

## Summary – Seizure Disorders and Epilepsy Dr. Mary Kay Koenig

### Introduction

- What seizure disorders are common for children & adults with mitochondrial disease?
- How do stroke-like episodes, memory loss and other neurological issues relate to seizure disorders for people with mito?
- How are seizure disorders and epilepsy classified?
- What are the treatments, recommendations and special precautions for mito patients?

Dr. Mary Kay Koenig is an Assistant Professor of Pediatrics and Neurology at the University of Texas-Houston Medical School. Her clinical research interests include General Pediatric Neurology, Mitochondrial Disorders and Neurometabolic Disorders.

As the Director of the Mitochondrial Center at UT Houston she sees mostly children, but also some adult Mito patients in the course of her clinical research. Her goal for all her patients is to provide treatments which will increase their quality of life. Please use the slides posted on the MitoAction site to follow along with this summary of her talk.

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### The Brain

The brain is the key to the nervous system since it regulates and controls all that comes in and all that goes out. The brain triples in size during the first year of life; it is made up of one billion cells. Though it only represents 2% of the body's weight, the brain uses 20% of the body's energy. The complex functioning of the brain makes it a high energy demanding organ which reacts to any decrease or loss in energy.

### Seizures

**Definition:** uncontrolled electrical activity in the brain that may or may not produce a physical convulsion. Epilepsy is a condition of recurrent unprovoked seizures. A person can have a seizure that does not involve a convulsion.

#### **Seizure classification:**

- *Partial Onset* seizures begin in only one part of the brain
- Simple partial onset seizure: seizure starts in one part of the brain and stops there. The person does not lose consciousness, but they may have some twitching or tremors.
- Complex partial onset seizure: seizure starts in one part of the brain and the person will lose consciousness at the beginning of the seizure.
- Partial onset with secondary generalized seizure: seizure starts in one part of the brain and then spreads and the person will lose consciousness when it becomes generalized
- *Generalized onset seizures* begin in the entire brain at the same time.

#### **Seizure types:**

- *Tonic*: a stiffening of arms and legs - the limbs remain straight.
- *Tonic-Clonic*: periods of time the limbs are straight interspersed with bending of extremities; this is the "classic" seizure.
- *Absence*: person does not move at all.
- *Focal*: a single part of the body moves.
- *Sensory*: person develops sensations like a tingling in the arm or face - no motor component just sensation.
- *Myoclonic*: a "jerking" motion.
- *Atonic*: "drop attack" - that is all the muscle strength is lost at once and a person who might

be standing suddenly falls to the ground; happens quickly, less than 5 seconds, and this often results in injury.

**The important things for a neurologist to note about a seizure are:**

- What caused the onset of the seizure
- What type of seizure was it (ie, what did it look like)

There are special considerations for seizures in people with mitochondrial disease. These seizures may change over time, partial onset seizures becoming generalized. The types of seizures seen in Mito patients are different than those seen in others because the cause in Mito is NOT structural damage or scarring to the brain. For this reason, Mito seizures can be difficult to treat. These seizures may be related to or triggered by metabolic changes in the body. **One drug that should always be AVOIDED in Mito is DEPAKOTE (valproic acid). This drug is often used for seizure disorders but is toxic to Mito patients.**

**Myoclonus**

**Definition:** brief, involuntary twitching of muscles which may or may not be associated with a seizure. It is caused by abnormal electrical currents in muscles or nerves, not the brain. Myoclonus is often associated with mitochondrial disease, can be very debilitating and can cause injury. There are medications to help with these symptoms such as:

- Levetiracetan (Keppra)
- Clonazepam (Klonopin)
- Topiramate (Topomax)
- Acetazolamide (Diamox)

Neurologists unfamiliar with Mitochondrial disease will want to prescribe Depakote; Do NOT take Depakote; it has been found to be toxic for those with mito making the disease worse.

**Ataxia**

**Definition:** a lack of coordinated movements when performing voluntary actions. Ataxia often arises out of degeneration of the cerebellum that can be seen on an MRI. Often seen in mito patients, ataxia can begin with hand tremors and then progress slowly to the point where a person may have difficulty walking. Symptoms include tremor, poor balance, wide based gait, breathy speech and scanning eye movements.

**Treatment:** Although there is no medical treatment for ataxia, there are therapies that patients are encouraged to seek. These include physical therapy to build strength and enhance mobility, occupational therapy to help with daily living tasks like eating, and speech therapy to improve speech and aid swallowing. Because ataxia increases the risk of falls and injury and is often progressive in Mito patients, assistive devices like canes and/or walkers are recommended. The use of assistive devices should be seen as a sign of strength in a person - someone who is willing to continue to live a full life.

**Strokes**

**Definition:** a rapidly developing loss of brain function from a disrupted supply of blood to the brain. Strokes can be caused by a number of events.

**Causes of strokes:**

- Clotted blood vessel

- Common in older people
- Emboli
  - An embolus is a small particle (of fat or blood or other substance) that moves into a vessel and blocks blood flow to the brain
    - Lack of oxygen to the brain
      - caused by global lack of oxygen, such as in drowning
    - Bleeding
      - A hemorrhagic stroke
      - Vasospasm
        - A sudden, unnecessary constriction of a blood vessel, which results in a decreased blood flow to that part of the brain
        - Usually the cause of strokes in Mito patients, especially those with MELAS

In most patients between 60 and 70 years of age, strokes are caused by either bleeding or a clot. A CAT scan will reveal which. If it is an ischemic stroke (caused by a clot blocking the blood supply), then tPA treatment is begun immediately (the clot buster drug) in order to break down the clot and allow blood flow back to the brain. However, in Mito patients, the cause of strokes (which occur at a much earlier age) is generally NOT clots but rather vasospasms and these will NOT respond to tPA treatment (it could even make it worse).

Nitric Oxide is a chemical produced by the body's cells that causes blood vessels to dilate. Nitric Oxide production requires L-arginine. Research has demonstrated that those people with MELAS do not seem to have enough L-arginine in their blood. A vasospastic stroke, therefore, may be helped by using either L-arginine or L-citrulline in order to increase the body's production of Nitric Oxide. **Mito patients who develop a vasospastic stroke should receive L-arginine via intravenous route; this may decrease the severity of the stroke.** Those at high risk for vasospastic strokes may also be placed on daily oral L-arginine as a preventative measure. If a patient has MELAS this therapy should be discussed with their neurologist (contact Dr. Koenig directly if there are questions or concerns).

## Migraines

**Definition:** chronic headache syndrome where patients develop moderate to severe headaches. Migraines are common in Mito patients.

### **Common Symptoms:**

- Photophobia (sensitivity to light)
- Phonophobia (sensitivity to sound)
- Nausea
- Vomiting.

### **Types of migraines:**

- Without an aura
  - Most common type of migraine
- With an aura (an aura is a neurological symptom that occurs before a migraine - usually seeing spots or tunnel vision)
  - Confusional aura: become confused about 30 minutes to an hour before the migraine; these are difficult to diagnose
  - Hemiplegic: one side of the body becomes weak before the onset of the migraine; can be confused with a stroke but there is no brain damage; the hemiplegia gets better and then the headache occurs

- Basilar: dizziness due to decreased blood flow to the back of the head (basilar area of the brain); often confused with a stroke
- Acephalic: present with an aura but no headache; hard to diagnose
- Cyclic vomiting/abdominal migraine
  - Often seen in children; with episodes of nausea and vomiting for a day or two every few weeks. There is no headache present and the N & V resolves itself. These often develop into migraine headaches later in life. In such cases where GI causes have been ruled out, they should be treated not with GI medications, but rather with migraine treatments.
  - Similarly, abdominal migraines present with abdominal pain, especially in children, and once GI causes have been excluded, treatment should be for the migraine.
  - Retinal migraine
    - The aura is a loss of vision for about 30 - 60 minutes
    - Ophthalmoplegic migraine
      - the eye muscles are paralyzed during the aura and the person cannot move his/her eyes

Migraines are fairly common in Mito patients. Since the migraines often have a vascular component, L-arginine may help. In some cases, however, it may make the migraine worse. Riboflavin (Vitamin B2) has also been found to be helpful for some Mito patients with migraines. Other prophylactic treatments (used to prevent migraines from happening) that have been successful for some Mito patients with migraines are topomax, elavil and propranolol, but never use DEPAKOTE. To help alleviate the symptoms of a migraine once it occurs, ibuprofen or Aleve is suggested. Tylenol is not suggested for Mito patients due to the potential liver toxicity, and aspirin also may not be beneficial to Mito patients. Neurologists may prescribe Triptans to alleviate symptoms once a migraine occurs. However, Dr. Koenig is hesitant to recommend Triptans to Mito patients for fear that they might precipitate a stroke.

**Summary** People with mitochondrial disease experience common neurological problems, and the frequency of these is higher and the symptoms may occur at a younger age. Treatments for these symptoms may also be different for Mito patients because the causes are different. Neurologists with knowledge of mitochondrial diseases are best able to deal with these complex issues. When in doubt, however, if someone is having stroke-like symptoms, it is best to seek immediate care in a local ER rather than "waiting it out" at home. If the neurological symptoms are reoccurring, then a plan should be pursued with your neurologist. Mitochondrial disease is a challenge for both patients and doctors who need to work together.