

# Valproate in Utero May Affect Child's Language

BY MICHELE G. SULLIVAN

BANGKOK, THAILAND — Expressive and receptive language abilities are significantly poorer in 3-year-olds who were exposed to sodium valproate in utero than they are in children who were exposed to other individual antiepileptic drugs during gestation, based on a subanalysis of the Neurodevelopmental Effects of Antiepileptic Drugs study.

Valproate exposure was associated with a 10-point difference on both language measures compared with exposure to phenytoin, carbamazepine, or lamotrigine—a difference that is not only statistically significant, but clinically important as well, Gus A. Baker, Ph.D., said at the World Congress of Neurology.

The differences apparent in these 3-year-old subjects will likely expand as the groups grow older, said Dr. Baker, director of the division of neurosciences at the Walton Centre for Neurology and Neurosurgery in Liverpool, England. “We can expect the difference in the magnitude to get greater and not smaller

with age,” he said. Already, Dr. Baker noted, valproate-exposed 3-year-olds in the U.K. portion of the study are lagging behind a group of matched controls. “Well over a third of those exposed to valproate have been referred for speech therapy, so we see that this 10-point difference has real meaning in terms of day-to-day practice.”

The prospective, observational Neurodevelopmental Effects of Antiepileptic Drugs (NEAD) study included 303 pregnant women who were taking sodium valproate, carbamazepine, lamotrigine, or phenytoin as monotherapy. Enrollment occurred during 1999-2004 in 25 epilepsy centers in the United States and the United Kingdom. Separate investigations in the United States and the United Kingdom were later combined. The primary outcome was cognitive performance of the children at 6 years of age.

Dr. Baker, a primary investigator in the U.K. study and coinvestigator in the overall study, presented the results of the

drugs' effect on expressive and receptive language development among 234 children who were 3 years old at assessment. The children all underwent testing of verbal and nonverbal commu-

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nication, including expressive and receptive language, visual motor construction, and nonverbal intellectual ability.

Their abilities in these areas were determined by calculating subscores on screening tests called the Differential Ability Scales (2nd ed.) and the Preschool Language Scale (4th ed.). The scores were adjusted for factors known to affect child intellect.

“We saw that maternal IQ, antiepileptic drug (AED) dose, maternal age, gestational age, and preconceptional exposure to folate were significant factors

predicting the scores, as we would expect,” he said. “But we also showed that overall, the scores for valproate-exposed children were significantly lower than all other drugs and the magnitude of the effect was greater for verbal than nonverbal language.”

Testing showed that the children exposed to valproate scored significantly lower on measures of expressive language (mean score of 91 vs. 102 for carbamazepine, 104 for lamotrigine, and 101 for phenytoin) and receptive language (mean score of 89 vs. 97 for carbamazepine, 101 for lamotrigine, and 101 for phenytoin). On visual motor construction and nonverbal intellectual ability, children exposed to valproate scored lower, but not significantly lower, than children exposed to the other drugs.

In terms of developmental milestones, this finding could bode ill for the valproate-exposed children, said Dr. Baker. “Without a cohesive and intact language system, a child's

neurodevelopmental progress will be limited.”

Unlike the physical results of in utero valproate exposure, which can be surgically corrected to at least some degree, the cognitive effects cannot be erased, he pointed out. The best hope for such children is early identification and intervention.

“If we identify them now, we have to think about an appropriate intervention now. If we leave it for later, the gains they might make will be limited.”

“For women for whom sodium valproate is the first choice because of the nature of their seizures, we should be thinking about reducing the dose to the least possible effective level,” he said.

“In an ideal world, we would have preconception counseling and would be thinking of an alternative drug several years before pregnancy.” ■

**VITALS** **Disclosures:** The NEAD study is funded by the National Institutes of Health. Dr. Baker said he had no financial disclosures.

## Mother-to-Infant *S. aureus* Transmission Horizontal

BY ROBERT FINN

SAN FRANCISCO — Infants most often acquire *Staphylococcus aureus* infections from their mothers horizontally after birth and not vertically during birth, based on a prospective, longitudinal study of 158 pregnant women and their offspring.

Of the participating women, 54 (34%) were *S. aureus* carriers, and 17 of the children born to them (31%) acquired *S. aureus* before discharge, Dr. Eyal Leshem and colleagues at Chaim Sheba Medical Center, Tel Hashomer, Israel, wrote in a poster presentation at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy, sponsored by the American Society for Microbiology.

By contrast, only 3% of the children born to noncarrier mothers acquired *S. aureus*. The investigators found that the mother's carriage status was a very strong predictor of the infant's status. Children born to carriers were 22 times more likely to acquire *S. aureus* than other children. The investigators controlled for the sex of the child, carriage status of the mother, breastfeeding, gestational age, antibiotic treatment, type of delivery, and smoking status. This increase in risk was highly statistically significant.

The only other statistically significant predictor of mother-to-infant transmission was smoking status.

Of the 54 maternal carriers, 38 were nasal carriers, 9 were vaginal carriers, and 7 were both vaginal and nasal carriers. Among 11 of the newborns who acquired *S. aureus* from their carrier mothers, 9 had strains that were genetically identical to the mother's nasal strain, but only 2 had strains identical to the mother's vaginal strain. This suggests that the transmission was horizontal rather than vertical.

Two other pieces of evidence supported the hypothesis that most transmission was horizontal. Only 5% of newborns had acquired *S. aureus* by 1 hour after birth, but this figure increased to 8% at 24-48 hours and to 12% by 72-100 hours. Also, there were no significant differences in transmission rates between infants born vaginally and those born by cesarean section. If a vertical transmission were dominant, one would expect a greater rate of transmission in vaginal births. ■

**VITALS** **Disclosures:** Dr. Leshem and associates reported no conflicts of interest.

## Chronic Kidney Disease Ups Risk For Poor Pregnancy Outcomes

BY DOUG BRUNK

SAN DIEGO — Although pregnant women with chronic kidney disease face an elevated risk of adverse maternal and fetal outcomes, most are able to deliver a surviving newborn, according to results from a multicenter study.



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DR. ALGHONAIM

The current analysis is believed to be the second largest of its kind and supports earlier findings in the medical literature, Dr. Mohammed Alghonaim said in an interview during a poster session at the annual meeting of the American Society of Nephrology.

“These women need vigilant care,” said Dr. Alghonaim of the nephrology section in the department of medicine at King Saud University, Riyadh, Saudi Arabia. “If they've had a previous pregnancy, I would not advise them to get pregnant again if they have advanced-stage chronic kidney

disease because of the potential for adverse maternal and fetal outcomes.”

In a study led by his associate at the university, Dr. Abdulkareem Alsuwaida, researchers at five tertiary hospitals in the Middle East reviewed 101 pregnancies in women (mean age, 32 years) with chronic kidney disease to estimate the rate of fetal, maternal, and neonatal complications.

The mean serum preconception creatinine concentration was 81.2  $\mu\text{mol/L}$ , and the mean 24-hour urine proteinuria was 1.97 g/day. A total of 21 women (21%) had renal impairment, with a mean serum creatinine of 144  $\mu\text{mol/L}$ .

In 10 pregnancies (10%), levels of serum creatinine rose more than 25% from preconception levels. Overall maternal and fetal complications included cesarean section (39%), preeclampsia (23%), preterm delivery (22%, with 4% delivered at less than 30 weeks' gestation), and intrauterine growth retardation (19%). Six infants (6%) were stillborn.

“Renal impairment was the most important predictor for both maternal and fetal complications,” Dr. Alghonaim said. ■

**VITALS** **Disclosures:** Dr. Alghonaim said he had no financial conflicts of interest.