

there is no reason why clearly abnormal results on compression ultrasonography would not establish a firm diagnosis of DVT. Furthermore, in a study of the use of negative results on compression ultrasonography during pregnancy or the postpartum period, Le Gal et al.¹ found that no patient with a negative compression ultrasonogram had a thromboembolic event after 3 months of follow-up. However, any diagnostic test must be interpreted in the clinical context, and if any doubt exists, further diagnostic testing should be performed.

Dholakia and De Mendonca state that CTPA is a better diagnostic tool than ventilation–perfusion scanning. We cannot dispute this point except to note that many radiology departments have a strong preference for one imaging study or another, especially for use in pregnant patients. A survey of members of the Society of Thoracic Radiology reported that 53% perform CTPA as the initial study for pregnant women with suspected pulmonary embolism, whereas 30% begin with ventilation–perfusion scanning.² Furthermore, recent data involving nonpregnant patients suggest that CTPA may be overly sensitive, detecting microemboli that may not be clinically significant.³

Hoftman is correct that the ASRA recommends the initiation of low-molecular-weight heparin no earlier than 24 hours postoperatively, regardless of the anesthetic technique used, and that the first dose of low-molecular-weight heparin should be delayed for at least 2 hours after an epidural cath-

eter is removed.⁴ In our practice (and, we assume, in the vast majority of obstetric practices), the epidural catheter is removed at the conclusion of a cesarean delivery, so that a 24-hour postoperative delay in restarting therapeutic low-molecular-weight heparin is the same as a 24-hour post-catheter delay. The primary authors of the ASRA paper have more recently stated that thromboprophylaxis “should be held until at least 12 hours after vaginal delivery or epidural removal (whichever is later). After cesarean delivery, thromboprophylaxis should be held for at least 24 hours.”⁵

Paul E. Marik, M.D.

Lauren A. Plante, M.D., M.P.H.

Thomas Jefferson University
Philadelphia, PA 19107
paul.marik@jefferson.edu

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Prevalence of Mitochondrial 1555A→G Mutation in European Children

TO THE EDITOR: Aminoglycoside antibiotics are used worldwide to treat gram-negative sepsis. Since these drugs are ototoxic and nephrotoxic, drug levels are closely monitored. However, their effect on patients with the mitochondrial DNA mutation m.1555A→G is dramatic. Carriers of this mutation have permanent, profound hearing loss after receiving aminoglycosides, even when drug levels are within the therapeutic range.^{1,2} A review of previous studies indicates that after aminoglycoside exposure, penetrance of deafness in this population is close to 100%.³

Estimates of the prevalence of the m.1555A→G mutation have been hampered because of the small numbers of patients in such studies, many of which have involved the ascertainment of either one or a few patients. We genotyped the m.1555A→G variant in the Avon Longitudinal Study of Parents and Children (ALSPAC) birth cohort, a cohort of children who were not selected for hearing loss (www.bristol.ac.uk/alspac).⁴ Pure-tone audiometry and tympanometry were performed prospectively in children at ages 7 and 9 years. Of 9371 children who were tested, 18 had

the m.1555A→G mutation, providing a population prevalence of 1 in 520, or 0.19% (95% confidence interval, 0.10 to 0.28) (for details, see the Supplementary Appendix, available with the full text of this letter at NEJM.org). The children with the mutation all had hearing thresholds in the clinically normal range at 9 years, indicating that only

genetic testing could have revealed those at risk for deafness (Fig. 1). (See the Supplementary Appendix for details regarding hearing thresholds and tympanometry results for the entire cohort.)

None of the children had a history of admission to a neonatal intensive care unit, where children most commonly receive aminoglycosides.

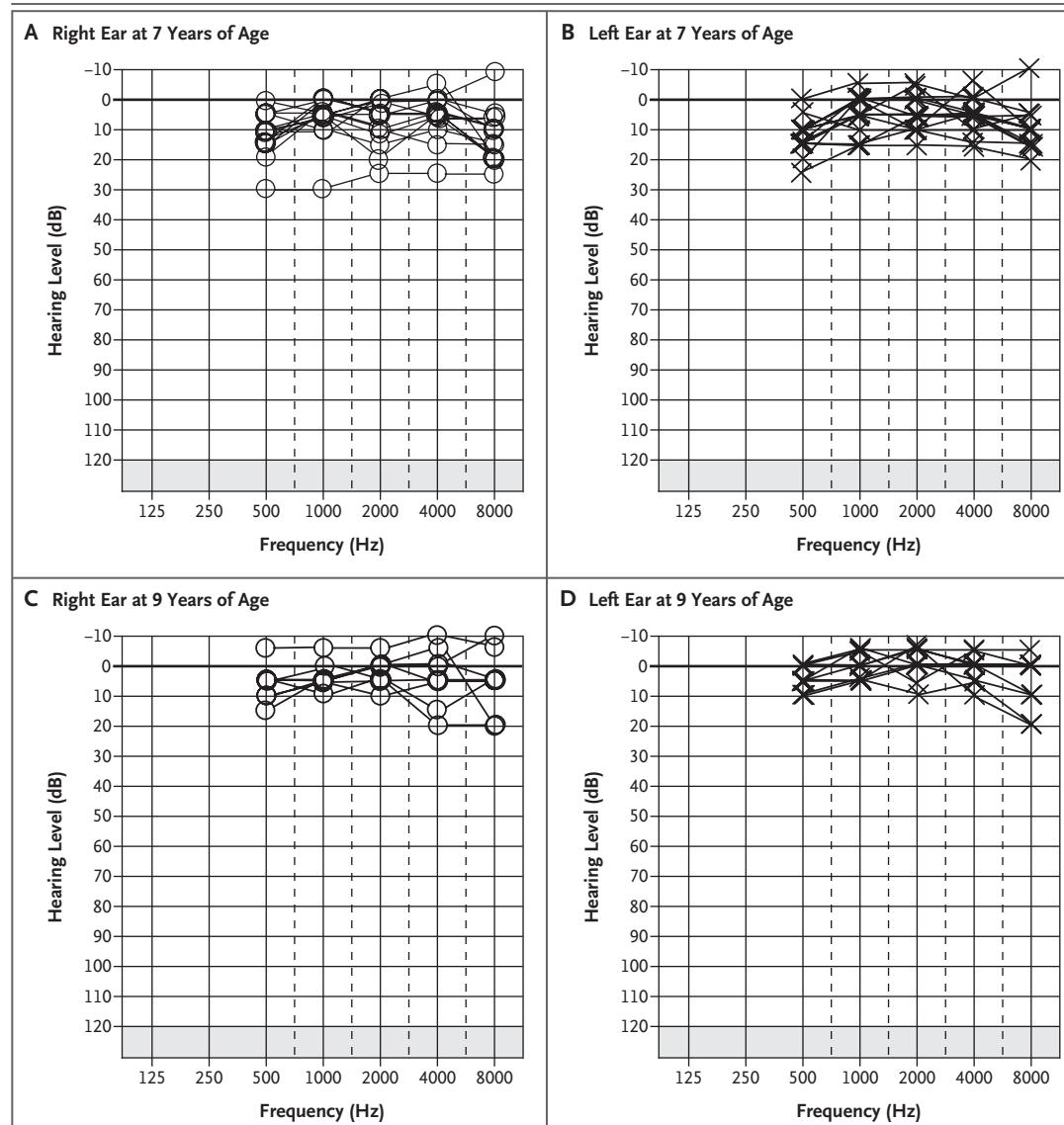


Figure 1. Results of Pure-Tone Audiometry in Children with the m.1555A→G Genotype.

Of 18 children with the m.1555A→G mutation, audiometric data were available for 14 at the age of 7 years and for 9 at the age of 9 years. The results of testing of the right ear (Panel A, circles) and the left ear (Panel B, crosses) are shown in the 7-year-olds. One of these children had a hearing threshold of 25 to 30 dB at 0.5 to 8 kHz in the right ear only. This child had mild eustachian-tube dysfunction on tympanometry. A second child had a slightly raised threshold of 25 dB at 500 Hz in the left ear only. At the age of 9 years, both of these children had thresholds of less than 20 dB at all frequencies, and all the children who underwent testing had normal hearing thresholds in both ears (Panels C and D).

This finding is consistent with a lack of penetrance of the mutation in this cohort.

On the basis of a mutation frequency of 0.19% in this population, genetic screening before aminoglycoside administration is cost-effective when balanced against the costs of lifelong deafness or the need for cochlear implantation.⁵ In this issue of the *Journal*, a letter by Vandebona et al.⁶ reports a prevalence of 0.21% for the m.1555A→G mutation in an aging population of European descent, but the prevalence of the mutation in non-European populations is unknown. Clearly, robust studies involving other ethnic groups are required to determine whether screening is appropriate.

On the basis of our findings, we recommend that elective genetic testing be performed on a case-by-case basis to prevent hearing loss, although in an acute, life-threatening situation, the best interests of the patient may require the administration of aminoglycosides before the results of genetic testing are available. Children with leukemia and patients with tuberculosis could be tested at diagnosis, and those allergic to beta-lactam antibiotics could be tested in the surgical outpatient department. Universal screening of neonates would not be effective in preventing 100% of deafness related to m.1555A→G, since admission to a neonatal intensive care unit usually occurs before such screening could take place. Screening all pregnant women for the mutation would be an alternative approach, since the mutation is maternally inherited and is almost al-

ways homoplasmic. Such an approach would not detect low levels of heteroplasmy.

Maria Bitner-Glindzicz, F.R.C.P., Ph.D.

Marcus Pembrey, F.R.C.P., F.Med.Sci.

Andrew Duncan, Ph.D.

UCL Institute of Child Health

London WC1N 1EH, United Kingdom

mbitner@ich.ucl.ac.uk

Jon Heron, Ph.D.

Susan M. Ring, Ph.D.

Amanda Hall, Ph.D.

University of Bristol

Bristol BS8 1TH, United Kingdom

Shamima Rahman, F.R.C.P.C.H., Ph.D.

MRC Centre for Neuromuscular Diseases

London WC1N 3BG, United Kingdom

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Prevalence of Mitochondrial 1555A→G Mutation in Adults of European Descent

TO THE EDITOR: Sensorineural hearing loss is the most common type of sensory impairment worldwide.¹ We have found that pathogenic mitochondrial DNA (mtDNA) mutations, such as the m.3243A→G mutation associated with mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS), are prevalent and can cause sensorineural hearing loss in adults of European descent.² Polymorphisms within mtDNA can modify a patient's risk of hearing loss.³ The m.1555A→G mutation, which is located in the 12S ribosomal RNA gene of the mitochondrial ge-

nome, is known to cause hearing loss, especially after exposure to aminoglycoside antibiotics.⁴

We prospectively collected audiologic data and DNA from blood and hair-follicle samples from 2856 subjects over the age of 49 years who were noninstitutionalized permanent residents of two suburban areas west of Sydney (known as the Blue Mountains Hearing Study cohort)² and screened them for the m.1555A→G mutation, using polymerase-chain-reaction-restriction-fragment-length polymorphism techniques. We also carried out mitochondrial DNA haplogroup