The Ketogenic Diet: Is it another fad?

Thanks for joining us! We will get started soon. While you’re waiting you can get handouts, etc. by following the link below.

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Jessica M Lowe, MPH RD CSP | Ketogenic Dietitian

• Presented 9 abstracts and 10 presentations related to ketogenic diet therapy for epilepsy at regional, national, and international conferences

• Invited reviewer for The Academy of Nutrition and Dietetics practice paper on ketogenic diet therapy for epilepsy, published in 2017

• Research Interests:
  - Alternative use of the ketogenic diet, especially pediatric traumatic brain injury
  - Impact of social support networks on adherence of ketogenic diet for children and adults with epilepsy
Disclosures

• Employer:
  – Department of Neurology, Keck School of Medicine of USC
  – Department of Pediatrics, LAC+USC Medical Center
  – Clinical Nutrition Services, Children’s Hospital Los Angeles

• Research Funding: Vitaflo Ltd.

• Programmatic Funding:
  – The Epilepsy Foundation of Greater Los Angeles
  – The Charlie Foundation
  – The Carley Eissman Foundation
Objectives

• Define the ketogenic diet using language and protocols outlined in the standard of care for epilepsy

• Discuss the science behind the ketogenic diet’s role in the treatment of chronic disease (i.e. obesity and type II diabetes) as well as athletic performance

• Discuss strategies to streamline sessions with patients interested in ketogenic diets
Epilepsy is a neurological disorder caused by malfunctioning nerve cell activity in the brain. These malfunctions cause episodes called seizures.

Epilepsy

Epilepsy: the 4th most common neurological disorder

• Epidemiology
  – Prevalence: 2.5-3 million
  – Refractory: \( \frac{1}{3} \) of those with epilepsy

• Etiology:
  – Age dependent:
    • Neonates: metabolic disorders, brain malformations, HIE, ICH
    • Infants and children: fever, brain tumor, infections
    • Children & adults: congenital or genetic factors, head trauma
    • Seniors: Alzheimer’s, stroke, head trauma
  – Idiopathic: \( \frac{1}{3} \) of all epilepsies
Ketogenic Diet

The ketogenic diet is high in fat, supplies moderate protein, and is low in carbohydrate. This metabolic shift results in the production of ketone bodies.

Fat

\[
\begin{align*}
\text{O} \\
\text{C} &\quad \text{R} \\
\text{OH} &
\end{align*}
\]

Ketone

\[
\begin{align*}
\text{O} \\
\text{C} &\quad \text{R} &\quad \text{R}^1
\end{align*}
\]
Ketogenic Diet: epilepsy

How did this come about?

• Hippocrates: fasting
• King James version Mark 9:14-29
  – “He fell on the ground and wallowed foaming…and he said unto them, this kind can come forth by nothing but prayer and fasting”.
• 1920’s
  – Geyelin (endocrinologist): 1st reported fasting as a treatment for epilepsy
  – Wilder (Mayo Clinic): ketogenic diet

Ketogenic Diet: epilepsy

How did this come about? continued

• 1940: development of antiepileptic drugs
• 1994: The Charlie Foundation
  – Dateline segment
  – “…First Do No Harm”
  – Impact: publications
    • 1994: 3
    • 1995: 20
    • 2018: 420

www.webofscience.com
The ketogenic diet should be strongly considered in a child who failed two to three anticonvulsant therapies, regardless of age or gender, and particularly in those with symptomatic generalized epilepsies.

Ketogenic Diet: epilepsy

How well does medication work?
• 1\textsuperscript{st} drug trial: 49% seizure freedom
• 2\textsuperscript{nd} drug trial: 13% seizure freedom
• 3\textsuperscript{rd} drug trial: 4% seizure freedom

How well does the diet work?
• Seizure control:
  – ≥50% reduction in frequency: 65%
  – ≥90% reduction in frequency: 30%
  – Freedom: 10-15%

• Other noted benefits:
  – Cognition and learning
  – Behavior and alertness

Ketogenic Diet: epilepsy
Ketogenic Diet: epilepsy

Defining the Ketogenic Ratio
• Fat (g) to combined carbohydrate (g) and protein (g)
• Purpose: regulate degree of ketosis
• Example: 4:1

Fat  Fat  Fat  Fat  X 9 kcals = 36 kcals

CHO + Protein  X 4 kcals = 4 kcals

36 kcals + 4 kcals = 40 kcals per Dietary Unit
1000 kcals x Dietary Units ÷ 40 kcals = 25 Dietary Units
25 Dietary Units x 4 = 100g Fat
25 Dietary Units x 1 = 25g CHO + Protein

Ketogenic Diet: epilepsy

Defining the Ketogenic Ratio

<table>
<thead>
<tr>
<th>Diet Therapy</th>
<th>Ratio</th>
<th>Fat (g)</th>
<th>Protein (g)</th>
<th>CHO (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classic</td>
<td>4:1</td>
<td>100</td>
<td>17</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>3:1</td>
<td>97</td>
<td>18</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>2:1</td>
<td>91</td>
<td>20</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>1:1</td>
<td>77</td>
<td>30-50</td>
<td>20-40</td>
</tr>
<tr>
<td>MCT Oil</td>
<td>1:1</td>
<td>78</td>
<td>25</td>
<td>50</td>
</tr>
<tr>
<td>MAD</td>
<td>1:1</td>
<td>72</td>
<td>52-62</td>
<td>10-20</td>
</tr>
<tr>
<td>LGIT</td>
<td>1:1</td>
<td>70</td>
<td>40-60</td>
<td>40-80</td>
</tr>
<tr>
<td>Regular Diet</td>
<td>0.2:1</td>
<td>33</td>
<td>35</td>
<td>140</td>
</tr>
</tbody>
</table>

# Ketogenic Diet: epilepsy

<table>
<thead>
<tr>
<th>Diet Characteristics</th>
<th>The Classic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories: adequate, controlled</td>
<td>Calories: adequate, controlled</td>
</tr>
<tr>
<td>Protein: adequate</td>
<td>Protein: adequate</td>
</tr>
<tr>
<td>Fat &amp; Carbohydrates:</td>
<td>Fat &amp; Carbohydrates:</td>
</tr>
<tr>
<td>• Age</td>
<td>• Age</td>
</tr>
<tr>
<td>• Tolerance</td>
<td>• Tolerance</td>
</tr>
<tr>
<td>• Seizure control</td>
<td>• Seizure control</td>
</tr>
<tr>
<td>Initiation</td>
<td>Inpatient, but…</td>
</tr>
<tr>
<td>Education</td>
<td>Recipes provided by RDN</td>
</tr>
<tr>
<td></td>
<td>Foods weighed on gram scale</td>
</tr>
</tbody>
</table>

Ketogenic Diet: epilepsy

The MCT Oil

• Fatty Acids:
  – Caproic acid (C6:0)
  – Caprylic acid (C8:0)
  – Capric acid (C10:0)
  – Lauric acid (C12:0)

• Used as an energy source for:
  – Pancreatic insufficiency
  – Impaired chylomicron transportation

• Physiology:
  – Bypasses lymphatic system
  – Yields more ketones of kcal

• Side effect: GI disturbance

**Ketogenic Diet: epilepsy**

<table>
<thead>
<tr>
<th>Diet Characteristics</th>
<th>The MCT Oil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories: adequate, controlled</td>
<td>Calories: adequate, controlled</td>
</tr>
<tr>
<td>Protein: 12% kCals or 2 x RDA</td>
<td>Protein: 12% kCals or 2 x RDA</td>
</tr>
<tr>
<td>Fat:</td>
<td>Fat:</td>
</tr>
<tr>
<td>• Total: 70-80% kCals</td>
<td>• Total: 70-80% kCals</td>
</tr>
<tr>
<td>• MCT: 30-60% kCals</td>
<td>• MCT: 30-60% kCals</td>
</tr>
<tr>
<td>Carbohydrates: 10% kCals</td>
<td>Carbohydrates: 10% kCals</td>
</tr>
<tr>
<td>Initiation</td>
<td>Inpatient or Outpatient</td>
</tr>
<tr>
<td>Education</td>
<td>Options:</td>
</tr>
<tr>
<td></td>
<td>• RDN provides recipes from gram scale</td>
</tr>
<tr>
<td></td>
<td>• Exchange list and household measures</td>
</tr>
</tbody>
</table>

# Ketogenic Diet: epilepsy

The MAD

<table>
<thead>
<tr>
<th>Diet Characteristics</th>
<th>Calories: adequate, but not controlled</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Protein: ad lib</td>
</tr>
<tr>
<td></td>
<td>Fat: encouraged</td>
</tr>
<tr>
<td></td>
<td>Carbohydrates: 10-30g daily</td>
</tr>
<tr>
<td></td>
<td>• Any type of carbohydrate</td>
</tr>
<tr>
<td></td>
<td>• Can be eaten all at once</td>
</tr>
<tr>
<td></td>
<td>• Total versus net (subtract fiber)</td>
</tr>
<tr>
<td>Initiation</td>
<td>Outpatient</td>
</tr>
<tr>
<td>Education</td>
<td>Carbohydrate counting</td>
</tr>
</tbody>
</table>

## Ketogenic Diet: epilepsy

### The LGIT

| Diet Characteristics | Calories: adequate, controlled  
Protein: adequate  
Fat: 60% kCals  
Carbohydrates: 40-60g daily  
• Glycemic Index: <50  
• Total carbohydrates counted |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiation</td>
<td>Outpatient</td>
</tr>
<tr>
<td>Education</td>
<td>Exchange list and household measures</td>
</tr>
</tbody>
</table>
Ketogenic Diet: epilepsy

The Clinical Pathway

Neurological Evaluation
- Metabolic screening
- Referral to KD
- Insurance authorization

Consultations
- Dietitian
- Social worker
- Pharmacist

Elective Admission (3-5 days)
- Diet initiation
- Labs (BMP, BHB)
- Education

The Clinical Pathway continued

**Post-Hospitalization**

- Phone support
- F/U at 1m & q3m
- Monitor: labs, growth, seizures
- If indicated: adjust Rx and/or diet

**Diet Discontinuation**

- Ineffective: rapid after 3-6 months
- Effective: gradual after 18-24 months
- Serious complications

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Ketogenic Diet: epilepsy

The KD causes a physiologic and metabolic shift

- Drug-nutrient interactions
- Laboratory monitoring
- Side effects

The KD is restrictive

- It is not easy
- Nutritionally incomplete
Ketogenic Diet: epilepsy

Drug-Nutrient Interactions

• Steroids: increases glucose levels and negates ketosis
• Anti-epileptic drugs
  – Carbonic anhydrase inhibitors
    • Medications: topiramate, zonisamide, Diamox
    • Side effects: metabolic acidosis, kidney stones
  – Valproic acid
    • Brands: Depakote, Depakene
    • Side effects: VPA induced carnitine deficiency
  – Pentobarbital IV:
    • Can cause necrotic bowel
    • Interferes with absorption of formula
  – Propofol: one death related to use of ketogenic diet with concomitant propofol in intubated patient

Ketogenic Diet: epilepsy

Carbohydrate Content <1000mg daily

• Avoid syrup, elixirs, and chewables
  – Depakene syrup (250mg/5mL): 7.5mL TID: 21.9g CHO
  – Depakote sprinkles (125mg caps): 3 caps TID = 0g CHO

• Impact on ketogenic ratio:
  – 4:1 at 1000kcals
    • Depakene syrup: reduces ketogenic ratio to 2.13:1
## Ketogenic Diet: epilepsy

### Carbohydrate Content – intravenous medications

<table>
<thead>
<tr>
<th>Intravenous Product</th>
<th>Strength</th>
<th>Carbohydrate</th>
<th>Fat</th>
<th>Alcohol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenobarbital</td>
<td>130mg/mL</td>
<td>Propylene glycol 702mg</td>
<td>-</td>
<td>79mg</td>
</tr>
<tr>
<td>Diazepam</td>
<td>5mg/mL</td>
<td>Propylene glycol 414mg</td>
<td>-</td>
<td>79mg</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>2mg/mL</td>
<td>Propylene glycol 753mg</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>50mg/mL</td>
<td>Propylene glycol 414mg</td>
<td>-</td>
<td>79mg</td>
</tr>
<tr>
<td>Pentobarbital</td>
<td>50mg/dL</td>
<td>Propylene glycol 414mg</td>
<td>-</td>
<td>79mg</td>
</tr>
<tr>
<td>Famotidine</td>
<td>10mg/dL</td>
<td>Mannitol 20mg</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Propofol</td>
<td>19mg/mL</td>
<td>Glycerol 22.5mg</td>
<td>Soybean Oil 100mg</td>
<td>-</td>
</tr>
</tbody>
</table>

Ketogenic Diet: epilepsy

Laboratory Monitoring

- Plasma Amino Acids*
- Urine Organic Acids*
- Plasma Acylcarnitine Profile*
- CMP
- CBC
- Fasting Lipids
- Prealbumin
- Free & Total Carnitine

- Ionized Calcium
- Phosphorus
- Magnesium
- Zinc
- Selenium
- 25-Hydroxy Vitamin D
- Urinanalysis
- Betahydroxybutyrate

Ketogenic Diet: epilepsy

Side Effects

- Reflux
- Constipation
- Acidosis
- Carnitine Deficiency
- Hypoglycemia
- Hyperlipidemia

**Ketogenic Diet: epilepsy**

**It’s Not Easy**


### LAC+USC: Challenges Reported in Clinic (2016)

<table>
<thead>
<tr>
<th>Challenge</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accessibility</td>
<td>25.6% (n=11/43)</td>
</tr>
<tr>
<td>Cultural</td>
<td>44.2% (n=19/43)</td>
</tr>
<tr>
<td>Lack of support</td>
<td>16.3% (n=7/43)</td>
</tr>
<tr>
<td>Meal preparation</td>
<td>23.3% (n=10/43)</td>
</tr>
</tbody>
</table>


Nutritionally Incomplete

Figure 2.
Percent of dietary reference intake (DRI) for ages 4–6, minerals.
*Epilepsia* © ILAE
Questions
Does it work? The Short Term

• Moreno, et al (2014)

Ketogenic Diet: obesity

Does it work? The Long Term

• Moreno, et al (2016)

Ketogenic Diet: obesity

How might it work? Satiety

<table>
<thead>
<tr>
<th>Visual Analogue Scale rating</th>
<th>LC diet (ketogenic)</th>
<th>MC diet (nonketogenic)</th>
<th>SED</th>
<th>$p^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motivation to eat</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hunger</td>
<td>16.8</td>
<td>21.4</td>
<td>1.76</td>
<td>0.014</td>
</tr>
<tr>
<td>Fullness</td>
<td>54.3</td>
<td>54.2</td>
<td>2.02</td>
<td>0.975</td>
</tr>
<tr>
<td>Desire to eat</td>
<td>18.7</td>
<td>23.0</td>
<td>2.59</td>
<td>0.093</td>
</tr>
<tr>
<td>Prospective consumption</td>
<td>23.1</td>
<td>26.4</td>
<td>1.92</td>
<td>0.070</td>
</tr>
<tr>
<td>Thirst</td>
<td>33.7</td>
<td>33.7</td>
<td>1.2</td>
<td>0.970</td>
</tr>
<tr>
<td>Preoccupation with thoughts</td>
<td>13.6</td>
<td>15.6</td>
<td>1.410</td>
<td>0.177</td>
</tr>
<tr>
<td>of food</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postmeal ratings</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pleasantness</td>
<td>86.6</td>
<td>88.8</td>
<td>1.67</td>
<td>0.213</td>
</tr>
<tr>
<td>Satisfying</td>
<td>86.0</td>
<td>88.5</td>
<td>1.67</td>
<td>0.164</td>
</tr>
</tbody>
</table>

Ketogenic Diet: diabetes

Does it work? Type 2

Ketogenic Diet: diabetes

Does it work? Type 1


TABLE 2: Participant-Reported Clinical Variables

<table>
<thead>
<tr>
<th>Clinical Variables</th>
<th>No. Responses</th>
<th>Finding, Mean ± SD or No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse events</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes-related hospitalizations, persons per y²</td>
<td>300</td>
<td>7 (2)</td>
</tr>
<tr>
<td>DKA</td>
<td></td>
<td>4 (1)</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td></td>
<td>2 (1)</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td>4 (1)</td>
</tr>
<tr>
<td>Diabetes-related emergency encounters, persons per y</td>
<td>301</td>
<td>10 (3)</td>
</tr>
<tr>
<td>DKA</td>
<td></td>
<td>3 (1)</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td></td>
<td>2 (1)</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td>7 (2)</td>
</tr>
<tr>
<td>Hypoglycemia with seizure and/or coma, persons per y²</td>
<td>298</td>
<td>7 (2)</td>
</tr>
<tr>
<td>Hypoglycemia requiring help from others, adults per y</td>
<td>174</td>
<td>20 (12)</td>
</tr>
<tr>
<td>Hypoglycemia requiring glucagon, persons per y²</td>
<td>299</td>
<td>11 (4)</td>
</tr>
<tr>
<td>Symptomatic hypoglycemic episodes, persons per mo</td>
<td>297</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td></td>
<td>92 (31)</td>
</tr>
<tr>
<td>1–5</td>
<td></td>
<td>112 (38)</td>
</tr>
<tr>
<td>5–10</td>
<td></td>
<td>40 (13)</td>
</tr>
<tr>
<td>10–20</td>
<td></td>
<td>30 (10)</td>
</tr>
<tr>
<td>≥21</td>
<td></td>
<td>23 (8)</td>
</tr>
<tr>
<td>Monthly symptomatic hypoglycemic episodes</td>
<td>101</td>
<td>6.1 (8.5)</td>
</tr>
</tbody>
</table>

Ketogenic Diet: diabetes

Diabetic Ketoacidosis

- Plasma ketones: ↑
- Plasma glucose: ↑
- Glycosuria: +
- Plasma pH: ↓

Nutritional Ketosis

- Plasma ketones: ↑
- Plasma glucose: □
- Glycosuria: –
- Plasma pH: □

↑ Increase
↓ Decrease
+ Positive
- Negative
□ No Change

Ketogenic Diet: athletics

Keto-Adaption

The human body can adapt to use fat as its primary fuel during submaximal exercise, while at the same time freeing itself from obligate high rate of live and muscle glycogen.

Ketogenic Diet: athletics

Does it work?

  – Self-selected:
    • Group 1: high carbohydrate (n=10)
    • Group 2: low carbohydrate (n=10)
  – Findings:
    • Group 2 had a greater reduction in BMI (-5.9 v -0.8, p=0.006)
    • Low carbohydrate group had a greater reduction in body fat % (-4.6% v 0.7%, p=0.008)
    • Group 2 had a significant increase in the six second sprint peak power test (+0.8 v -0.01, p=0.025)
    • Group 2 had a significant increase in peak power for the critical power test (+1.4 v -0.7, p=0.047)

Ketogenic Diet: athletics

How does it work?
  – Elite, ultra-marathoners & iron man triathletes (n=20)
  – Matched groups:
    • Group 1: high carbohydrate
    • Group 2: low carbohydrate
  – Findings:
    • Group 2 had a two-fold higher rates of peak fat oxidation during graded exercise (p<0.0001) AND sustained submaximal running (p<0.0001)
    • Group 2 had a greater capacity to oxidize fat at higher exercise intensities (p<0.0001)
    • No difference in rate of glycogenolysis pre- and during exercise, and rate of glycogen synthesis during recovery

Ketogenic Diet: so what now?

Message 1: “Nothing about me without me”
– Valerie Billingham

• Patient involvement
  – Patient goals
  – Shared decision making
  – Partnership
  – Empowerment

• Individualized care
  – Psychosocial experience
  – Tailoring treatment
  – Communication
  – Patient as priority
  – Accessible care

Ketogenic Diet: so what now?

Message 2: communicate with their primary provider
• Collaboration enhances care coordination and continuity of care
• The ketogenic diet results in a physiologic and metabolic shift
• The ketogenic diet is nutritional incomplete
• Unknown long-effects of the ketogenic diet
Ketogenic Diet: so what now?

Message 3: The Ketogenic Diet has a reputation

• Bacon and butter
• Trendiest diet in 2018
  – Google: >27,600,000 results
  – Amazon: >3000 cookbooks
    • Developed by RD: 2
Ketogenic Diet: so what now?

Message 4: apps are our friends

• Set macronutrient goals
• Comprehensive food database
• Tracks macro- and micronutrient intake
• App dependent
  – Calculating net carbohydrates
  – Export data
Ketogenic Diet: so what now?

Message 5: it’s ok to not have all the answers

• Large network of Ketogenic Dietitians
  – Charlie Foundation website
  – Nutricia website
• Annual conferences
  – September 2019: Phoenix, Arizona
  – October 2020: Brighton, England
Conclusion

• The Ketogenic Diet is an efficacious treatment option for refractory epilepsy for both adults and pediatric patients

• While the evidence for the use of the Ketogenic Diet in disease states other than epilepsy are limited, we are starting to understand how it may play a role in chronic disease management and athletics

• As practitioners, we should support the decisions our clients/patients make and assist them in making healthful
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MFLN Nutrition & Wellness

Upcoming Event

International Lifestyle Recommendations for Polycystic Ovary Syndrome (PCOS)

- Thursday, March 28, 2019
- 11:00 am – 12:00 pm Eastern
- RSVP: militaryfamilieslearningnetwork.org/event/22060

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