activity after one or two weeks.
- Should dysuria, bleeding or other problems occur, the patient is instructed to contact the surgeon immediately.
- All surgical instruments are subject to wear and damage under normal use. Before use, the instrument should be visually inspected. Defective instruments or instruments that appear to be corroded should not be used and should be discarded.
- As with other incontinence procedures, de novo detrusor instability may occur following these procedures. To minimize this risk, make sure to place the tape tension-free in the midurethral position.
- Do not contact the PROLENE mesh with any staples, clips or clamps as mechanical damage to the mesh may occur.
- Do not sterilize any single-use devices or components. Discard opened, unused devices.
- Prophylactic antibiotics can be administered according to the surgeon's usual practice.

WARNINGS AND PRECAUTIONS – additional for GYNECARE TVT / GYNECARE TVT with abdominal guides

- The abdominal guide should not be used to pull the interlocked system upward toward the abdomen.
- Ensure there is a snug connection between the guide and coupler and the coupler and TVT needle.
- Cystoscopy should be performed to confirm bladder integrity or recognize a bladder perforation.
- The rigid catheter guide should then be gently pushed into the Foley catheter so that the catheter guide does not extend into the holes of the Foley catheter.
- When removing the rigid catheter guide, open the handle completely so that the catheter retains properly in place.

WARNINGS AND PRECAUTIONS – additional for GYNECARE TVT Obturator System

- Although bladder injury is unlikely to occur with this technique, cystoscopy may be performed at the discretion of the surgeon.
- Transient leg pain lasting 24-48 hours may occur and can usually be managed with mild analgesics.

ADVERSE REACTIONS

- Punctures or lacerations of vessels, nerves, bladder, urethra or bowel may occur during needle passage and may require surgical repair.
- Transitory local irritation at the wound site and a transitory foreign body response may occur. This response could result in extrusion, erosion, fistula formation or inflammation.
- As with all foreign bodies, PROLENE mesh may potentiate an existing infection. The plastic sheaths initially covering the PROLENE mesh are designed to minimize the risk of contamination.
- Over correction, i.e. too much tension applied to the tape, may cause temporary or permanent lower urinary tract obstruction.

References: 1. Nilsson CG, Rezapour M, Falconer C. 7 year follow-up of the tension-free vaginal tape (TVT) procedure. *Int Urogynecol J*. IUGA Abstract 116 (89), October 2003. 2. American Medical Systems receives patent for innovative SPARC Sling System. American Medical Systems Web site. Available at: <http://www.AmericanMedicalSystems.com>. Accessed January 13, 2004.

GYNECARE WORLDWIDE, a division of ETHICON, INC., a JOHNSON & JOHNSON company
* Trademark

© ETHICON, INC., 2004

OP, Vacuum Combo Raises Anal Sphincter Injury Risk

WHITE SULPHUR SPRINGS, W. VA. — Occiput posterior fetal head position during a vacuum delivery incrementally increases the risk of anal sphincter injury above the risk imposed by the vacuum alone, Jennifer Wu, M.D., said at the annual meeting of the South Atlantic Association of Obstetricians and Gynecologists.

In her retrospective study, vacuum delivery from the OP position was four times more likely to result in a sphincter-injuring third- or fourth-degree tear than vacuum delivery from the occiput anterior (OA) position.

"This is an important issue to consider when weighing the risks and benefits of performing a vacuum delivery from the OP position, especially when one of the goals is to reduce the risk of maternal perineal trauma," said Dr. Wu of the University of North Carolina, Chapel Hill.

She retrospectively analyzed a total of 393 vacuum deliveries performed at the university from 1996 to 2003. Anal sphincter injury was defined as a third- or fourth-degree laceration.

position and 345 deliveries from the OA position. Women in the OP group were significantly younger than those in the OA group (24 years vs. 28 years), more likely to be nulliparous (87% vs. 74%), and more likely to have received an episiotomy (35% vs. 14%).

The infants' gestational age, head circumference, and birth weight were not significantly different between the groups.

The overall anal sphincter injury rate was 24%. Significantly more women in the OP group sustained an anal sphincter injury (42% vs. 22%).

DR. WU
In a multivariate analysis that took into account fetal head position, body mass index, race, nulliparity, length of second stage, episiotomy, birth weight and head circumference, the OP position was four times more likely to be associated with an anal sphincter injury than the OA position. In a previous retrospective study of 588 forceps deliveries, Dr. Wu also found an increased anal sphincter injury rate among OP deliveries, compared with OA deliveries (51% vs. 33%).

—Michele G. Sullivan

