NON PHARMACOLOGICAL TREATMENTS FOR EPILEPSY

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NEUROLOGY-EPILEPSY
OUTLINE

• Options of treatment for epilepsy

• Approach to pharmaco-resistant epilepsy
  • Options of treatment

• Other non-pharmacological options

• The Future..
EPILEPSY
OPTIONS OF TREATMENT

Deep Brain Stimulation (DBS) for Epilepsy

Surgery
Lifestyle
ASDs
Ketogenic Diet
Neuro-stimulation

An implant that relieves epilepsy
The IRES device is surgically implanted in the skull and is designed to prevent or halt seizures.
BACKGROUND
EPIDEMIOLOGY

• 10% of the world's population will have *at least one seizure during their lifetime* and 1/3 of these will develop epilepsy at any given time

• 1% of the world's population has active epilepsy

• **30-40%** of patients with epilepsy have pharmaco-resistant epilepsy

BURDEN OF EPILEPSY

• According to the World Health Organization, disability due to epilepsy accounts for approximately 1% of the global burden of disease, as measured by disability-adjusted life years (DALYs), which ranks epilepsy just after major affective disorders, dementias, and alcohol dependence among primary disorders of the nervous system, and comparable to the worldwide burden due to breast and lung cancer.

EPILEPSY: GOALS OF CARE

• Lifelong seizure freedom without adverse effects: the most clinically relevant outcome of any intervention for epilepsy
PHARMACO-RESISTANT EPILEPSY
PHARMACO-RESISTANT (REFRACTORY) EPILEPSY

• The failure of adequate trials of two appropriately chosen and tolerated ASDs (anti-seizure drugs) - whether as monotherapies or in combination - to achieve sustained seizure freedom

PHARMACO-RESISTANT (REFRACTORY) EPILEPSY

• *appropriate treatment* should be proven to be effective for the patient’s epilepsy and seizure type

• treatment used should be at an adequate strength/dosage for a sufficient length of time

• *no seizures including auras:*
  • for *at least three times the longest pre-intervention inter-seizure interval or 12 months, whichever is longer*
  • *any other outcome is considered a treatment failure*
<table>
<thead>
<tr>
<th>Number of ASDs</th>
<th>Number of patients</th>
<th>Number of seizure-free patients</th>
<th>Seizure-free patients (% of total cohort)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1,098</td>
<td>543</td>
<td>49.5</td>
</tr>
<tr>
<td>2</td>
<td>398</td>
<td>146</td>
<td>13.3</td>
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<td>68</td>
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<td>1.0</td>
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</tr>
<tr>
<td>9</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

The chance of seizure freedom declines with successive ASD regimens, most markedly from the first to the third, among patients with epilepsy. Modified from Brodie et al. (19).

PHARMACO-RESISTANT (REFRACTORY) EPILEPSY

• Early identification of pharmaco-resistant epilepsy can direct patients to other options of treatment

• Caution: *apparent* pharmaco-resistance maybe related to:
  • Non-compliance
  • ASD-related (ex: inadequate doses, drug interactions)
  • Lifestyle factors (ex: substance abuse, including alcohol)
  • Misdiagnosis of seizure type or syndrome
  • Non-epileptic seizures
Pharmaco-resistant epilepsy accounts for ~80% of the annual cost attributed to epilepsy.

Ref: Healthcare utilization and costs in adults with stable and uncontrolled epilepsy; Joyce A. Cramer et al; Epilepsy & Behavior 31 (2014) 356-362
APPROACH TO PHARMACO-RESISTANT EPILEPSY
PHARMACO-RESISTANT EPILEPSY

Rule out ‘apparent’ causes for resistance

EMU ADMISSION:
1) CONFIRM DIAGNOSIS
2) DEFINE SEIZURE TYPE(S), SYNDROME

FOCAL ONSET SEIZURES
1. CANDIDATE FOR EPILEPSY SURGERY
   - MTLE & others
   - GKS
   - LASER

GENERALIZED ONSET SEIZURES
1. NEUROMODULATION
   - VNS
   - RNS
   - DBS
   - TNS
2. DIET
3. CAM
PHARMACO-RESISTANT EPILEPSY: OPTIONS OF TX

- SURGERY
- NEURO-MODULATION
- CAM (Complementary and Alternative Medicine)
- OTHER/NEWER/FUTURE OPTIONS
"Nurse, get on the internet, go to SURGERY.COM, scroll down and click on the 'Are you totally lost?' icon."
EPILEPSY SURGERY: THE RATIONALE

• If selection criteria are met, the chances of improvement with surgery is **2 in 3**

• Surgery is associated with a much higher incidence of seizure-free state, reduction in the need for ASD and greater improvement in QOL

Ref: Surgery for epilepsy: a systematic review of current evidence; West S et al; Epileptic Discord. 2016 Jun 1;18(2):113-21

Ref: Surgical versus medical treatment of drug-resistant epilepsy: a systematic review and meta-analysis; Liu, J et al; Epilepsy and Behavior, 2018-05-01, Volume 82, Pages 179-188
MTLE & EPILEPSY SURGERY

• The most common type of epilepsy is MTLE (mesial temporal lobe epilepsy)
  • It is also the most common difficult-to-treat epilepsy
  • **70-90%** of patients become *seizure-free* after antero-mesial temporal lobectomy *(Class I evidence -> AAN practice parameter, 2003)*
  • Improvements in QOL were best in patients who had early surgery (within 2 years)
  • Mortality rates post-surgery were close to **zero** *(vs higher risk with intractable seizures, including SE, SUDEP and suicide)*

Ref: The timing of surgical intervention for MTLE; Engel, J; Neurotherapeutics, Nov 1999
EPILEPSY SURGERY: HOW COMMON?

• Fewer than 1% of patients out of ~ 1,000,000 patients with pharmaco-resistant epilepsy are referred for epilepsy surgery
  • Only ~ 2000-3000 undergo surgery

• Patients who are referred typically have had epilepsy for ~ 22 years and > 10 years after failure of 2 ASDs

Ref: The current place of epilepsy surgery; Engel Jr; Curr Opin Neurol 2018 Apr;31(2):192-197; Diagnosis and surgical treatment of drug-resistant epilepsy Anyanwu C and Motamedi, GK; Brain Sci 2018 Apr 8(4):49
Ref: How long does it take for partial epilepsy to become intractable? Berg AT et al; Neurology. 2003;60(2):186-190
BARRIERS TO SURGERY
FACTORS INFLUENCING DECISION-MAKING

Ref: Perceptions of epilepsy surgery: a systematic review and explanatory model of decision-making; Dewar SR and Pieters HC; Epilepsy and Behavior, 2015-03-01, Volume 44, Pages 171-178
Fear

- Brain surgery provokes fear, and is therefore seen as only a ‘last’ resort.

Physician

Patient
**RISKS VS. BENEFITS**

- Patients overestimate surgical risks and tend to underestimate the risks of uncontrolled seizures.

**COMPARISON:**

<table>
<thead>
<tr>
<th>18 mo data from a Level I Trauma Ctr</th>
<th>GEN SURG</th>
<th>VASC SURG</th>
<th>GEN SURG + TRAUMA</th>
<th>CT SURG</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOTAL</td>
<td>1363</td>
<td>978</td>
<td>914</td>
<td>1403</td>
</tr>
<tr>
<td><strong>TOTAL COMPLIC RATE</strong></td>
<td>30.3%</td>
<td>42.4%</td>
<td>32.3%</td>
<td>26.9%</td>
</tr>
<tr>
<td><strong>MORTALITY RATE</strong></td>
<td>1.83%</td>
<td>3.33%</td>
<td>2.28%</td>
<td>3.34%</td>
</tr>
</tbody>
</table>

Ref: *Complications in Surgical Patients; Healey M et al; Arch Surg. 2002;137(5):611-618*
MORBIDITY & MORTALITY FROM EPILEPSY SURGERY (ATL)

• Operative mortality: **0.1% to 0.5%**
  • mortality is higher for extratemporal procedures (1.4%) than for temporal lobe operations (0.4%)

• Temporary neurologic complications: ~ 10% patients
  • more likely in children and in patients undergoing extratemporal resections

• Overall morbidity: 8%

PRE-SURGICAL EVALUATION
GOALS OF PRE-SURGICAL EVALUATION

- Define the epileptogenic zone
- Identify the *minimum* area of cortex that needs to be resected to attain seizure freedom

APPROACH TO SURGICALLY REMEDIABLE EPILEPSIES

Based on the complexity of pre-surgical evaluation

SELECTION VIA NON-INVASIVE STUDIES

REQUIRE FUNCTIONAL STUDIES

&/OR

INVASIVE STUDIES
NON-INVASIVE STUDIES SUFFICE IN:

Patients who can be selected by non-invasive studies
- Mesial temporal lobe epilepsy associated with hippocampal sclerosis
- Circumscribed epileptogenic lesions (not near eloquent areas)
  - Benign neoplasms
    - Ganglioglioma
    - Dysembryoplastic neuroepithelial tumour
    - Low-grade astrocytoma
    - Oligodendroglioma
  - Vascular malformations
  - Atrophic scars
- Large unihemispheric epileptogenic lesions (for hemispherotomy)
  - Hemiconvulsion Hemiplegia Epilepsy (HHE)
  - Sturge-Weber syndrome
  - Rasmussen’s encephalitis
  - Hemimegalencephaly
- Epileptic encephalopathies and multifocal disease (for corpus callosotomy)
  - Lennox-Gastaut syndrome
Patients who require functional imaging/mapping and/or invasive studies
- Temporal lobe epilepsy with
  *Discordant electroclinical data*
  *Bilateral mesial temporal sclerosis*
  *Normal MRI*
- Extratemporal circumscribed epileptogenic lesions close to eloquent area
- Malformations of cortical development
- Dual pathologies
<table>
<thead>
<tr>
<th><strong>Table 1: Description of cortical zone and lesions (Rosenow and Luders, 2001).</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Epileptogenic zone</strong></td>
</tr>
<tr>
<td><strong>Irritative zone</strong></td>
</tr>
<tr>
<td><strong>Seizure onset zone</strong></td>
</tr>
<tr>
<td><strong>Epileptogenic lesion</strong></td>
</tr>
<tr>
<td><strong>Ictal symptomatogenic zone</strong></td>
</tr>
<tr>
<td><strong>Functional deficit zone</strong></td>
</tr>
<tr>
<td><strong>Eloquent cortex</strong></td>
</tr>
</tbody>
</table>
PRE-SURGICAL EVALUATION

<table>
<thead>
<tr>
<th>CORTICAL ZONE</th>
<th>METHOD OF ASSESSMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatogenic zone</td>
<td>History and Video of the seizure</td>
</tr>
<tr>
<td>Irritative zone</td>
<td>EEG, MEG, f-MRI triggered by EEG</td>
</tr>
<tr>
<td>Ictal onset zone</td>
<td>EEG, ictal SPECT</td>
</tr>
<tr>
<td>Functional deficit zone</td>
<td>Physical exam, Neuro-Psy testing, EEG, PET, SPECT, MRS</td>
</tr>
<tr>
<td>Epileptogenic lesion</td>
<td>MRI</td>
</tr>
<tr>
<td>Eloquent cortex</td>
<td>Cortical stimulation, f-MRI, EP, MEG, trans-cranial magnetic stimulation</td>
</tr>
<tr>
<td>Epileptogenic zone</td>
<td>None (theoretical construct)</td>
</tr>
</tbody>
</table>

Ref: Luders et al
EPILEPTOGENIC ZONE

• “area of cortex that is necessary for initiating seizures and whose removal or disconnection is necessary for complete abolition of seizures” *

• “the minimum amount of cortex that must be resected (inactivated or completely disconnected) to produce seizure freedom”

SEIZURE-FREE AFTER SURGERY

The epileptogenic zone

Actual seizure onset zone

Potential seizure onset zone

Surgical excision
PRE-SURGICAL EVALUATION: THE STEPS
STEP 1:

PATIENT ACCEPTS RISK/BENEFIT RATIO OF SURGERY

YES

NO

DEFER

INTIAL INVESTIGATIONS

EMU EVALUATION
MRI BRAIN (3T)
NEURO-PSYCHOLOGY
NEURO-PSYCHIATRY
SOCIAL & OCCUPATIONAL

MULTI-DISCIPLINARY CONFERENCE

PATIENT DOES NOT WISH TO PROCEED

CONTRA-INDIC TO SURGERY

RESECTION NOT FEASIBLE

ASD; OTHER OPTIONS

Modified from: Ref: Concept of epilepsy surgery and presurgical evaluation; Rathore C and Radhakrishnan K. Seminar in Epileptology; Epileptic Discord 2015; 17 (1): 19-31
STEP: 2

MULTIDISCIPLINARY CONFERENCE

Willing patient

CONCORDANT DATA

LANGUAGE, MOTOR f-MRI, VF: IF NEAR THESE AREAS

POTENTIAL SURGICAL CANDIDATE

DISCORDANT DATA

MRI NEGATIVE

POTENTIAL RESECTION NEAR ELOQUENT CORTEX

ADDITIONAL TESTING

INTERICTAL-FDG-PET

ICITAL SPECT

f-MRI

MSI & ESI

EEG-fMRI & Wada

INTRACRANIAL EEG CORTICAL STIM & MAPPING

YES

TESTABLE HYPOTHESIS RE EPILEPTOGENIC ZONE

NO

PALLIATIVE MEASURES: ASD, KD, NS

SURGERY

EPILEPTOGENIC ZONE LOCALIZED & CAN BE RESECTED

YES

Willing patient

Modified from: Ref: Concept of epilepsy surgery and presurgical evaluation; Rathore C and Radhakrishnan K. Seminar in Epileptology; Epileptic Discord 2015; 17 (1): 19-31
## INTRACRANIAL MONITORING

### MTLE
- Normal MRI
- Bilateral mesial temporal sclerosis on MRI
- Dual pathology
- Electroclinical discordance: investigations are equivocal or contradictory

### EXTRA-TEMPORAL EPILEPSY
- To define epileptogenic zone with indistinct lesion(s)
- Epileptogenic zone is located near eloquent cortex

Ref: Clinical challenges in invasive monitoring in epilepsy surgery; Sperling MR; Epilepsia 1997; 38(4):S6-12
Ref: How to establish causality in epilepsy surgery; Asano E et al. Brain Dev 2013;35: 706-20
INTRACRANIAL EEG

• Subdural surface electrodes
  • grids and strips

• Depth electrodes

• Number and location of placement of electrodes based on individual findings and hypothesis

Ref: Value of non-invasive testing when there are independent bitemporal seizures in scalp EEG. Jenssen S et al. Epilepsy Res 2006, 68, 115-122
STEREO-EEG (SEEG)

• Originally developed in the 1950s (Talairach and Bancaud)
  • Frameless (ease of use; reduced patient discomfort)
  • Robot-assisted (increased accuracy to <2 mm; shorter time (less than 3.5h) for implantation)

• Best for deep foci

• Requires formulating precise hypothesis regarding the epileptogenic zone

Ref: Surgical outcome and prognostic factors of frontal lobe epilepsy surgery. Jeha L et al; Brain 2007, 130, 574–584
EPILEPSY SURGERY: THE PROCEDURE
THE EARLY DAYS...

• The surgical treatment of epilepsy is not a recent innovation: as early as ancient Greek and Roman times, and in the Middle Ages, *trepanation* (the opening of the skull) was occasionally carried out on people with epilepsy.

• It was thought that opening the skull cap would cause the demons of the sickness, poisonous gases or disease-causing juices to escape.

• *Epilepticus sic curabitur* ('The way to cure an epileptic')

RECENT HISTORY

• Victor Horsley pioneered epilepsy surgery: 1886
  • Operated on a 22yo M who developed epilepsy s/p TBI

• Until 1940s, surgery was mostly aimed at removal of tumors and scars and confined to the convexity of cerebral cortex

RELATIVE CONTRA-INDICATIONS TO SURGERY:

- Minor seizures not impairing the quality of life (risk vs benefit)
- Progressive medical or neurological disorder
- Active psychosis, not related to peri-ictal period
- Behavioral issues that impair rehabilitation
- Poor contra-lateral memory – in TL resection

Ref: Concept of epilepsy surgery and presurgical evaluation; Rathore C and Radhakrishnan K. Seminar in Epileptology; Epileptic Discord 2015; 17 (1): 19-31
TYPES OF SURGERY:

• ATL (Anterior Temporal Lobectomy): the most common epilepsy surgery (for pharmaco-resistant MTLE)
  • Standard (en bloc) resection: 3–6 cm of anterior temporal neocortex and 1–3 cm of mesial structures (amygdala and hippocampus)

• SAH (Selective Amygdalo-Hippocampectomy)
  • selectively removing mesial temporal structures leaving the neocortical region intact – to minimize language deficits

STEREOTACTIC LASER ABLATION SURGERY
(VISUALASE; NEUROBLATE)

• Useful for both TLE and extra-TLE
• Less invasive; similar efficacy but less morbidity than open procedure
• Used for both lesional and non-lesional cases, including failed prior surgeries and deep inaccessible lesions

• *Principle:* to necrotize soft tissues through interstitial irradiation or thermal therapy under MRI guidance (MRIgLITT)

MTLE: T1 MRI

STEREOTACTIC LASER THERMO-ABLATION

Images courtesy: Minimally invasive surgical approaches for temporal lobe epilepsy. Chang EF et al; Epilepsy Behav 2015 Jun;47:24-33
STEREOTACTIC RADIOSURGERY (SRS)

• Utilizes stereotactic radioactive cobalt to deliver radiation to a focal region in the brain while leaving the remaining brain tissue intact

• Similar outcomes as ATL

• Effects (seizure control) take as much as 12-12 months to develop

• Minimal side-effects, no neurocognitive decline post-op

Ref: Gamma knife surgery for mesial temporal lobe epilepsy; Rejies J et al; J Neurosurg. 2000 Dec; 93 Suppl 3():141-6
Ref: The role of gamma knife surgery in the treatment of severe epilepsies; Rejies J et al; Epileptic Disord. 2000 Jun; 2(2):113-22
Images courtesy: Minimally invasive surgical approaches for temporal lobe epilepsy. Chang EF et al; Epilepsy Behav 2015 Jun;47:24-33
Comparison of surgical treatments for temporal lobe epilepsy.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior temporal lobectomy (ATL)</td>
<td>Supported by class I evidence; best seizure outcomes</td>
<td>Largest incision and craniotomy; questionable neuropsychological implications of lateral cortex resection</td>
</tr>
<tr>
<td>Selective amygdalohippocampectomy (SAH)</td>
<td>Preservation of lateral cortex; smaller incision and craniotomy</td>
<td>Slightly worse seizure outcomes than ATL; still requires open surgery</td>
</tr>
<tr>
<td>Transsylvian approach</td>
<td>Complete preservation of lateral cortex</td>
<td>Technically challenging; damage to temporal stem</td>
</tr>
<tr>
<td>Transcortical approach</td>
<td>Technically less challenging</td>
<td>Damage to lateral cortex</td>
</tr>
<tr>
<td>Subtemporal approach</td>
<td>Avoids both sylvian fissure and lateral cortex</td>
<td>Possible retraction damage to basal temporal lobe</td>
</tr>
<tr>
<td>Gamma knife radiosurgery (GKRS)</td>
<td>No invasive surgery</td>
<td>Antiseizure effects delayed by 12–24 months</td>
</tr>
<tr>
<td>Stereotactic laser thermo-ablation (STA)</td>
<td>Only burr hole required; preliminarily favorable neuropsychological outcomes</td>
<td>Higher risk of persistent seizures than resection; long-term outcomes require further study</td>
</tr>
</tbody>
</table>
OTHER TYPES OF SURGERY:

• CORPUS CALLOSOTOMY

• Palliative

• When there is no focally resectable lesion:
  • disconnection of CC causes decreased frequency and severity of focal onset seizures with bilateral spread (ex: drop attacks)

OTHER TYPES OF SURGERY:

• MULTIPLE SUBPIAL TRANSECTION

• When seizure foci is near to or overlapping with eloquent cortex

• Can be of value; but not as much as resective surgery

OTHER TYPES OF SURGERY:

• HEMISPHERECTOMY

• Mostly in children when refractory epilepsy is confined to one hemisphere
• Most commonly used in Rasmussen encephalitis, hemimegalencephaly etc.

• ANATOMICAL: consist of resection of all cortical tissue on one hemisphere + various amounts of subcortical tissue

• FUNCTIONAL: consist of more disconnection and less resection than the anatomic hemispherectomy

• Success of the epilepsy surgery depends on the precise localization and delineation of the extent of the epileptogenic zone, and its complete and safe removal.

Ref: Concept of epilepsy surgery and presurgical evaluation. Rathore C and Radhakrishnan K; Epileptic Discord 2015; 17 (1): 19-31
OUTCOMES: THE NUMBERS

ATL (Anterior Temporal Lobectomy)

• Seizure-free at 1-2 years post-op: 60-80%
• 50% at 10 years
• Low risk of significant morbidity (2%); improved life span, neuro-psy profile and QALY compared to pre-surg baseline

SURGERY: OTHER OUTCOMES

• Less effective with:
  • extratemporal lesions
  • no structural lesion
  • or both
• Better outcomes with: hippocampal sclerosis and benign tumors than other pathologies
• Seizure-free outcomes are similar between children and adults

OTHER NON-PHARMACOLOGICAL TREATMENTS FOR EPILEPSY
DIETARY OPTIONS
KETOGENIC DIET

• Fasting has been recognized as a ‘cure’ for epilepsy since 500 BC

• Fasting is the only treatment against epilepsy recorded in Hippocratic collection

• Introduced as a treatment for epilepsy in modern times in 1920s

Ref: History of Ketogenic diet; Wheless JW; Epilepsia Nov 2008, Vol 49, s8, p 3-8
KETOGENIC DIET IN ADULTS

- 32% of KD treated patients achieved >/= 50% seizure reduction
- 9% of KD treated patients achieved > 90% seizure reduction
- The effects persists long-term but may not outlast treatment
- Effects are seen within days to weeks
- Side-effects are benign – hyperlipidemia is the most serious – reversible with d/c of treatment
- High rates (51%) of diet discontinuation

MODIFIED ATKINS DIET (MAD) IN ADULTS

• 29% of MAD treated patients achieved ≥ 50% seizure reduction
• 5% of MAD treated patients achieved > 90% seizure reduction
• The effects persists long-term but may not outlast treatment
• Effects are seen within days to weeks
• Side-effects are benign – hyperlipidemia is the most serious – reversible with d/c of treatment
• High rates (42%) of diet discontinuation

CAM:
(COMPLEMENTARY AND ALTERNATIVE MEDICINE)
Complementary and alternative medicine (CAM) is a diverse group of health care practices and products that fall outside the realm of traditional Western medical theory and practice and that are used to complement or replace conventional medical therapies.

• Up to 44% of adult patients and 12% of children with epilepsy use some form of CAM tx – based on surveys
CAM OPTIONS

• Acupuncture
• Biofeedback
• Yoga
• Nutritional supplements
• Herbal supplements
• Music therapy
• Stress elimination etc...

Ref: Complementary and Alternative Therapies in Epilepsy: Relation to Western Medicine. Levine J and Devinsky D. Book ch 1 in CAM Treatment for Epilepsy 2005
LIFESTYLE MODIFICATIONS

• *Avoid* seizure triggers:
  • Sleep deprivation
  • Excessive alcohol use

• *Avoid* stress

• Adequate physical exercise

Ref: Effect of physical training on aerobic capacity, seizure occurrence, and serum level of antiepileptic drugs in adults with epilepsy. Nakken KO et al; Epilepsia. 1990 Jan-Feb; 31(1):88-94
PSYCHOLOGICAL APPROACHES

• To abort seizures:
  • Biofeedback
  • Avoidance/aversive therapy

• To promote overall well-being:
  • Yoga
  • Relaxation techniques

• To find appropriate coping strategies:
  • Psychotherapy
  • CBT

Ref: Psychological treatments for epilepsy. Ramaratnam S et al; Cochrane Database Syst Rev. 2005 Oct 19; (4)
# NUTRITIONAL SUPPLEMENTS

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin B6</td>
<td>Case reports, uncontrolled clinical trials</td>
</tr>
<tr>
<td>Magnesium</td>
<td>Clinical observations and lab findings</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>Double-blind trials</td>
</tr>
<tr>
<td>Manganese</td>
<td>Clinical observations and lab findings</td>
</tr>
<tr>
<td>Taurine</td>
<td>Uncontrolled trials</td>
</tr>
<tr>
<td>Dimethylglycine</td>
<td>Case report, negative follow-up studies</td>
</tr>
<tr>
<td>Thiamine (to improve cognitive function)</td>
<td>Clinical observations and lab findings</td>
</tr>
<tr>
<td>Folic acid</td>
<td>Clinical observations and lab findings</td>
</tr>
<tr>
<td>Biotin</td>
<td>Clinical observations and lab findings</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>Clinical observations and lab findings</td>
</tr>
<tr>
<td>Omega-3 fatty acids</td>
<td>Uncontrolled and double-blind trials</td>
</tr>
<tr>
<td>L-Carnitine (to prevent valproate toxicity)</td>
<td>Clinical observations and lab findings</td>
</tr>
<tr>
<td>Vitamin K (to prevent drug-induced deficiency)</td>
<td>Uncontrolled trial</td>
</tr>
<tr>
<td>Melatonin</td>
<td>Uncontrolled trial</td>
</tr>
<tr>
<td>Progesterone</td>
<td>Uncontrolled trial</td>
</tr>
</tbody>
</table>

Ref: Natural Approaches to Epilepsy. Gaby AR; Alternative Medicine Review Vol 12 No 1, 2007
OTHER OPTIONS

- Aromatherapy
- Hypnosis

promising results when used together: 1/3 patients became seizure-free for > 12 mo

- Herbal medicine and Homeopathy:
  - Herbal medicines are used as *first line* treatments for all illnesses in an estimated 80% of the world's population

- Acupuncture: *no evidence to support*

"I go home today. They cured me using this new miracle drug. I'm afraid it'll be years before it's approved for humans."
IN CONSIDERATION, IN DEVELOPMENT OR IN INFANCY..

• Non-invasive stimulation
  • TNS: transcutaneous Trigeminal nerve stimulation
  • TMS: transcranial magnetic stimulation
  • tDCS: transcranial direct current stimulation

• Novel drug delivery mechanisms
• Optogenetics
• Focal brain cooling mechanisms

OTHER CONSIDERATIONS..

- **Bioinformatics**: innovations can harness the large amount of data and information available and utilize machine learning and processing to improve understanding and care.

- **Precision Medicine**: understanding the genetics of epilepsy and mechanisms of epileptogenesis.

SUMMARY
APPROACH TO TREATMENT OF EPILEPSY

• Ensure correct diagnosis, type of seizure/epilepsy

• Treatment to fit patient profile; informed decisions

• *Goals of care*: no seizures and no side-effects of treatment, with better quality of life
APPROACH TO PHARMACO-RESISTANT EPILEPSY

• Consider non-pharmacological approaches when appropriate

• Consider epilepsy surgery *earlier* than later
  • Low morbidity and mortality with best results
    • With appropriate patient selection
    • Managed at a level 4 Epilepsy center
NON-PHARMACOLOGICAL TX OF EPILEPSY

- Patient and public education of epilepsy/seizures
  - High risk of SUDEP, SE and suicide with pharmaco-resistant epilepsy

- Strive to remove the fear of brain (epilepsy) surgery

- Understanding and educating patients about the role of CAM in the treatment of epilepsy
ONE PERSON WITH EPILEPSY + ONE NORMAL PERSON = TWO NORMAL PEOPLE