Other Treatments: Beyond Anti-Seizure Medications

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• Dietary treatments
• Epilepsy Surgery
• Stimulation
  - Vagus nerve stimulation
  - Brain stimulation
A substantial minority of children with epilepsy have continued seizures despite adequate trials of standard antiseizure medications. To maximize seizure control and thereby optimize their neurodevelopmental outcomes, alternate nonmedication therapies should be considered for these patients. Dietary therapies, including the ketogenic diet and its variations, have been available for years. With a recent resurgence in popularity and expansion of indications, these treatments can lead to freedom from seizures or a significantly reduced seizure burden for a large number of patients. For carefully selected individuals, resective epilepsy surgery may offer the best hope for a cure. For others, palliation may be achieved through additional surgical approaches, such as corpus callosotomy and multiple subpial transections, or through neurostimulation techniques, such as the vagus nerve stimulator. In this review, we present these nonmedication approaches to treatment-resistant childhood epilepsy, with attention to patient selection and the potential risks and benefits. 

Ketogenic diet

• Starvation reported as a treatment for seizures in the early part of the 20th century
• Popular in the 1930’s when the only other treatments of epilepsy were phenobarbital and bromides
• Fell out of favor when newer drugs (phenytoin and others) were discovered
• Interest renewed since the early 1990’s
Ketogenic diet

• High fat, low CHO-protein and low calorie diet
• Usually long chain triglycerides are used
• Minimum amount of protein factored in to allow growth
• Switches metabolism from CHO to fat, creating ketone bodies, notably betahydroxy butyrate
Ketogenic diet

- Not a “natural” therapy for epilepsy
- Strict, regimented and restricted diet
- Labor intensive
  - Intensive parent education
  - Precise weighing of foods
  - Ensuring that EVERY last bit of food is eaten
  - Close follow-up by clinician and dietician
Optimal clinical management of children receiving the ketogenic diet: Recommendations of the International Ketogenic Diet Study Group


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Indications

- Traditionally the KD has been used to treat drug resistant epilepsy
- More commonly used in individuals who don’t have a focal epilepsy, or in whom surgery is not an option
Indications

• Specific types of epilepsy
  – Lennox Gastaut Syndrome
  – Myoclonic Astatic Epilepsy (Use the diet early)
  – Dravet syndrome (SCN1A mutations)
  – Infantile spasms (Kossoff et al 2010)

• Non-epilepsy indications
  – GLUT1 deficiency
  – Pyruvate Dehydrogenase Deficiency
  – Cerebral gliomas (Scheck et al 2011)
Contraindications

- Fatty Acid Oxidation Defects
  - MCAD, SCAD, LCAD
- Carnitine deficiency
  - Primary Carnitine deficiency
  - CPT I or II deficiency
- Pyruvate Decarboxylase deficiency
- Porphyria

Source
## Side Effects

<table>
<thead>
<tr>
<th>During initiation</th>
<th>After initiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>Constipation</td>
</tr>
<tr>
<td>Emesis/Dehydration</td>
<td>Anorexia (usually gets better)</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>Effects of nutrient deficiencies</td>
</tr>
<tr>
<td>Lethargy</td>
<td>- Vitamin D (bone health)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>- Zinc</td>
</tr>
<tr>
<td>Refusal to eat</td>
<td>- Selenium</td>
</tr>
<tr>
<td>Acidosis (decreased CO2)</td>
<td>- Carnitine</td>
</tr>
<tr>
<td></td>
<td>- Fat malabsorption</td>
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<tr>
<td></td>
<td>- Growth deceleration</td>
</tr>
<tr>
<td></td>
<td>- Kidney stones</td>
</tr>
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<td></td>
<td>- Hyperlipidemia</td>
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</tbody>
</table>
Side Effects

- Effects on the family
  - Disruption of mealtimes
  - Behavior effects
  - Halloween and other holidays, birthdays can be challenging
Mechanism

- Exact mechanism is not known
- 4 mechanisms suggested (Danial et al 2013)
  - Carbohydrate reduction
  - Activation of ATP sensitive K-channels by mitochondrial metabolism
  - Inhibition of mammalian target of rapamycin pathway
  - Inhibition of glutamateric synaptic transmission
Efficacy

• An estimated third of patients show significant improvement in seizure frequency on the KD

• RCT by Neal et al:
  – 38% children on the KD had > 50% seizure reduction compared with 6% controls (p<0.0001),
  – 7% in the KD group had greater than 90% seizure reduction compared with no controls (p=0.0582)

Epilepsy Surgery

- Resective surgery: Removal of epileptogenic focus
  - Most common: temporal lobectomy in mesial temporal sclerosis
  - Resection of cortical dysplasias, tumor
  - Hemispherectomy
  - Corpus Callosotomy
  - Multiple subpial transections
Resective Surgery

• Principle
  • Identify Epileptogenic zone
  • Resect Epileptogenic Zone without loss of neurological function
Presurgical Evaluation

• Clinical Assessment
  • Candidates
    • Drug resistant focal epilepsy
    • Treatment resistant generalized epilepsies such as Lennox Gastaut syndrome
  • Work up
    • Ictal localization with EEG telemetry to determine seizure onset
    • Supportive data for further localization
Imaging Data

- High quality MRI is cornerstone
- Often special imaging protocols are employed, using 3T (or higher) magnets surface coil MRIs or thin cuts to get optimal image resolution
MRI scan showing mesial temporal sclerosis
Imaging: Cortical Dysplasia

Please have a picture inserted here
Presurgical Evaluation

Other functional imaging studies
- Positron Emission Tomography (PET) scan
- Ictal SPECT scan
- Functional MRI
- Magnetoencephalography (MEG)
Presurgical Evaluation
Functional Localization: fMRI

Right Finger tapping
Other Supportive Data

• Neuropsychological testing
• Speech and Language testing
• These evaluations yield useful data about dominant vs. non-dominant hemisphere dysfunction, frontal vs. temporal lobe etc
Multidisciplinary Epilepsy Conference

- Group meeting (similar to Tumor Board)
- Usually attended by: epilepsy specialists, neurosurgeon, neuropsychologist, speech pathologist, neuroradiologist, social worker
- Above data presented
- Decision made......
Surgical Evaluation Techniques, When Scalp EEG Isn’t Enough

- Invasive Monitoring
  - Mapping
  - Localization
  - Surface
  - Depth Electrodes
A RANDOMIZED, CONTROLLED TRIAL OF SURGERY FOR TEMPORAL-LOBE EPILEPSY

SAMUEL WIEBE, M.D., WARREN T. BLUME, M.D., JOHN P. GIRVIN, M.D., PH.D., AND MICHAEL ELIASZIW, PH.D., FOR THE EFFECTIVENESS AND EFFICIENCY OF SURGERY FOR TEMPORAL LOBE EPILEPSY STUDY GROUP*
Vagus Nerve Stimulator

• Used in the treatment of refractory epilepsy
• FDA approved in 1997 for patients above 12 years of age
• Device that delivers a programmed electrical impulse to the left vagus nerve.
• About 30% of patients experience > 50% reduction in seizures
• Side effects: hoarseness of voice, discomfort, dyspnea, small risk of asystole during implantation wound, infection
• Patients also report greater alertness (? due to fewer seizures, smaller AED doses, less prn benzodiazepines, ? direct VNS effect)
Brain Stimulation

- Thalamic stimulation
- Responsive neurostimulation