EMERGENCY CARE AID FOR ALTERNATING HEMIPLEGIA OF CHILDHOOD (AHC) PATIENTS

A Reference Guide for Medical Professionals

AHC DEFINITION: *(Handb Clin Neurol. 2013; 112:821-6)*

Alternating hemiplegia of childhood (AHC) is a very rare disease characterized by recurrent attacks of loss of muscular tone resulting in hypomobility of one side of the body. The etiology of the disease is due to ATP1A3 gene mutations in the majority of patients. AHC has an onset in the first few months of life. Hemiplegic episodes are often accompanied by other paroxysmal manifestations, such as lateral eyes and head deviation toward the hemiplegic side and a very peculiar monocular nystagmus. Movement disorders such as dystonia and abnormal movements are frequent. Cognitive delay of variable degree is a common feature. Epilepsy has been reported in 50% of the cases, but seizure onset is usually during the third or fourth year of life. Many drugs have been used in AHC with very few results. Flunarizine has the most supportive anecdotal evidence regarding efficacy.

AHC RISK FACTORS:

TREATMENT: *(Neurol Genet. 2017 Apr; 3(2): e139)* There is no specific treatment for AHC. There is no approved medication or device that alters the underlying deficit in the Na+/K+ pump (see Flunarizine next page).

NEUROLOGICAL: *(Neurology. 2019 Sep 24;93(13))* Epilepsy is present in over 50% of AHC patients. Epilepsy in AHC can be focal or generalized seizures. Dystonia is also a common feature that affects the majority of patients dealing with AHC. Patients with AHC can deteriorate either abruptly or gradually at the motor and intellectual function level, depending on the severity of their disease. Specific mutations (see below) may influence the susceptibility to functional decline and severity of epilepsy as well.

RESPIRATORY: (*Brain Res. 2017 Jul 1; 1666:27-37 and J Clin Sleep Med. 2019 Jan 15; 15(1): 65–70)*

Abnormal respiratory patterns have been identified in AHC mouse models. Sleep dysfunction is common among children with AHC and can consist of obstructive sleep apnea, difficulty falling asleep, difficulty staying asleep, behavioral insomnia of childhood, or delayed sleep-wake phase syndrome.

CARDIAC: *(Brain 2015 Oct; 138(10): 2859–2874 and Intractable Rare Dis Res. 2019 May; 8(2): 134–137)*

Electrocardiogram abnormalities are common in AHC and have characteristics reflecting those of inherited cardiac channelopathies and most likely amount to impaired repolarization reserve. AHC has been associated with an increased risk of sudden death that may be caused by lethal cardiac arrhythmias. Cardiac dysfunction may account for some of the unexplained premature mortality of patients with AHC.

SUDDEN UNEXPLAINED DEATH: **(Neurol Genet. 2017 Apr; 3(2): e139 and Brain. 2015 Oct; 138(10): 2859–2874)** AHC patients who have died suddenly have had documented evidence of cardiac structural abnormalities, including ventricular hypertrophy, on autopsy studies. Sudden premature death in AHC is not always explained and may be seen in patients with and without epilepsy. It has been ascribed to cardiorespiratory dysfunction.

AHC HEMIPLEGIC ATTACK VS SEIZURE:

Hemiplegic Attack: As the attack progresses, hemiplegia can shift to the other side of the body. Sometimes the attack can provoke bilateral paralysis, and these patients may have severe clinical impairment, with difficulty in swallowing and breathing. Hemiplegic attacks may be triggered by different stimuli, like bath in warm water, motor activity, or emotion. The frequency of attacks is high, usually several in a month or in a week. The duration is variable from a few minutes to several hours or even days. Sleep can stop the attack. Understandably, these episodes may be mistaken for epileptic seizures, but typically lack any significant EEG changes during a spell. If possible, continuous EEG may

help in clarifying events, especially given that some patients with AHC may have exacerbation of non-epileptic spells when exposed to new medications.

AHC SYMPTOMS: include paroxysmal, neurological, and central nervous system events

Paroxysmal

Abnormal ocular movements – Dystonia – Ataxia – Hypotonia - Bulbar Palsy - Choreoathetosis

Neurological

Hemiplegia – Quadriplegia – Seizures - Developmental Delay – Regression - Mood Disorders - Executive Function Disorder - Behavioral Manifestations - Memory and Thought - Cognitive

Central Nervous System

Hypertonia (Spasticity) – Hypotonia – Autonomic Dysfunction including:
Heart Rate (blood pressure), Body Temperature (perspiration), Breathing Rate, Digestion (bowel & bladder function), Apnea, Other (color changes, pupillary abnormalities, fatigue, lightheadedness, feeling faint or passing out, weakness, impairment in the body's ability to handle gravity)

AHC TRIGGERS: *(Gene Reviews ATP1A3-Related Neurologic Disorders, Updated 2018 Feb 22).*

Triggers include psychological stress / excitement; environmental stressors (e.g., bright light, excessive heat or cold, excessive sound, crowds); water exposure (e.g., bathing, swimming); certain foods or odors (e.g., chocolate, food dyes); missed meals; excessive or atypically strenuous exercise; illness; irregular sleep (missing a nap, delayed bedtime).

AHC GENETICS: *(Nat Genet. 2012 Sep; 44(9): 1030–1034 and Neurology. 2014 Feb 11;82(6):482-90)*

ATP1A3 mutations are responsible for at least 74% of AHC cases and is the primary cause of AHC. AHC cases are caused by one of seven recurrent ATP1A3 mutations. AHC-causing mutations in this gene cause consistent reductions in ATPase activity without affecting the level of protein expression. The two most common missense mutations of ATP1A3 are Glu815Lys and Asp801Asn. Clinical severity of AHC is extremely variable. The Glu815Lys genotype appears to be associated with the most severe AHC phenotype. Although AHC is not generally seen as a progressive disorder, it should be considered a disorder that deteriorates abruptly or in a stepwise fashion, particularly in patients with the Glu815Lys mutation.

FLUNARIZINE: *(Brain Dev. 2001 Aug;23(5):303-5)*

Although currently unavailable within the US, Flunarizine is the most commonly used long-term treatment for AHC; it reduces duration and frequency of attacks in 50% of patients and decreases intensity in 32.1%. No other drug has shown to be more effective than flunarizine. Flunarizine anecdotally has shown both short-term (i.e. it reduced the hemiplegic attacks) and long-term effects on the motor and intellectual development in some patients with AHC. Additionally, flunarizine should not be stopped suddenly due to possible catastrophic consequences. While not FDA approved, flunarizine is used within the US through compassionate use status.

GENERAL EMERGENCY RECOMMENDATIONS:

Provide a calm environment with less external stimulation: noise, cold, light. Let the child or adult sleep spontaneously or prescribe drugs (benzodiazepines) which may prove helpful in terminating a spell. Monitor vital constants: risk of disorders of the autonomous system (respiratory disorders, bradycardia, tachycardia, pallor, vomiting, or mydriasis) while avoiding audible alarms. Presence of the parents is desirable (including after hours) for patient comfort and can be of great help in the assessment of crises and patient behavior, especially when patient is "non-communicating" or difficult to understand.

EMERGENCY CARE AID FOR ALTERNATING HEMIPLEGIA OF CHILDHOOD (AHC) PATIENTS

A Reference Guide for Medical Professionals

PERSONAL EMERGENCY CARE AID

NAME:_____ **AGE:**_____ **DATE:** _____

MAJOR DIAGNOSES: (list all important ones)

CRITICAL RISKS: (such as allergies, seizure risks, behavioral risks, or fall risks)

MEDICATIONS: (list time to be administered, how often, concentration, dose, and the administration route (oral, G or J-tube, IV, etc.))

DAILY MEDICAL PROCEDURES: (ex: nebulizer treatments, cough assist treatments, vest treatments, suctioning, catheterization)

CODE STATUS: (Check one - This is critical for the hospital staff to know if you aren't present)

☐ FULL CODE - If you want your child to be intubated or resuscitated.

☐ DNR (Do Not Resuscitate ☐ DNI (Do Not Intubate) ☐ No CPR

☐ POLST/ MOLST (Physician/Medical Order for Life Sustaining Treatment).
(If you have a POLST/MOLST, or other similar order, send a copy with your child.)

RELIGIOUS AFFILIATION: _____

MOTHER: _____ **Phone Number:**_____

FATHER: _____ **Phone Number:**_____

EMERGENCY CARE AID FOR ALTERNATING HEMIPLEGIA OF CHILDHOOD (AHC) PATIENTS

A Reference Guide for Medical Professionals

PERSONAL EMERGENCY CARE AID

NAME:_____ **AGE:**_____ **DATE:** _____

NOTABLE BEHAVIORS:

SOOTHING TECHNIQUES: (strategies to help reduce stress and anxiety)

NUTRITION: (what is fed, when, how fast/slow, and by what route such as oral, G-tube, IV)

SPECIAL EQUIPMENT: (supplies or equipment needed during hospitalization)

MOTHER: _____ **Phone Number:**_____

FATHER: _____ **Phone Number:**_____