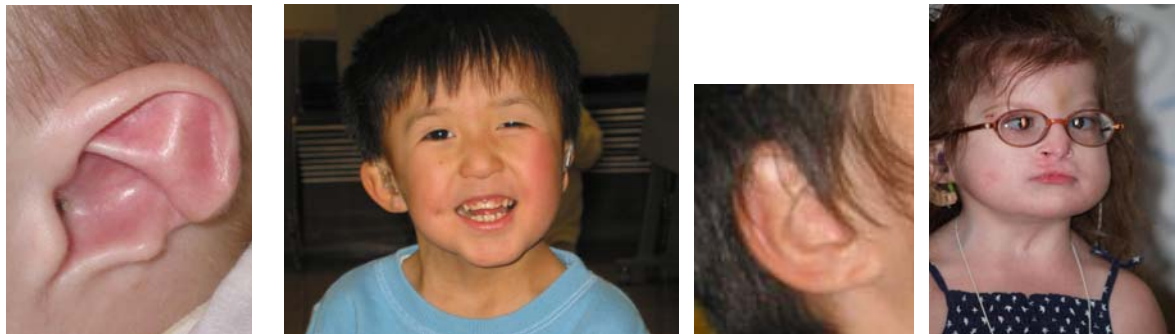


CHARGE Syndrome: Multiple Congenital Anomalies Including Disorders of All Senses and Speech, Language, Feeding, Swallowing, and Behavior

Ears and Hearing by James W. Thelin and Lori A. Swanson

CHARGE syndrome is a genetic disorder (one in 10,000 to 15,000 live births) with multiple physical, sensory, and behavioral anomalies. Children with CHARGE typically undergo 10 surgeries before age 3. Although early mortality rates have been 10% to 20%, survival rates have improved with cardiac treatment. Individuals with CHARGE may have deficits in every sensory modality and frequently exhibit challenging behaviors. CHARGE is presently the leading genetic cause of deaf-blindness at birth in the United States.

For those children who survive the challenges of early life, parents focus their concerns on development, communication, and education. The ultimate level of functioning is significantly enhanced by early intervention from audiologists and speech-language pathologists. In children with CHARGE syndrome, the value of services offered by SLPs and audiologists is enhanced when other aspects of the disorder, such as clinical and genetic diagnosis, feeding and swallowing, behavior, and education, are understood. Information on behavior and development appeared in a 2004 special CHARGE syndrome edition of the *American Journal of Medical Genetics*. [available at www.chargesyndrome.org Resources Tab]



Ears and Hearing

In CHARGE, every part of the auditory system may be involved. External ear anomalies are so distinctive that, at times, it is possible to make a preliminary diagnosis of the syndrome on the basis of pinna shape alone. (See photos above right and page 7, right.) Middle-ear ossicular anomalies can cause conductive losses as great as 70 dB and chronic otitis media secondary to eustachian tube dysfunction is nearly universal. Underdevelopment of the cochlear and vestibular structures (including Mondini's dysplasia) is common and often causes sensory losses in hearing and balance. Auditory nerve diameter may be reduced; latencies may be prolonged on auditory brainstem response tests; and agenesis of the corpus callosum has been reported. Typical losses are mixed losses with very large conductive components and substantial cochlear involvement that is usually greatest in the high frequencies. The prevalence of severe-profound hearing loss is approximately 50%.

Audiologic evaluation of children with CHARGE is challenging for several reasons:

- 1) Many children do not speak or sign.
- 2) Visual problems interfere with sound field audiometry.
- 3) Tactile defensiveness is common.
- 4) Hearing losses are often large and asymmetrical.
- 5) There may be resistance to and risks associated with sedation.

Aural habilitation also can be made difficult by: soft pinnas that do not support hearing aids well, large hearing losses that require tightly fitting earmolds to prevent feedback, and stenosed ear canals with drainage from chronic otitis media. Selecting and fitting appropriate amplification is often difficult. Some individuals have benefitted from cochlear implants and others from bone-anchored hearing aids.

Despite these challenges associated with multiple physical and sensory deficits, many children with CHARGE who are significantly involved have learned to communicate using symbolic language. Those with the greatest success have had consistent and innovative audiologic intervention very early in life and communication training (spoken and signed language)-even when the child's health was poor and hospitalizations were frequent.

Communication and Related Issues

About 60% of children with CHARGE acquire symbolic language and communicate with spoken language, signs, and/or visual symbols. The mechanics of speech may be affected by craniofacial anomalies, breathing problems, and clefts. Success in acquiring symbolic language is related to communication training begun before age 3, success in overcoming hearing loss, and the ability to walk independently. One explanation for this latter finding is that an ambulatory child has the ability to move into his or her own communication bubble-the space in which the child can see and hear a communication partner optimally. Among children who use symbolic language, however, speech and language problems are common. Children who use symbolic forms often have problems in maintaining a topic and in effective turn-taking.

Children who do not acquire symbolic language may learn to demonstrate higher forms of prelinguistic communication such as use of gestures and vocalizations to regulate the behavior of others. Those who are most impaired may produce pre-intentional behaviors, which parents and caregivers may interpret as intentional. Since children with CHARGE often demonstrate a high rate of repetitive behaviors, parents and caregivers may have difficulty assigning meaning to potential communication acts.

Adapted Prelinguistic Milieu Teaching (PMT, Warren & Yoder, 2002) is currently being tested as a means to increase the rate and variety of prelinguistic communications in the deaf-blind population by Bashinski and Brady at the University of Kansas. PMT focuses on increasing use of gestural forms (e.g., distal points, gives, shows, and leading gestures), increasing rate of communication, and improving parent responsivity, which appear to be predictors of increased communication skills in children with disabilities (Brady, Marquis, Fleming, & McLean, 2004). Gestures may have some advantages over symbolic forms of communication. Unlike signs, they are readily understood by most communication partners. Most importantly, gestures may facilitate understanding of the give and take between people that underlies communication.

Children with CHARGE often also have feeding and swallowing difficulties, behavior problems unique to the syndrome, and very special educational needs. Before CHARGE was recognized as a unique disorder, individuals with the disorder were believed to have a collection of unrelated anomalies. They received treatment from many specialists that was not coordinated. Now that CHARGE is recognized, it is clear that optimal treatment results from the collaboration of specialists in medicine, communication, behavior, and education.

Problems related to CHARGE often are inter-related, and communication is an essential part of an effective clinical response. As an example, investigators at the University of Tennessee asked parents how the communication of their child with CHARGE was affected by their child's behavior. The parents responded that in many cases an inability to communicate was the cause of inappropriate behavior.

Emerging evidence suggests that early intervention by speech-language pathologists, audiologists, and educators of the deaf can enhance the acquisition of symbolic language that is crucial to communication development, social interaction, and learning. Early and persistent intervention for speech, language, swallowing, and hearing disorders can greatly enhance the quality of life for children with CHARGE syndrome-even for those who have frequent illness and those who are severely involved. An increased awareness of CHARGE syndrome should lead to enhanced services provided by professionals in our field.

James W. Thelin is an associate professor in the Department of Audiology and Speech Pathology at the University of Tennessee, Knoxville (UTK). Contact him at jthelin@utk.edu.

Lori A. Swanson is an associate professor in the Department of Audiology and Speech Pathology at UTK. Contact her at lswanon@utk.edu.



Genetic Diagnosis

by Conny van Ravenswaaij

Although CHARGE syndrome is usually sporadic, there always has been evidence that it is caused by a genetic factor. The concordance rate in monozygotic twins is very high and affected sibling pairs do occur. We found a very small deletion of chromosome 8 in two children with CHARGE. This tiny region on chromosome 8 appeared to harbor a new gene: CHD7. Mutations in this gene were found in 16 of 17 well-selected patients. At present large groups of patients suspected for CHARGE syndrome are being studied and a mutation in CHD7 is found in about 60% of these patients. In the patients who fulfill the diagnostic clinical criteria, the mutation detection rate is as high as 90%. However, mutations can be found in patients who do not fulfill these criteria, and the mild end of the clinical spectrum is not yet known.

CHARGE syndrome has a recurrence risk of 1-2%. This can be explained by germ line mosaicism. That means that although the parent is not affected, some of his/her sperm or egg cells carry the same CHD7 mutation. Sometimes, in affected siblings, a mosaic mutation of CHD7 can be detected in one of the parents. In this situation the recurrence risk is increased. Therefore DNA studies are recommended in all parents of children with a CHD7 mutation. Prenatal diagnosis with 100% reliability is possible with chorionic villi sampling. A person with CHARGE syndrome has a risk of 50% to pass on the CHD7 mutation. However, infertility is very common in CHARGE syndrome and as a result parent-to-child transmission is rare. Further studies are in progress to determine if genes other than CHD7 can cause CHARGE syndrome.

Conny van Ravenswaaij is a clinical geneticist/cytogeneticist in the Department of Human Genetics at the University Medical Centre Groningen, the Netherlands.



Clinical Diagnosis

by Meg Hefner and Sandra L. H. Davenport

Although CHARGE syndrome is a genetic condition most often caused by mutations in the CHD7 gene (see Genetic Diagnosis, p. 40), the diagnosis is still clinical, based on the presence of specific major and minor characteristics. Beyond the major and minor diagnostic characteristics are many additional findings in CHARGE that may be critically important in management.

Major characteristics are ocular coloboma, choanal atresia, cranial nerve abnormalities (anosmia, facial palsy, severe suck and swallow incoordination), and characteristic ears (outer ear shape, ossicular anomalies and eustachian tube dysfunction, cochlear and/or semicircular canal abnormalities). The most common features in CHARGE are cochlear and semicircular canal anomalies, which are found in >90% of children with CHARGE when imaged by MRI. Minor characteristics are those which are common in CHARGE syndrome, but are either less specific to CHARGE (e.g., heart defects), or more difficult to evaluate consistently (e.g., characteristic CHARGE syndrome face). Minor characteristics are congenital heart defects, genital hypoplasia, renal anomalies, tracheo-esophageal fistula/esophageal atresia, cleft lip or palate, growth retardation, and characteristic face and hands.

Occasional findings in CHARGE syndrome are features which may not be diagnostic by themselves, but which support a diagnosis of CHARGE and may be important in management. These include DiGeorge sequence in the absence of 22q11.2 deletion, omphalocele or umbilical hernia, bony scoliosis or hemivertebrae and additional dysmorphic features (thumb or limb anomalies, short webbed neck with sloping shoulders, nipple anomalies). If a diagnosis of CHARGE syndrome is being considered in an older individual, the typical CHARGE behavioral profile may be helpful as well. Many other syndromes (especially 22q deletion syndrome and some chromosome abnormalities) have features which overlap with CHARGE. Diagnosis of CHARGE syndrome should be made by a medical geneticist familiar with CHARGE.

Children with CHARGE syndrome show marked delays in motor development due to vestibular dysfunction in combination with prolonged hospitalization, truncal hypotonia with ligamentous laxity, decreased visual acuity and hearing impairment. Many children are reluctant to crawl, often moving by scooting in a combat crawl, pushing with their feet in the supine position or using a five-point crawl (head down). The average age of walking is 3-4 years. Language development is delayed due to multiple sensory deficits, motor deficits, and delay in establishment of an appropriate communication system.

Although developmental delays might be expected in children with CHARGE syndrome, the incidence of cognitive impairment in CHARGE syndrome is probably 50% or less. Factors which correlate with better apparent development in the teen years include age of walking and degree of visual impairment. Some children with CHARGE syndrome have specific learning disabilities such as difficulty understanding math. Many adults with CHARGE syndrome live independently and several are college graduates.

Meg Hefner is a clinical associate professor, Division of Medical Genetics, Department of Pediatrics at Saint Louis University School of Medicine.

Sandra L. H. Davenport is a pediatric geneticist and developmental pediatrician in Bloomington, MN. She works with the Minnesota Deaf-Blind Project.



Feeding and Swallowing

by Sara Rosenfeld-Johnson

Feeding problems are common in individuals with CHARGE syndrome; the causes and severity of the feeding difficulties vary greatly. The most severe of the disorders is, as the medical diagnosis states, "dysphagia: not approved for oral feedings." In this case the child could not receive any liquids or foods by mouth. Swallow studies of individuals with this diagnosis have identified physiological deficits in the swallowing mechanism. Thus, food or liquid intake can result in choking, gagging, and/or food aspiration. These individuals cannot receive food or liquid by mouth until medical approval is given.

The medical diagnosis for the second group is "dysphagia: approved for only specified food or liquid textures." Swallow studies have identified, based on the physiological deficits in the swallowing mechanism, safe and unsafe food and liquid textures. These individuals will have a diet prescribed by a speech-language pathologist trained in feeding and swallowing therapy. Changes in food textures cannot be implemented without direct communication with the physician.

The third group consists of individuals with muscle deficits secondary to weakness and/or motor-planning disorders. The swallow mechanism is intact in this group, but the preparation of the bolus for swallowing is impaired. Weakness in the muscles of the jaw, lips and tongue is often seen.

There is an additional overlying problem seen in nearly all individuals with CHARGE syndrome: sensory deficits. A complete oral sensory examination will determine the presence of oral hyposensitivity, oral hypersensitivity, mixed oral sensitivity, or fluctuating oral sensitivity. Tactile defensiveness, a fear-response to the presence or placement of certain textures within the mouth, may be superimposed over any of these.

Sara Rosenfeld-Johnson is a speech-language pathologist and oral-motor specialist at TalkTools™/ Innovative Therapists International in Tucson, AZ.

Behavioral Phenotype

by Timothy S. Hartshorne

Children with CHARGE develop behavioral difficulties, some of which may be described as autistic-like, and obsessive-compulsive, with attention difficulties and tic disorders also present. There are potentially multiple sources for these difficulties, and research is attempting to sort them out. Multi-sensory impairments, communication frustrations, and physical pain and discomfort all have been implicated. However, some children with fairly good sensory abilities, adequate communication, and little apparent discomfort may still have challenging behavior. Cognitive impairment has been implicated in some but not all cases. It seems likely that some neuropsychological problems exist. Recent research supports the presence of executive dysfunction, or problems with shifting, initiating, inhibiting, or sustaining actions based on prefrontal cortex activity.

Another area being explored is the presence of a regulatory disorder making it difficult for the child to regulate complex processes such as their sleep-wake cycle, hunger-satiety cycle, their ability to console themselves, to manage their emotions, and to plan their motor activities. Recent research has found indications of significant sleep disorders in well over half of these children, which can have a significant impact on behavior. The presence of significant stress and perhaps Post-Traumatic Stress Disorder due to pain, illness, multiple surgeries, and difficulties experienced in school and sometimes at home is also being studied. Several researchers have found that the age the child first walks is a predictor for behavioral and communication difficulties. Most children with CHARGE walk by about 3 years of age, but those who walk later are at more risk for difficulties. The behavioral difficulties are frequently managed by medication, and a wide variety of drugs have been used. Children with CHARGE may have paradoxical reactions to medications, and frequently the drugs gradually lose their effectiveness. Well-developed behavioral interventions based on functional analysis of the behavior and involving functional communication training are important.

Timothy S. Hartshorne is a professor in the Department of Psychology at Central Michigan University.



Education

by Kathleen Stremel

Evidence has been accumulating that children with CHARGE derive the greatest benefit from early intervention and education programs that address functional hearing and vision simultaneously. Spoken and signed language together may benefit children with auditory and visual deficits. Children who are totally blind may need habilitation techniques that include tactile (e.g., touch cues, tactile sign language), movement, and sensorimotor strategies. Current early intervention and educational placements for children with CHARGE include a range of educational settings, including residential schools, separate schools, home schooling, separate classes, and regular classes. Perkins School for the Blind has the only classroom specifically for children with CHARGE.



A coordinated effort among families, early intervention specialists, and state deaf-blind projects must be a priority if children with CHARGE are to receive well-coordinated services, appropriate adaptations to access their environments, early communication systems, and intervention within the context of daily routines in natural environments. Educators in programs that serve these children are currently focusing on the following issues: the effects of multiple disabilities on educational outcomes, educational expectations with cochlear implantation, and pragmatics in communication. There is a great need for appropriate curricula for children with CHARGE, as well as parent training materials and qualified service providers.

The National Technical Assistance Consortium (NTAC) maintains the national census of individuals with deaf-blindness and provides technical assistance to deaf-blind projects in all states. These services will be continued by a new organization called the National Technical Assistance and Dissemination Center for Children and Youth Who are Deaf-Blind. The Web site for this new organization describes how the addresses for all state deaf-blind projects can be accessed. Children with CHARGE should be registered with their state deaf-blind project, which provides technical assistance to families and service providers for appropriate educational programming and other activities.

Kathleen Stremel is project director of the National Technical Assistance and Dissemination Center for Children and Youth Who Are Deaf-Blind, and is affiliated with the Teaching Research Institute at Western Oregon University.

References

Clinical and Genetic Diagnosis

Blake, K., Davenport, S.L.H., Hall, B.D., Hefner, M.A., Pagon, R., Williams, M.S., et al. (1998). CHARGE association - an update and review for the primary pediatrician. *Clinical Pediatrics*, 31, 159-174.

Hefner, M.A., & Davenport, S.L.H. (2002). *CHARGE syndrome: A management manual for parents, Version 2.1*. Columbia, MO: CHARGE Syndrome Foundation

Visser, L.E.L.M., van Ravenswaaij, C.M.A., Admiraal, R., Hurst, J.A., de Vries, B.B.A., Janssen, I.M., et al. (2004) Mutations in a new member of the chromodomain gene family cause CHARGE syndrome. *Nature Genetics*, 36, 955-957.

Hearing

Bauer, P.W., Wippold, F.J., 2nd, Goldin, J., & Lusk, R.P. (2002). Cochlear implantation in children with CHARGE association. *Archives of Otolaryngology Head & Neck Surgery*, 128(9), 1255-1262.

Edwards, B.M., Kileny, P.R., & Van Riper, L.A. (2002). CHARGE syndrome: a window of opportunity for audiologic intervention. *Pediatrics*, 110 (1 Pt 1), 119-126.

Shah, U.K., Ohlms, L.A., Neault, M.W., Willson, K.D., McGurit, W. F., Hobbs, et al. (1998). Otolgic management in children with the CHARGE association. *International Journal of Pediatric Otorhinolaryngology*, 44, 139-147.

Thelin, J.W., Hartshorne, T., & Hartshorne, N. (1999). Audiologic and educational management of hearing loss in CHARGE syndrome. *Journal of Educational Audiology*, 7, 34-41.

Communication

Brady, N.C., Marquis, J., Fleming, K., & McLean, L. (2004). Prelinguistic predictors of language growth in children with disabilities. *Journal of Speech, Language, and Hearing Research*, 47, 663-677.

Thelin, J.W., & Fussner, J.C. (2005). Factors related to the development of communication in CHARGE syndrome. *American Journal of Medical Genetics*, 133A, 282-290.

Yoder, P., & Warren, S. (2002). Effects of prelinguistic milieu teaching and parent responsivity education on dyads involving children with intellectual disabilities. *Journal of Speech, Language, and Hearing Research*, 45, 1158-1175.

References cont'd

Feeding and Swallowing

Rosenfeld-Johnson, S. (2001). *Oral-Motor Exercises for Speech Clarity*. Tucson, AZ: Innovative Therapists International.

Rosenfeld-Johnson, S. (2002). *The Drooling Program*. Tucson, AZ: Innovative Therapists International.

Rosenfeld-Johnson, S. (2005). *Assessment and Treatment of the Jaw: Putting it All Together-Sensory, Feeding and Speech*. Tucson, AZ: Innovative Therapists International.

Behavior

Brown, D. (2005). CHARGE syndrome "behaviors": Challenges or adaptations? *American Journal of Medical Genetics*, 133A, 268-272.

Hartshorne, T.S., & Cypher, A.D. (2004). Challenging behavior in CHARGE Syndrome. *Mental Health Aspects of Developmental Disabilities*, 7(2), 41-52.

Hartshorne, T.S., Grialou, T.L., & Parker, K.R. (2005). Autistic-like behavior in CHARGE syndrome. *American Journal of Medical Genetics*, 133A, 257-261.

Hartshorne, T.S., Hefner, M.A., & Davenport, S.L. (2005). Behavior in CHARGE syndrome: Introduction to the special topic. *American Journal of Medical Genetics*, 133A, 228-231.

Nicholas, J. (2005). Can specific deficits in executive functioning explain the behavioral characteristics of CHARGE syndrome: A case study. *American Journal of Medical Genetics*, 133A, 300-305.

Salem-Hartshorne, N., & Jacob, S. (2005). Adaptive behavior in children with CHARGE syndrome. *American Journal of Medical Genetics*, 133A, 262-267.

Education

Stremel, K., Haynes, D., & Killoran, J. (2001). It's never too early collaborating with state early childhood programs. *Deaf-Blind Perspectives*, 9(2), 3-6.

Stremel, K., & Malloy, P. (2006). Cochlear implants for young children who are deaf-blind. *Deaf-Blind Perspectives*, 12(3), 1-8.