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Early childhood hearing loss: Clinical and molecular genetics. An educational slide set of the American College of Medical Genetics

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An educational slide set entitled "Early Childhood Hearing Loss: Clinical and Molecular Genetics" is offered by the American College of Medical Genetics (ACMG). The slide set is produced in Microsoft PowerPoint 2002. It is extensively illustrated and supported with teaching tools, explanations of each slide and figure, links to Internet resources, and a bibliography. The slide set is expected to be used as a resource for self-directed learning and in support of medical genetics teaching activities. The slide set is available through the ACMG (http://www.acmg.net) for $20, plus applicable tax and shipping. It is the first in a series of educational slide sets to be developed by the ACMG. ***Genet Med* 2003:5(4):338–341.**

Key Words: *education, hearing loss, deafness, slides*

Hearing loss affects 1 to 3 per 1000 infants born in the United States. More than half of early childhood hearing loss has a genetic etiology. Rapid advances in gene discovery and mutation identification have revealed extensive genetic heterogeneity.[1] Recognizing the need for comprehensive continuing education in this fast moving area of clinical and molecular genetics, a slide set on early childhood hearing loss was developed under the direction of the ACMG Education and CME committee in 2000. Quickly outdated by the continuing accomplishments in the field, the original slide set was revised in early 2002 by a six-member working group, with comments from a four-member review panel and the Education and CME committee of the ACMG. The revised slide set was approved by the ACMG Board of Directors in January 2003.

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**Slide set working group (in alphabetical order); #Slide set reviewers (in alphabetical order).*

Four sample slides, in Notes Page View Format, are available via the ArticlePlus feature at the Genetics in Medicine *Web site, www.geneticsinmedicine.org.*

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This newly revised slide set is intended as an educational resource for both self-directed learning and in support of medical genetics teaching activities.[1] As a self-directed learning tool, it provides comprehensive coverage of the clinical and molecular genetic aspects of hearing loss, complete with references and resources for further study. As a resource for teaching activities, it includes talking points for speakers and teaching tools such as learning objectives (Table 1), sample review questions (Table 2), and a content outline (Table 3).

The charge and mission of the Education and CME committee of the ACMG includes a responsibility to "plan, organize and conduct various educational activities of the College." The development of this slide set supports this educational mission. It is the first in a series of educational slide sets planned by the ACMG. At the present time, the College does not plan to offer credit for review of the slide set.

Format

The slide set is produced in Microsoft PowerPoint 2002 and is available on CD. The CD is compatible with both Mac and PC platforms. The CD is programmed to auto-launch the slide set in the Notes Page View format of PowerPoint. Additional instructions for manually launching the program are provided on the back of the CD's cover sleeve. The notes sections of the slides can also be accessed manually, by selecting "View" and "Notes Page" from the top menu bar of PowerPoint. System requirements for running the CD are as follows: PC—Windows 98 or greater, Microsoft PowerPoint 97 or greater; Macintosh—OS 9 or greater, Microsoft PowerPoint 97 or greater. The slide set contains 68 slides and is extensively illustrated with diagrams, images, and photographs. Due to its

Table 1
Learning objectives

Upon completion of this educational activity, participants should be able to do the following:

1. Cite the incidence and etiologies of early childhood hearing loss in the United States.
2. Describe the most common causes of congenital genetic hearing loss and recognize their clinical features.
3. Provide basic information about recurrence risks associated with common forms of genetic hearing loss.
4. Identify and utilize resources for clinical genetics consultation, genetic counseling, and genetic testing for hearing loss and other genetic disorders.
5. Appreciate the complexity of medical genetics and understand the role of the clinical geneticist, genetic counselor, and laboratory geneticist in the care of patients and families with hearing loss and other genetic disorders.
6. Recognize the value and potential benefits of appropriate referral and a multidisciplinary approach that includes clinical genetics and genetic counseling for the care of patients and families with hearing loss and other genetic disorders.

Table 2
Slide set review questions

Questions	Possible answers
1. Approximately what percentage of early childhood hearing loss in the United States is believed to be primarily genetic in etiology?	A. 10% B. 40% C. 60% D. 90%
2. Approximately what percentage of early childhood genetic hearing loss is nonsyndromic?	A. 5% B. 30% C. 70% D. 95%
3. The carrier rate for *GJB2* (Connexin 26) gene mutations in the United States Caucasian population is estimated to be approximately:	A. 1 in 10 B. 1 in 35 C. 1 in 375 D. 1 in 500
4. The carrier rate for *GJB2* (Connexin 26) gene mutations in the Ashkenazi Jewish population is estimated to be approximately:	A. 1 in 20 B. 1 in 50 C. 1 in 100 D. 1 in 500
5. Nonsyndromic hearing loss caused by recessive mutations in the gene *GJB2* (Connexin 26):	A. Varies from mild to profound. B. Can vary among siblings. C. Carries a 25% recurrence risk for carrier couples. D. All of the above.
6. Hearing loss associated with mutations in *SLC26A4:*	A. Has been associated with nonsyndromic hearing loss but not with syndromic hearing loss. B. Is inherited in an autosomal dominant manner. C. May also be associated with enlarged vestibular aqueduct and/or Mondini malformation. D. All of the above.
7. With regard to Usher syndrome (US):	A. US Type I is a genetically heterogeneous disorder. B. Children with US Type II may be developmentally delayed because of vestibular abnormalities. C. US Type III is the most severe form with the earliest age of onset and most severe degree of hearing loss and the earliest age of onset of retinitis pigmentosa. D. All of the above.
8. A mutation in the mitochondrial 12S rRNA gene known as A1555G:	A. Has been associated with genetic susceptibility to aminoglycoside induced ototoxicity. B. Has been associated with hearing loss in the absence exposure to aminoglycoside antibiotics. C. Is inherited only from mothers and never from fathers. D. All of the above.

comprehensive content and numerous illustrations, the size of the PowerPoint file is ≈20 megabytes.

Background material for each slide is provided in the Notes Page View format of PowerPoint. It includes learning objectives (Table 1), review questions (Table 2) with answers and explanations, a content outline (Table 3), explanations of each slide, detailed descriptions of the clinical and scientific content, figure legends, talking points for speakers who use the slides in teaching activities, citations for images, funding sources, suggested reading, and references.

When the slide set is used in teaching presentations, users can select "View" and "Slide Show" from the top menu bar of PowerPoint, or click on the slide show icon in the lower menu bar of PowerPoint. This will launch the slide show presentation, hiding the notes sections of the slides, and showing only the presentation content of the slides.

Content

Focused primarily on early childhood hearing loss, the slide set contains a comprehensive review of genetic hearing loss, highlights its extreme etiologic and phenotypic heterogeneity, and includes a discussion of genetic forms of hearing loss characterized by later onset.

The slide set opens with introductory materials including the title slide, recognition of the working group and reviewers, and a legal statement slide. The notes sections of these slides contain the learning objectives (Table 1), review questions (Table 2), and content outline (Table 3).

The slide set continues with an idealized case (Fig. 1 and Table 4), an introduction to the biomechanics of hearing, and a description of the basic tools of audiology. The incidence and etiologies of early childhood hearing loss are described, as are the various patterns of inheritance of genetic traits and conditions.

Several common forms of syndromic hearing loss and their genetic bases are highlighted including branchio-oto-renal

Table 3
Slide set content outline

Topic	Number of slides
Introductory materials	3
Case Presentation	2
Introduction	
A. How hearing occurs	2
B. Audiologic assessment of hearing	3
Early childhood hearing loss	
A. Incidence and etiologies	3
B. Modes of inheritance	2
C. Genetic causes of hearing loss	
1. Syndromic forms of hearing loss	16
2. Nonsyndromic forms of hearing loss	8
3. Online resources for additional information on genetic forms of hearing loss	2
GJB2: The most common cause of nonsyndromic genetic hearing loss	
A. *GJB2* function and the physiologic basis of *GJB2*-based hearing loss	3
B. Incidence of *GJB2*-based hearing loss	1
C. Genetic mutations associated with *GJB2*-based hearing loss	2
Summary of ACMG statements and guidelines on hearing loss	4
The role of genetics in evaluation and care of patients with genetic disease	
A. How a genetics consult will help patients and families	1
B. How to identify and utilize clinical genetics resources for patient care	2
C. How genetic testing can be used to assist patients and families	1
D. How to identify and utilize clinical genetics resources for genetic testing	1
Resolution of presented case	
A. DNA test results	1
B. Interpretation of test results	1
C. Consideration of test limitations	1
Other resources for information and continuing education	3
Summary	3
Acknowledgements	1
Suggested reading, online resources, references, answers to review questions	2

(BOR) syndrome, Waardenburg syndrome, Pendred syndrome, Jervell and Lange-Nielsen syndrome (JLNS), Alport syndrome, and Usher syndrome, among others. The genes known to be associated with nonsyndromic hearing loss are delineated and a description of Internet resources for additional information and continued learning is provided.

The most common cause of nonsyndromic genetic hearing loss, mutations in the gene *GJB2*, encoding Connexin 26, is explored. The slides describe gap junction channel function and provide a possible explanation of *GJB2*-based hearing loss. The frequency of *GJB2*-based hearing loss and a summary of common genetic mutations in *GJB2* are also discussed.

ACMG statements and guidelines on newborn screening for hearing loss and the etiologic diagnosis of congenital hearing loss are reiterated, highlighting the clinical applications of knowledge about the molecular genetics of hearing loss.[2,3] Also included are descriptions of the role of clinical genetics and genetic counseling in evaluation and care of patients with hearing loss and other genetic disorders, the potential benefits of clinical genetics consultation, resources for the identification and utilization of clinical genetics services, the capabilities, limitations, benefits and risks of genetic testing, and mechanisms for identifying and utilizing laboratory genetics services.

In the conclusion slides, the case presented earlier (Fig. 1 and Table 4) is resolved through the presentation of DNA test results, with interpretation of the results, their implications, and limitations. Additional resources for information and continuing education are provided, as is a series of summary slides. Acknowledgments, additional online resources, suggested reading, references, and answers to review questions are found in the notes sections of these final slides.

Availability

The slide set is available through the Web site of the American College of Medical Genetics: http://www.acmg.net. The slide set is offered for $20, plus $5 shipping and handling ($10 shipping and handling for overseas or express rate shipping) and applicable sales tax.

Four sample slides, in Notes Page View Format, are available via the ArticlePlus feature at the Web site of the journal *Genetics in Medicine*, 2003: http://www.geneticsinmedicine.org

Future ACMG slide sets

Working groups are assembled to develop additional educational slide sets in a format similar to this one. Slide sets are planned on cystic fibrosis, newborn screening, and the genetics of cardiovascular disease. Suggestions on topics for future slide sets are welcome and can be directed to Raye Lynn Alford, PhD, FACMG, Chair of the 2003 ACMG Education and CME committee.

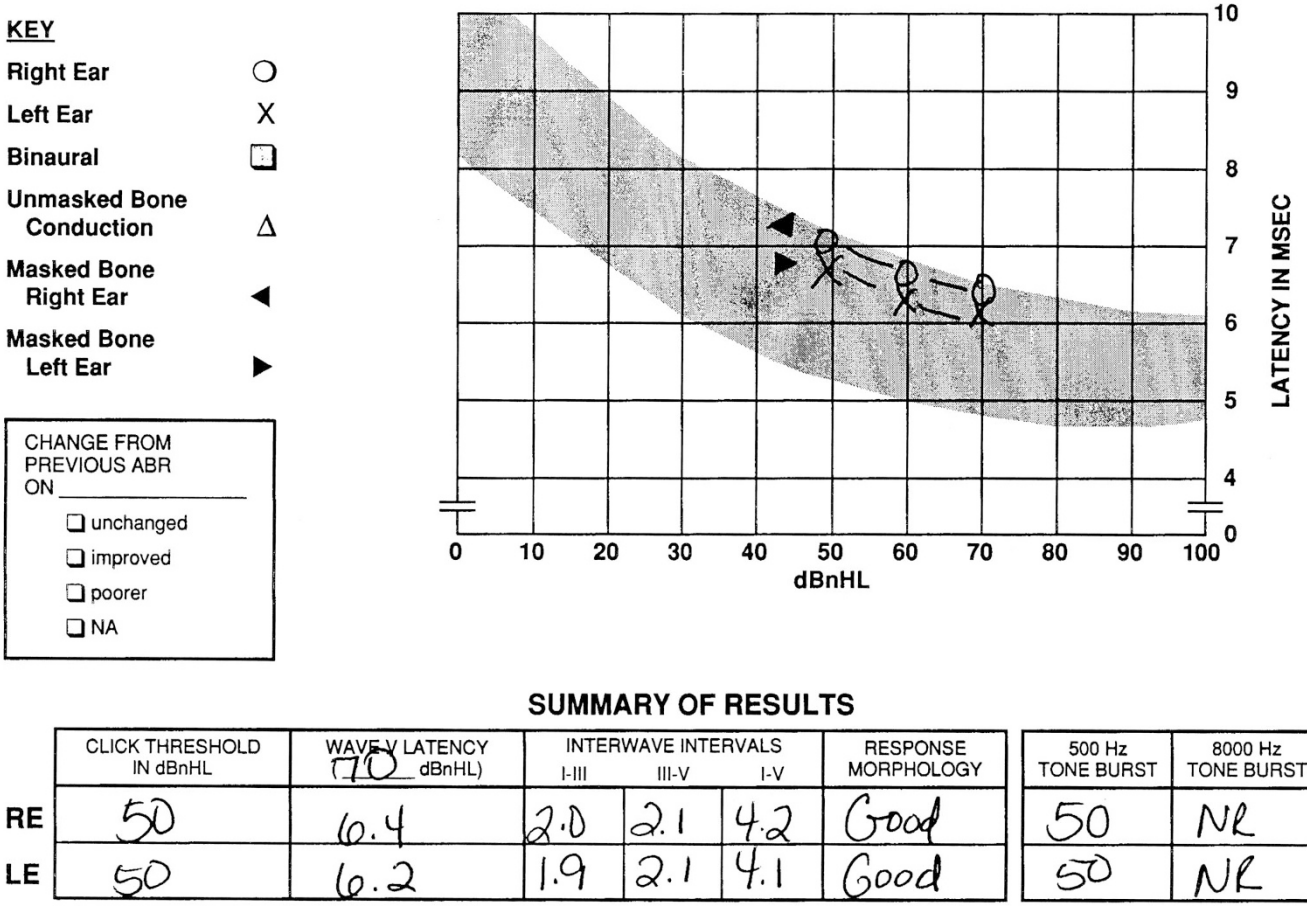

Fig. 1 Case presentation. Idealized click ABR evaluation for a child with moderate to severe sensorineural hearing loss. *X*-axis shows the decibels (dB) normed to hearing level. *Y*-axis shows the Wave V Latency in milliseconds. The gray area delineates normal ranges. Wave V latency was not obtained below 50 dB (decibels). Response to 500-Hz tone burst occurred at 50 dB. No response to tone burst at 8000 Hz was obtained. Bone and air conduction thresholds were matching, indicating a sensorineural hearing loss. The 50-dB click threshold indicates a moderate to severe hearing loss.

Table 4
Case presentation

The following case presentation is provided early in the slide set, to frame the educational activity:

- JD is a healthy 2-month-old Caucasian female, product of a normal pregnancy and delivery.
- Newborn hearing screening by OAE at day 2 of life indicated a possible hearing loss. Follow-up testing by diagnostic ABR at 1 month of age confirmed at least a moderate to severe, bilateral, sensorineural hearing loss (Fig. 1).
- JD was born at 38.5 weeks gestational age.
- Birth weight was 3.2 kg (7.05 pounds).
- JD has no history of ototoxic medications, asphyxia, hyperbilirubinemia, or infection. TORCH titers are negative. (The TORCH test measures antibodies to toxoplasmosis, other infections, rubella [german measles], cytomegalovirus, and herpes simplex virus. Other infections also tested for in a TORCH test may include syphilis, hepatitis B, coxsackie, Epstein-Barr, varicella zoster, and human parvovirus.)
- JD has no additional clinical findings, dysmorphic features, or syndromic stigmata.
- There is no family history of hearing loss. JD's parents both have normal hearing.
- JD's mother has just asked you why her daughter is deaf.

References

1. Early Childhood Hearing Loss: Clinical and Molecular Genetics. An educational slide set of the American College of Medical Genetics. American College of Medical Genetics World Wide Web home page, 2003, http://www.acmg.net.
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