NMDC221 Session 16: Nervous System Disease Part III
Recommended Reading

Website for MS
https://overcomingms.org/
Topic Summary

Nervous System: Part III

- Nutritional considerations of complex & multisystem conditions with a consideration of drug-nutrient interactions
  - Myasthenia gravis
  - Multiple sclerosis
  - Epilepsy
Myasthenia Gravis
Myasthenia Gravis

- Progressive auto-immune condition characterized by weakness and fatigue of the muscles of the limbs, mouth, throat and eyes. Respiratory muscles can be affected.
- The body produces antibodies to Acetylcholine receptors and tyrosine kinase receptors.
- Thymic hyperplasia is also present in 70% of cases.
- Myasthenia gravis is associated with thyroid disease, rheumatoid arthritis, pernicious anaemia & SLE.
- The antibodies to ACh weaken the immune system making the individual more receptive to infection.

(Romi et.al, 2005; Rozsa et.al. 2006; Mahan & Escott-Stump, 2008)
Myasthenia Gravis

From *Immunity: The Immune Response in Infectious and Inflammatory Disease* by DeFranco, Locksley and Robertson

Nutritional Considerations in MG:

Individuals fatigue easily while eating so the following should be observed:

- Nutritionally dense foods at the beginning of the meal is easier to chew before the individual tires.
- Small, frequent meals.
- Limit physical activity before meals.
- Fatigue while eating can increase the chances of food aspiration.

(Schlenker & Long, 2007; Mahan & Escott-Stump, 2008)
# Myasthenia Gravis

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Dosage</th>
<th>Therapeutic Actions</th>
</tr>
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<tbody>
<tr>
<td>Calcium</td>
<td>800-1200mg</td>
<td>Depleted by immuno-suppressant drugs</td>
</tr>
<tr>
<td>magnesium</td>
<td>400-1,000mg</td>
<td></td>
</tr>
<tr>
<td>Chromium</td>
<td>100-600mcg</td>
<td></td>
</tr>
<tr>
<td>Vitamin D</td>
<td>1000-5000iu</td>
<td></td>
</tr>
<tr>
<td>Acetyl-L-Carnitine</td>
<td>500-6,000mg</td>
<td>Improves neuronal energetics. Enhances or mimics acetylcholine function.</td>
</tr>
</tbody>
</table>
| Phosphatidyl-
  choline    | 100-400mg    | Acetylcholine substrate.                                                            |
| Lipoic acid      | 200-600mg    | Improve antioxidant recycling                                                       |
| Inositol         | 750-13,000mg | Secondary messenger for cholinergic receptors                                         |
| Vitamin E        | 100-1000iu   | Cell membrane, supports circulation                                                 |

Myasthenia Gravis

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<tr>
<td>Vitamin B1</td>
<td>50-200mg</td>
<td>Cofactor. Also for acetylcholine &amp; fatty acid synthesis. Cellular energetics. Deficiency causes dementia like symptoms</td>
</tr>
<tr>
<td>Vitamin B5</td>
<td>50-500mg</td>
<td>Cofactor. Synthesis of acetylcholine.</td>
</tr>
<tr>
<td>Vitamin B6</td>
<td>150-200mg</td>
<td>Methylation, reduces hyper-homocysteinemia</td>
</tr>
<tr>
<td>Folate</td>
<td>500-1,000mcg</td>
<td></td>
</tr>
<tr>
<td>Vitamin B12</td>
<td>500-2,000mg</td>
<td>(Malouf &amp; Evans, 2008)</td>
</tr>
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# Myasthenia Gravis

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<th>Drug</th>
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<th>Side Effects</th>
<th>Interactions</th>
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<tr>
<td>Acetyl-cholinesterase Inhibitors</td>
<td>Inhibit acetyl-cholinesterase thereby reducing ACh breakdown at nicotinic &amp; muscarinic receptor sites.</td>
<td>Increased muscle activity in the eyes (pupil constriction), bradycardia, diarrhoea, muscle twitching, bronchoconstriction. Also hypotension, increased lacrimation &amp; sweating</td>
<td>None listed</td>
</tr>
</tbody>
</table>

(Romi et.al, 2005; Rosza et.al. 2006; Bullock et.al. 2007; Bryant & Knights, 2011)
# Myasthenia Gravis

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<tr>
<td>Methotrexate</td>
<td></td>
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<td></td>
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(Romi et.al, 2005, Bullock, et.al, 2007; Kumar & Clark, 2009; Sarris & Wardle, 2010; Bryant & Knights, 2010)
# Myasthenia Gravis

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<th>Drug</th>
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<th>Side Effects</th>
<th>Interactions</th>
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<tbody>
<tr>
<td><strong>Immunosuppressant</strong></td>
<td>Corticosteroids can alter thymus action</td>
<td>Increased appetite, weight gain, fluid retention, nervousness, insomnia</td>
<td>Calcium &amp; Vitamin D: reduced absorption &amp; metabolism.</td>
</tr>
<tr>
<td><strong>Systemic Corticosteroids</strong></td>
<td>Used in acute phase flare-ups of the condition to alter cell mediated and humoral immunity responses.</td>
<td>Protein losses (thinning skin, hair, reduced wound healing, immune dysregulation)</td>
<td>Chromium &amp; Zinc: Increased excretion</td>
</tr>
<tr>
<td>Prednisolone</td>
<td></td>
<td>Adrenal atrophy</td>
<td><strong>Potassium &amp; Vitamin B3:</strong> depletes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bone thinning</td>
<td><strong>Vitamin B12 &amp; Folate:</strong> reduced serum levels</td>
</tr>
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(Harkness & Bratman, 2003; Mahan & Escott-Stump, 2008; Stargrove et al. 2008)
Multiple Sclerosis
Multiple Sclerosis

- A chronic neuromuscular condition characterised by destruction of the myelin sheath and the formation of scar tissue.
- Destruction leads to the distortion or interruption of nerve impulses.
- Myelin sheath are composed of lipoprotein layers formed in early life & function to promote transmission of a neural impulse along an axon.
- No known cause but potential triggers include:
  - Genetic (HLA-A3, B7, D2 and DR2)
  - Infection – viral infections may precipitate
  - Diet (increased consumption of saturated fat) (Kumar & Clark, 2009)

**Symptoms**

- Numbness and/or tingling in the limbs
- Loss of coordination
- Weakness
- Paralysis
- Blurred vision or loss of vision
Types of Multiple Sclerosis

- Relapsing-remitting (RR) MS
- Primary-progressive (PP) MS
- Secondary-progressive (SP) MS
- Progressive-relapsing (PR) MS

Multiple Sclerosis

- The most common form of MS is relapsing-remitting MS
  - Characterised by alternating periods of exacerbation and remission of symptoms without progressive worsening of symptoms.

- Approximately half of individuals diagnosed with relapsing-remitting MS progress to secondary-progressive MS within 10 years
  - The severity of symptoms begin to progressively worsen.

(Nelms et. al 2007)
Multiple Sclerosis – Considerations when planning nutritional interventions

1. Neurotransmitters
   - Melatonin, noradrenaline and serotonin deficiencies have presented in MS cases.

2. Autoimmunity
   - T helper/ T suppressor cell ratios are increased.
   - Raised IgG4 & lymphocyte are commonly present.
   - Th1 dominant autoimmunity disease
     - Excessive IL-12, TNF-α
     - Suppression of TH2 & IL-10

(Osiecki, Meeke & Smith, 2005, p. 226)
Multiple Sclerosis

3. Vitamin $B_{12}$
   - Vitamin $B_{12}$, demyelination, re-myelination and repair in multiple sclerosis
   - Multiple sclerosis and vitamin $B_{12}$ deficiency share common inflammatory and neurodegenerative pathophysiological characteristics.
   - Due to similarities in the clinical presentations and MRI findings, the differential diagnosis between vitamin B12 deficiency and MS may be difficult.
   - Additionally, low or decreased levels of vitamin B12 have been demonstrated in MS patients.

(Miller et.al. 2005)
Multiple Sclerosis

3. Vitamin B12 Cont.
   o Moreover, recent studies suggest that vitamin B12, in addition to its known role as a co-factor in myelin formation, has important immuno-modulatory and neurotrophic effects.
   o These observations raise the questions of possible causal relationship between the two disorders, and suggest further studies of the need to close monitoring of vitamin B12 levels as well as the potential requirement for supplementation of vitamin B12 alone or in combination with the immunotherapies for MS patients.
   o 3-6 years are required to become cobalamin deficient if absorption is ceased abruptly.
   o Inadequate intake (vegetarians).

(Miller et.al. 2005)
Multiple Sclerosis

3. Vitamin $B_{12}$ Cont.
   o Malabsorption:
     • Inadequate production of intrinsic factor (low HCl levels)
     • Disorders of terminal ileum (Crohn’s disease)
     • Competition for cobalamin (intestinal worms)
   o Impaired conversion of homocysteine to methionine
   o Defect in DNA synthesis
   o Megaloblastic cell maturation
   o Defective choline and phosphatidylcholine production
   o Increase in tissue methylmalonyl CoA which is then incorporated into neuronal lipids.
     • These fats are non-physiologic and can be partly responsible for the damage to myelin sheaths
   o Defective central myelin may trigger the autoimmune process

(Miller et.al. 2005)
1. Vitamin B12 deficiency may lead to dysformed myelin which may become a target for autoimmune attacks → aggravating MS

2. Vitamin B12 deficiency is associated with reduction of its immunomodulatory activity → aggravating MS

3. Vitamin B12 deficiency is associated with reduction of its neurotrophic activity → aggravating MS

4. Inflammatory and demyelinating activity in MS is associated with attempts of remyelination leading to consumption of Vitamin B12 → Vitamin B12 Deficiency

5. Immunotherapies induce Th1 to Th2 shift that may lead to:
   a. Increase repair and consumption of Vitamin B12 → Vitamin B12 Deficiency
   b. Possible induction of auto Abs including anti IF and anti PC → pernicious anemia and Vitamin B12 deficiency
Multiple Sclerosis

Nutritional Considerations
Testing for Vitamin B$_{12}$ deficiency
- Common test is serum B$_{12}$ levels - very inaccurate
- Methylmalonic acid and homocysteine levels is much more accurate
  - May be affected by folic acid levels

(Miller et.al. 2005)
Multiple Sclerosis

Nutritional Considerations

Food Allergy
- Increased IgM & low IgA can indicate food intolerances.
- Common foods implicated include dairy & wheat.
- Malabsorption is a common issue linked with altered immune responses.

(Osiecki, Meeke & Smith, 2005, p. 227)
Multiple Sclerosis

Nutritional Treatment Aims
Alleviate Symptoms
  o Support nervous system function
  o Reduce inflammation
Promote Healing
  o Support nervous system repair
Address Underlying/Concomitant Conditions
  o Investigate food intolerances
  o Promote gut repair

(Osiecki, 2006)
Multiple Sclerosis

Nutritional Treatment

- Avoid stimulants to the HPA axis as this will increase the need for nutrients that are involved in NT synthesis
- Avoid dried & cured meats. Nitrophenols have been linked to the presentation of autoantibodies against the myelin sheath
- Avoid overly refined foods and “junk” foods.
- Avoid high saturated fat food sources.
- Assist absorption of key nutrients at the GIT mucosa.
- Enhance intra-transportation of nutrients within the body.

( Osiecki, Meeke & Smith, 2005; Osiecki, 2006; Mahan & Escott-Stump, 2008)
Multiple Sclerosis

Nutritional Treatment

- Investigate digestive dysfunction, serum B12 & Vitamin D
- Avoid stimulants to the HPA axis as this will increase the need for nutrients that are involved in NT synthesis
- Check copper & mercury levels (hair mineral analysis)
- Check for food sensitivities or allergies (elimination diet)
- Visual evoked Response test (VER) measures a reduction in nerve conduction.
  
  (Osiecki, Meeke & Smith, 2005; Osiecki, 2006; Mahan & Escott-Stump, 2008)
Multiple Sclerosis

**Swank Diet**

- Dr Roy Swank, neurologist observed a correlation between high saturated fat diet and MS progression.
- In a prospective cohort study that commenced in 1949 he observed that maintenance of a low saturated fat diet, less than 20gm/day was associated with significantly lower disability. These subjects were followed by 34 years.
- Not all subjects were able to adhere to the Swank diet and the ‘poor dieters’ had significantly poorer health outcomes, higher rates of mortality and more rapid disease progression.
- The ‘good dieters’ consumed on average 16gms of saturated fat/day whereas the ‘poor dieters’ approximately 38gms of saturated fat/day. [http://www.overcomingmultiplesclerosis.org/Recovery-Program/Diet/](http://www.overcomingmultiplesclerosis.org/Recovery-Program/Diet/)
Swank Diet

- **Summary:**
  - Saturated fat should not exceed 15 grams per day.
  - Unsaturated fat (oils) should be kept to 20-50 grams per day.
  - No red meat for the first year.
  - After the first year, 3 oz. of red meat is allowed once per week.
  - Dairy products must contain 1% or less butterfat unless otherwise noted.
  - No processed foods containing saturated fat.
  - Cod liver oil (1 tsp. or equivalent capsules) and a multi-vitamin and mineral supplement are recommended daily.

Multiple Sclerosis

- **What Can You Eat?**
  - **Grains:** Grains and cereals are allowed, with 4 servings encouraged; watch for hidden fats in baked goods and in granola.
  - **Eggs:** Eggs are allowed, count 5 grams of saturated fat in the yolks.
  - **Pasta and rice:** Any amount, whole grain pasta & brown rice preferred.
  - **Poultry:** White meat chicken or turkey, no skin or visible fat.
  - **Fruits:** People should eat least 2 servings a day of fruit. Avocados and olives should be limited, due to their fat content.
  - **Vegetables:** At least 2 servings of vegetables a day are part of the Swank Diet (1 serving=1 cup). Unlimited servings.
  - **Fish:** All whitefish and shellfish is allowed in unlimited amounts; fatty fish must be counted in daily fat allowance.
  - **Coffee:** No more than 3 cups/day of caffeine-containing beverages.
  - **Nuts:** Nuts and seeds, must be counted towards daily oil allowance.

Dietary recommendations

- Further to Roy Swanks research, Professor George Jelinek has published his dietary approach and recommendations for people living with MS.
- Professor Jelinek has adapted the Swank diet although it maintains the primary principle of a low saturated fat diet.
- The resources available on the following website are valuable for people living with MS
  
  http://www.overcomingmultiplesclerosis.org/
# Multiple Sclerosis

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<th>Dosage</th>
<th>Therapeutic Actions</th>
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<tr>
<td>ALA</td>
<td>1000-6000mg (up to 9,000mg)</td>
<td>Suppresses the inflammatory response (enhancing PGE-3 response = down regulation of PGE-2). Decrease Th1 levels</td>
</tr>
<tr>
<td>EPA</td>
<td>500-5,000mg</td>
<td></td>
</tr>
<tr>
<td>Vitamin E</td>
<td>100-1000iu</td>
<td>Due to it action as an antioxidant of lipid peroxides or alternatively in diminishing PGE-2 activity.</td>
</tr>
<tr>
<td>Choline</td>
<td>1000-3,500mg</td>
<td>Useful for myelin sheath production. Addresses ataxia.</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>1000-5000iu</td>
<td>Intake associated with reduced risk of MS development. Prevalence increases the further away an individual resides from the equator thereby having limited sun exposure. Suppresses autoimmunity, regulates suppressor T-cells. Inhibits the production of IL-1, IL-2 &amp; TNF-α</td>
</tr>
<tr>
<td>Calcium</td>
<td>800-1200mg</td>
<td>High intake with vitamin D, results in decreased lymphocytes and increased IL-4 and TGF-b1</td>
</tr>
</tbody>
</table>

(Kidd, 2005; Osiecki, Meeke & Smith, 2005; Osiecki, 2006)
## Multiple Sclerosis

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<tr>
<td>Lipoic acid</td>
<td>200-600mg</td>
<td>Increases nitric oxide synthesis. Reduced glutathione peroxidase levels in MS –</td>
</tr>
<tr>
<td></td>
<td>100-500mg</td>
<td>implicated in increased lipid peroxidation of myelin sheaths</td>
</tr>
<tr>
<td></td>
<td>100-1,500mg</td>
<td></td>
</tr>
<tr>
<td>Glutathione</td>
<td>100-500mg</td>
<td></td>
</tr>
<tr>
<td>N-Acetyl Cysteine</td>
<td>100-1,500mg</td>
<td></td>
</tr>
<tr>
<td>Tyrosine</td>
<td>400-1,500mg</td>
<td>Abnormal stress responses common in MS &amp; are implicated in adrenergic fatigue leading to depletion in noradrenaline precursors</td>
</tr>
<tr>
<td>Phenylalanine</td>
<td>150-600mg</td>
<td></td>
</tr>
<tr>
<td>Vitamin B6</td>
<td>50-200mg</td>
<td></td>
</tr>
<tr>
<td>Vitamin B12</td>
<td>500-8000mcg</td>
<td></td>
</tr>
<tr>
<td>Folate</td>
<td>50-200mcg</td>
<td></td>
</tr>
<tr>
<td>Zinc</td>
<td>10-100mg</td>
<td></td>
</tr>
<tr>
<td>Magnesium</td>
<td>300-800mg</td>
<td></td>
</tr>
</tbody>
</table>

(Kidd, 2005; Osiecki, Meeke & Smith, 2005; Osiecki, 2006)
## Multiple Sclerosis

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<tr>
<td>Threonine</td>
<td>250-1,000mg (up to 10,000mg)</td>
<td>Decreases spasticity</td>
</tr>
<tr>
<td>Lactobacillus Plantarum</td>
<td>10-40 billion org</td>
<td>Moderates T-cell activity &amp; balances Th1/Th2</td>
</tr>
<tr>
<td>Tryptophan</td>
<td>300-4000mg</td>
<td>Serotonin production</td>
</tr>
<tr>
<td>Bioflavonoids anthocyanins</td>
<td>600-3,000mg</td>
<td>Strengthen the blood brain barrier. Potent antioxidants</td>
</tr>
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</table>

(Kidd, 2005; Osiecki, 2006)
## Multiple Sclerosis

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<th>Drug</th>
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<tbody>
<tr>
<td>Centrally Acting Skeletal Muscle Relaxants - (Baclofen, Diazepam)</td>
<td>GABA receptor agonists. Diazepam is specific for GABA-A receptors &amp; Baclofen for GABA-B receptors.</td>
<td>Diarrhoea, nausea, vomiting Dizziness, fatigue, Respiratory depression</td>
<td>Phenylalanine / High protein meal: reduces absorption of Baclofen. Take 2 hrs before or 4 hrs after. Glutamine &amp; Vitamin B6: additive effect with Diazepam Vitamin B3: stimulates GABA receptors without binding, concurrent high dosages could theoretically have an additive effect.</td>
</tr>
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(Stargrove et.al 2008; Kumar & Clark, 2009; Braun & Cohen, 2010; Bryant & Knights, 2011)
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<tr>
<td>Peripherally Acting Skeletal Muscle Relaxants: Dantrolene</td>
<td>Blocks calcium from stimulating an action potential in skeletal muscle</td>
<td>Diarrhoea, nausea, vomiting, Dizziness, fatigue, Respiratory depression</td>
<td>None listed</td>
</tr>
</tbody>
</table>

(Kumar & Clark, 2009; Bryant & Knights, 2011)
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<td>Immuno-suppressant</td>
<td>Corticosteroids can alter thymus action</td>
<td>Increased appetite, weight gain, fluid retention, nervousness, insomnia</td>
<td>Calcium &amp; Vitamin D: reduced absorption &amp; metabolism.</td>
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<td>Systemic Corticosteroids</td>
<td>Used in acute phase flare-ups of the condition to alter cell mediated and humoral immunity responses.</td>
<td>Protein losses (thinning skin, hair, reduced wound healing, immune dysregulation)</td>
<td>Chromium &amp; Zinc: Increased excretion</td>
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<td>Prednisolone</td>
<td>Used in acute relapse stages of MS</td>
<td>Adrenal atrophy</td>
<td>Potassium &amp; Vitamin B3: depletes</td>
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<td></td>
<td></td>
<td>Bone thinning</td>
<td>Vitamin B12 &amp; Folate: reduced serum levels</td>
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(Harkness & Bratman, 2003; Mahan & Escott-Stump, 2008; Stargrove et al. 2008)
Epilepsy
Epilepsy

General name given to a group of disorders that are characterised by recurrent convulsive seizures due to over-firing of neurons across the cerebral cortex.

Symptoms include:
- Loss of consciousness
- Muscle jerking
- Prodromal sights & smells
- Prodromal unusual behaviour

(Bryant & Knights 2011)
Epilepsy

There are different types of epilepsy:

**Partial simple motor (Jacksonian)**
- One part of the brain is stimulated causing single body parts to jerk. This may end quickly or exacerbate until more muscle is affected.

**Partial complex (psychomotor)**
- Quick loss of consciousness, ‘tics’, temperature fluctuations, confusion & feeling of loss of reality. These may progress to a more serious form of epilepsy

**Generalized absence seizures” or ‘petit mal’**.
- “Daydreaming” - actuality there is loss of consciousness for seconds. This can turn into more serious forms in adulthood

(Bryant & Knights 2011, p297)
Epilepsy

Triggers may include:
- Stress
- Brain ischemia.
- Diet
- High aspartic acid
- Environmental toxins.
- Bright lights, loud noises.

(Osiecki, 2006)
Nutritional Treatment
Commonly deficient in epileptics:
- Minerals: Magnesium, Manganese, Zinc
- Vitamins: B1, B3, B6, B12, C, E, Biotin, Folate,
- Amino acids: Adenosine, Glutamine, Taurine, and Tryptophan

Melatonin
- Epileptic children have a high incidence of sleep disturbances. Epilepsy exacerbated by sleep deprivation.
  (Osiecki, 2006)
Epilepsy

Nutritional Treatment
Increase GABA (Glutamine +P5P)
- Found to be low in patients suffering with epilepsy. Neuro-inhibitory effects.

Taurine
- High concentrations in brain tissue. Inhibitory NTM, stabilizes cell membrane electrical conductivity. Acts as a conjugating agent for detoxification processes

Adenosine
- Inhibits nerve firing and has sedative and anti-convulsant activity. Protects brain tissue from injury caused from ischaemia (e.g. during seizures)

(Osiecki, 2006)
Epilepsy

Nutritional Treatment

Histidine
- Precursor to brain histamine (acts as a neuro-inhibiting agent). Promotess relaxation of excitatory tissue.

Trimethylglycine and Dimethylglycine
- Effective in alleviating seizures in rats and humans with hyperhomocysteinemia. Preliminary evidence suggests that it is beneficial in seizures with long-standing mental retardation (Pizzorno & Murray, 2006)
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<td>Adenosine</td>
<td>100-200mg</td>
<td>Regulates nerve impulses</td>
</tr>
<tr>
<td>Histidine</td>
<td>1,000-6,000mg</td>
<td>Neuro-inhibitory agent</td>
</tr>
<tr>
<td>Glutamine</td>
<td>500-3000mg</td>
<td>Cofactor for GABA</td>
</tr>
<tr>
<td>Taurine</td>
<td>250-2,000mg</td>
<td>Calcium flux regulator. Supports brain tissue</td>
</tr>
<tr>
<td>Tryptophan</td>
<td>300-4,000mg</td>
<td>Cofactor for Melatonin. Sleep cycle regulator – induces sleep and decreases brain neuronal stimulation</td>
</tr>
<tr>
<td>Magnesium</td>
<td>300-1000mg</td>
<td>Cofactor for Neurotransmitters</td>
</tr>
<tr>
<td>Selenium</td>
<td>25-250mcg</td>
<td>Antioxidant</td>
</tr>
<tr>
<td>Zinc</td>
<td>10-100mg</td>
<td>Cofactor for Neurotransmitters</td>
</tr>
<tr>
<td>Trimethylglycine</td>
<td>180 mg</td>
<td>Implicated in relieving seizures (Osiecki, 2006; Pizzorno &amp; Murray, 2006)</td>
</tr>
<tr>
<td>Dimethylglycine</td>
<td></td>
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</tbody>
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Epilepsy

Nutritional Treatment

- Eliminate all stimulants – caffeine, sugar, refined CHO’s.
- Increase Magnesium containing foods – nuts, wholegrain cereals, eggs, cashews, almonds
- Remove processed foods from diet – usually high in sugar and fat
- Epileptics have a tendency to development of alkalosis. Ketogenic diet helps to normalise nerve conduction

Ketogenic diet – quality protein foods e.g. legumes, cereals, grains, nuts, seeds, lean meats.

(Osiecki, 2006; Mahan & Escott-Stump, 2008)
Epilepsy

Ketogenic Diets

- Traditionally fasting was the mainstay for this disorder with epilepsy diets metabolically mimicking starvation (carbohydrate deprivation).
- Ketogenic diets are generally high-fat and low-carbohydrate and induce a metabolic shift of energy utilisation within some tissues including the brain.
- This is a viable option for the 30% of epilepsy patients that are intractable to anti-epileptic drugs.

(Nelms et. al. 2011)
## Epilepsy

### Outline of Classic Ketogenic Therapy used for Seizure Control

| Strict clinical supervision by a qualified medical team and registered nutritionist required | Sugar-free multivitamin, calcium and vitamin D supplement to meet AI and other supplements as needed |
| Fat in grams calculated at a 4:1 ratio to protein. 75% Kcal from fat & protein calculated at 1gm/kg/day. Carbohydrate makes up the rest - negligible | Minimal fluid requirements established and fluid encouraged – not to exceed 2L/day |
| Establish energy and protein requirements for individual patients | Monitor urine for maintenance of ketosis |
| In-hospitalisation diet initiation (or outpatient when appropriate) with follow-up visits at least every 3 months for the first year | Lab studies typically include routine monitoring of CBC with platelets, Comprehensive Metabolic Panel (CMP), magnesium, phosphorus, fasting lipid panel, urinalysis, urine calcium & creatinine, and others as needed |

(Mahan & Escott-Stump, 2008, p. 1090; Nelms et. al. 2011)
Epilepsy

Ketogenic Diets

- For infants, children and adolescents, impaired ability to consume adequate nutrients, limited food choices (due to restrictive (ketogenic) diets and drug-nutrient interactions may impair optimal growth and development.

- Supplementation of fibre (will affect ketogenic diet) and calcium (and other nutrients) is recommended due to the lack of these factors in ketogenic diets.

(Nelms et. al, 2011)
Epilepsy

*Ketogenic Diet*
- Appears to increase cerebral energy (ATP) as it changes brain fuel from glucose to acetones and ketones.
  - May help reverse mood symptomatology present in Bipolar (Freeman Kossoff & Hartman, 2007, p. 535, 542)

Summary of a ketogenic diet
Epilepsy

**Ketogenic Diet**

<table>
<thead>
<tr>
<th>Recommended food in low-carbohydrate ketogenic diet</th>
<th>Recommended and restricted food in a low-carbohydrate ketogenic diet and a sample low-calorie diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proteins</td>
<td>fish: tuna, sardine prawns, shrimps, lobster meat; kebabs; sausages; minced poultry; chicken; eggs; cheese: full-fat cheese</td>
</tr>
<tr>
<td>Vegetables/fruit</td>
<td>spinach, watercress, eggplant, parsley, mulberry, coriander, mint, artichoke, okra, cabbage, mushroom, avocado, leek, carrot, radish, celery, cauliflower, green pepper, lettuce, cucumber, tomato, 10–15 olives/d, lemon, strawberry 6/d, avocado, berries 10/d</td>
</tr>
<tr>
<td>Oil</td>
<td>olive oil (5 tbsp, added to salad), flax seed oil</td>
</tr>
<tr>
<td>Restricted food in low-carbohydrate ketogenic diet</td>
<td>flour, potato, macaroni spaghetti, noodles, bread, rice, sugar, sweets, honey, cakes, all fruit juices, all soft drinks</td>
</tr>
</tbody>
</table>

Sample 2200-calorie low-calorie diet

- **Breakfast**: coffee with caffeine (12 oz); cottage cheese 1% fat (1.5 cup); cream, fluid, half and half (1 tbsp); fruit cocktail (0.5 cup)
- **Lunch**: medium apple with peel, medium banana (1 each)
- **Morning snack**: medium apple with peel (1 each); bread whole wheat slice (2 each); cheddar cheese (2 in.³); mayonnaise (tuna salad, 0.15 cup); turkey breast/white meat (3 oz)
- **Dinner**: Bread slice rye 7 grain (2 each); jelly: any fruit flavor (4 tsp); peanut butter (2 tbsp); chicken breast/white meat (4 oz); rice: white cook steamed (1.5 cups); low-calorie thousand island dressing (salad); Kraft mayonnaise (4 tbsp); croutons (cook cuts bred into small cubes) plain (0.25 cup); 1 small garden salad with tomato, onion

- This is a restrictive diet and supplementation will be needed.

Hussain et al. 2012
Epilepsy

Nutritional Treatment

- Increase EFA’s – especially EPA/DHA which supports brain function and integrity of cell membranes – anti-inflammatory effect
- Maintain blood glucose levels consistent – low GI diet. Hypoglycaemia – glucose levels can trigger a seizure in epileptics
- Increase green leafy vegetables – folate content. Low levels have been detected in epileptic patients.

(Osiecki, 2006; Pizzorno & Murray, 2006)
Epilepsy

Nutritional Treatment

- Food allergies/sensitivities – particularly additives, preservatives, gluten has been suspected in some people
- Pesticides, herbicides – inhibits GABA activity

(Osiecki, 2006; Pizzorno & Murray, 2006)
## Epilepsy

<table>
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<tr>
<th>Drug</th>
<th>Action</th>
<th>Side Effects</th>
<th>Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepine: suffix “azepam”</td>
<td>Alter chloride channels = reduced excitability of neurons (enhance GABA levels). Bind to GABA receptors enhancing the action of GABA (muscle relaxation, sedation &amp; anticonvulsant activity)</td>
<td>CNS depression: Sedation (useful for insomnia), Drowsiness, Depression, Cognitive impairment, Ataxia, Inco-ordination, Amnesia. Short action due to dependence, tolerance &amp; withdrawal issues.</td>
<td>Chamomile: additive effect Stimulatory agents may counteract drug effect (caffeine etc…) Glutamine &amp; B6: additive effect Niacinamide: stimulates GABA receptors without binding = additive effect.</td>
</tr>
</tbody>
</table>

(Stargrove et.al. 2008; Braun & Cohen, 2010; Bryant & Knights, 2011)
### Epilepsy

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</tr>
</thead>
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<tr>
<td>Anti-convulsants: Phenytoin, Carbamazepine</td>
<td>Inhibits sodium channels thereby reducing nerve firing</td>
<td>Low therapeutic window Neurotoxic effects (drowsiness, dizziness), vision changes, changes to speech, dizziness, confusion &amp; hallucinations Skin reactions</td>
<td>Carnitine, &amp; folate: Reduced drug toxicity when combined. Drug depletes folate Vitamin B6: reduced drug effects Vitamin B12, vitamin D, beta-carotene, biotin; depleted by drug usage</td>
</tr>
</tbody>
</table>

(Bullock et.al. 2007; Braun & Cohen, 2010; Bryant & Knights, 2007)
Case Discussion – Tutorial

Working in small groups:

- Based on the principles of the ketogenic diet, design a suitable diet with breakfast, lunch, and dinner suggestions that may be applied for someone who wishes to follow, whilst under full medical supervision for their epilepsy. Consider meal choices and systems of the body that need supporting whilst dietary planning.

- What supplements, if any, could be paired with the diet to support the patient and in what dose would they be used for an adult.
References


References


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