

A Century of Progress

Ketogenic Diets for Epilepsy in Children and Adults

Eric H. Kossoff, MD

Professor, Neurology & Pediatrics

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March 3, 2017



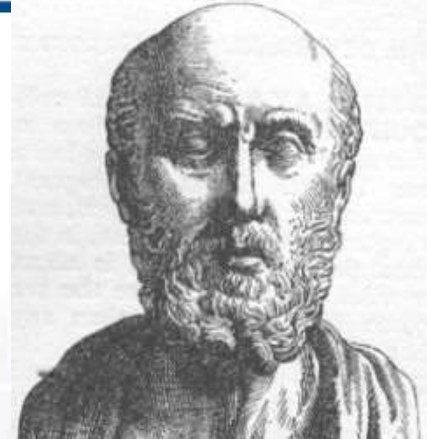
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M E D I C I N E

Disclosures

- Grant support: Nutricia
- Consultant: Atkins Nutritionals, Nutricia
- Data Safety Monitoring Board: GW Pharma
- Royalties: Demos, UpToDate, Oxford

Fasting for epilepsy in history

- Hippocrates ~400 BC
 - Man with body burns and seizures
 - “complete abstinence from food and water”
- Galen ~200 BC
 - Recommended “abstinence from daily use of such food as engenders unhealthy humors”



The Bible: King James version

Mark 9: 14-29

- “he fell on the ground, and wallowed foaming”
- “Jesus took him by the hand, and lifted him up; and he arose”
- “And he said unto them, this kind can come forth by nothing, but by prayer and fasting”



THE CLINIC BULLETIN

VOL 2

WEDNESDAY, JULY 27, 1921

NO. 307

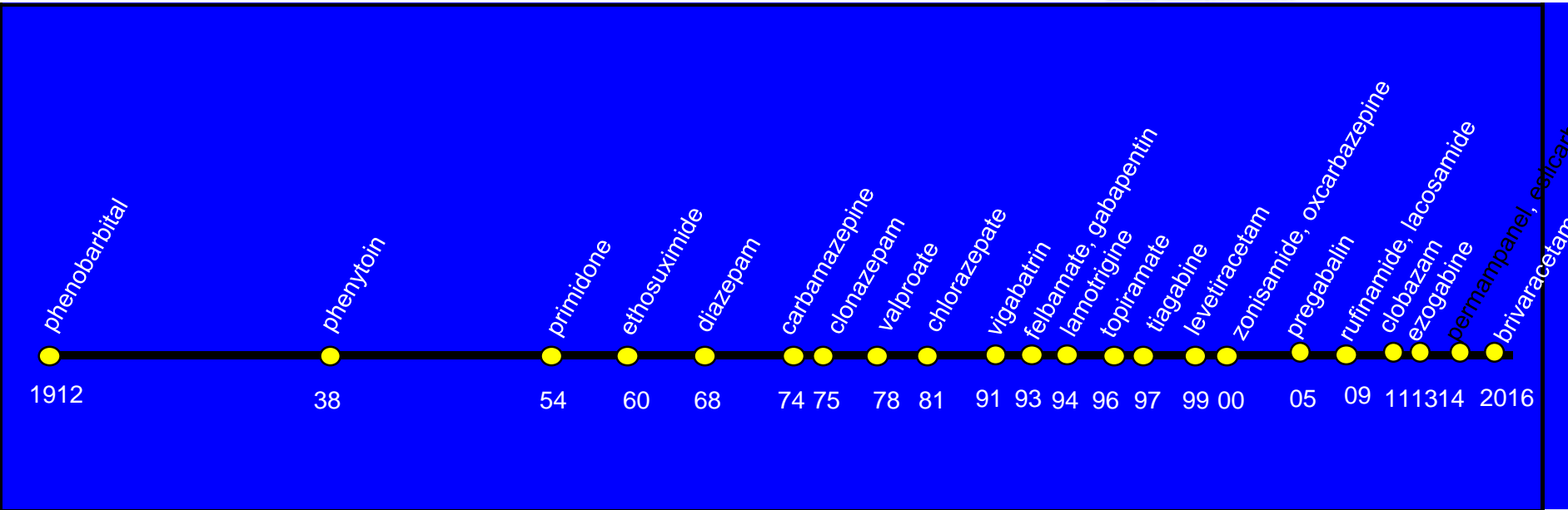
THE EFFECT OF KETONEMIA ON THE
COURSE OF EPILEPSY ✓

4.00

Intendant

Dr. Wilder at Mayo Clinic,
Rochester, MN creates a
high fat, low carbohydrate
diet to mimic fasting state

Anticonvulsant Drug Explosion



Early 1990s

- Used in a few centers in the US and only as a last resort for children
- No interest at American Epilepsy Society annual meetings
- Perceived as “alternative medicine”

TIME Healthland

A Healthy Balance of the Mind, Body and Spirit

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DIET

Sometimes a 90% Fat Diet Is Good For You

By **MEREDITH MELNICK** @meredithcm November 19, 2010 **17**

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This weekend, the *New York Times Magazine* has an [article](#) written by Fred Vogelstein, a contributing editor to *Wired* and father to a young boy with epilepsy. Sam's condition is severe: at one point, the boy was having up to 130 seizures a day and was not responsive to medication. To treat him, the family has put Sam on a special diet: a typical breakfast consists of eggs mixed



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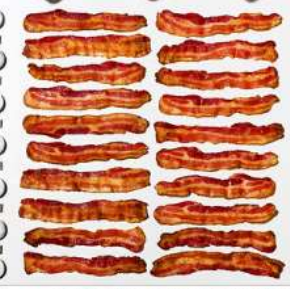
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AUTOS

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Prepared by GCG [Click here for more information](#)


Epilepsy's Big Fat Miracle







Stephen Lewis for The New York Times; Food Stylist: Brad Kuzivski


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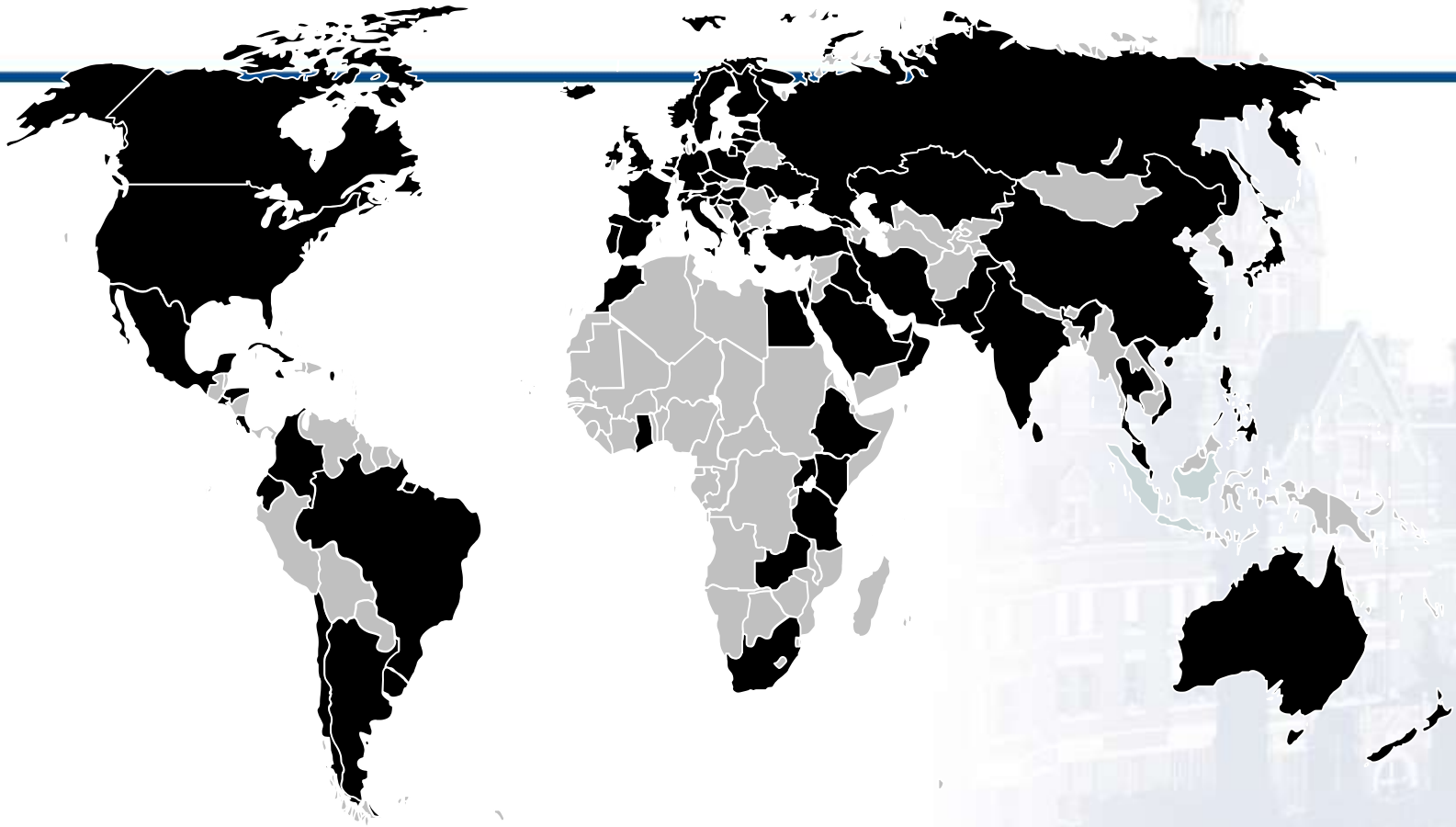
What's Popular Now

The Yankees, a Summer Symphony in 9 Innings 

Seeing Trends, Coalition Works to Help a River Adapt 

CLICK FOR SOUND







September 20-24, 2016
5th Ketogenic Diet
Symposium
Banff, Alberta, Canada



What Changed?!?!?

1. A dynamic parent support group
2. High quality, multicenter research
3. Patience with the larger epilepsy medical community...

November 1993



[THERAPIES](#) [LEARN](#) [AM I A CANDIDATE](#) [RECIPES](#) [STORE](#) [RESOURCES](#) [ABOUT](#)

IN 1993 THE KETOGENIC DIET CURED CHARLIE ABRAHAM'S EPILEPSY

OUR STORY

WHAT IS KETOSIS ?

The term ketosis refers to a byproduct of the breakdown of fat into useable energy, called ketones. This fat can be derived directly from the food we eat, known as nutritional ketosis, or from stored body fat. Ketones are alternative energy sources for both the brain and body.

AM I A CANDIDATE ?

Hundreds of studies have been performed showing therapeutic benefits of the Ketogenic Diet for a variety of diseases. Originally studied for its effects on epilepsy, the diet is now showing promise for a multitude of illnesses that have an underlying metabolic element.

FIND SUPPORT

Visit our database of hospitals that specialize in ketogenic therapies for epilepsy as well as our list of independent Ketogenic Professionals who are available to consult on a variety of disorders. We advise medical supervision with all ketogenic therapies.



0:16 / 9:55

2004 Dateline NBC (part one)



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INTERNATIONAL SYMPOSIUM

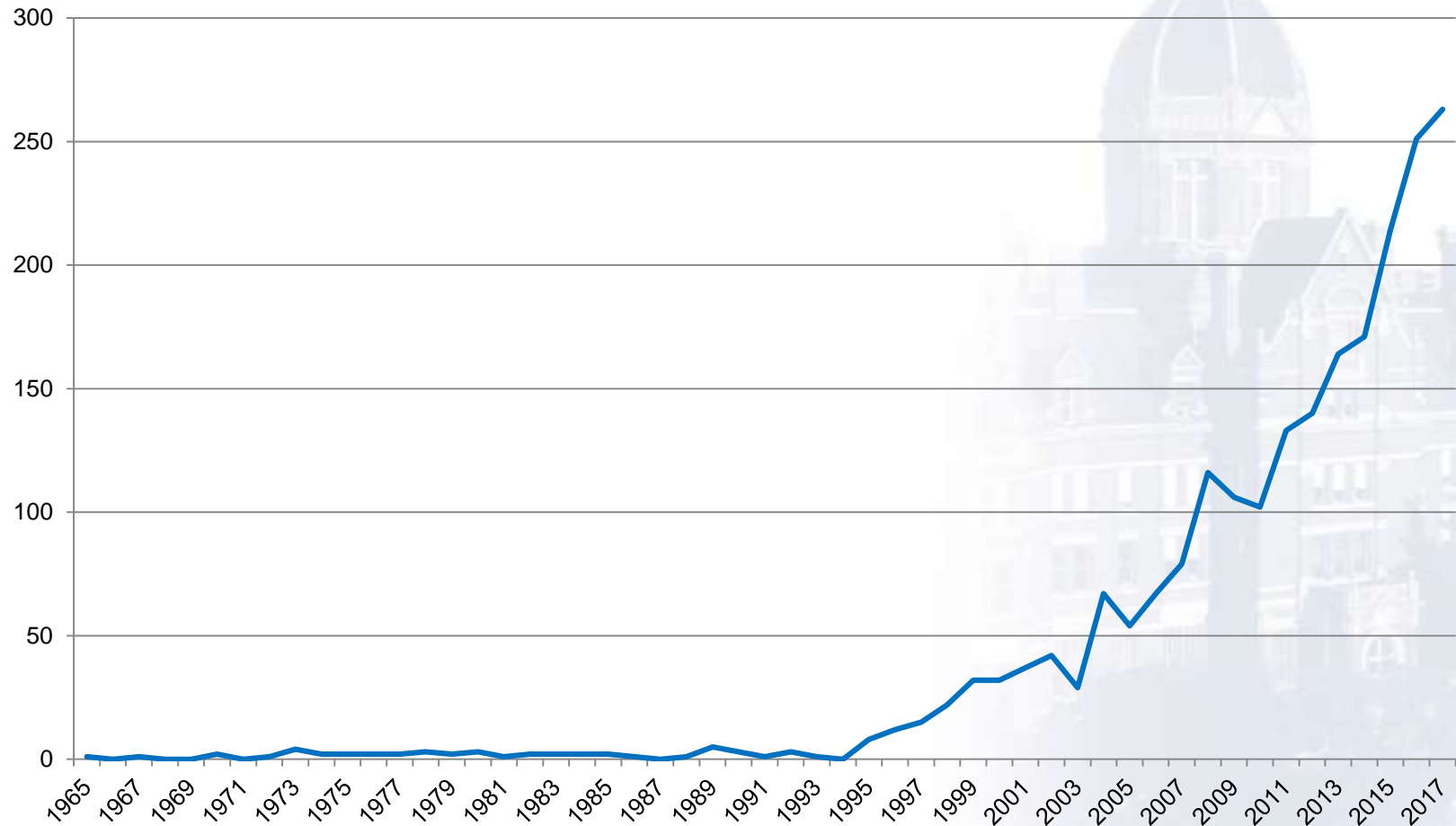
ON DIETARY THERAPIES FOR EPILEPSY
AND OTHER NEUROLOGICAL DISORDERS

April 2-5, 2008
The Ritz-Carlton Phoenix



Sponsored by The Charlie Foundation, CURE and Nutricia N.A.
Hosted by the Barrow Neurological Institute at St. Joseph's Hospital & Medical Center


Ketogenic Diet Studies Published



BRIEF COMMUNICATION

A blinded, crossover study of the efficacy of the ketogenic diet

*John M. Freeman, *Eileen P.G. Vining, *Eric H. Kossoff, *Paula L. Pyzik, *Xiaobu Ye, and †Steven N. Goodman

➔  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, Geogianna Fitzsimmons, Andrea Whitney, J Helen Cross

FULL-LENGTH ORIGINAL RESEARCH

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

*¹Suvasini Sharma, *²Naveen Sankhyan, *Sheffali Gulati, and †Anuja Agarwala

Acta
Neurologica
Scandinavica

Acta Neurol Scand DOI: 10.1111/ane.12592

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ACTA NEUROLOGICA
SCANDINAVICA

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

Lambrechts DAJE, de Kinderen RJA, Vles JSH, de Louw AJA, Aldenkamp AP, Majoie HJM. A randomized controlled trial of the ketogenic diet in refractory childhood epilepsy.

Acta Neurol Scand: DOI: 10.1111/ane.12592.

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D. A. J. E. Lambrechts¹,
R. J. A. de Kinderen^{2,3,4},
J. S. H. Vles^{1,2,5}, A. J. A. de
Louw^{1,6}, A. P. Aldenkamp^{2,5,6,7},
H. J. M. Majoie^{1,2,5,8}

2012

Ketogenic diet and other dietary treatments for epilepsy (Review)

Levy RG, Cooper PN, Giri P, Pulman J



“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.”



Epilepsia, 50(2):304–317, 2009
doi: 10.1111/j.1528-1167.2008.01765.x

SPECIAL REPORT

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

*Eric H. Kossoff, †Beth A. Zupec-Kania, ‡Per E. Amark, §Karen R. Ballaban-Gil, ¶A. G. Christina Bergqvist, #Robyn Blackford, **Jeffrey R. Buchhalter, ††Roberto H. Caraballo, ‡‡J. Helen Cross, ‡Maria G. Dahlin, §§Elizabeth J. Donner, ¶¶Joerg Klepper, §Rana S. Jehle, ###Heung Dong Kim, §§Y. M. Christiana Liu, ***Judy Nation, #Douglas R. Nordli, Jr., †††Heidi H. Pfeifer, ‡‡‡Jong M. Rho, §§§Carl E. Stafstrom, †††Elizabeth A. Thiele, *Zahava Turner, ¶¶¶Elaine C. Wirrell, ###James W. Wheless, ****Pierangelo Veggiotti, *Eileen P. G. Vining and The Charlie Foundation, and the Practice Committee of the Child Neurology Society

Ketogenic Diet

Elevated FFA

Chronic
Ketosis

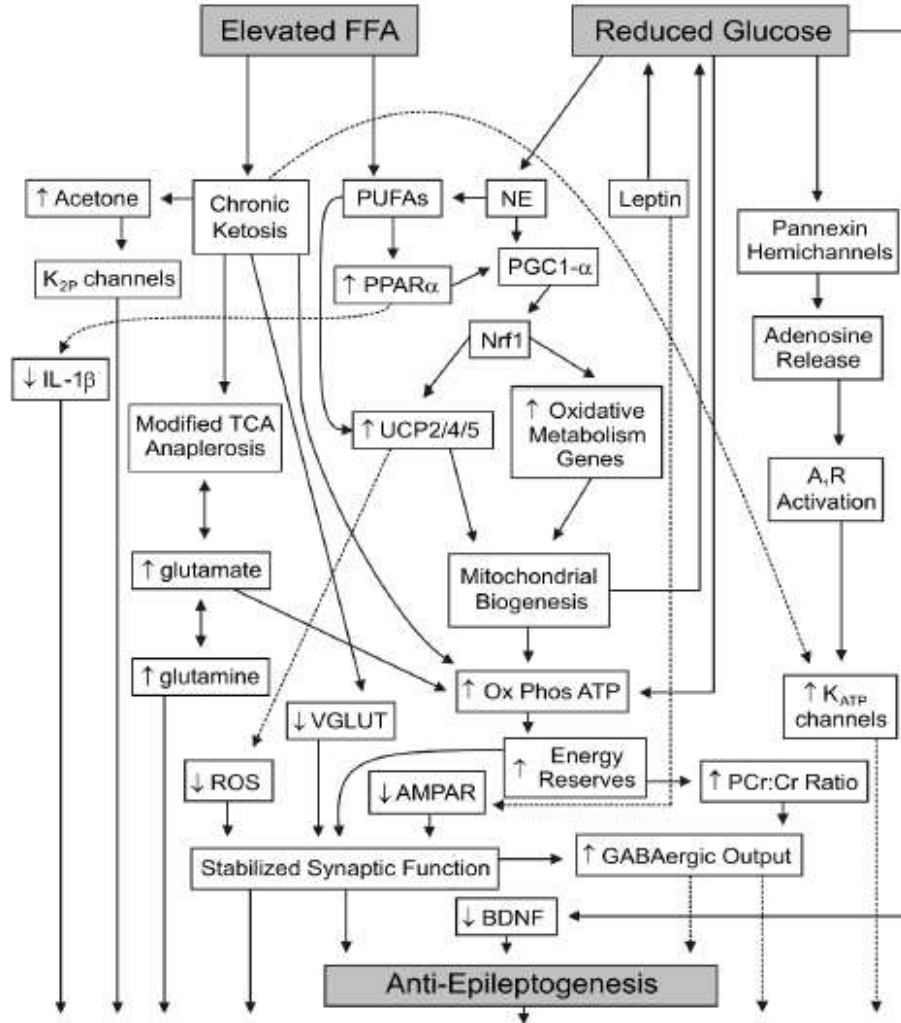


Anticonvulsant Action



Masino & Rho 2012

Ketogenic Diet



Anticonvulsant Action



Masino & Rho 2012

Diets for Epilepsy

1. How is it started?
2. Who should be started on the diet?
3. Preventing side effects
4. The future!

Ketogenic Diet: Initiation

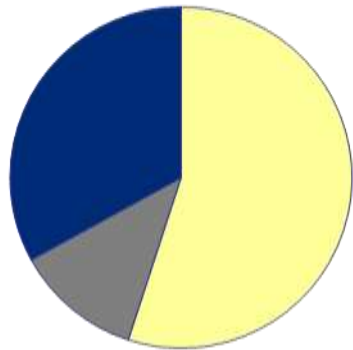
- Traditionally started gradually in the hospital over 2-3 days, after an optional 24 hour fast
 - Families educated daily
- Ratio (fat: carbs and protein)
 - 4:1 more strict
 - 3:1 for infants and adolescents
- Calories and fluids calculated





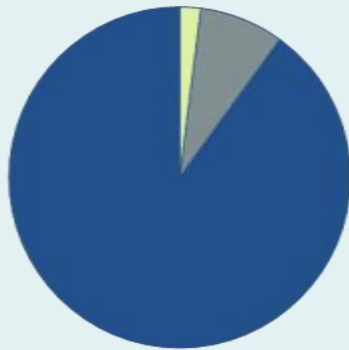
Four Ketogenic Diets

Standard
"Normal"
Diet



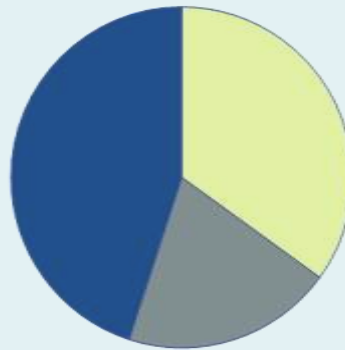
■ Carbohydrates
■ Protein
■ Fat

Ketogenic Diet



■ Carbohydrates
■ Protein
■ Fat

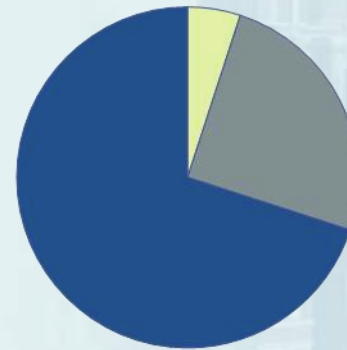
Medium
Chain
Triglyceride
Diet



■ Carbohydrates
■ Protein
■ Fat

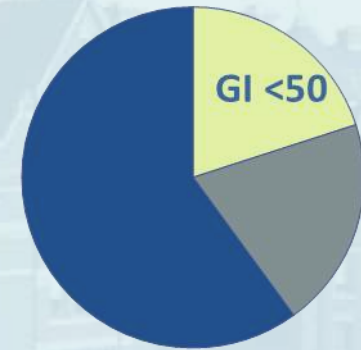
Modified
Atkins Diet

10-20 g



■ Carbohydrates
■ Protein
■ Fat

Low Glycemic
Index
Treatment



■ Carbohydrates
■ Protein
■ Fat

Maintenance

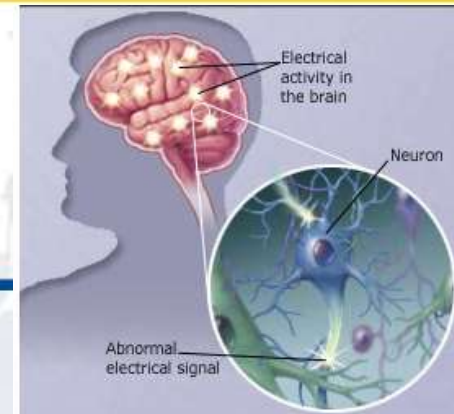
- Children seen every 3-6 months
- Labs, dietitian, neurologist evaluation to assess efficacy and safety
- After ~2 years if successful (3 months if not), *in children*, the ketogenic diet is slowly weaned back to previous foods



Diets for Epilepsy

1. How is it started?
- 2. Who should be started on the diet?**
3. Preventing side effects
4. The future!

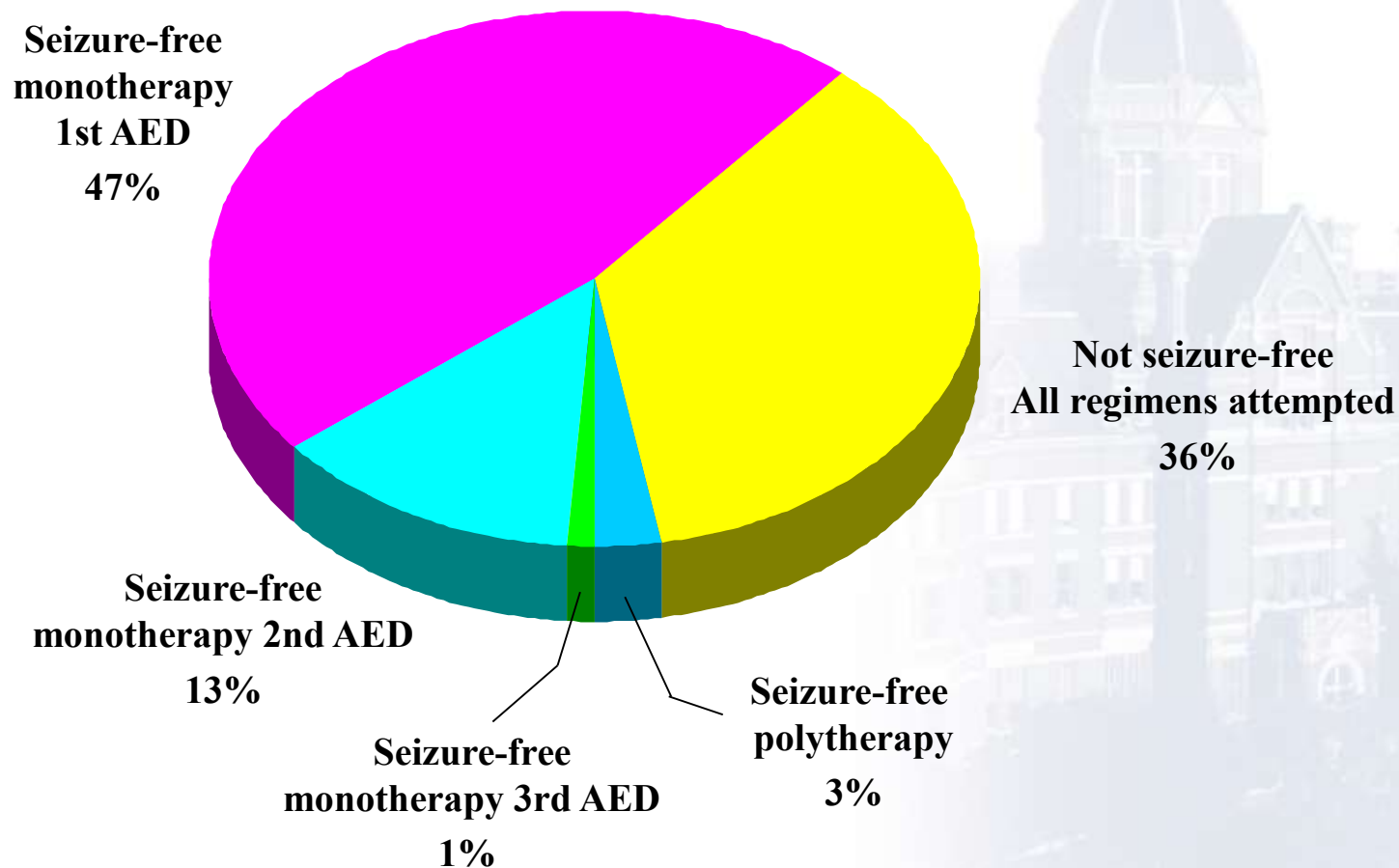
What is Epilepsy?

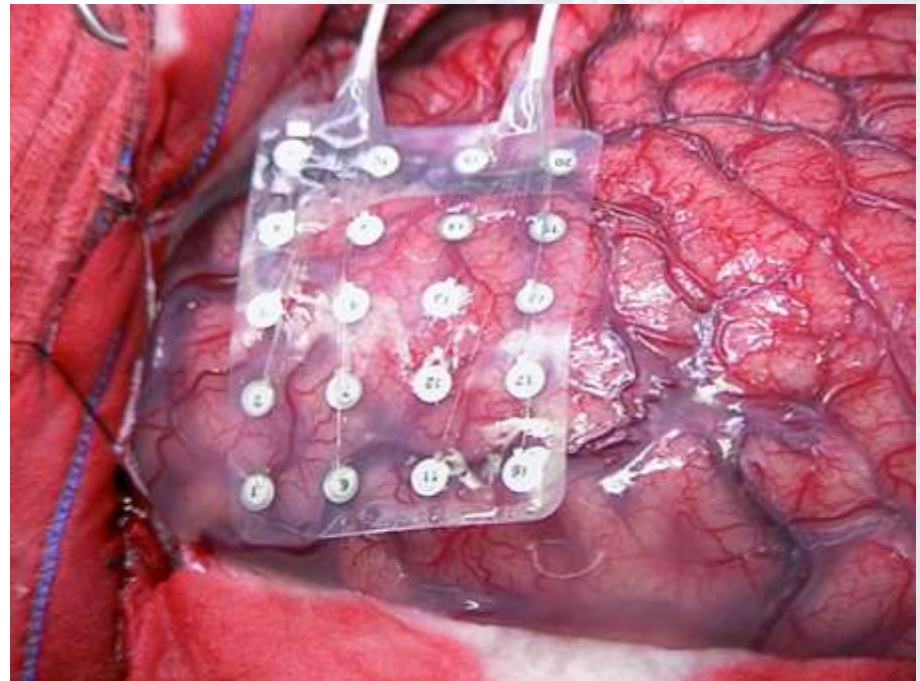


- Periodic, unpredictable electrical discharges of the brain
 - Multiple causes, often genetic
- Common, but *private* condition
- Spectrum of severity
 - Mild cases that are outgrown in childhood...
 - Severe cases which do not respond to any treatment



Seizure-Free Rates In Adults with Epilepsy





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

Probable benefit (at least two publications)

Glucose transporter protein 1 (GLUT-1) deficiency

Pyruvate dehydrogenase deficiency (PDHD)

Myoclonic-astatic epilepsy (Doose syndrome)

Tuberous sclerosis complex

Rett syndrome

Severe myoclonic epilepsy of infancy (Dravet syndrome)

Infantile spasms

Children receiving only formula (infants or enterally fed patients)

Suggestion of benefit (one case report or series)

Selected mitochondrial disorders

Glycogenosis type V

Landau-Kleffner syndrome

Lafora body disease

Subacute sclerosing panencephalitis (SSPE)



ELSEVIER

Official Journal of the European Paediatric Neurology Society



Review article

Ketogenic diet guidelines for infants with refractory epilepsy

Elles van der Louw ^{a,*}, Dorine van den Hurk ^b, Elizabeth Neal ^c,
 Bärbel Leiendecker ^d, Georgiana Fitzsimmon ^e, Laura Dority ^f,
 Lindsey Thompson ^g, Maddelena Marchió ^h, Magdalena Dudzińska ⁱ,
 Anastasia Dressler ^j, Joerg Klepper ^k, Stéphane Auvin ^l, J. Helen Cross ^m

^a Erasmus Medical Center Sophia Children's Hospital, Wytemaweg 80, 3015 CN, Rotterdam, The Netherlands

^b Wilhelmina Children's Hospital, University Medical Center Utrecht, The Netherlands

^c Matthews Friends Clinics, Lingfield, UK

^d University of Essen, Children's Hospital, Germany

^e Great Ormond Street Hospital for Children, London, UK

^f Medical University of South Carolina, USA

^g Children's Mercy Hospital and Clinics, Overland Park, KS, USA

^h University of Modena and Reggio Emilia, Italy

ⁱ Center of Pediatrics and Oncology, Chorzow, Poland

^j Medical University Vienna, Austria

^k Klinikum Aschaffenburg-Alzenau, Germany

^l Pediatric Epilepsy & Child Neurology Paris-Diderot University, France

^m UCL Institute of Child Health, Great Ormond Street Hospital for Children NHS Trust, London, UK





Contents lists available at ScienceDirect

Epilepsy & Behavior

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



Establishing an Adult Epilepsy Diet Center: Experience, efficacy and challenges



Mackenzie C. Cervenka ^{a,*}, Bobbie J. Henry ^b, Elizabeth A. Felton ^{a,1}, Katlyn Patton ^{a,2}, Eric H. Kossoff ^{a,c}

^a Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD, United States

^b Institute for Clinical and Translational Research, Johns Hopkins University School of Medicine, Baltimore, MD, United States

^c Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD, United States

- Started August 6th, 2010
- >300 adults seen in clinic to date
 - 80% never have tried a dietary therapy before
 - Most started on the modified Atkins diet



Table 2. Contraindications to the use of the KD

Absolute

- Carnitine deficiency (primary)
- Carnitine palmitoyltransferase (CPT) I or II deficiency
- Carnitine translocase deficiency
- β -oxidation defects
 - Medium-chain acyl dehydrogenase deficiency (MCAD)
 - Long-chain acyl dehydrogenase deficiency (LCAD)
 - Short-chain acyl dehydrogenase deficiency (SCAD)
 - Long-chain 3-hydroxyacyl-CoA deficiency
 - Medium-chain 3-hydroxyacyl-CoA deficiency.
- Pyruvate carboxylase deficiency
- Porphyria

Relative

- Inability to maintain adequate nutrition
- Surgical focus identified by neuroimaging and video EEG monitoring
- Parent or caregiver noncompliance

Diets for Epilepsy

1. How is it started?
2. Who should be started on the diet?
- 3. Preventing side effects**
4. The future!

Side Effects in Children (with KD)

- Constipation
 - Gastroesophageal reflux
 - Acidosis
- COMMON**
- Renal stones
 - Growth slowing
 - Dyslipidemia
 - Vitamin D deficiency
- SPORADIC**
- Carnitine deficiency
 - Pancreatitis
 - Bone fractures
 - Cardiomyopathy (due to selenium deficiency)
- RARE**

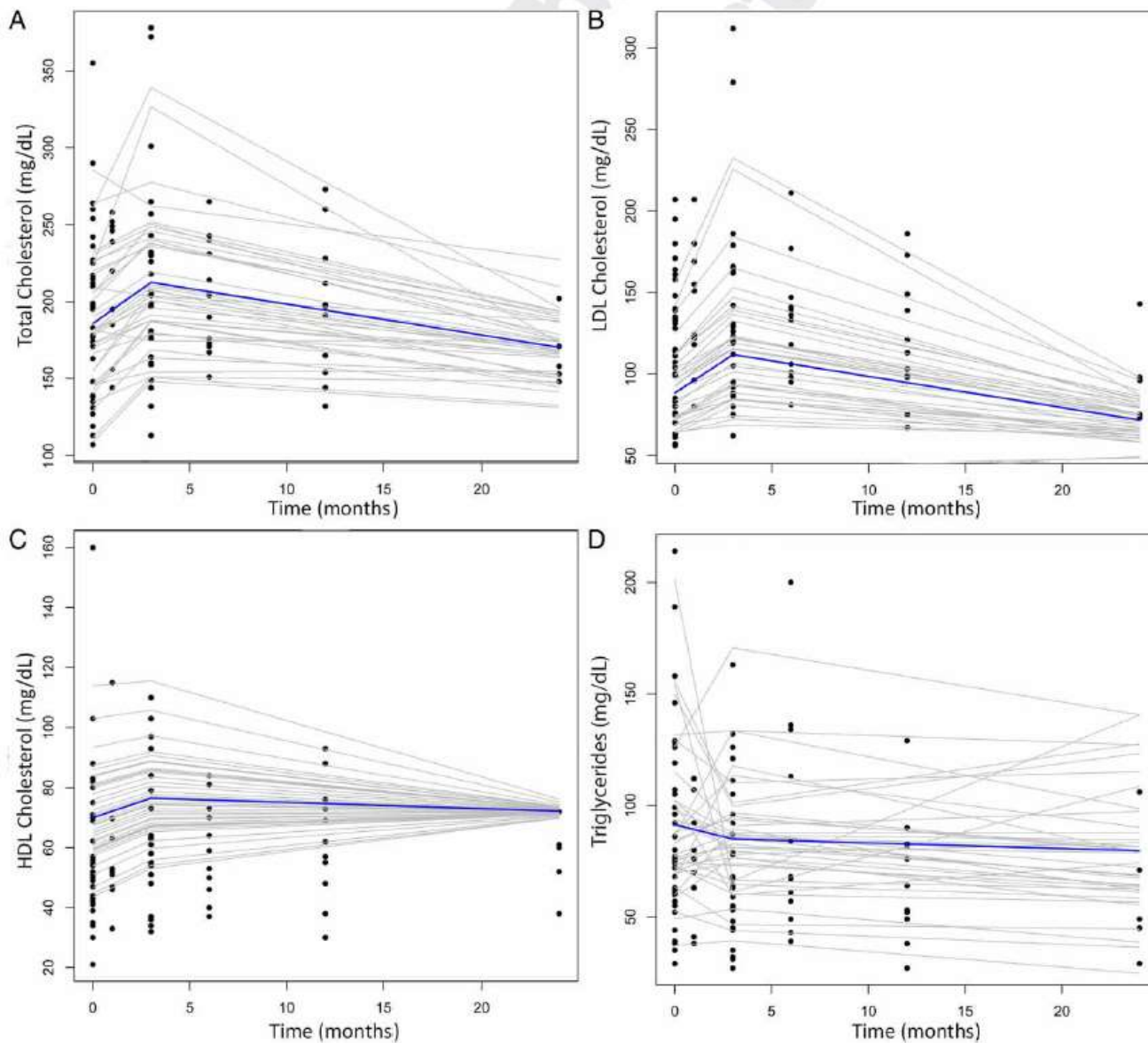


Figure 2 Total cholesterol (A), LDL (B), HDL (C), and triglyceride (D) levels plotted over time on the MAD using a random effects model with two linear spline terms. Points represent values (mg/dl) for all patients plotted over 0–24 months. Light gray lines represent cholesterol trends over time. Dark gray lines show the average of these values.

McDonald et al,
Epilepsy Behav
 2017

Kidney stones and Oral Citrates

- Kidney stones had been occurring in 6% of children on KD
- Due to acidic and hypercalciuric urine
- Polycitra K (30 meq twice daily)
 - Reduces risk of kidney stones on the KD from 6 to <1%



Table 4. Supplementation recommended for children receiving the KD

Universal recommendations

- Multivitamin with minerals (and trace minerals)
- Calcium with vitamin D

Optional extra supplementation

- Oral citrates (Polycitra K)
- Laxatives: Miralax, mineral oil, glycerin suppository
- Additional selenium, magnesium, zinc, phosphorus, vitamin D
- Carnitine (Carnitor)
- MCT oil or coconut oil (source of MCT)
- Salt (sodium to add to modular formulas if used for greater than age 1 year)

All supplements listed should be provided as carbohydrate-free preparations whenever possible.

Diets for Epilepsy

1. How is it started?
2. Who should be started on the diet?
3. Preventing side effects
4. **The future!**



Commission on Medical Therapies



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Ketogenic Diets

View in  Spanish  English

Welcome! Here you will find information and resources regarding the ketogenic diet, a high fat, low carbohydrate treatment for epilepsy. This treatment started in the United States in 1921, fell out of favor in the 1940s, but has seen a resurgence since the 1990s. In the past decade, the ketogenic diet has seen exponential growth around the world

ILAE Task Force for Dietary Therapies was created to help meet the growing need for information and resources regarding the ketogenic diet.

We hope you find this site useful in your region of the world. Please **email us** with questions and ideas!

News on Dietary Therapy

Cutting edge, brand new information about dietary therapies for epilepsy from the Task Force

Articles about the Ketogenic Diet

Links to free access articles about the Ketogenic Diet, organized by date

Basics of the Ketogenic Diet

What it is, how it works, and other key information

Book List

Books in multiple languages providing ketogenic diet guidance

Congresses and Other Events

Listings of international congresses, workshops, and other events

Helpful Links

Ketogenic diet resources from around the world

International Ketogenic Centers

Physicians providing the ketogenic diet who participated in this survey, listed alphabetically by country within regional areas.

Ketogenic Diet Products

Complete nutrition products, modular products (lipid-based, carbohydrate, and protein) and special products for use in ketogenic diets

Recipes for Ketogenic Diets

An international selection of recipes

Dietary Therapies Task Force Members

Ketogenic diet task force member listing with contact information







SPECIAL REPORT

What are the minimum requirements for ketogenic diet services in resource-limited regions? Recommendations from the International League Against Epilepsy Task Force for Dietary Therapy

***Eric H. Kossoff, †Nabil Al-Macki, *Mackenzie C. Cervenka, ‡Heung D. Kim, §Jianxiang Liao, ¶Katherine Megaw, #Janak K. Nathan, **Ximena Raimann, ††Rocio Rivera, ‡‡Adelheid Wiemer-Kruel, §§Emma Williams, and ¶¶Beth A. Zupec-Kania**

Epilepsia, **(*) :1–6, 2015
doi: 10.1111/epi.13039



The Keilah Foundation: Making the ketogenic diet viable for children in Africa

*Katherine Megaw and †Jo M. Wilmshurst

Epilepsia, **(*)1-3, 2014
doi: 10.1111/epi.12770

Brief Communication

First Application of Ketogenic Diet on a Child With Intractable Epilepsy in Ghana

Child Neurology Open
July - September 2015: 1-3
© The Author(s) 2015
DOI: 10.1177/2329048X15604593
cno.sagepub.com



Dezhi Cao, MD¹, Eben Badoe², Yanwei Zhu, BA¹, Xia Zhao, MD¹, Yan Hu, MD¹, and Jianxiang Liao, MD, PhD¹

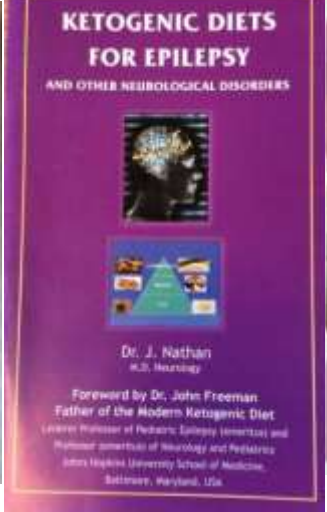
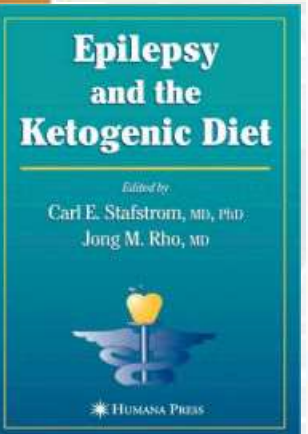
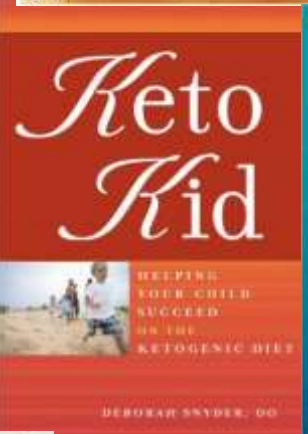
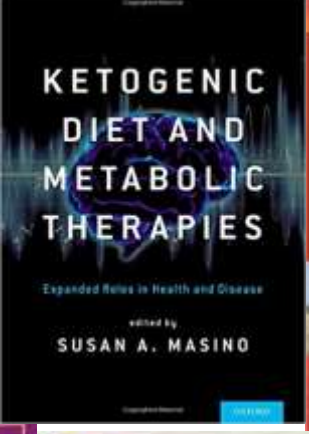
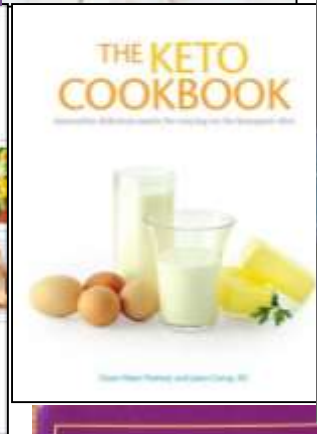
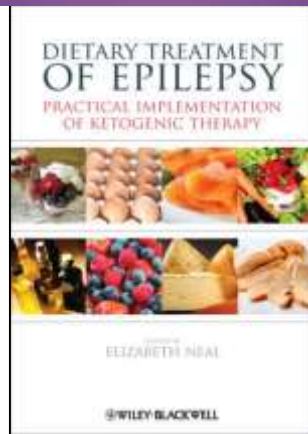
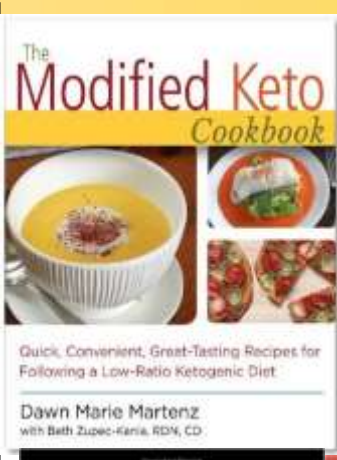
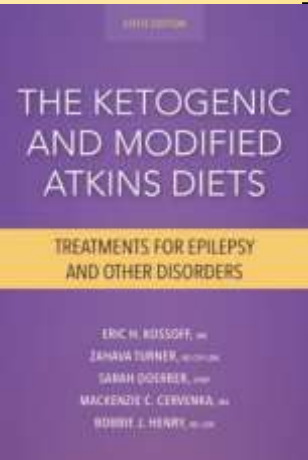
Why should modified Atkins diet be encouraged for treating epilepsy in emerging countries?

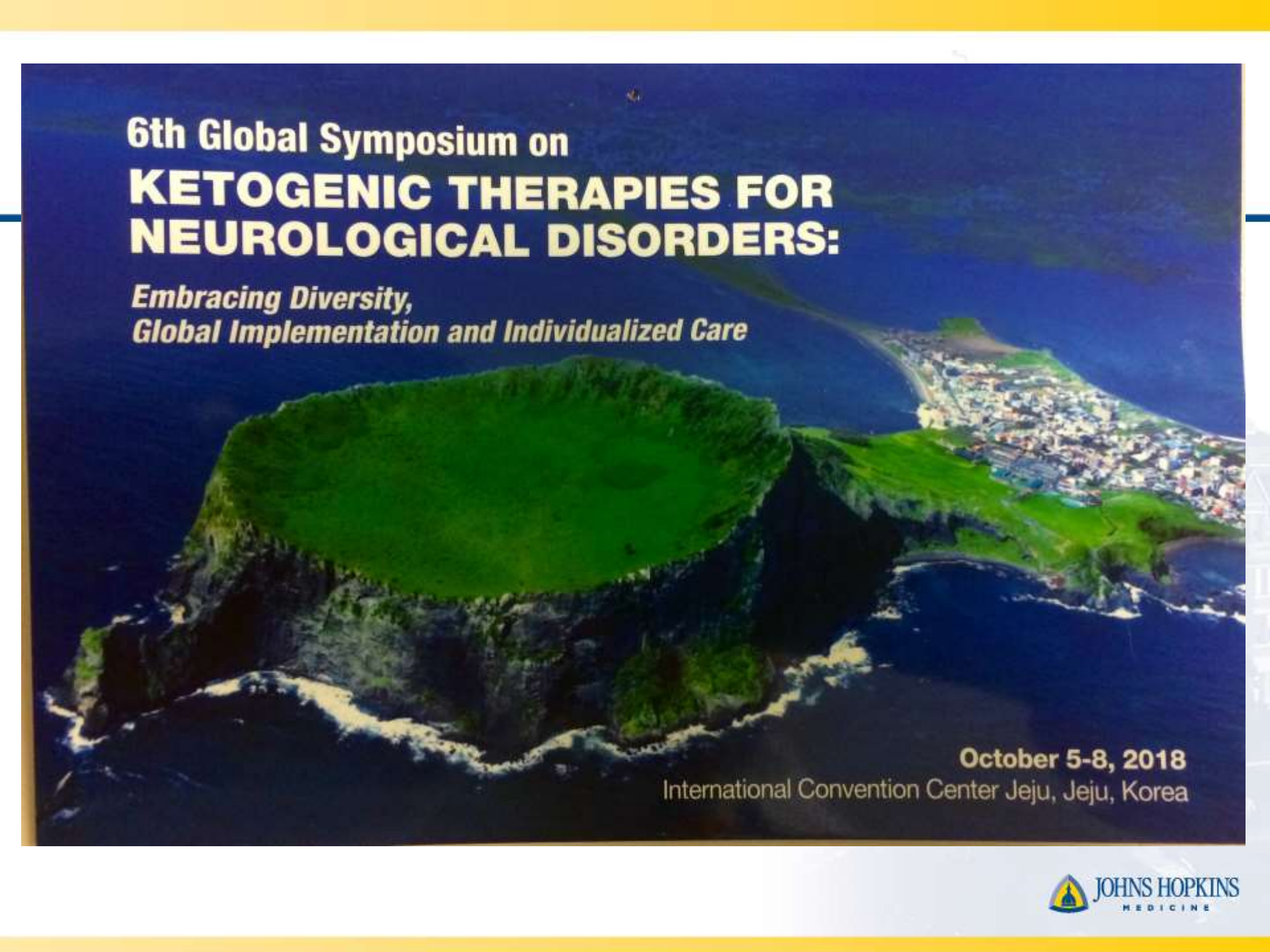
Amal Satte², Eric Heath Kossoff¹, Mohamed Belghiti³, Abderrahim Zerhouni², Hamid Ouhabi², Hassania Guerinech³, Jamal Mounach²



Evaluation of a simplified modified Atkins diet for use by parents with low levels of literacy in children with refractory epilepsy: A randomized controlled trial

Suvasini Sharma (MD, DM)^{a,*}, Shaiphali Goel (MSc)^a, Puneet Jain (MD, DM)^{b,c}, Anuja Agarwala (MSc)^d, Satinder Aneja (MD)^a



An aerial photograph of a coastal town and a large green island. The town is built on a peninsula, and the island is a large, flat, green expanse. The ocean is dark blue, and the sky is a lighter blue. The text is overlaid on the top left of the image.

**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

Johns Hopkins Ketogenic Diet Center

Eric Kossoff MD

Sarah Doerrer PNP

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Zahava Turner RD

Courtney Haney RD

Bobbie Henry RD

Stacey Bessone RD

Tony Stanfield

Gerry & Mike Harris

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Tarah Majestic

Anita Charpentier, PharmD

Sapana Edwards, RN

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