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REPLY

Sudden infant death syndrome (SIDS) has been linked to such environmental factors as maternal smoking, infections, drug abuse, and air pollution. Endocrine-disrupting chemicals (EDCs) are an emerging contributor to this syndrome. Recent evidence suggests that both brainstem and inner ear abnormalities, which affect respiratory control, are risk factors for SIDs.[1] The extent to which EDCs cross placental and the blood-brain barriers to affect the auditory brainstem and hypothalamus is largely unknown. Pusiol et al[2] have demonstrated that organochlorine pesticides (OCPs) and organophosphorus pesticides (OPPs) are detected in the brain samples of infants and fetuses who died of SIDS or sudden intrauterine death syndromes (SIUDS), respectively. It will be of great interest to learn the route of exposure in neonates (via breast milk or environmental contamination, such as house dust) and whether the levels of chemicals found by Pusiol et al are significantly higher in SIDS/SIUDS compared with healthy prenatal and neonatal brains from the same region of Italy and in studies of other populations. Pusiol et al make an important contribution by demonstrating that EDCs can cross the placental and blood-brain barrier during fetal development. It is well-known that OCPs and OPPs are associated with neurotoxicity and neurodegeneration[3]; therefore, the presence of these EDCs at parts-per-million levels in fetal and neonatal brain tissue is concerning, per se. OCPs and OPPs are primarily targeted against the cholinergic system,[3] which is intriguing because automatic responses controlled by the brainstem, such as respiration, are modulated primarily by acetylcholine neurotransmission. Thus, determining whether these OCPs and OPPs are linked to SIDS/SIUDS via the cholinergic pathway or instead via their known effects on hormonal signaling pathways is an important and open question for the future. ■

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Confusion between analytic validity and clinical validity

TO THE EDITORS: Recently Lefkowitz et al[1] (Sequenom Laboratories, San Diego, CA) reported a validation study of fetal/placental copy number variants by sequencing the cell-free DNA of maternal plasma. The clinical sensitivity was 97.7% (42 of 43 copy number variants detected).

Unfortunately, the authors have confused the concepts of analytic validity (the correct response for the sample tested) with clinical validity (the correct response for the patient tested). Among the 43 cases, 9 were identified by cell-free DNA sequencing as being autosomal trisomies (3 trisomy 8, 1 trisomy 14, 3 trisomy 16, 1 trisomy 21, and 2 trisomy 22). All 9 had normal karyotypes (8 after amniocentesis and 1 after chorionic villus sampling). Ordinarily, these 9 would be classified as confined placental mosaicisms and the test results