POSSIBLE TOPICS FOR FUTURE RESEARCH

The following list has been compiled but by no means is meant to be a comprehensive inventory of all the research that is needed on CHARGE Syndrome.1

BEHAVIORAL ISSUES:

- Is there truly a behavioral phenotype that is part of CHARGE, or is it a result of the multiple sensory impairments, inability to communicate adequately, and medical issues?
- When are psychotropic medications truly indicated? What about drug-drug interactions?

CHOCHLEAR IMPLANTS AND VESTIBULAR ISSUES:

- When is cochlear implantation truly contraindicated? What are the otologic criteria that accurately predict surgical success or failure? What is the relationship between presurgical diagnostic criteria and the range of auditory outcomes—including no benefit, awareness of environmental sounds, and ability to use the auditory channel as the primary mode for communication? What cochlear anatomy predicts when implants will be helpful for environmental awareness and when for speech detection and/or acquisition? What are appropriate expectations from a cochlear implant?
- Congenital vestibular dysfunction clearly causes major balance issues. Dizziness is not involved: Is this because the sensory cells have never formed and, therefore, are not causing dizziness as they are attacked by infections or agents, or are other factors involved? What are the best methods to promote and encourage motor development and upright and balanced posture? How does the vestibular dysfunction interact with the other sensory impairments? How does vestibular dysfunction affect cognition, the acquisition of symbolic language, and behavior?

CONTROL OF EXCESS SALIVARY SECRETIONS:

- Excess salivary secretions in infancy and early childhood have been controlled successfully with Botox injections in one child we know of and not in another. This is another area that needs further investigation.

ENURESIS:

- Why does enuresis (urinary accidents) persist into childhood and even teenage years?

GENETICS:

- Understanding of the functions of the CHD7 gene is advancing at a rapid pace, thanks in part to the development of at least two animal models (mouse and zebra fish). Further study may elucidate significance of particular mutations within the gene, interaction of the CHD7 protein with other genes, and their effects on the huge variety of clinical and developmental outcomes seen in individuals with CHARGE. Other genes likely will be identified, which either influence the expression of CHD7 or result in similar clinical findings.

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[1] Based on recommendations for further research on CHARGE Syndrome found in ***CHARGE Syndrome: A Volume in the Genetics and Communication Disorders Series*** by Timothy S. Hartshorne, Margaret A. Hefner, Sandra L. H. Davenport, and James W. Thelin, Plural Publishing, San Diego, 2010.

GROWTH, BONE, CARTILAGE AND MUSCLE DEVELOPMENT:

- Hypotonia of the shoulder girdle and trunk has not yet been explained. Are there weak muscles that can be strengthened, or are some muscles abnormal in size or internal structure or even missing? Is scoliosis caused by the weakness of particular muscle groups? Can progression of scoliosis be avoided by appropriate preventive physical therapies or exercises? How do hypotonia, scoliosis, and vestiblular anomalies interact?
- Why is osteoporosis such a major problem beginning in adolescence (or even earlier)? Is there a problem with bony mineralization involving not just the lack of sex hormones or even growth hormone but also a problem with calcium, magnesium, and vitamin D? Or is it related more to nutrition and exercise?
- What is the effect of growth hormone on both skeletal growth and muscle strength over time? Can it stave off the early development of osteoporosis?
- Why is the cartilage of the ear soft in many cases and cartilage in the trachea soft in some?
- When is tracheostomy a necessity? For instance, if excessive secretions are avoided or breathing obstruction treated, can tracheostomy be avoided?

IMMUNOLOGY:

- Infections are a constant factor in the lives of children with CHARGE. Very little is known about possible immunological factors that influence these infections.
- The relationship between enlarged adenoids (and sometimes tonsils) and breathing obstruction has been noted in many cases and has even caused seizure-like episodes. However, as adenoids and tonsils are the first line of defense against infective agents that arrive through the nose and throat, a careful investigation of the benefits and risks of removing adenoids or tonsils should involve both otolaryngologists and immunologists.

HORMONES, FERTILITY:

- What is the range of sex hormone production over adolescence and adulthood? Do the levels follow normal patterns, or is there something distinctive about CHARGE?
- What is the fertility rate in males? In females? What factors predict success in childbearing?

LIFE CYCLE ISSUES:

- We know that there are many adults with CHARGE who have not been diagnosed. How are they functioning? What kinds of developmental and educational support did they receive?
- What is the typical life span for individuals with CHARGE, and what unique medical issues emerge in adolescence, adulthood, and old age?
- How can case management in medical, educational, and rehabilitation settings be optimized?

NEUROLOGICAL ISSUES:

- Which structural brain abnormalities correlate with seizures, intellectual functioning, and/or behavioral changes?
- What kinds of seizures are the most prevalent, and is treatment any different from treatment of seizures in children with other syndromes?
- Why are some cranial nerves involved and not others, or are they all involved, but not as clearly manifested?
- Are the cranial nerve nuclei in the brain malformed, or is the problem the connection with the end organ, e.g., vestibule and cochlea, or does the malformation of the end organ cause retrograde destruction of the connecting nerves?

- Is the autonomic nervous system (ANS) malfunctioning? This system controls muscle functions not under voluntary control such as breathing and peristalsis. Peristalsis is the neurologically based propulsion of food down the esophagus and gut, the regulation of voiding, and other functions. Is the persistent troublesome constipation more related to peristalsis or diet and exercise?
- Are the pain sensors of the body malformed or not functioning properly? Is there a high threshold for pain in this population, or is there a difference in response to painful stimuli or both?
- What brain factors predict central auditory or central visual processing issues?

SLEEP DISTUBANCES:

- Sleep disturbance is a major issue. Although some of the problem is related to lack of sensory input and/or obstructive sleep apnea, disturbances in diurnal rhythm need further investigation.

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