CHARGE Syndrome

Second Edition

Timothy S. Hartshorne, PhD
Margaret A. Hefner, MS
Kim D. Blake, MD

Plural Publishing Inc.

PLURAL PUBLISHING
INC.

5521 Ruffin Road
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e-mail: information@pluralpublishing.com
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Foreword

This second edition of *CHARGE Syndrome* offers a significantly expanded and contemporary compilation of information on CHARGE syndrome (CS) and its protean manifestations and management issues. For early interventionists, health care providers, educators, families, and advocates of those impacted by CS, this textbook provides a tremendous foundation upon which to begin building a working understanding of the breadth and scope of challenges and opportunities presented by CS.

Since the first edition's publication in 2011, the interest in CHARGE and research on this syndrome have increased exponentially. As one result, this second edition incorporates expanded clinical content that covers the multiple organ systems and conditions that are associated with CS. The rapidly growing and evolving knowledge base about the clinical and developmental features of CS and the optimal management of specific conditions are presented in each of the chapters by clinicians with tremendous firsthand experience and unique expertise.

This valuable content is enhanced and refined by editorial oversight and contributions by three of the world-renowned experts on CHARGE (Tim Hartshorne, Meg Hefner, and Kim Blake). Their combined decades of research and work on CS have provided an outstanding perspective in editing this work. Their high-level editorial supervision has kept the authors tightly focused on CHARGE-related content, kept the material relevant to potential readership, and ensured the highest levels of validity and accuracy.

Taken as a whole, this second edition of *CHARGE Syndrome* offers a unique and superb foundational textbook on CHARGE. Whether the reader's background is academic, clinical, educational, research, or other domain, the content is readable at many levels, inclusive by means of its diverse chapters, and allows the reader to begin exploring and understanding the complexities of CS.

Daniel I. Choo, MD
Director, Division of Pediatric Otolaryngology—Head and Neck Surgery
Professor, UC Department of Pediatrics
UC Department of Otolaryngology—Head and Neck Surgery
Cincinnati Children's Hospital Medical Center
Cincinnati, Ohio





Introduction to CHARGE Syndrome

"Communication, communication, communication."

For more than 30 years, this has been the mantra regarding what children with CHARGE syndrome (CS) need. CS is a very complex syndrome encompassing a wide variety of medical, developmental, and personality traits. Many children struggle just to survive. However, the biggest barrier to ultimate success for individuals with CS is communication. Children who are able to establish abstract communication in childhood ultimately do far better than those who do not. The barriers to communication are extensive, including life-threatening medical issues; decreased hearing, vision, and balance; difficulty handling secretions and moving the face; and an educational system that is ill prepared to meet the childrens' diverse needs.

Each individual with CHARGE has a unique set of features, making generalizations difficult and not very useful. There is no "average" or "typical" child with CS. There are, however, many similarities between cases. Experienced observers have learned a lot about individuals with CS and have developed ways to assess the strengths and the weaknesses of each child. It is necessary to understand the world of the child—how each child experiences and interacts with their environment—to be able to implement therapies and set up environments that will be conducive to the establishment of effective communication systems.

Where Did the Name CHARGE Come From?

The "CHARGE" acronym was coined in 1981 using some of the features recognized in many of the children described: C = coloboma of the eye, H = heart defects, A = atresia of the choanae, R = restriction of growth and development, G = genitourinary abnormalities, E = ear anomalies and hearing

loss (Pagon, Graham, Zonana, & Yong, 1981). Even in 1981, it was recognized that the acronym did not encompass all of the recognized features or even perhaps some of the most important features (e.g., cranial nerve anomalies). The acronym features should never be used for diagnosis or even to describe the syndrome.

How Is CHARGE Diagnosed?

History

Since the first description in 1981 by Pagon et al., there have been numerous revisions of the clinical diagnostic criteria for CHARGE, most notably in 1998 by Blake et al. and in 2007 by Sanlaville and Verloes. Vissers et al. (2004) were the first to identify pathogenic variants (mutations) in a single gene (*CHD7*) as a cause of CHARGE syndrome, confirming the genetic basis of the syndrome. However, not all *CHD7* variants cause CS, and a significant number of individuals with CS (~10%) do not appear to have identifiable *CHD7* variants. Therefore, although *CHD7* sequencing is extremely helpful (and always recommended), the diagnosis of CHARGE syndrome remains a clinical diagnosis—based on the combination of genetic, medical, and developmental characteristics. The field of medical genetics is in a state of extremely rapid evolution—we are only just beginning to understand the complexity of interactions between multiple genes and the environment, which come together to create a "syndrome." Suffice to say, there may be many avenues to arrive at "CHARGE syndrome" other than pathogenic variants in the *CHD7* gene.

Diagnostic Criteria

The diagnosis of CHARGE syndrome should always be made by a medical geneticist, preferably one who is familiar with CS. Tables 0–1 and 0–2 illustrate one current version of the major and minor clinical diagnostic criteria for CS, with the approximate percentage of people with CS who have each feature. The criteria for clinical diagnosis of definite/typical CS require the presence of at least two (preferably three) major features and several minor features. Individuals with fewer features may be diagnosed as atypical CS or CHARGE-like. *It is important to note that there is no single cardinal feature of CHARGE among affected individuals. Every characteristic ranges from absent to present and, when present, can vary from mild to severe*. The most common features are the inner ear malformations, particularly hearing loss and vestibular abnormalities. Features notable on brain imaging may also be extremely common in individuals with CS but may not be routinely investigated (de Geus et al., 2017). Detailed reviews of many issues related to CS, including diagnostic criteria, how *CHD7* affects the developing embryo, and genetic counseling, can be found in the December 2017 issue of the *American Journal of Medical*

Table 0–1. Major Diagnostic Characteristics of CHARGE Syndrome

Characteristic	Manifestations	Frequency
Coloboma of the eye	Coloboma of the iris, retina, choroid, disc; microphthalmos	80%–90%
Choanal atresia or stenosis[1,2]	Unilateral/bilateral: bony/membranous, atresia/stenosis	50%–60%
Cranial nerve dysfunction or anomaly	I: Hyposmia or anosmia/arhinencephaly	80%–90%
	VII: Facial palsy (unilateral or bilateral)	40%–50%
	VIII: Hypoplasia of auditory nerve	>80%
	IX/X: Swallowing problems with aspiration and gut motility issues.	70%–80%
Characteristic CHARGE outer ear[3]	Short, wide ear with little or no lobe, "snipped off" helix, prominent antihelix that is often discontinuous with tragus, triangular concha, decreased cartilage, often protruding, usually asymmetric	80%–90%
Characteristic CHARGE middle or inner ear	Ossicular malformations	>80%
	Abnormal cochlea	>80%
	Absent or hypoplastic semicircular canals	>95%

[1] Choanae are passages in the back of the nose that are blocked (atretic) or narrowed (stenotic).

[2] Cleft palate may substitute for this characteristic in some cases.

[3] See Figure 8–4.

Genetics, Part C, devoted entirely to CHARGE syndrome and summarized in the article by van Ravenswaaij-Arts and Martin (2017).

As many of the diagnostic features of CS (as well as additional "occasional findings") have an impact on language and other developmental skills, they are discussed in detail in this volume. From a practical standpoint, the information in this volume should be extremely useful to anyone caring for an individual with typical CHARGE syndrome, atypical CHARGE, or who presents as "CHARGE-like."

Development and Communication in CHARGE Syndrome

Over 90% of individuals with CHARGE have both vision loss and hearing loss (classified as deafblindness), and most also have vestibular (balance) abnormalities that further inhibit and delay development. Most spend the first two

Table 0–2. Minor Diagnostic Characteristics of CHARGE Syndrome

Characteristic	Manifestations	Frequency
Genital hypoplasia	Males: Micropenis, cryptorchidism Females: Hypoplastic labia	50%
	Both: Delayed puberty	>50%, 90% in males
Cardiovascular malformation	Especially conotruncal defects (e.g., tetralogy of Fallot), aortic arch anomalies	75%–85%
Growth deficiency	Short stature Growth hormone deficiency	70% 15%
Orofacial cleft	Cleft lip and/or palate	20%–40%
Tracheoesophageal (T-E) fistula	T-E defects of all types	15%–25%
Renal anomalies	Ectopic or solitary or duplex kidney, uteropelvic junction obstruction, reflux, hydronephrosis	30%–40%
Distinctive facial features	Square face with broad prominent forehead, prominent nasal bridge and columella, flat midface, small chin that gets larger with age	70%–80%
Palmar crease	Hockey-stick palmar crease	50%
CHARGE behavioral profile	Obsessive-compulsive disorder or other perseverative behavior	>50%

to three years of life in and out of hospitals and clinics because of surgeries and airway-, heart-, and feeding-related problems. Since medical issues can have a profound impact on growth and development, the medical section in this volume provides detailed descriptions and references for each affected system.

Because the focus in early childhood is typically on overcoming life-threatening medical challenges, scant attention is often paid to development and communication. However, the establishment of an adequate communication system is crucial to learning and to living a meaningful life. Research on hearing impairment demonstrates that some mode of communication needs to be established in the first few months of life for development of symbolic language (Vohr et al., 2008). Due to the complexities of cochlear malformations, tracheostomies preventing verbal output, along with visual

impairment, standard speech therapy and sign language methods need to be modified. Despite best efforts, some of these children may never attain easily recognizable verbal speech. Creative approaches utilizing all available modes of communication are often required. It is important to understand, however, that *all behavior is communication*. Families and professionals should document and shape behavior while still striving for a formal communication system.

ORGANIZATION OF THIS VOLUME

CHARGE syndrome may be the only disorder that presents with deficits of all of the senses (Part I). These deficits alone make many aspects of life challenging. However, the greater issue is the combined consequences of *multiple* sensory issues superimposed on a distinctive constellation of medical and physiologic disorders (Part II) that give rise to a unique course of individual development (Part III) and result in restricted forms of uncommon communication (Part IV). The sum of the individual challenges governs the resulting patterns of behavior, as well as factors that are critical to take into account in parenting, education, and developing appropriate social interaction (Part V).

The purpose of this volume is to provide allied health professionals (as well as families and educators) a comprehensive picture of the sensory, physical, and psychological issues that challenge children with CHARGE and to explore a variety of ways to overcome the challenges in assessment of each involved organ system and of the child as a whole. In spite of our goal of making each chapter reader friendly, there is a lot of technical information that we believe is critical to include for those professionals who are deeply involved with particular issues. We hope that each reader will find that the information most critical to their work with individuals with CS is readily accessible in these chapters.

CHARGE syndrome is highly complex, highly variable, and has a profound impact on those with the syndrome, their families, and those who interact with them. It is our hope that this volume will be a valuable tool in working towards the goals of understanding the multiple interconnected challenges that CHARGE syndrome presents and in maximizing all aspects of development.

Margaret A. Hefner, MS

REFERENCES

Blake, K. D., Davenport, S. L., Hall, B. D., Hefner, M. A., Pagon, R. A., Williams, M. S., . . . Graham Jr, J. M. (1998). CHARGE association: An update and review for the primary pediatrician. *Clinical Pediatrics, 37*(3), 159–174.

de Geus, C. M., Free, R. H., Verbist, B. M., Sival, D. A., Blake, K. D., Meiners, L. C., & van Ravenswaaij-Arts, C. M. A. (2017). Guidelines in CHARGE syndrome and the missing link: Cranial imaging. *American Journal of Medical Genetics Part C: Seminars in Medical Genetics, 175*(4), 450–464.

Pagon, R. A., Graham Jr, J. M., Zonana, J., & Yong, S. L. (1981). Coloboma, congenital heart disease, and choanal atresia with multiple anomalies: CHARGE association. *Journal of Pediatrics, 99*(2), 223–227.

Sanlaville, D., & Verloes, A. (2007). CHARGE syndrome: An update. *European Journal of Human Genetics, 15*(4), 389–399.

van Ravenswaaij-Arts, C., & Martin, D. M. (2017). New insights and advances in CHARGE syndrome: Diagnosis, etiologies, treatments, and research discoveries. *American Journal of Medical Genetics Part C: Seminars in Medical Genetics, 175*(4), 387–406.

Vissers, L. E., van Ravenswaaij, C. M. A., Admiraal, R., Hurst, J. A., de Vries, B. B., Janssen, I. M., . . . van Kessel, A. G. (2004). Mutations in a new member of the chromodomain gene family cause CHARGE syndrome. *Nature Genetics, 36*(9), 955–957.

Vohr, B., Jodoin-Krauzyk, J., Tucker, R., Johnson, M. J., Topol, D., & Ahlgren, M. (2008). Early language outcomes of early-identified infants with permanent hearing loss at 12 to 16 months of age. *Pediatrics, 122*(3), 535–544.

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This book is dedicated to the families who have the urgent need for information to help their children with CHARGE syndrome and to the professionals who make the special effort to understand this rare syndrome.





Contributors

Véronique Abadie, MD, PhD
Head of the General Pediatrics Unit
Necker Hospital
Professor of Pediatrics
Paris Descartes University
Paris, France
Chapter 4

Susan M. Bashinski, EdD
Professor of Special Education
Interim Dean of the Graduate School
Missouri Western State University
Saint Joseph, Missouri
Chapter 25

Kim D. Blake, MD, MRCP, FRCPC
Professor, Medicine
Department of Pediatrics, IWK Health Centre
Dalhousie University
Halifax, Nova Scotia, Canada
Chapters 10 and 11

David M. Brown, MA, DSc (Hon)
Consultant Teacher of the Deafblind
Emeritus Educational Specialist
California Deafblind Services
San Francisco State University
San Francisco, California
Chapter 7

Dianne E. Campbell, MD, PhD
Department of Allergy and Immunology
Children's Hospital at Westmead

Discipline of Paediatrics and Child Health
University of Sydney
Sydney, Australia
Chapter 15

Daniel I. Choo, MD
Director, Division of Pediatric Otolaryngology—Head and Neck Surgery
Professor, UC Department of Pediatrics
UC Department of Otolaryngology—Head and Neck Surgery
Cincinnati Children's Hospital Medical Center
Cincinnati, Ohio
Chapter 8

Sarah E. Curtis, AuD, ABA-C
Doctor of Audiology
Practice Owner
Sounds of Life Hearing Center, LLC
Concord Township, Ohio
Chapter 3

Michael Daugherty, MD
Assistant Professor
Division of Pediatric Urology
Cincinnati Children's Hospital Medical Center
Cincinnati, Ohio
Chapter 13

Sandra L. H. Davenport, MD
Clinical Genetics and Pediatrics
Sensory Genetics/Neurodevelopment
Bloomington, Minnesota
Chapters 1 and 23

Laurie S. Denno, PhD, BCBA-D
Behavior Analyst
Behavior and Learning Consultation
Vineyard Haven, Massachusetts
Chapter 21

Eniolami O. Dosunmu, MD, FAAP
Assistant Professor of Ophthalmology
Abrahamson Pediatric Eye Institute
Cincinnati Children's Hospital Medical Center
Department of Ophthalmology

University of Cincinnati
Cincinnati, Ohio
Chapter 2

Elizabeth E. Gilles, MD
Child Neurology Solutions, PLLC
Saint Paul, Minnesota
Chapter 11

Pamela Haibach-Beach, PhD
Professor of Motor Behavior
Associate Director of the Honors College
Co-Director of the Institute of Movement Studies for Individuals with Visual Impairments and Deafblindness
State University of New York College at Brockport
Brockport, New York
Chapter 20

Catherine K. Hart, MD, MS
Assistant Professor
Pediatric Otolaryngology
Cincinnati Children's Hospital Medical Center
University of Cincinnati College of Medicine
Cincinnati, Ohio
Chapter 9

Timothy S. Hartshorne, PhD
Professor of Psychology
Central Michigan University
Mount Pleasant, Michigan
Chapters 27 and 31

Alexander Hatton
Co-Op Student
Cincinnati Children's Hospital Medical Center
Department of Cardiovascular Surgery
Cincinnati, Ohio
Chapter 12

Margaret A. Hefner, MS
Genetic Counselor
Division of Medical Genetics
Department of Pediatrics
Saint Louis University School of Medicine

St. Louis, Missouri
Introduction and Chapter 1

Christine H. Heubi, MD
Assistant Professor
Pediatric Otolaryngology Head and Neck Surgery
ABOTO-Certified in Sleep Medicine
Cincinnati Children's Hospital Medical Center
Cincinnati, Ohio
Chapter 9

Peter Hsu, MBBS, FRACP, PhD
Department of Allergy and Immunology
Kids Research
The Children's Hospital at Westmead
Discipline of Adolescent and Child Health
The University of Sydney
Sydney, Australia
Chapter 15

Alexandra S. Hudson, MD
Resident Physician
University of Alberta
Edmonton, Canada
Chapter 10

Benjamin Kennert, PhD
Central Michigan University
Mount Pleasant, Michigan
Chapter 22

Jeremy M. W. Kirk, MD, FRCP, FRCPCH
Professor
Department of Pediatric Endocrinology
Birmingham Children's Hospital
Birmingham, United Kingdom
Chapter 14

Lauren J. Lieberman, PhD
Distinguished Service Professor
Kinesiology, Sport Studies, and Physical Education Department
State University of New York at Brockport
Co-Director
The Institute on Movement Studies for Individuals with
Visual Impairment or Deafblindness
Founder and Director

Camp Abilities
Brockport, New York
Chapter 20

Sam Mehr, MD
Department of Allergy and Immunology
Royal Children's Hospital
Parkville, Australia
Chapter 15

Emily King Miller, MA, CCC-SLP
Clinical Team Leader Speech Language Pathology
Blount Memorial Total Rehabilitation Pediatrics
Alcoa, Tennessee
Chapter 26

Claes Möller, MD, PhD
Professor in Audiology and Disability Science
Örebro University/Örebro University Hospital
Örebro, Sweden
Chapter 5

David Luís Simóne Morales, MD
Professor of Pediatrics and Surgery
Clark-Helmsworth Chair
Director, Congenital Heart Surgery—Heart Institute
Cincinnati Children's Hospital Medical Center
Cincinnati, Ohio
Chapter 12

Jude Nicholas, PsyD
Consultant Clinical Neuropsychologist
Haukeland University Hospital
Statped Center for Special Needs Education
Bergen, Norway
Chapter 6

Dominique Pancotto, MS
Board Certified Behavior Analyst
Capella University
Minneapolis, Minnesota
Chapter 22

Melanie E. Perreault, PhD
Associate Professor of Motor Behavior
Department of Kinesiology, Sport Studies, and Physical Education
State University of New York at Brockport
Communications Director
Institute of Movement Studies for Individuals with Visual Impairments
Brockport, New York
Chapter 20

Pramod P. Reddy, MD
Director
Division of Pediatric Urology
Professor of Surgery
Cincinnati Children's Hospital Medical Center
The University of Cincinnati, College of Medicine
Cincinnati, Ohio
Chapter 13

Meilan M. Rutter, MD, BCh, FRACP
Associate Professor of Pediatrics
Division of Endocrinology
Cincinnati Children's Hospital Medical Center
University of Cincinnati College of Medicine
Cincinnati, Ohio
Chapter 14

Nancy Salem-Hartshorne, PhD, NCSP
Professor of Psychology
Delta College
University Center, Michigan
Chapters 18 and 23

Megan C. Schmittel, MS
School Psychologist
Perkins School for the Blind, Deafblind Program
PhD Candidate
Central Michigan University
Member of the Central Michigan University CHARGE
Syndrome Research Lab
Mount Pleasant, Michigan
Chapters 19 and 23

Michael P. Scott, AuD, CCC-A
Clinical Research Auditory Implant Program Coordinator
Cincinnati Children's Hospital Medical Center, Division of Audiology

University of Cincinnati, Communication Sciences and Disorders
Cincinnati, Ohio
Chapter 3

Lillian J. Slavin, MA, TLLP
School Psychology Doctoral Candidate
Central Michigan University
Mount Pleasant, Michigan
Chapter 32

Nancy K. Steele, MEd
Educational Consultant
Maryville, Tennessee
Chapter 26

Kasee K. Stratton, PhD, NCSP, LP
Associate Professor and Director
TK Martin Center for Technology and Disability
Bulldog CHARGE Syndrome Research Lab
College of Education
Mississippi State University
Mississippi State, Mississippi
Chapters 23, 29, and 30

Lori A. Swanson, PhD, CCC-SLP
Professor of Communication Sciences and Disorders
Department of Communication Sciences and Disorders
University of Wisconsin—River Falls
River Falls, Wisconsin
Chapters 24 and 26

Karthik Thangappan, MD
University of Cincinnati Medical Center General Surgery Resident, PGY-3
Congenital Heart Surgery Research Fellow
Cincinnati Children's Hospital Medical Center
Department of Cardiovascular Surgery
Cincinnati, Ohio
Chapter 12

James W. Thelin, PhD
Associate Professor Emeritus
Department of Audiology and Speech Pathology
University of Tennessee—Knoxville
Knoxville, Tennessee
Chapter 26

Sara J. Thelin, MA CCC-SLP
Speech-Language Pathologist (Retired)
Knoxville, Tennessee
Chapter 26

Susan Wiley, MD
Developmental and Behavioral Pediatrics
Cincinnati Children's Hospital Medical Center
Professor of Pediatrics
University of Cincinnati
Cincinnati, Ohio
Chapters 17 and 28

Marc S. Williams, MD, FAAP, FACMG, FACMI
Professor and Director Emeritus
Genomic Medicine Institute
Geisinger
Danville, Pennsylvania
Chapter 16

PART I

Sensory Issues in CHARGE Syndrome

CHARGE syndrome (CS) has features that overlap with a multitude of other genetic conditions. However, the multisensory impairment associated with CS makes it unique. Among genetic conditions, CS is the leading cause of congenital deafblindness (dual-sensory impairment). Individuals with CS can have disturbances not only in hearing and vision, but in all seven senses (hearing, vision, smell, taste, touch, proprioception, and inner ear balance). The impact of multisensory impairment is not additive, but multiplicative. First and foremost, understanding CS requires an understanding of sensory impairment.





CHAPTER 1

Overview and Sensory Issues

MARGARET A. HEFNER AND
SANDRA L. H. DAVENPORT

INTRODUCTION

Humans have receptors for five "input" senses which allow access to external stimuli, namely, vision, hearing, smell, taste, and touch (including cold/hot, smooth/rough, light touch, two-point discrimination, tickle, itch, vibration, pressure, pain, and more). In addition, the body has other receptors that allow the body to recognize its position in space and in relation to itself, namely vestibular and proprioceptive senses. In CHARGE syndrome (CS), all of these senses may be affected.

Vision, hearing, smell, and balance are all affected in most individuals with CHARGE. This means that children with CS may not see you unless you are at a specific distance and in their visual field, or they may see only parts of you and not see you as a person. These children may not hear your natural voice, or they may not hear you at all. They may not smell properly, hindering their ability to identify food, perfumes, or other common odors, and they may not have enough balance to attain normal motor milestones. These children are *input impaired*—the information they are receiving from the outside world is often absent and/or distorted.

Most children with CHARGE do not have significant abnormalities on brain imaging studies and, therefore, must be presumed to have normal brain

function until proven otherwise. Before a child with CS can be said to have anything other than normal intelligence, they must have been relatively healthy and have been in settings with appropriate adaptations to address their multiple sensory issues for a number of years. Appropriate adaptations are not obvious. Most adaptations for people who are hearing impaired use visual enforcers. However, a visually impaired individual who also has hearing loss may not see or understand these enforcers. Likewise, most adaptations for visually impaired individuals are auditory and are completely lost to those who are hearing impaired in addition to visually impaired. Dual sensory loss (deafblindness) requires unique adaptations (see "Definition of Deafblindness" below). Hearing, vision, and smell are the primary "distance" senses. In other words, sounds, sights, and smells orient a person to their setting and alert one to the approach or presence of a person, animal, or other object. If all three distance senses are decreased or absent, the person with CS may not be aware of someone who is present until physical contact is made. This can be both startling and frightening, leading one to being "jumpy" and sometimes having significant tactile and oral aversions. Incidental learning, including most "socially appropriate behavior," which typical

Definition of Deafblindness

In the United States, "deafblindness" is an educational term used when determining eligibility for specific services. One might assume defining deafblindness is straightforward (i.e., no hearing, no vision), but that is not the case. Most children classified as "deafblind" have at least some usable hearing and/or some usable vision. There are actually many definitions, and while most U.S. states have a definition, they are not all identical. Although all states indicate that deafblindness involves both hearing and vision impairment, some specify the degree of impairment that must exist, whereas others allow "functional" definitions. Some state deafblind projects automatically serve children with CHARGE, while others require that the child have specific vision and auditory losses before they may receive services.

The U.S. federal definition of deafblindness is as follows:

> Deafblindness means concomitant hearing and vision impairments, the combination of which causes such severe communication and other developmental and educational needs that they cannot be accommodated in special education programs solely for children with deafness or children with blindness [34 CFR 300.8 (c) (2)].

The U.S. Code, Title 29-Labor, Chapter 21-Sec. 1905 also has a definition, established when funding was authorized for the Helen Keller National Center:

(2) the term "individual who is deaf-blind" means any individual—

(A) (i) who has a central visual acuity of 20/200 or less in the better eye with corrective lenses, or a field defect such that the peripheral diameter of visual field subtends an angular distance no greater than 20 degrees, or a progressive visual loss having a prognosis leading to one or both these conditions;

(A) (ii) who has a chronic hearing impairment so severe that most speech cannot be understood with optimum amplification, or a progressive hearing loss having a prognosis leading to this condition; and

(A) (iii) for whom the combination of impairments described in clauses (i) and (ii) cause extreme difficulty in attaining independence in daily life activities, achieving psychosocial adjustment, or obtaining a vocation;

(B) who despite the inability to be measured accurately for hearing and vision loss due to cognitive or behavioral constraints, or both, can be determined through functional and performance assessment to have severe hearing and visual disabilities that cause extreme difficulty in attaining independence in daily life activities, achieving psychosocial adjustment, or obtaining vocational objectives; or

(C) meets such other requirements as the Secretary may prescribe by regulation.

children achieve by observing those in their environment, will not happen without specific instruction.

While hearing impairment leads primarily to delayed language acquisition, vision impairment combined with vestibular dysfunction leads to delayed motor milestones. Hartshorne et al. (2007) reported that crawling in children with CHARGE occurred on average at 1 year, 8 months (range: <1 to 5 years old, 88 participants), and walking occurred on average at 3 years, 1 month (range: 1 to 10 years, 95 participants). In addition to the sensory losses, some children have bilateral facial palsy, resulting in a complete lack of facial expression (Figure 1–1). If all of these conditions are present, all developmental milestones are significantly delayed, and intellectual disability is often

Figure 1–1. Bilateral facial palsy.

presumed. Usually, this is a false assumption (see Chapters 20, 23, 24 and 32). If central vision is affected (as with a macular coloboma; see Chapter 2), the individual with CS will not make direct eye contact. Lack of apparent eye contact, combined with lack of language development in the presence of unusual behaviors, may lead to a diagnosis of autism. Usually, this is also an inaccurate assumption (see Chapter 27).

SPECIFIC ANOMALIES THAT AFFECT SENSORY FUNCTION

Eyes and Vision

The primary cause of visual impairment is a coloboma of the eye globe (see detailed discussion in Chapter 2). This is a congenital defect in which a cleft fails to close in the bottom of the retinal layer lining the inside of the eye. The affected retina cannot process images coming from the upper visual field. Since glasses cannot correct this impairment, all visual gestures or materials must be presented within the individual's visual communication bubble (i.e., in front and to the sides of the person with CHARGE, where people, hands,

or objects can be seen) (Figure 1–2). The size and location of the coloboma has major implications for vision since the cleft can extend from the iris in the front to the optic nerve in the back. A coloboma may be so tiny that vision is hardly impaired at all, or it may be very large, in which case the entire eye may be small (microphthalmic), and vision may be severely impaired or even absent.

If the coloboma involves the macula, the central vision may be affected. This is the area that allows one to see things clearly, and it is measured using standard eye charts. When the macula is affected, people and objects may be blurred or even completely missing when one looks directly at them. This causes the person to look above or to the right or left of the object in order to figure out what it is. If the coloboma is in the optic nerve, the effect may be similar to a moderately sized retinal coloboma in that the vision in that eye can be significantly reduced.

Auditory System and Hearing

All structures of the peripheral and central auditory systems may be involved in CHARGE (see Chapters 3 and 8). Some anomalies have little or no effect on hearing, while others have significant effects. Misshapen external ears or

Figure 1–2. The communication bubble. Note how close the boy is to his work.

pinnas, which are a very recognizable characteristic of CS, almost never cause hearing loss. Malformations of the ossicles or other structures of the middle ear typically cause conductive hearing loss that can be moderate to severe. Congenital anomalies of the inner ears typically cause cochlear or sensorineural hearing losses that are usually greatest in the high frequencies, which are critical to understanding speech. The combined (mixed) conductive and cochlear losses are often asymmetrical, with one ear worse than the other. About half of individuals with CS have severe to profound mixed hearing loss. Even a mild hearing loss can have major developmental implications when combined with other sensory deficits.

The craniofacial anomalies in CHARGE often cause eustachian tube dysfunction, which, in turn, leads to middle ear disease with recurrent ear infections and chronically draining ears. Most individuals with CS have several sets of tympanostomy tubes inserted surgically in an attempt to overcome middle ear disease. By late childhood, ear infections become less frequent, but sinus infections become increasingly frequent and even chronic. Frequent infections (middle ear and sinus) result in pain, decreased stamina, and fluctuating hearing loss. Draining middle ears and floppy outer ears can complicate the use of amplification devices.

Olfactory System and Smell

The sense of smell is notoriously difficult to evaluate (see Chapter 4). However, one study in France was able to demonstrate that all 25 individuals with CHARGE who were evaluated had either a decreased or absent sense of smell (Chalouhi et al., 2005). Imaging of the brain also showed abnormal olfactory bulbs (Pinto et al., 2005). Since smell is a primary contributor to the enjoyment of food, the lack of smell may decrease the motivation to eat. Smell is also involved with memory and can be a powerful way to recognize people, pets, and different environments. In addition, if both hearing and vision are gone, smell is the remaining distance sense. If it is decreased or absent, then only touch, taste, and proprioception are available to communicate and learn about the environment.

Gustatory System and Taste

Taste buds detect sweet, sour, salty, bitter, and umami (savory) substances. To our knowledge, these are not affected in CHARGE, but no studies have been done to verify this. The taste buds are partially supplied by the chorda tympani, a branch of the facial nerve (cranial nerve VII) that passes through the middle ear. Because the facial nerve in CS is often in an unusual place, it can be damaged either in development or during surgery. Taste buds are also supplied by cranial nerve IX, the glossopharyngeal nerve, which is thought