and provides for some flexibility in approach, which may be the best it can do, both ethically and legally.

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Since publication of their article, the authors report no further potential conflict of interest.


Noninvasive Prenatal Diagnosis of a Fetal Microdeletion Syndrome

TO THE EDITOR: The definitive diagnosis of fetal aneuploidy and genomic imbalances requires invasive collection of fetal cells through amniocentesis or chorionic villus sampling. These methods are associated with fetal loss and parental anxiety. Analyses of DNA in maternal plasma have shown the potential for noninvasive diagnosis of common aneuploidies.

A couple presented for prenatal genetic counseling at the Magee–Womens Hospital of the University of Pittsburgh Medical Center. They had previously had a child with developmental delay and dysmorphic features in whom a paternally inherited 4.2-Mb deletion on chromosome 12 between bands 12p11.22 and 12p12.1 had been diagnosed (Fig. 1A). Amniocentesis was performed at 21 weeks of gestation, and microarray-based comparative genomic hybridization identified the same heterozygous deletion in the male fetus (Fig. 1B).

A maternal blood sample was drawn at 35 weeks of gestation, and plasma DNA was extracted without further enrichment. Real-time polymerase-chain-reaction assay revealed that the relative prevalence of fetal DNA was 5.7%. The maternal plasma DNA was then used as a substrate for Illumina HiSeq2000 DNA sequencing, generating 243,340,714 single-end reads, of which 75% mapped uniquely and perfectly to the Genome Reference Consortium human genome (build 37), GRCh37. Seven maternal plasma samples in which both the mother and fetus...
were known to be diploid for chromosomes 12 and 14 were also sequenced as reference libraries. Using our previously described method,2 we determined whether the maternal sample (PL565) was diploid in each of 22 nonoverlapping 4-Mb regions on chromosomes 12 and 14 through a pairwise comparison with each of the reference libraries. We detected a 4-Mb depletion in DNA copy number on chromosome 12p in PL565 in all seven pairwise comparisons with a normal sample (adjusted P≤0.05 for all comparisons) (Fig. S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org). Tests for all other 21 regions resulted in nonsignificant adjusted P values for all seven pairwise comparisons (Table S1 in the Supplementary Appendix).

In summary, we have shown proof of concept that a fetal chromosomal microdeletion can be identified by means of noninvasive analysis of DNA in maternal plasma.

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CORRECTIONS

SHANK3, the Synapse, and Autism (July 14, 2011;365:173-5). The phrase “lower amplitude and frequency of action potentials” should have been “lower amplitude and frequency of miniature excitatory postsynaptic currents (mEPSCs)” in three instances: the first sentence of the fifth paragraph (page 173), beginning “Consistent . . . ”; the fourth sentence of the figure legend (page 175), beginning “Dendrites . . . ”; and the third sentence of the penultimate paragraph (page 175), beginning “Given . . . . ” The article is correct at NEJM.org.

Specialist Physician Practices as Patient-Centered Medical Homes (April 29, 2010;362:1555-8). In the fourth paragraph, beginning “The extent . . . ” (page 1556), the number of practices mentioned in the third sentence should have been 372, rather than 373. In the fifth paragraph (page 1556), the percentages of practices given in the first sentence should have been 84.6%, 10.3%, and 1.7%, rather than 81%, 12.5%, and 2.7%. Because one pulmonary practice was counted twice and the weights used to calculate values given in the table were not the final weights, the reported percentages of specialist practices serving as primary care physicians were incorrect. The article is correct at NEJM.org.

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