Ketogenic Diet
A first-line treatment choice?

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4 February 2023

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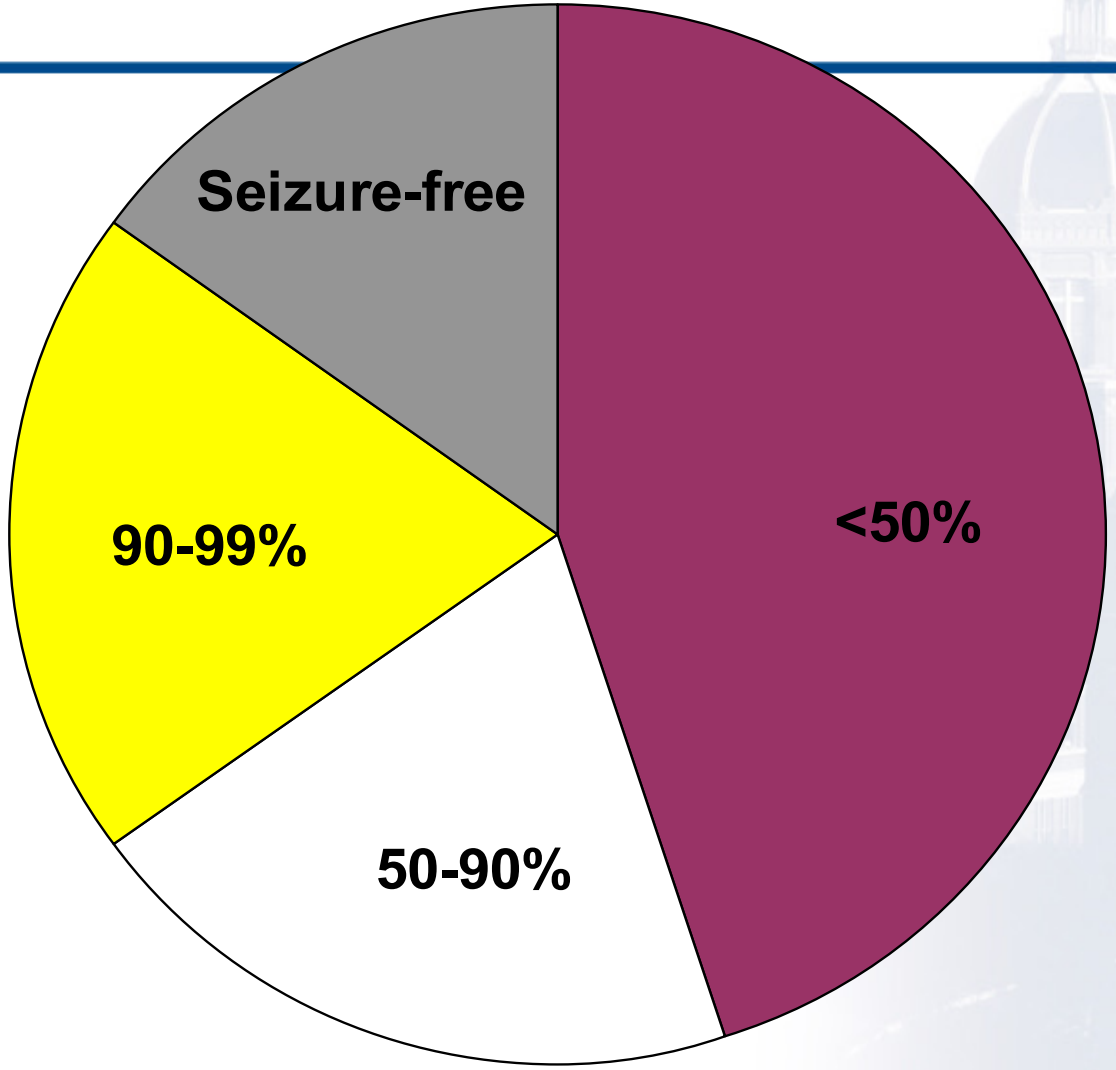
MEDICINE

INTERNATIONAL
NEUROLOGICAL
KETOGENIC SOCIETY

Disclosures

- Consultant: Atkins Nutritionals, Nutricia, Cerecin, Bloom Science, Aquestive, LivaNova
- DSMB: NeuroPace
- Royalties: Springer, UpToDate, Oxford, Johns Hopkins University Press

6-Month Seizure Reduction

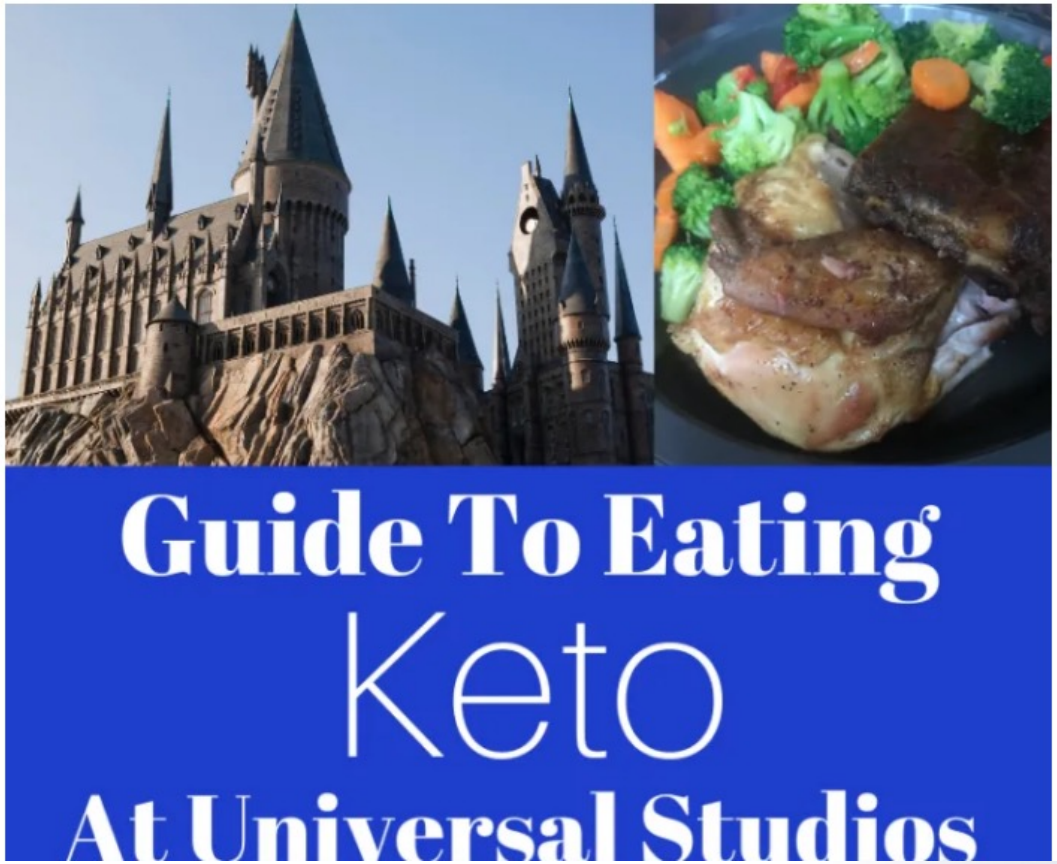



LARD LAD
DONUTS


Universal Orlando
VOODOO
DOUGHNUT
UNIVERSAL · ORLANDO
AmateurTraveler.com

Tips For Eating Keto At Universal Studios

It's so easy for me to stay on track and diet when I'm at home. Yet, a one week vacation can wreak havoc on my diet and undo a lot of my hard work. Instead of fearing the weight gain, I arm myself with the best possible choices at any destination. Here's my complete guide to eating **Keto at Universal Studios & Islands of Adventure** in Orlando, Florida. These low carb theme park options will be your best friend!



Using the diet earlier for DEEs?

1. What do the guidelines say?
2. Is there published evidence for first-line use?
3. The future…

Epilepsia Open® The Open Access Journal of the International League Against Epilepsy

Open Access

SPECIAL REPORT

Optimal clinical management of children receiving dietary therapies for epilepsy: Updated recommendations of the International Ketogenic Diet Study Group

[1]Eric H. Kossoff, [2]Beth A. Zupec-Kania, [3]Stéphane Auvin, [4]Karen R. Ballaban-Gil, [5]A.G. Christina Bergqvist, [6]Robyn Blackford, [7]Jeffrey R. Buchhalter, [8]Roberto H. Caraballo, [9]J. Helen Cross, [10]Maria G. Dahlin, [11]Elizabeth J. Donner, [12]Orkide Guzel, [13]Rana S. Jehle, [14]Joerg Klepper, [15]Hoon-Chul Kang, [16]Danielle A. Lambrechts, [17]Y.M. Christiana Liu, [18]Janak K. Nathan, [19]Douglas R. Nordli Jr, [20]Heidi H. Pfeifer, [21]Jong M. Rho, [22]Ingrid E. Scheffer, [23]Suvasini Sharma, [24]Carl E. Stafstrom, [20]Elizabeth A. Thiele, [25]Zahava Turner, [26]Maria M. Vaccarezza, [27]Elles J.T.M. van der Louw, [28]Pierangelo Veggiotti, [29]James W. Wheless, [30]Elaine C. Wirrell, The Charlie Foundation, Matthew's Friends, and the Practice Committee of the Child Neurology Society

Epilepsia Open, 3(2):175–192, 2018
doi: 10.1002/epi4.12225

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Guidelines

- Use KDT after 2.6 (SD 0.9) drugs have been tried

- "Consider earlier use for certain situations or indications?"
  - 88% of the consensus group voted YES

Table 1. Epilepsy syndromes and conditions (listed alphabetically) for which KDT has been consistently reported as more beneficial (>70%) than the average 50% KDT response (defined as >50% seizure reduction).

Angelman syndrome[56,57]
Complex I mitochondrial disorders[51,55]
Dravet syndrome[35,36]
Epilepsy with myoclonic–atonic seizures (Doose syndrome)[34,37,38]
Glucose transporter protein 1 (Glut-1) deficiency syndrome (Glut1DS)[27,29–32]
Febrile infection–related epilepsy syndrome (FIRES)[44–47]
Formula-fed (solely) children or infants[48,49]
Infantile spasms[10,39,40]
Ohtahara syndrome[50–52]
Pyruvate dehydrogenase deficiency (PDHD)[28]
Super-refractory status epilepticus[44,46,53,54]
Tuberous sclerosis complex[41–43]

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Using the diet earlier for DEEs?

1. What do the guidelines say?
2. **Is there published evidence for early use?**
3. The future

Experience in the Use of the Ketogenic Diet as Early Therapy

James E. Rubenstein, MD*; Eric H. Kossoff, MD*; Paula L. Pyzik, BS; Eileen P. G. Vining, MD; Jane R. McGrogan, RD; John M. Freeman, MD

Table 1. Patients on Either Zero or One Anticonvulsant Prior to Diet Initiation

Patient	Prior Medication	Age at Diet Onset (yr)	Seizure Duration Prior to Diet (yr)	Seizure Type	6-Month Efficacy (%)	Diet Duration (yr)
1	None	0.33	0.33	Myoclonic	< 50	0.50
2	None	0.42	0.00	Infantile spasms	Seizure free	0.50
3	None	0.50	0.08	Infantile spasms	< 50	0.06
4	None	0.51	0.09	Infantile spasms	> 90	3.22
5	None	0.66	0.08	Infantile spasms	< 50	0.36
6	None	1.08	0.16	Lennox-Gastaut syndrome	50–90	1.73
7	None	3.00	0.00	Infantile spasms	Seizure free	0.42
8	Valproic acid	3.25	0.25	Lennox-Gastaut syndrome	> 90	1.00*
9	Valproic acid	4.25	0.75	Neuronal ceroid-lipofuscinosis	< 50	0.75
10	Valproic acid	6.00	5.67	Lennox-Gastaut syndrome	> 90	1.50
11	Clonazepam	0.40	0.07	Infantile spasms	> 90	0.86
12	Clonazepam	0.42	0.17	Complex partial (prior infantile spasms)	50–90	4.50*
13	Phenobarbital	0.50	0.50	Infantile spasms	Seizure free	1.87

*Currently on the ketogenic diet.

J Child Neurol 2005

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- Mostly children under age 1 year
- Several with side effects from the first drug

- "When presented in a favorable manner and compared with the unknown effects of many anticonvulsants on the developing brain, it is not surprising that parents elected to initiate the ketogenic diet rather than wait until their child experienced multiple anticonvulsant failures."

J Child Neurol 2005

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J Child Neurol 2005

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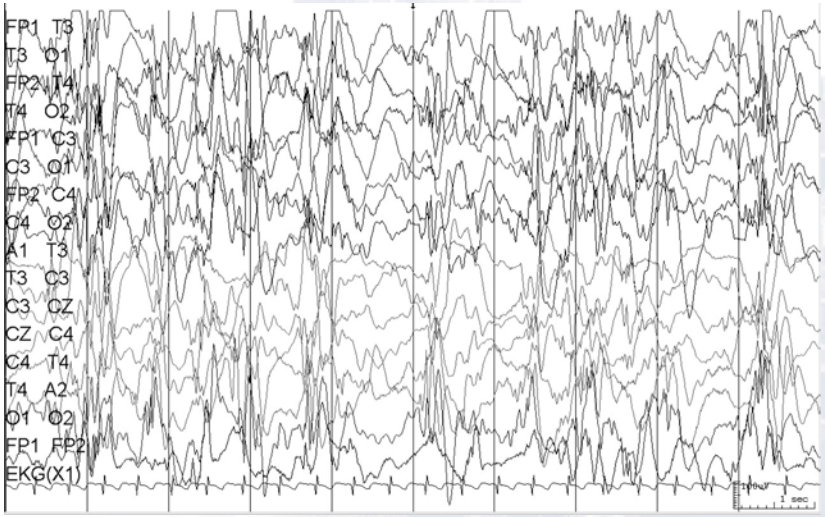
C.H.

- 5 month old previously healthy girl with the acute onset of infantile spasms
- Seen in ER after 3 days
  - ACTH and vigabatrin offered
- Family chose to try KD first



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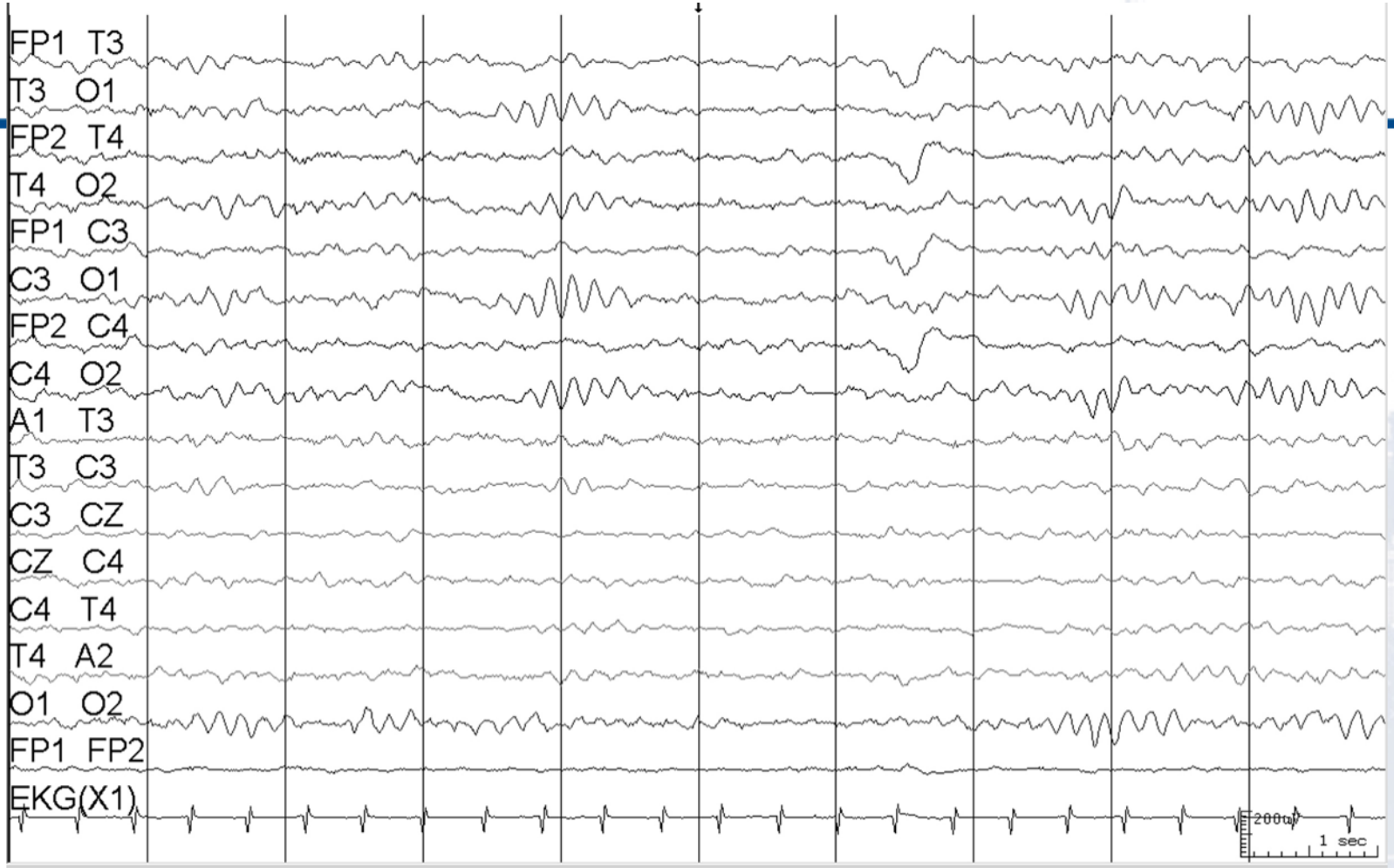

2 months later

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The Carson Harris Foundation

What is the keto diet?

It is a high fat, low carbohydrate diet that has been in use since 1921.

JHH KETOGENIC DIET PARENT SUPPORT GROUP

Held monthly during the keto admission week at Johns Hopkins Hospital.

Watch our last webinar!

"Advances and Practical Application of the Modified Atkins Diet"

DONATE TODAY

Donations provide support of clinical and research efforts on the diagnosis and treatment of epilepsy.

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Carson's Story

In February of 2007, we took our 5-month old daughter, Carson, to Johns Hopkins Hospital because she was having what appeared to be seizures. (http://www.youtube.com/user/CarsonHarrisFDN?feature=mhsn) Twelve hours, a spinal tap and an EEG scan of her brain later we were told that she has a rare form of Epilepsy called "Infantile Spasms". There are no words to describe the emotions we experienced upon hearing the news that our daughter had about a 20% chance of recovering. Fortunately for us, Johns Hopkins has one of the best pediatric epilepsy programs in the country so we were immediately seen by specialists who have hands on experience with this rare disorder. We were offered multiple forms of treatment, including a regiment of steroids called ACTH, Vigabatrin, Topamax and a more radical approach that Hopkins happens to specialize in called the ketogenic diet.

The Ketogenic Diet

Normally, our bodies run on energy from glucose, which we get from food. We can't store large amounts of glucose, however. We only have about a 24-hour supply. When a child has no food for 24 hours -- which is the way the diet begins, usually in a hospital -- he or she uses up all the stored glucose. With no more glucose to provide energy, the child's body begins to burn stored fat. The ketogenic diet keeps this process going. It forces the child's body to burn fat round the clock by keeping calories low and making fat products the primary food that the child is getting. In fact,

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A case-control evaluation of the ketogenic diet versus ACTH for new-onset infantile spasms

	KD (n=13)	ACTH (n=20)	*P*-value
Spasm free at 1 month	8 (62%)	18 (90%)	0.06
Median days to spasm freedom (range)	6.5 (1-18)	4 (1-21)	0.18
Normal EEG at 1 month	1 (9%)	9 (53%)	0.02
Normal EEG at 3-6 months *(for responders)	8 (100%)	13 (76%)	0.19
Developmental delay (moderate/severe)			
At follow-up (median 12 months)	5 (38%)	7 (35%)	0.28
Recurrence rate for responders	1 (12.5%)	6 (33%)	0.23

Kossoff et al. *Epilepsia* 2008

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Received: 25 October 2018 | Revised: 29 January 2019 | Accepted: 29 January 2019
DOI: 10.1111/epi.14679

FULL-LENGTH ORIGINAL RESEARCH

Epilepsia

Efficacy and tolerability of the ketogenic diet versus high-dose adrenocorticotropic hormone for infantile spasms: A single-center parallel-cohort randomized controlled trial

Anastasia Dressler[1] | Franz Benninger[2] | Petra Trimmel-Schwahofer[1] | Gudrun Gröppel[1] | Barbara Porsche[1] | Klaus Abraham[1] | Angelika Mühlebner[1] | Sharon Samueli[1] | Christoph Male[1] | Martha Feucht[1]

- 101 infants, randomized controlled trial
- For New Onset (no vigabatrin):
  - At 1 month: 80% ACTH vs. 47% KD (p=0.02)
  - *At last visit: 21% ACTH vs. 48% KD (p=0.05)*

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KD for New-onset Spasms today

- I will offer it when infants present within 2 weeks of onset
  - *Usually Friday 1pm*
- 14/29 patients spasm-free (48%)
  - When not successful, parents still very appreciative!
- Most common reasons for refusal:
  - Ease of oral steroids AND breastfeeding

GLUT-1 Deficiency Syndrome

- 80% of patients have >90% seizure reduction on the KD or MAD
  - 64% no longer require anticonvulsants
- Highly effective for cognition and movements as well

There are several specific conditions in which the group considered the KD could be used potentially even earlier (Table 1). The diet is the treatment of choice for two distinct disorders of brain energy metabolism: GLUT1 deficiency syndrome (Klepper & Leiendecker, 2007) and pyruvate dehydrogenase deficiency (PDHD) (Wexler et al., 1997). In GLUT1 deficiency syndrome, glucose transport across the blood-brain barrier is impaired resulting in seizures, developmental delay, and a complex movement disorder (Klepper & Leiendecker, 2007). Twenty-four members of the consensus (92%) believed the KD should be considered as a first-line therapy for GLUT1 deficiency syndrome. In PDHD, a severe mitochondrial

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Received: 3 May 2020 | Revised: 13 June 2020 | Accepted: 16 June 2020

DOI: 10.1002/epi4.12414

SPECIAL REPORTS

Epilepsia Open®
Open Access

Glut1 Deficiency Syndrome (Glut1DS): State of the art in 2020 and recommendations of the international Glut1DS study group

Joerg Klepper[1] | Cigdem Akman[2] | Marisa Armeno[3] | Stéphane Auvin[4] | Mackenzie Cervenka[5] | Helen J. Cross[6] | Valentina De Giorgis[7] | Adela Della Marina[8] | Kristin Engelstad[2] | Nicole Heussinger[9] | Eric H. Kossoff[10] | Wilhelmina G. Leen[11] | Baerbel Leiendecker[8] | Umrao R. Monani[12] | Hirokazu Oguni[13] | Elizabeth Neal[14] | Juan M. Pascual[15] | Toni S. Pearson[16] | Roser Pons[17] | Ingrid E. Scheffer[18] | Pierangelo Veggiotti[19] | Michél Willemsen[20] | Sameer M. Zuberi[21] | Darryl C. De Vivo[2]

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Consensus: Glut1 and KDT

- Should the KD be used “very early” in the course of treatment?
  - **88% YES (2018)**
  - **100% YES (2020)**

- Use the diet before other keto-like drugs?
  - **96% YES (2018)**
  - **92% YES (2020)**

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Case Report

Ketogenic Diet in Glut 1 Deficiency Through the Life Cycle: Pregnancy to Neonate to Preschooler

Child Neurology Open
1-4

DOI: 10.1177/2329048X211034655
journals.sagepub.com/home/cno
SAGE

Jennifer Kramer, MS, RD[1] and Lisa Smith, MD[1]

"This case helps validate the concept that very early treatment of the presymptomatic infant is consistent with normal neurological development."

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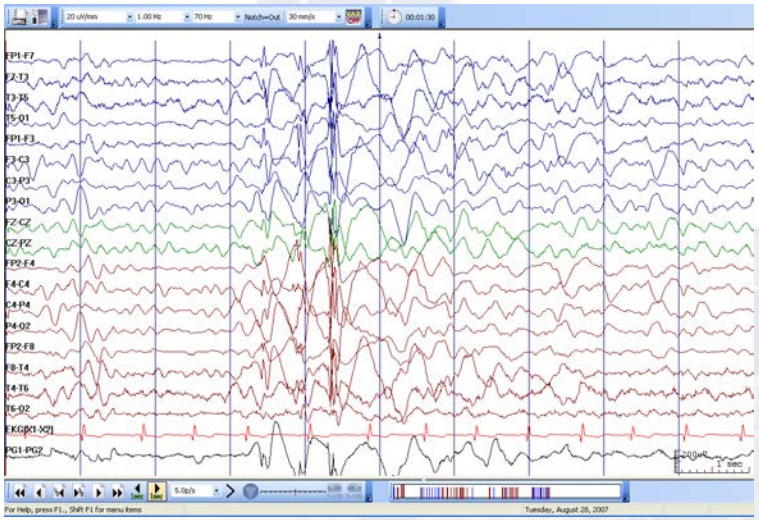
EMAS (Doose syndrome)

- Young children aged 3-5
- Intellectually normal
- Sudden onset of drop seizures



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Epilepsy with myoclonic-atonic seizures (Doose syndrome): Clarification of diagnosis and treatment options through a large retrospective multicenter cohort

Katherine Nickels[1] | Eric H. Kossoff[2] | Krista Eschbach[3] | Charuta Joshi[3]

- Drugs 26% (top 3)
  - Valproate 31%, Levetiracetam 17%, all others 26%
    - Others typically diazepam, topiramate, zonisamide, ethosuximide
- Diet 79% ($p<0.005$)
  - Used in 57% of this 161 patient cohort eventually

Epilepsia 2021.

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Epilepsy with myoclonic-atonic seizures (Doose syndrome): Clarification of diagnosis and treatment options through a large retrospective multicenter cohort

Katherine Nickels[1] | Eric H. Kossoff[2] | Krista Eschbach[3] | Charuta Joshi[3]

"Not only does this study support the use of diet therapy in the treatment of EMAS, but we would also suggest using it early in the epilepsy course."

Epilepsia 2021.

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Epilepsy & Behavior 68 (2017) 45–50

Contents lists available at ScienceDirect

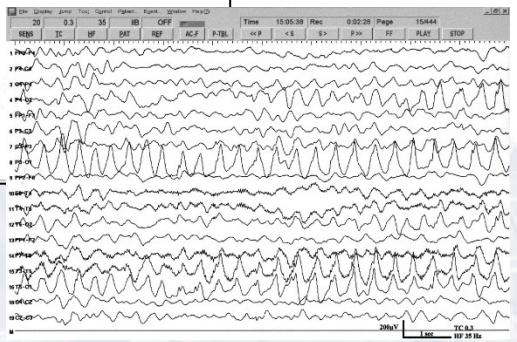
Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Low glycemic index treatment for seizure control in Angelman syndrome: A case series from the Center for Dietary Therapy of Epilepsy at the Massachusetts General Hospital

Olivia R. Grocott, Katherine S. Herrington, Heidi H. Pfeifer, Elizabeth A. Thiele, Ronald L. Thibert *

Angelman Syndrome Clinic and Center for Dietary Therapy of Epilepsy, Massachusetts General Hospital, Boston, MA, United States



Five subjects attempted LGIT monotherapy at some point during treatment. One subject remains seizure-free on LGIT monotherapy and has never used an AED. Two other subjects were on LGIT monotherapy

Epilepsy Research 144 (2018) 1–6

Contents lists available at ScienceDirect

Epilepsy Research

journal homepage: www.elsevier.com/locate/epilepsyres

Efficacy and safety of ketogenic diet for treatment of pediatric convulsive refractory status epilepticus

Ravindra Arya[a,b,*], Katrina Peariso[a,b], Marina Gaínza-Lein[c,d], Jessica Harvey[a], Ann Bergin[c], J. Nicholas Brenton[e], Brian T. Burrows[f], Tracy Glauser[a,b], Howard P. Goodkin[e], Yi-Chen Lai[g], Mohamad A. Mikati[h], Iván Sánchez Fernández[c], Dmitry Tchapyjnikov[h], Angus A. Wilfong[f], Korwyn Williams[f], Tobias Loddenkemper[c], for the pediatric Status Epilepticus Research Group (pSERG)

[a] Division of Neurology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA
[b] Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, OH, USA
[c] Division of Epilepsy and Clinical Neurophysiology, Department of Neurology, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA
[d] Facultad de Medicina, Universidad Austral de Chile, Valdivia, Chile
[e] University of Virginia Health System, Charlottesville, VA, USA
[f] Barrow Neurological Institute at Phoenix Children's Hospital, Phoenix, AZ, USA
[g] Baylor College of Medicine, Texas Children's Hospital, Houston, TX, USA
[h] Duke University Medical Center, Durham, NC, USA

ARTICLE INFO

Keywords:
Electrographic seizure resolution
Suppression burst ratio
Continuous infusions
Multi-center cohort

ABSTRACT

Purpose: To describe the efficacy and safety of ketogenic diet (KD) for convulsive refractory status epilepticus (RSE).

Methods: RSE patients treated with KD at the 6/11 participating institutions of the pediatric Status Epilepticus Research Group from January-2011 to December-2016 were included. Patients receiving KD prior to the index RSE episode were excluded. RSE was defined as failure of ≥ 2 anti-seizure medications, including at least one non-benzodiazepine drug. Ketosis was defined as serum beta-hydroxybutyrate levels > 20 mg/dl (1.9 mmol/l). Outcomes included proportion of patients with electrographic (EEG) seizure resolution within 7 days of starting KD, defined as absence of seizures and ≥ 50% suppression below 10 μV on longitudinal bipolar montage (suppression-burst ratio ≥ 50%); time to start KD after onset of RSE; time to achieve ketosis after starting KD; and the

ICU Protocol

- Remove dextrose from intravenous fluids
- D/C current enteral formula
- Remove carbohydrates from medications and parenteral fluids
- Check fasting lipid profile, CMP, CBC, selenium levels, urine ketones
- Nutrition consult
- Begin 4:1 ketogenic formula at half RDA of calories for first 24 hours then advance to full calories
- Begin multivitamin and calcium via GT/NG crushed and mixed in water
- Document baseline weight and height
- Check glucose every 6 hours
- Consider wean of pentobarbital drip after 1 week

Courtesy Mackenzie Cervenka

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Dietary Management of Children With Super-Refractory Status Epilepticus: A Systematic Review and Experience in a Single UK Tertiary Centre

Natasha E. Schoeler[1], Zoe Simpson[2], Runming Zhou[1], Suresh Pujar[3], Christin Eltze[3] and J. H. Cross[1,3,4]*

- 85/141 (60%) responded
- No relationship to the age, ketogenic ratio
- More likely to respond if female, shorter period of status epilepticus

Frontiers in Neurology, 2021

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Using the diet earlier for DEEs?

1. What do the guidelines say?
2. Is there published evidence for early use?
3. **The future**

Flexibility in how to start

• No fasting	Vaisleib, 2004 Kim, 2004 Bergqvist, 2005 Morrison, 2008 Lin, 2017
• Ratio daily change	Bansal, 2014
• No admission	Vaisleib, 2004 Nathan, 2009 Lord, 2010
• Gradual introduction	Fabe, 2014
• Telemedicine	Armeno, 2022 Lima, 2020 Kossoff, 2020 Zini, 2018

.

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NUTRICIA
KetoCal 3:1
NUTRICIA
KetoCal 4:1
Liquigen


Microlipid
3 FL OZ (88.7 mL)


KetoGEN
4:1 ratio product


KETOGENIC DIET
Net:250ml


CAMBROOKE THERAPEUTICS
KetoVie
4:1
chocolate
CAMBROOKE THERAPEUTICS
KetoVie
4:1
vanilla


A nutritionally complete, ketogenic supplement
in a 4:1 ratio
KetoKid
Ketogenic Diet Specially Formulated For Epilepsy
Natural Vanilla Flavour


SOL CARB
When extra calories are needed.
Pour un apport supplémentaire en calories.
Net 227 g


carb zero
250ml
8.43 fl oz


beta quik
250ml
8.43 fl oz


RCF
Reduced Carbohydrate Free
SOY FORMULA BASE WITH IRON
Concentrated Liquid
13 FL OZ (384 mL)


Namyang
KETONIA
180 mL


MEIJI
特殊ミルク
No.817-B
ケトンフォーミュラ


KetoVOLVE
4:1 Ratio Powder
Medical Food


SAMPLE
日清 MCT
パウダー
たんぱく質ゼロ
加えるだけで
エネルギーアップ!
(764kcal/100g) 250g

Modified Atkins Diet : 2023 approach

- Basics – 1) push fat, 2) carbs 20g/d, 3) modest protein, 4) lots of fluid
- I provide families and teens with a USB and PDF handout
  - Most information in our *Ketogenic Diets 8th ed* book
- 30 minute counselling session to go over the handout (if desired)
- Rare baseline labs today
- Dietitian available later for questions or emails
- Contact back in 1 month if the diet is helping

Seizure: European Journal of Epilepsy 103 (2022) 61–67

Contents lists available at ScienceDirect

Seizure: European Journal of Epilepsy

journal homepage: www.elsevier.com/locate/seizure

Modified Atkins diet versus levetiracetam for non-surgical drug-resistant epilepsy in children: A randomized open-label study☆

Archna [a], Divyani Garg [b], Shaiphali Goel [a], Sharmila B Mukherjee [a], Harish K Pemde [a], Puneet Jain [c], Suvasini Sharma [a,*]

[a] Department of Pediatrics (Neurology division), Kalawati Saran Children's Hospital and Lady Hardinge Medical College, New Delhi, India
[b] Department of Neurology, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India
[c] Epilepsy Program, Division of Neurology, Department of Pediatrics, Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada

- 51 children – MAD, 50 children – LEV
- Mean # drugs – 3
- *Vast majority with DEE's*
  - *47 LGS, 21 infantile spasms, 4 EMAS, 4 CSWS…*

Seizure: European Journal of Epilepsy 103 (2022) 61–67

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journal homepage: www.elsevier.com/locate/seizure

Modified Atkins diet versus levetiracetam for non-surgical drug-resistant epilepsy in children: A randomized open-label study☆

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Table 2
Seizure outcomes in the study cohort at 12 weeks.

Seizure outcome	Modified Atkins Diet ($n = 51$)	Levetiracetam ($n = 50$)	P value
Change in seizure frequency	−47.33 ± 39.57	−31.15 ± 32.18	0.03
Proportion of children with >90% seizure reduction	6 (11.8)	3 (6)	0.49
Proportion of children with >50% seizure reduction	27 (52.9)	11 (22)	0.001
Seizure-free	6 (11.8)	2 (4)	0.27

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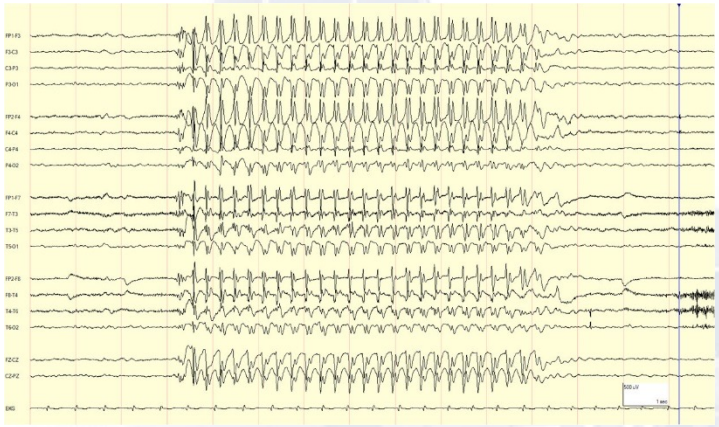
New-onset Absence Epilepsy?

- 3 month prospective trial
  - Single center
- Age 3-12 years
- Modified Atkins Diet vs. Ethosuximide



clinicaltrials.gov:
NCT04274179

The Carson Harris Foundation

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New-onset Absence Epilepsy?

- 1. What will parents do when given a choice?
- 2. Is the MAD feasible to start in a clinic quickly (e.g. 30 minutes)?
- 3. Is the MAD preliminarily effective for absence?

Personal Thoughts

- Appeals to medication-averse families
- Needs to be simple and quick to initiate
- You need to have a sense of **belief** that KDT will work when discussing with parents
  - Be honest and share the data
- Discontinue after 2-4 weeks and try standard drugs if not successful

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INTERNATIONAL NEUROLOGICAL KETOGENIC SOCIETY

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Our Mission

To promote the practice and science of ketogenic diets and related metabolism-based therapies for neurological disorders.

Our Vision

Global accessibility and implementation of ketogenic and metabolic therapies for brain disorders through collaborative research, training, education and outreach.

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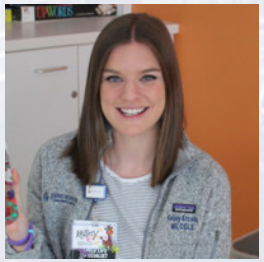


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