

## Usher Syndrome in Louisiana



By **Anita Jeyakumar, M.D.**, director of pediatric otolaryngology at Children's Hospital and assistant professor of Otorhinolaryngology at LSU Health Sciences Center and **Jennifer Lentz, Ph.D.**, assistant professor of Otorhinolaryngology at LSU Health Sciences Center. This issue of Pediatric Review is intended for pediatricians, family physicians and all other interested medical professionals. For CME purposes, the authors have no relevant financial relationships to disclose.

### OBJECTIVES

At the end of this activity, the participant should be able to:

1. Describe Usher syndrome, its types and symptoms
2. Discuss Usher syndrome's impact on Louisiana children
3. Review management of Usher syndrome in pediatric patients

### INTRODUCTION

Usher syndrome (Usher, USH) is the leading genetic cause of combined deafness and blindness.

There are three clinical types of Usher syndrome, USH1, USH2 and USH3, based on the severity and age of onset of deafness and blindness, and in some patients, vestibular areflexia. USH1, the most severe form, is characterized by congenital, bilateral, profound sensorineural hearing loss (SNHL), vestibular areflexia and adolescent-onset retinitis pigmentosa (RP). USH2 is the most frequent form characterized by congenital, bilateral SNHL that is mild to moderate in the low frequencies and severe to profound in the higher frequencies, intact vestibular responses, and RP that begins in the second to third decade of life. USH3 is characterized by post-lingual, progressive SNHL, late-onset RP and variable impairment of vestibular function. The RP in all forms of USH is a progres-

sive, bilateral, symmetric retinal degeneration that begins with night blindness and constricted visual fields (tunnel vision) and eventually includes decreased central visual acuity. The rate and degree of vision loss varies within and among families.

### HISTORY

Usher syndrome was first described in 1858 by Albrecht von Gräfe. However, the syndrome was named after Charles Howard Usher, a Scottish ophthalmologist, who described the syndrome in 1914 on 69 patients, in an article called "On the inheritance of Retinitis Pigmentosa, with notes of cases."

### WHO IS AFFECTED BY USHER SYNDROME?

The incidence of Usher is estimated at 1:6,000–20,000 individuals worldwide. Approximately 3–6% of hearing impaired children have Usher. An estimated 10% of children born with profound SNHL have Usher. Current reports indicate that Usher accounts for more than 50% of people who are both deaf and blind.

### WHAT CAUSES USHER SYNDROME?

Usher is inherited in an autosomal recessive manner. Both males and females can inherit Usher when he or she receives a mutation from each parent.

### HOW DO YOU DIAGNOSE USHERS SYNDROME?

Usher syndrome affects hearing, balance and vision. Diagnosis of Ushers includes evaluation of all three senses. Evaluation of the eyes includes a visual field test, an electroretinogram (measurement of the electrical response of the retina), and a retinal exam by an ophthalmologist. An ear evaluation often includes an audiologic exam by an audiologist, and an otologic examination by an otolaryngologist. Sometimes an electronystagmogram can be done to measure involuntary eye movements to check for balance problems.

Genetic testing is available for some of the genetic mutations that cause Ushers. Often times, the patient is diagnosed clinically, and genetic testing is reserved for select cases. It is important that patients are diagnosed early to enable the start of special education programs.



*"The Arrival of the Acadians in Louisiana" by Robert Dafford, a 12 x 30 foot mural which represents actual documented Acadian refugees who arrived in Louisiana from about 1764 to 1788, at the Acadian Memorial in St. Martinville, La. (Photo courtesy the Acadian Memorial)*

### HOW DOES USHER SYNDROME AFFECT LOUISIANA?

The Acadians are descendants of the 17th century French colonists who settled in Acadia. Many Acadians later settled in Louisiana, where they developed what became known as Cajun culture. Clinical scientists have recognized some Acadian cultural isolation in Louisiana through an increased incidence of particular diseases in subpopulations of Acadian descendants, including Friedreich ataxia, lack of coordination of the voluntary muscles resulting in irregular movements of the body. Ataxia can be brought on by an injury, infection, or degenerative disease of the central nervous system, e.g. (Barbeau et al. 1984), Tay-Sachs disease (McDowell et al. 1992), and Usher syndrome (Kloepfer et al. 1966).

Dr. H. W. Kloepfer and his colleagues first reported Usher syndrome in Louisiana Acadian patients in 1966. Because of founder affect, Usher type 1C is suggested to have a higher incidence in the

Acadian population than the general American population. In addition, a few patients with Usher type 2 have been reported within the Acadian population. Virtually all type 1 Usher syndrome in the Acadian populations of Louisiana and Canada are caused by a single mutation, the USH1C gene (216G>A).

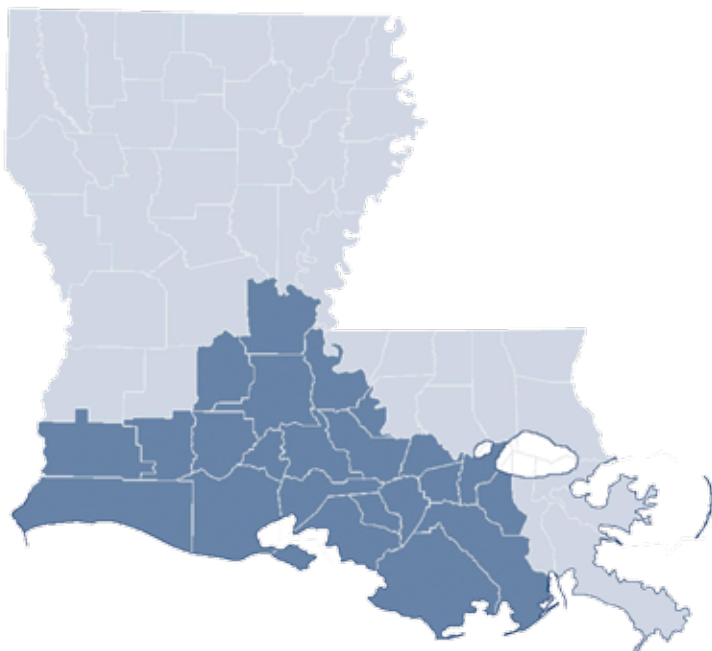
### MANAGEMENT OF USHER SYNDROME PATIENTS

The key to management of patients with Usher syndrome is early diagnosis. Early diagnosis enables adapted educational and patient management options. While there is no definitive cure for USH, there are a lot of treatments, and many of these treatments are most successful when begun early in life. The program is specific to each patient, is multidisciplinary, and is tailored to individual patient needs depending on the severity of the symptoms.

The team comprises specialists in otolaryngology, ophthalmology, genetics, audiology and nursing.

### SO WHAT IS IN THE FUTURE FOR PATIENTS WITH USHER SYNDROME?

Several advances have been made by Jennifer Lentz, Ph.D., and her team at Louisiana State University Health Science Center. They have created a mouse model of Usher that contains the same mutation responsible for Acadian Usher. More recently, they have developed a drug and shown rescue of hearing and vestibular function in the Usher mice



*The Acadians (Cajuns) settled in the shaded parishes (counties) of Louisiana after their exile from Canada's Maritime Provinces by the British in during the French and Indian War.*

after a single treatment early in life. The study was published in Nature Medicine (2013 March, Vol 19 (3), Pages 345 – 350). Preclinical animal testing is underway in Lentz’s research laboratory. While the treatment is a long way away from a clinical trial, it is a huge step in the right direction.

## RESOURCES FOR HEALTHCARE PROFESSIONALS

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### National Institutes of Health

Web: [www.ushersyndrome.nih.gov](http://www.ushersyndrome.nih.gov)

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### Coalition for Usher Syndrome Research

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  - b. Two
  - c. Three
  - d. Four
2. Usher syndrome was first described in \_\_\_\_\_.
  - a. 1858
  - b. 1885
  - c. 1958
  - d. 1985
3. Usher syndrome affects approximately \_\_\_\_\_% of hearing impaired children?
  - a. 1 – 3
  - b. 3 – 6
  - c. 6 – 9
  - d. 9 – 12
4. What Louisiana population was discussed in this article?
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  - c. Creoles
  - d. Acadians

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