Dietary Therapy For GLUT1
What are parents telling the experts?

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Disclosures

• I really like working with Glenna, Jason, Greg, April and the entire GLUT1DF

• Jason wrote a great chapter in our 6th edition Ketogenic Diets book

• I will travel anywhere that has a bicycle rental!
Dietary Treatment for GLUT1 2017

• The current state of dietary therapy

• What about GLUT1?

• The Orlando Survey and the future
Ketogenic Diet Studies Published
A blinded, crossover study of the efficacy of the ketogenic diet


The ketogenic diet for the treatment of childhood epilepsy: a randomised controlled trial

Elizabeth G. Neal, Hannah Chaffe, Ruby H. Schwartz, Margaret S. Lawson, Nicole Edwards, Georgianna Fitzsimmons, Andrea Whitney, J. Helen Cross

Use of the modified Atkins diet for treatment of refractory childhood epilepsy: A randomized controlled trial

*1Suvashini Sharma, *2Naveen Sankhyan, *Shefali Gulati, and †Anuja Agarwala

A randomized controlled trial of the ketogenic diet in refractory childhood epilepsy

These studies suggest that in children, the ketogenic diet results in short to medium term benefits in seizure control, the effects of which are comparable to modern antiepileptic drugs.
6-Month Seizure Reduction from Ketogenic Diet

- Seizure-free
- 90-99%
- 50-90%
- <50%
4.5 Witloof met mozzarella en spek

Ingredienten:

- 85 gr witloof
- 10 gr mozzarella
- 25 gr spek
- 15 gr Bescuit bakken en braden
☆做法：1. 將蛋打成蛋液，約用 MCT oil 5g 做蛋皮，
將紅蘿蔔及小黃瓜切條汆燙待用。
2. 飯加佐料，醋拌勻。
3. 蛋皮包所有材料捲起，切斜塊即可。
Four Different Diets Today

1. Classic ketogenic diet 1921
2. Medium chain triglyceride diet 1970
3. Modified Atkins Diet 2003
4. Low Glycemic Index Treatment 2005
• No calorie or fluid restriction
• No hospital admission
• No fasting
• No weighing of foods on gram scales
  • 15-20 grams carbohydrate/day
“Other more palatable but related diets, such as the modified Atkins KD, may have a similar effect on seizure control as classical KD but this assumption requires more investigation”
51 KD vs. 53 MAD

Similar efficacy and better tolerability with MAD

“The MAD might be considered as the primary choice...”
**SPECIAL REPORT**

Optimal clinical management of children receiving the ketogenic diet: Recommendations of the International Ketogenic Diet Study Group

### Table 1. Epilepsy syndromes and conditions in which the KD has been reported as particularly beneficial

<table>
<thead>
<tr>
<th>Probable benefit (at least two publications)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose transporter protein 1 (GLUT-1) deficiency</td>
</tr>
<tr>
<td>Pyruvate dehydrogenase deficiency (PDHD)</td>
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<tr>
<td>Myoclonic-astatic epilepsy (Doose syndrome)</td>
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<tr>
<td>Tuberous sclerosis complex</td>
</tr>
<tr>
<td>Rett syndrome</td>
</tr>
<tr>
<td>Severe myoclonic epilepsy of infancy (Dravet syndrome)</td>
</tr>
<tr>
<td>Infantile spasms</td>
</tr>
<tr>
<td>Children receiving only formula (infants or enterally fed patients)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Suggestion of benefit (one case report or series)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selected mitochondrial disorders</td>
</tr>
<tr>
<td>Glycogenosis type V</td>
</tr>
<tr>
<td>Landau-Kleffner syndrome</td>
</tr>
<tr>
<td>Lafora body disease</td>
</tr>
<tr>
<td>Subacute sclerosing panencephalitis (SSPE)</td>
</tr>
</tbody>
</table>
3 Key Questions from Houston

1. Is the MAD = KD?

2. What happens at puberty (and adulthood) on diets?
   - Can the KD ever be stopped in GLUT1?

3. Does the level of ketosis matter for seizure control?
“Pro” Argument

- GLUT1 deficiency syndrome has been historically reported as a “brain energy failure” condition
- Theoretically, higher ketosis would improve the situation
- At an early age, it would be logical to provide high quality and quantity fuel
  - Especially for cognition?
- Anecdotal reports of KD > MAD
“Con” Argument

- Anecdotal reports (and patient emails) of high ketones but persistent seizures and other issues
- MAD reported as helpful in cases for GLUT1
  - Many families reported switching diets successfully
- “the original concept that brain energy failure is reversible by means of a 3:1 or 4:1 KD apparently is far too simplistic” — Klepper *JCN* 2013
GLUT1 Ketoicnic Diet Survey

Participation in this survey is completely voluntary. No names will be recorded and no individual information will be shared.

1. What diet is your child currently receiving? (Circle) KETOGENIC DIET, MODIFIED ATKINS DIET, LOW GLYCEMIC INDEX, NONE

2. If your child is no longer receiving any of these diets, please state why it was stopped or why it was not started? (Leave blank if still on a diet)

3. My child is a BOY / GIRL (circle)

4. How old is your child now? _______ years

5. When was GLUT1 Deficiency syndrome diagnosed? _______ years

6. How old was your child when the diet was started? _______ years

7. KETOGENIC DIET INFORMATION

   a. Current Ratio: 4:1 3:1 2:1 Higher than 4:1
   b. Did your child fast the diet before? YES / NO
   c. Was your child admitted to the hospital? YES / NO
   d. Is your diet already on the diet? YES / NO

8. Has your ketogenic diet discussed coming off the diet ever? YES / NO
   a. If yes, what is the reason for stopping the diet? YES / NO
   b. Do you plan to take your child off ever? YES / NO
   c. Have you ever switched from KD to MAD or LGT? YES / NO

9. Has your ketogenic diet discussed transitioning to the MAD? YES / NO

10. Have you ever switched from KD to MAD or LGT? YES / NO

11. Do you check ketones through (circle all that apply): URINE / BLOOD / NEITHER

12. Do you see a relationship between seizures and ketones? YES / NO / NOT SURE / (NO SEIZURES)

13. Do you see a relationship between learning/behavior/movement (circle) and ketones? YES / NO / NOT SURE

14. If your child has reached puberty, did you see a change in ketones when puberty came? YES / NO

15. Is your child on any extra ketogenic diet supplements? (please circle any that apply)

   a. Calcium
   b. Extra oils (C7, MCT, etc)
   c. Polyunsaturated Fatty Acids
   d. Other

16. Is your child on antiepileptic medications? YES / NO. If yes, which ones?

17. Compared to before the diet, how much better are seizures now? (Circle)

   a. 100% gone (seizure-free)
   b. 90-95% gone (once in a while)
   c. 85-90% better (improved, but still frequent)
   d. 70-80% improved (really not better— we're thinking of coming off)

18. Have there been any side effects related to the diet? If so, please describe:

19. Have you discovered any tricks to allow your child to be successful on the diet for long periods that you'd like to share?

20. Any additional comments you'd like to add about your family's experience with the ketogenic diet?

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Thank you for your participation in this survey!

We will share the results at the next GLUT1 Deficiency Foundation meeting!

Eric Kossoff, M.D.
Glenna Steele
Caveats

- No verification of GLUT1 status, epilepsy, anti-seizure drugs
- Only families in active communication with GLUT1DF’s in US, UK, and Japan
- Not all questions universally completed
Use of dietary therapies amongst patients with GLUT1 deficiency syndrome

Hannah R. Kass\textsuperscript{a}, S. Parrish Winesett\textsuperscript{b}, Stacey K. Bessone\textsuperscript{b}, Zahava Turner\textsuperscript{c}, Eric H. Kossoff\textsuperscript{c,*}

\textsuperscript{a} University of Mary Washington, Fredericksburg, VA, USA
\textsuperscript{b} Johns Hopkins All Children’s Hospital, St. Petersburg, FL, USA
\textsuperscript{c} Johns Hopkins Hospital, Baltimore, MD, USA
Results: Overall

• 92 families completed the survey
  – 55% at the Orlando meeting

• Current age: 1-24 years (mean: 9.9 years)
  – GLUT1 diagnosis: 0.1 – 18 years (mean 4.8 years)

• 90 had been treated with diet therapy
Results: Wide Range of Diets!

- KD – 59
- MAD – 29
- MCT – 4
- LGIT – 2

- Switching was common! 27% changed diets during their treatment.
  - Mostly initiated by the neurologist
- Many started with KD and changed to MAD
Seizure Reduction Compared to Before Diets (n=82)

- Seizure-free: 80%
- 90-99%: 46%
- 50-89%: 34%
- <50%: 15%
<table>
<thead>
<tr>
<th>Factor</th>
<th>Presence (n = 38)</th>
<th>Absence (n = 46)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age at GLUT1 diagnosis (years), (SD)</td>
<td>3.8 (3.5)</td>
<td>5.3 (3.4)</td>
<td>0.05</td>
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<td>Mean age at diet onset (years), (SD)</td>
<td>4.0 (3.6)</td>
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<td>0.22</td>
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<tr>
<td>Mean current age (years), (SD)</td>
<td>8.2 (5.7)</td>
<td>11.6 (5.2)</td>
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<td>KD/MCT currently</td>
<td>28 (74%)</td>
<td>29 (63%)</td>
<td>0.30</td>
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<td>4:1 KD</td>
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<td>22 (58%)</td>
<td>25 (54%)</td>
<td>0.74</td>
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<td>Fasted at diet onset</td>
<td>17 (45%)</td>
<td>20 (43%)</td>
<td>0.91</td>
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<td>Gender (female)</td>
<td>19 (50%)</td>
<td>23 (50%)</td>
<td>1.00</td>
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<td>5 (13%)</td>
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<td>19 (50%)</td>
<td>24 (52%)</td>
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Results: Concurrent Medications

- 32 (36%) were on medications
  - Levetiracetam (8), acetazolamide (6), lamotrigine (6), ethosuximide (4), clonazepam (3)
- Only 1 with valproate, zero on phenobarbital
- Many were on “extra” supplementation
  - Carnitine (52), oral citrates (25), MCT oil (20)
  - None reported C7
Results: Other Diet Benefits

• 76 of 76 had improvement in abnormal movements and/or cognition
  – 84% “much” better
Results: Ketones

• Varied monitoring:
  – 34% only blood BOH, 34% only urine, 21% both, 11% neither
• 44/66 (67%) reported a correlation with ketones and seizures
• However, no difference in seizure freedom in those who checked blood vs. urine ketones
Results: Puberty

- 22 had reached (or finished) puberty
  - 14 (64%) reported a “change” in seizure frequency
  - 11 (50%) had a drop in ketosis
Results: Side Effects

- Side effects *reported* were common, but not overly problematic

- Constipation (24)
- Weight loss or hunger (6)
- Gastroesophageal reflux (5)
- Kidney stones (2)
- Acidosis (2)
- Elevated cholesterol (1)
Results: Discontinuation?

- Mean diet duration: 5.6 years
  - Range: 1 month - 20 years
  - 3 had stopped

- 8 (9%) planned to come off diet
- 22 (24%) said they had no plans to
- 60 (67%) were unsure
New Study #1

- 10 children with GLUT1 (2 were infants!) started on MAD
- Two patients switched from KD to MAD and improved weight, height, and endurance without change in seizures
- "Our data suggest that MAD provides a similar improvement to the ketogenic diet in patients with GLUT1-DS"
“Our study showed that the MAD was more palatable among the GLUT1DS patients and that its ketogenicity was comparable (or even better in some patients) to the classic KD”
New Study #3

- 181 patients in a G1D registry
- “The results of this study indicate a departure from canonical ketogenic diets”

<table>
<thead>
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<th>Category</th>
<th>No. (%) of Patients (N = 77)</th>
</tr>
</thead>
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<tr>
<td>Ketogenic diet</td>
<td>54 (70.1)</td>
</tr>
<tr>
<td>Ketogenic diet ratio</td>
<td></td>
</tr>
<tr>
<td>≤2:1</td>
<td>8 (10.4)</td>
</tr>
<tr>
<td>2.5:1</td>
<td>10 (13.0)</td>
</tr>
<tr>
<td>3.0:1</td>
<td>14 (18.2)</td>
</tr>
<tr>
<td>3.5:1</td>
<td>10 (13.0)</td>
</tr>
<tr>
<td>≥4.0:1</td>
<td>8 (10.4)</td>
</tr>
<tr>
<td>Modified Atkins diet</td>
<td>13 (16.9)</td>
</tr>
<tr>
<td>Other diets</td>
<td>10 (13.0)</td>
</tr>
</tbody>
</table>
Conclusions

- The results from this survey (and others) suggest GLUT1 families are implementing and switching successfully between various ketogenic diets
  - Incredible creativity

- Outcomes are outstanding and for extended periods of time
  - Great for seizures (and movements…)
  - 2/3 of patients without medications
Conclusions

• Day-by-day monitoring, drugs, and supplements are also variable

• Further study needed:
  – Puberty
  – Discontinuation?
  – Correlation with ketosis
  – Supplements?

• The future…
  – Cognition
  – Adults with GLUT1…
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Dr. Parrish Winesett
Stacey Bessone

Glenna Steele
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Mackenzie Cervenka MD
Parrish Winesett MD
Zahava Turner RD
Courtney Haney RD
Bobbie Henry RD
Stacey Bessone RD
Jamie Houdek RD
Tony Stanfield
Gerry & Mike Harris
Lindsay Brown
Tarah Majestic
Anita Charpentier, PharmD
Sapana Edwards, RN
Rebecca Fisher, RN
6th Global Symposium on
KETOGENIC THERAPIES FOR NEUROLOGICAL DISORDERS:

Embracing Diversity, Global Implementation and Individualized Care

October 5-8, 2018
International Convention Center Jeju, Jeju, Korea