NUTRITION AND EPILEPSY

Leo Galland MD
Foundation for Integrated Medicine
New York, New York

Nutritional Factors Related to Treatment of Epilepsy

- Food allergy may provoke seizures
- Ketogenic diet may control seizures
- Nutritional supplements may reduce seizures
- Anticonvulsant drugs may cause nutritional deficits

Food Allergy and Epilepsy: Background

- Cases of seizures induced by specific foods have been reported in allergy journals for over 50 years
- There is a higher frequency of allergy, eczema, and asthma among epileptic children and their families than controls
- EEGs of children with food-induced seizures become normal on an allergy elimination diet and become abnormal several days after eating the foods to which they are allergic

Food Allergy and Epilepsy: a Controlled Study-1

- 63 children with epilepsy treated at the Hospital for Sick Children, London
- “Oligoantigenic” (few foods) diet for 4 weeks:
  - 2 meats (lamb, turkey usually)
  - 2 starchy foods (rice, potatoes usually)
  - 2 fruits (cherries, pears usually)
  - 1 vegetable (green peas)
  - Calcium & multivitamin

Food Allergy and Epilepsy: a Controlled Study-2

- 36 children improved on diet therapy
  - 25 had no seizures
  - 11 had fewer seizures

Improvement occurred for generalized, petit mal and partial complex seizures and myoclonus.

Improvement only occurred in children who also had migraines, hyperactivity or abdominal pain (45 total).

Food Allergy and Epilepsy: a Controlled Study-3

- Systematic reintroduction of individual foods, one every 2 days, identified 31 foods that provoked seizures. Most children reacted to more than one food. All seizure-provoking foods also provoked headache, abdominal pain or hyperactive behavior
- Double-blind placebo controlled trial in 16 children: 8 had seizures provoked by the suspect foods, 15 developed other symptoms,

  0 reacted to the placebo

Food Allergy and Epilepsy: a Controlled Study-4

- Foods most likely to provoke seizures:

  Milk/cheese, wheat, corn, soy, egg, chocolate, orange, benzoate (a preservative), tomato, tartrazine (a dye), fish, pork, beef.

  Egger, Carter, Soothill and Wilson, Journal of Pediatrics 1989, volume 114, pp 51-58, 1989

Ketogenic Diet for Treatment of Intractable Epilepsy

- First used in the 1920's
- Increasing frequency of use past 10 years
- High fat, very low carbohydrate, moderate protein diet that produces ketones from the breakdown of fat
- Mechanism of benefit is unknown but it appears to change brain chemistry
- Usually started in the hospital; MCT oil may be used as a fat source

Guidelines for the Modified Ketogenic Diet

- Over 90% of calories come from fat (by weight, 80% of food eaten is fat)
- Oil, heavy cream and margarine are used as fat sources to supplement foods
  - Examples: One tablespoon of margarine for each Saltine cracker, 5 tablespoons of cream for 2 ounces of oatmeal, 3 teaspoons of oil in an ounce of apple sauce

http://www.ketogenic.org

Ketogenic Diets: Results

- Over 100 uncontrolled studies published and extensive research in animals
- Overall effectiveness in children with intractable epilepsy:
  - 16% become seizure-free
  - 16% more become almost seizure-free
  - 24% more have a greater than 50% reduction in seizure frequency

  56% response overall

  Similar results occur in adults

  Benefits maintained over a 3 to 6 year period. At Johns Hopkins, about 20-30% of children maintaining the diet become drug-free

Ketogenic Diets: Side Effects

- Increase in cholesterol (total and LDL) and triglycerides, decrease in HDL-cholesterol
- Decrease in blood levels of L-carnitine, may be temporary
- Loss of calcium in urine
- Abnormal electrocardiograms (rare)
- Kidney stones occur in 5-8%

Nutritional Deficits That May Cause Seizures

- Vitamin B1 (thiamine)*: alcoholism, malnutrition
- Vitamin B6 (pyridoxine): genetic or drug-induced
- Calcium: Vitamin D deficiency*(rickets), diet
- Magnesium*: diet, diarrhea, malabsorption, urinary losses, drug induced, stress
- Sodium: water intoxication
- Carnitine*: genetic or drug induced

*Paradox: anti-epileptic drugs may actually cause a deficiency of these nutrients

Vitamin B1 and Epilepsy

- Vitamin B1 (thiamin) is essential for brain function
- Depletion of vitamin B1 in alcoholics causes Wernicke's syndrome, which includes dementia, coma and/or seizures, which respond to thiamin administration
- Phenytoin (Dilantin) use is associated with lower thiamin in blood and spinal fluid
- Administering thiamin to adult epileptics at 50 mg/day improves cognitive function

Vitamin B1 and Epilepsy

- Epilepsy Res. 1993 Oct;16(2):157-63. **Thiamine and folate treatment of chronic epileptic patients: a controlled study with the Wechsler IQ scale. Botez MI, Botez T, Ross-Chouinard A, Lalonde R.**

- Can J Neurol Sci. 1982 Feb;9(1):37-9. **Cerebrospinal fluid and blood thiamine concentrations in phenytoin-treated epileptics.Botez MI, Joyal C, Maag U, Bachevalier J.**

Vitamin B6 Dependency

- An uncommon inherited disorder in which very high doses of vitamin B6 are needed to prevent seizures and neurological dysfunction (10-20 mg/pound)
- Low doses of Vitamin B6 (such as those found in a multivitamin) may prevent seizures without normalizing brain chemistry, complicating diagnosis

Magnesium, Calcium and Seizures

- Magnesium or calcium deficiency may cause “tetany”, a state of neuromuscular hyper-excitability associated with muscular spasms and seizures
- High doses of magnesium i.v. are used to treat eclampsia, a complication of pregnancy, in which seizures may occur
- Although magnesium or calcium deficiency are uncommon causes of seizures, the tetany syndrome is relatively common in adults and children, according to European researchers

SYMPTOMS OF TETANY SYNDROME

Asthenia (fatigue, muscle weakness)	(89%)
Irritability, anxiety	(72%)
Sleep disorders	(69%)
Muscle tension/spasm	
Headache	(69%)
Back pain	(62%)
Chest pain	(48%)
Difficulty swallowing	(47%)
Leg/foot cramps	(47%)
Constipation	(35%)
Palpitation	(65%)
Tingling, abnormal sensations	(67%)
Hyperventilation, sighing and lightheadedness	(18%)
Seizures	(5%)

- **Tetany syndrome occurs in 10-15% of a “healthy” population and correlates with abnormalities of the EEG and EMG and with reduced red blood cell magnesium.**

Individuals with seizures and symptoms of tetany may benefit from magnesium supplements

Anti-epileptic drugs may cause magnesium depletion

- Serum levels of magnesium are lower in patients with epilepsy than controls (Canelas et al, *J Neurol Neurosurg Psychiatry* 1954)
- Red blood cell magnesium decreases as blood levels of phenobarbital or phenytoin increase; this can be overcome with magnesium supplements (Steidl et al, *Magnesium* 1987)

Calcium and Seizures

- Low blood calcium can cause tetany and seizures
- Level of calcium in blood is influenced by intake of Vitamin D
- Most children with epilepsy do not consume the RDA for calcium or Vit D

Gough et al, *Quart J Medicine*, 1986

Anti-epileptic drugs deplete Vitamin D and calcium

- The use of all anticonvulsants except valproic acid (Depakote) is associated with evidence of Vitamin D and calcium deficiency, the more drugs the worse

  Gough et al, *Quart J Medicine*, 1986

- This effect is strongest is non-ambulatory children whose exposure to Vitamin D from sunlight is minimal

  Baer et al, *Am J Clin Nutr* 1997

Valproic acid may cause carnitine deficiency

- Carnitine is a nutrient needed for normal neurological function and metabolism
- Valproic acid (Depakote) may cause carnitine deficiency.
- Supplemental L-carnitine may reduce seizure frequency

De Vivo et al, Epilepsia. 1998, vol 39, pp 1216-25.

Anti-epileptic drugs may induce folic acid deficiency

- Folic acid is needed for normal neurological function
- Anti-epileptic drugs induce folic acid depletion in experimental animals
- Both anti-epileptic drugs and folic acid deficiency may cause birth defects in children of epileptic women
- Red blood cell levels of folic acid are decreased in patients taking anti-epileptic drugs (except for valproic acid)

Vitamin E and Epilepsy

- Children taking anti-epileptic drugs show lower vitamin E levels in blood than control children or epileptic children not on drug therapy
- Vitamin E may prevent seizures in animals
- Vitamin E has been reported to reduce seizure frequency in patients with intractable epilepsy
- Controlled studies in epileptic children have shown variable results

Vitamin E references

- **Ogunmekan,** Epilepsia. 1989, vol 30, pp 84-9.
  Can J Neurol Sci. 1979 6, pp 43-5.
  Am J Clin Nutr. 1979 . Vol 32, pp 2269-71.
- **Kataoka** et al, Dev Pharmacol Ther. 1989; vol 14, pp 96-101.
- **Raju** et al, Epilepsia, 1994, vol 35, pp 368-72

Nutrition and Epilepsy: Conclusions

- Children with epilepsy who also suffer from migraine headaches, abdominal pain or ADHD may have food allergies as triggers for epilepsy
- Children and adults with intractable epilepsy may benefit from a ketogenic diet
- Children and adults taking anti-epileptic drugs may require supplementation with B vitamins, calcium, vitamin D, vitamin E or magnesium