Ketogenic Diet Basics for the Non-Ketogenic Dietitian

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About the Ambassador
Zahava Turner

Zahava Turner is an Assistant Professor of Pediatrics and Neurology, Board Certified in pediatric nutrition working at the Johns Hopkins Hospital in Baltimore, Maryland sinc 2005. Prior to that, she worked at Schneider's Children's Hospital in New York. Zahava specializes in using the Ketogenic diet for infants and children with epilepsy and has spoken both nationally and internationally at several conferences on the ketogenic and Modified Atkins diet for epilepsy. She is a co-author of 19 publications and the widely-referenced book Ketogenic Diets 6th edition.

Topics

- History of the ketogenic diet
- Overview of the basics
- How to calculate the ketogenic diet
- Helpful tips for monitoring

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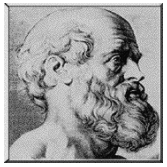
THE KETOGENIC DIET IN THE TREATMENT OF EPILEPSY*

A PRELIMINARY REPORT

M. G. PETERMAN, M.D.
ROCHESTER, MINN.

~400 BC



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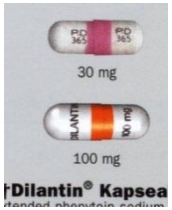

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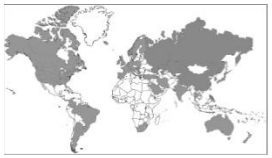

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"No thanks, I'm on a low carb diet."

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November 17 1993

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"After the ketogenic diet was started, Charlie did well and began to show a decrease in the amount of seizures he was having. By the time of discharge, the patient had had no seizures for several days."

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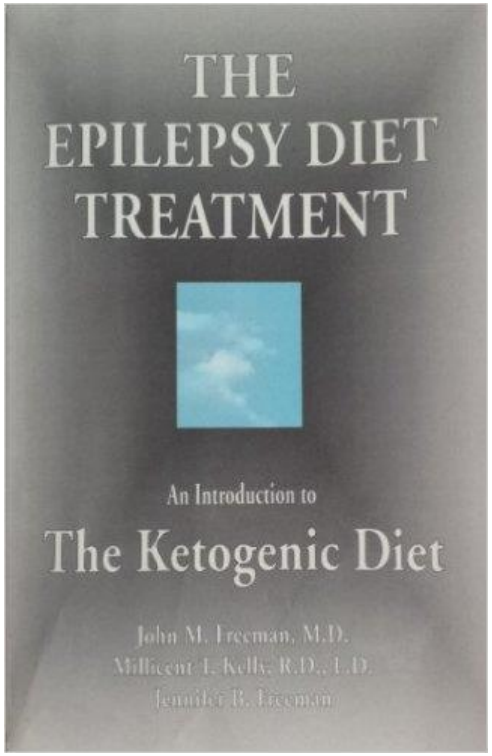
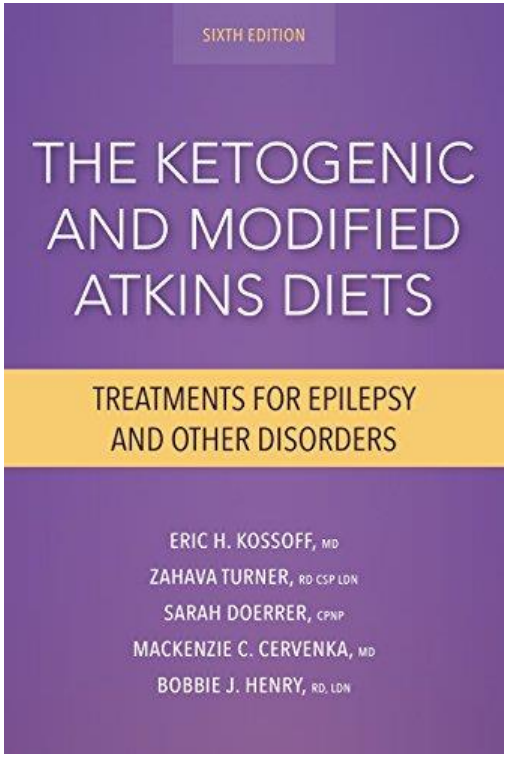
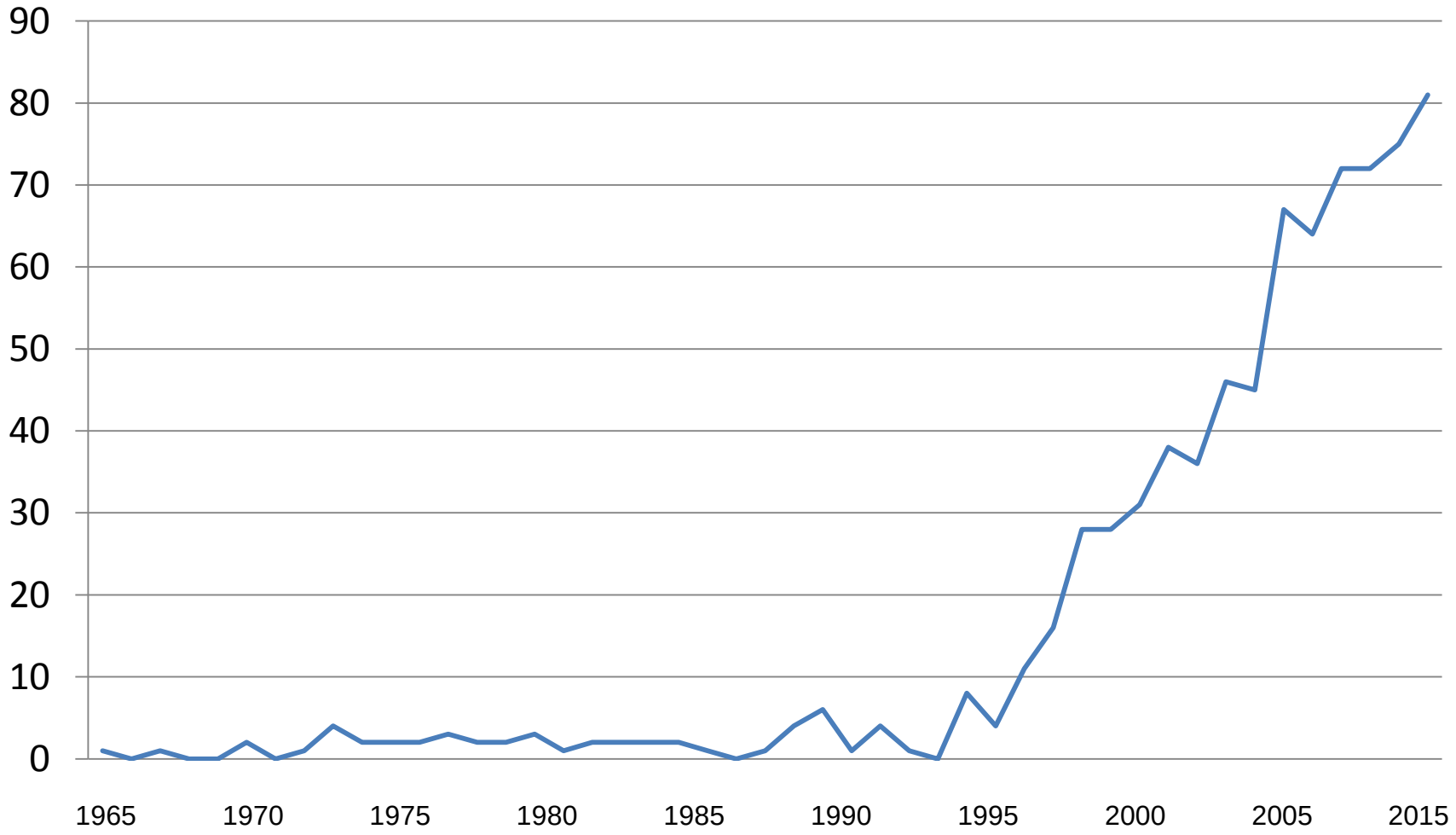
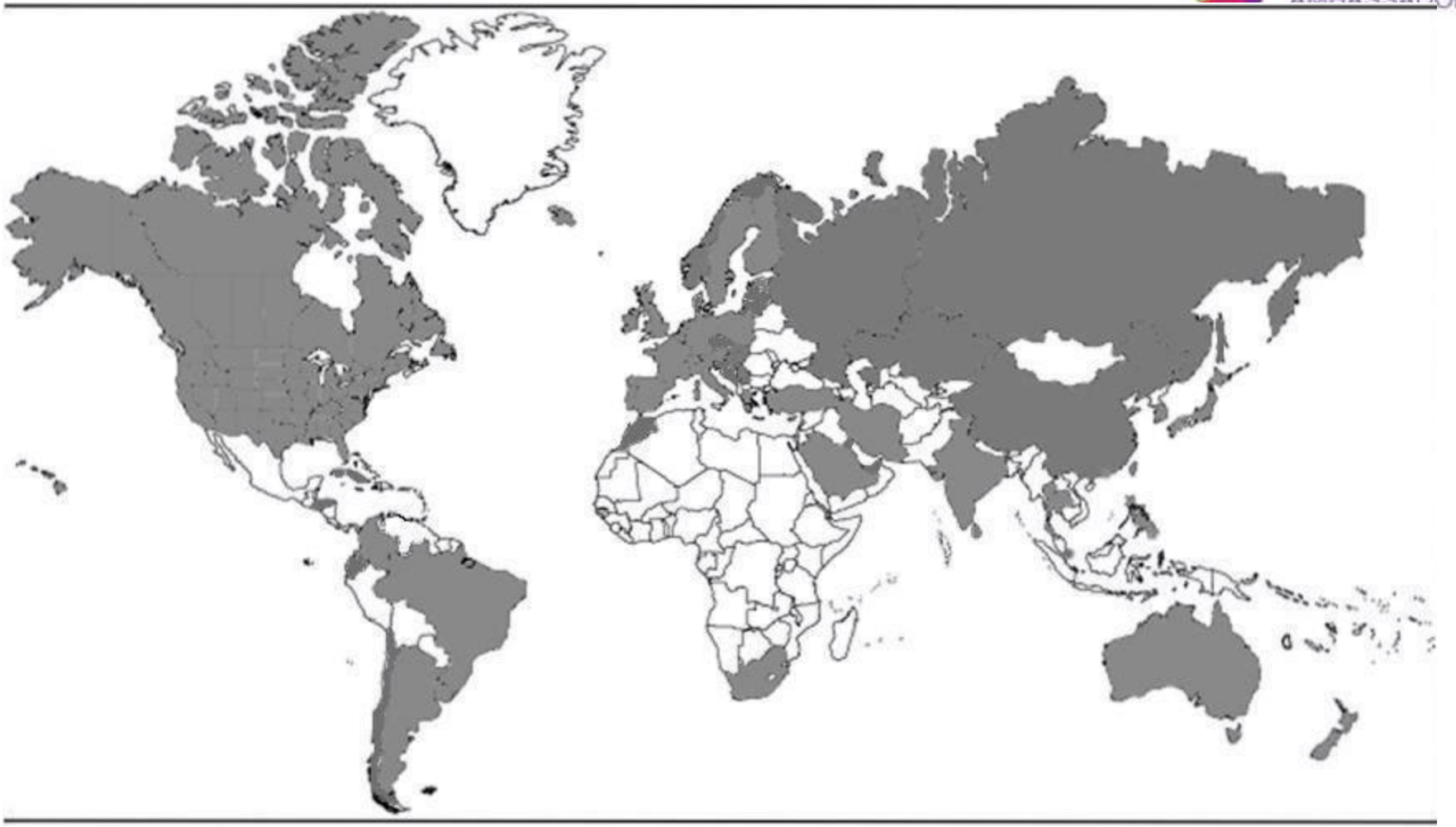




Ketogenic Diet Studies Published





Kossoff et al., *Epilepsia* 2005 (updated 2012)

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

Table 2. *Published Efficacy Studies of the Ketogenic Diet, Retrospective and Prospective, with 20 or More Patients, 1998–2008*

Reference	Study Type	Patients, no.	Age Range, yr	Seizure Improvement at 6 mo, %	
				>50% Reduction	>90% Reduction
Vining et al.,[75] 1998	Prosp.	51	1–9	53	29
Freeman et al.,[31] 1998	Prosp.	150	1–16	51	32
Hassan et al.,[76] 1999	Retrosp.	52	2–9	67	
Kankirawatana et al.,[77] 2001	Prosp.	35	0.2–13		75
Nordli et al.,[78] 2001	Retrosp.	32	0.5–1.5	55	
Kossoff et al.,[79] 2002	Retrosp.	23	0.5–2	72	39
Coppola et al.,[80] 2002	Prosp.	56	1–23	27	
Francois et al.,[81] 2003	Retrosp.	29	0.3–12.5	41	
Mady et al.,[82] 2003	Retrosp.	45	12–19	50	29
Klepper et al.,[83] 2004	Retrosp.	111	0.1–18	31	17
Vaisleib et al.,[84] 2004	Retrosp.	54	2–14	65	
Kang et al.,[85] 2005	Retrosp.	199	0.5–17.5	58	
Bergqvist et al.,[86] 2005	Prosp.	48	1–14	63*	38*
Eun et al.,[87] 2006	Retrosp.	43	0.5–4	81	63
Kossoff et al.,[88] 2007	Retrosp.	30	4–24	63	23
Seo et al.,[89] 2007	Prosp.	76	0.3–16	79	49
Hamdy et al.,[90] 2007	Retrosp.	90	0.3–14.8	74	44
Kossoff et al.,[28] 2008	Retrosp.	118	0.3–15	71	43
Neal et al.,[32] 2008	Prosp.	73	2–16	38*	7*
Freeman et al.,[29] 2009	Prosp.	20	1–10	80	
Total		1,335	0.3–24	56	24

Prosp. = prospective; Retrosp. = retrospective.
*At 3 months.

Kossoff, Rho *Neurotherapeutics*, 2009

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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

Freeman, et al. Epilepsia. 2009;50:322-5.
Neal, et al. Lancet Neurology. 2008;7:500-6.

Hopkins Double-Blinded Study

- 12-day study period
  - Start of the diet
  - Children with LGS
- Trend towards saccharin superiority in clinical seizures (p=0.07)
  - Median -34 seizures/day over 12 days (p=0.003)
- Probably an inadequate placebo state due to fasting twice

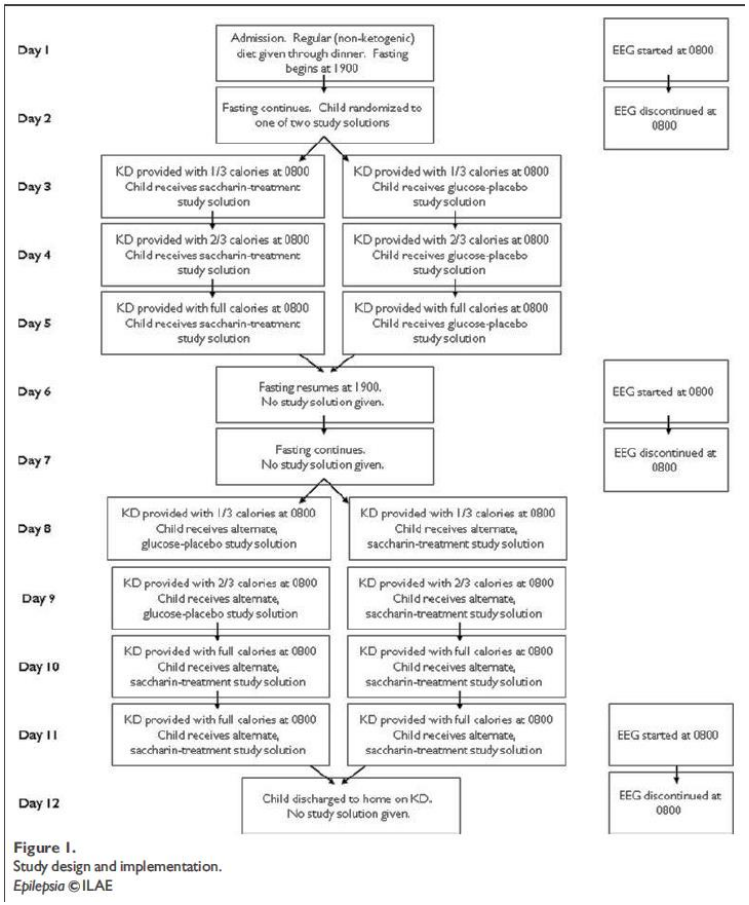

Figure 1.
Study design and implementation.
Epilepsia © ILAE

Freeman, et al. *Epilepsia*, 2009

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EUROPEAN JOURNAL OF PAEDIATRIC NEUROLOGY XXX (2016) 1–12

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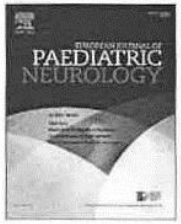
Official Journal of the European Paediatric Neurology Society



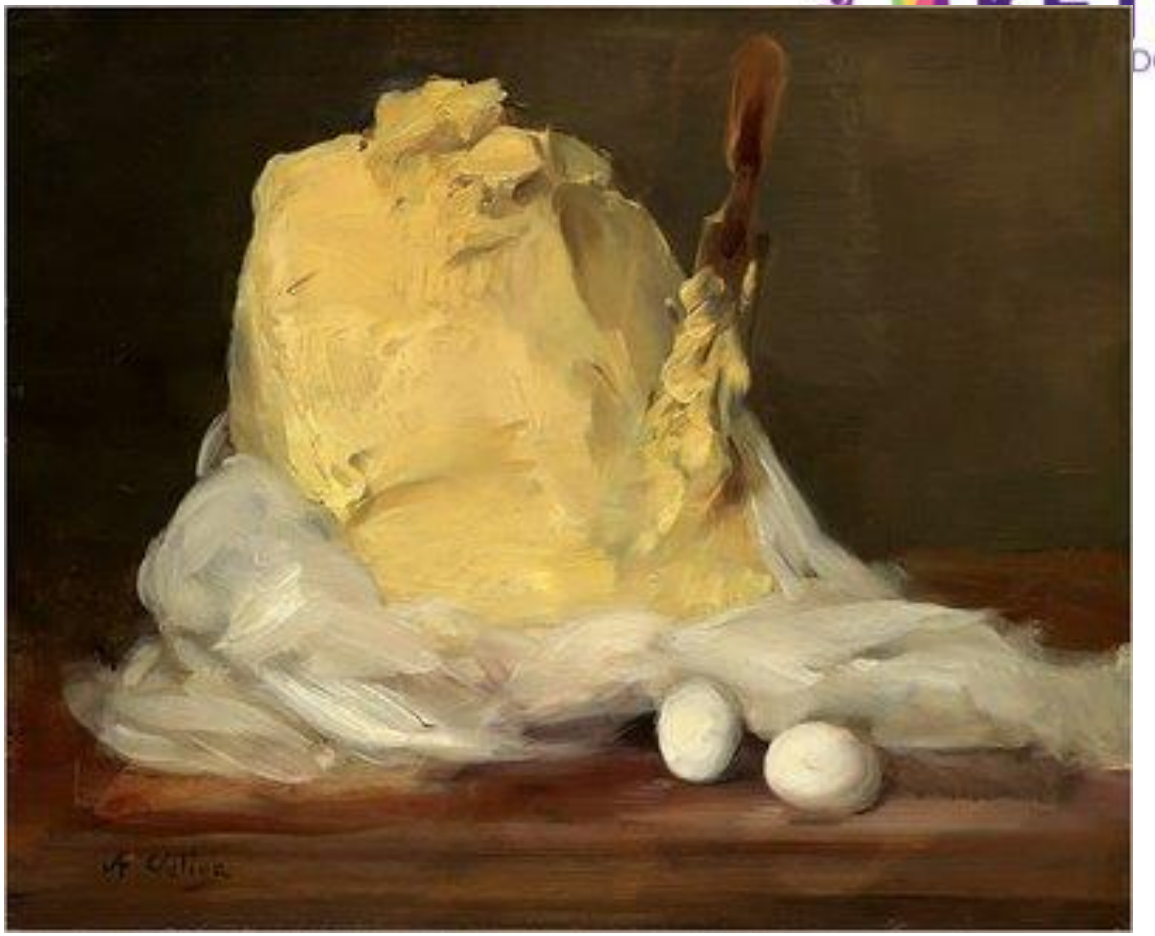
Review article

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]

Topics

- History of the ketogenic diet
- **Overview of the basics**
- How to calculate the ketogenic diet
- Helpful tips for monitoring



Keto Basics

- High fat, adequate protein and low carbohydrate
- Thought to mimic the metabolic state of fasting
  - By producing ketones
- Works on the mitochondrial level

Comparison

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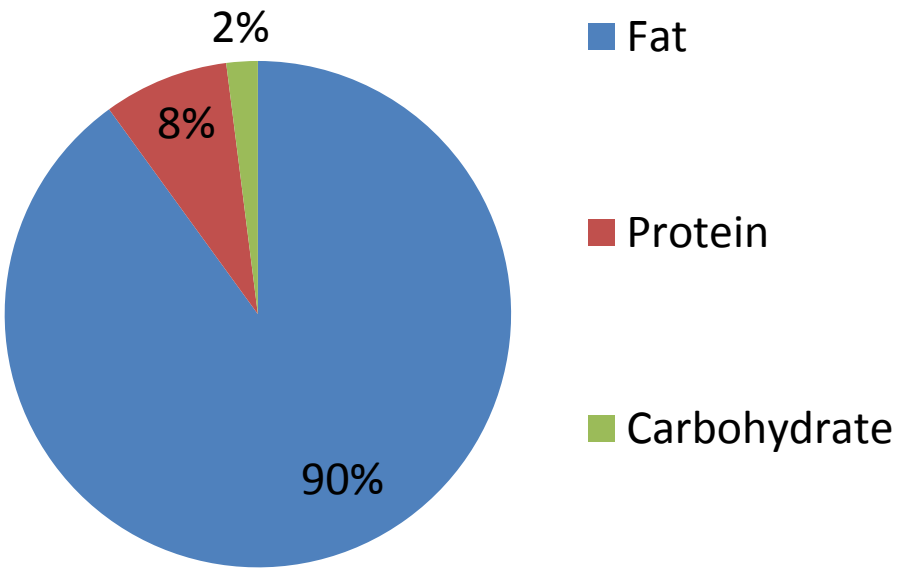
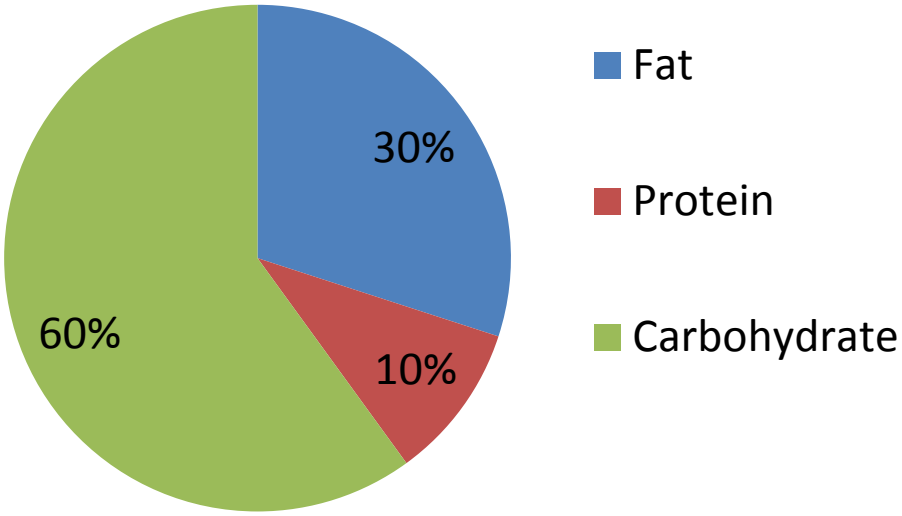
Ketogenic Diet 4:1



American Diet



Who gets placed on the diet?

- Patients who fail the traditional anti-convulsant therapy or are poor candidates for epilepsy surgery
- Can be used by all ages
- 3 months
- Average time 1-2 years

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)

Kossoff, et al. Epilepsia. 2009;50:304-17.

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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

Kossoff, et al. Epilepsia. 2009;50:304-17.

Calories, Protein & Fluid

- No calorie restriction
  - Use clinical judgment when estimating nutrition needs
- Current intake
  - GOAL: Meet adequate calories for growth
- DRI for protein
  - Adjust calories or ratio to meet protein needs
- 100% fluid maintenance

Ratio

- Ratio: Grams of fat: protein and carbohydrate combined
  - Example: 4:1 ratio is 4 grams of fat to 1 gram of protein and carbohydrate combined
- Typical ratio and uses
  - 3:1 Infants, teenagers & compromised patients
  - 4:1 > 2yo
- Higher the ratio the lower the amount of allowed protein and carbohydrates

Meal Plan

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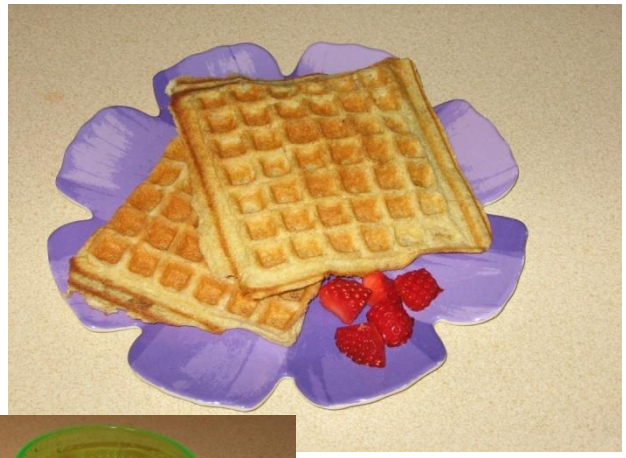
Basic Structure

- Heavy whipping cream
- Butter/ mayonnaise/ oil
- Protein
- Fruit or vegetable

Typical menu

- 40g 36% heavy cream
- 24g Chicken Breast
- 11g broccoli
- 21g fat
- 12g lettuce



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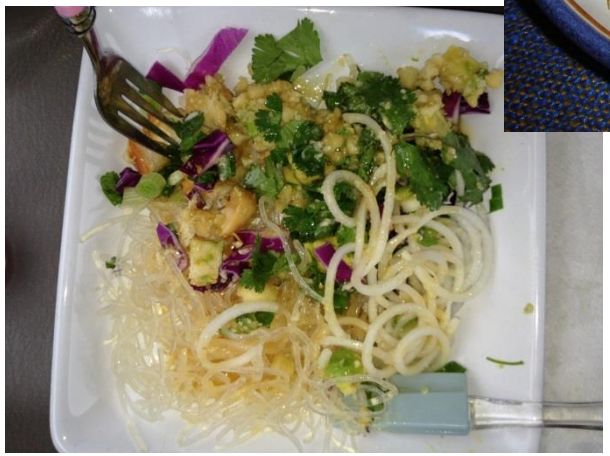

Products

Formulas that may be utilized for the ketogenic diet include:

- KetoCal® (Nutricia®)
  - KetoCal® 3:1 Powder (Unflavored)
  - KetoCal® 4:1 Powder (Vanilla Flavored)
  - KetoCal® 4:1 LQ Liquid (Flavored and Unflavored)
- RCF® (Abbott®) – Ross Carbohydrate Free Formula - soy based carbohydrate free formula
  - Used in milk protein allergy
  - Used when carbohydrates must be very limited due to low caloric needs
- KetoVolve™ (Nutr-e-volution)
  - Bland flavored powder
- KetoVie™ 4:1 (CamBrooke Therapeutics™)
  - Available in chocolate and vanilla flavors
  - Ready-to-feed liquid

The labels for KetoCal®, KetoVolve™ and KetoVie™ indicate these products are intended for use with children ages from 1 year plus.

Modular Products

A variety of modular products may need to be added to ensure nutrient needs are met and ketogenic ratios are correct.

Lipid

- Microlipid® (Nestle®) – safflower oil emulsion at 4.5 kcal/mL
- MCT Oil® (Nestle®) – fractionated coconut oil at 7.7 kcal/mL
- Liquigen® (Nutricia®) – MCT emulsion at 4.5 kcal/mL
- Betaquik™ (Vitaflo®) – MCT emulsion at 1.89 kcal/mL
- Carbzero™ (Vitaflo®) – LCT emulsion at 1.8 kcal/mL
- Retail Oils (Olive oil, coconut oil) – variable caloric density

Carbohydrate

- SolCarb powder (Solace®) – carbohydrate powder – maltodextrin - 3.75 kcal/g
- Polycal™ powder (Nutricia®) – carbohydrate powder – maltodextrin – 3.84 kcal/g

Protein

- Beneprotein® (Nestle®) – whey protein powder – 6 gm protein in 7 gm powder
- Complete Amino Acid Mix (Nutricia®) – 100% amino acid powder – 8.2 g protein in 10 g powder

Supplementation

- Diet deficient in:
  - B Vitamins
  - Vitamin C
  - Calcium, zinc, phosphorous
  - Fiber
  - Trace minerals
  - Carnitine, selenium
- Supplement with carbohydrate free multivitamin and mineral supplement

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.

Kossoff, et al. Epilepsia. 2009;50:304-17.

Estimating Calories Protein & Fluid

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Calories

- Dietary Reference Intake (DRI) + Activity Factor (AF)
  - Can use WHO, Schofield…
- 3 day food record
  - Important to compare estimated needs with food record and growth history
- No calorie restriction
- Use clinical judgment regarding patients with obesity and failure to thrive

Protein & Fluid

Protein

- RDA

Fluid

- Maintenance fluid calculation
- No fluid restrictions
- "Fluid Requirement"
  - Keep fluid level the same every day

Calculating Dietary Units

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Food Science:

- 1 g fat = 9 kilocalories
- 1g protein and 1 g carbohydrate= 4 kilocalories

Ratio	Calories per Dietary Unit	Example
2:1	22	**(2X9) + (1X4) =22**
3:1	31	**(3X9)+ (1X4) =31**
4:1	40	**(4X9)+ (1X4) =40**
5:1	49	**(5X9) +(1X4)=49**

Diet Calculation

- By dividing the dietary units of a given ratio into the determined total calories (age x calories per kg)
- The total grams of protein, carbohydrate, and fat in a given ketogenic diet can be determined.

Example of Calculation

- 5 year old female
  - Wt: 17.7kg (45%)
  - Ht 108 cm (50^{th}%)
  - BMI 50^{th}%
- Based on 3 day food record and EER for healthy children = 85-90kcals/kg
  - 1500 calories per day
- Team determined patient will go on 4:1

Diet Calculation

- Divide 40 into total calories
  - 1500/40= 37.5 Dietary Units
- Multiply Dietary Units by fat grams in ratio
  - 37.5 x 4= 150
- CHO/Pro = Multiply the dietary units by 1
  - 37.5 x1= 37.5
- Protein: determined by RDA
  - 5 year old = 1.1g/kg x 17.7= 19.5g/day
- Carbohydrates: Obtained by subtracting protein amount above
  - 37.5- 19.5 =18 g carbohydrates

Diet Prescription

- 1500 calories/ day 4:1
  - 150 grams fat per day
  - 19.5 grams protein per day
  - 18 grams carbohydrates per day
  - This can then be divided into 3 meals and 2-3 snacks or 4 even meals
    - Replicate prior feeding regimen

Other Considerations for Diet Calculation

- Sugar alcohols
- Dietary fiber
- Carbohydrate from medications

Keto Admission

- JHH Admission Protocol
  - 4 families at a time
  - Admission 3 days (Monday-Wednesday)
  - Education Daily
  - Blood Glucose levels monitored
  - Urine ketone levels
    - Blood ketone levels
- Typical process:
  - Initiate KD slowly:
  - 24 hour fast (optional, but usually done)
  - Goal ratio at 1/2 calorie strength for 24 hours
    - Eggnog or ketogenic formula until full strength
  - Advance to Full Strength
    - With actual food

Daily Education

Day	Topics Covered
Monday	MD review Diet basics Side Effects Diet initiation schedule Meet with floor team/nurses
Tuesday	RD: The basics of the ketogenic diet Meal Plan Guidelines Social worker meeting
Wednesday	Ketogenic Computer program What to do when your child gets sick Parent lecture Weighing and measuring foods Learning how to read recipes

Potential Side Effects

- Constipation
- Poor growth
- Osteopenia/ osteoporosis
- Kidney stones
- Hyperlipidemia
- Vitamin and mineral deficiency

Table 5. Recommendations for aspects of a follow-up KD clinic[a]

Nutritional assessment (registered dietitian)
Obtain height weight, ideal weight for stature, growth velocity, BMI when appropriate
Review appropriateness of diet prescription (calories, protein, and fluid)
Review vitamin and mineral supplementation based on dietary reference intake guidelines
Assess compliance to therapy
Adjust therapy if necessary to improve compliance and optimize seizure control
Medical evaluation (neurologist)
Efficacy of the diet (is the KD meeting parental expectations?)
Anticonvulsant reduction (if applicable)
Should the KD be continued?
Laboratory assessment
Complete blood count with platelets
Electrolytes to include serum bicarbonate, total protein, calcium, magnesium, and phosphate
Serum liver and kidney profile (including albumin, AST, ALT, blood urea nitrogen, creatinine)
Fasting lipid profile
Serum acylcarnitine profile
Urinalysis
Urine calcium and creatinine
Anticonvulsant drug levels (if applicable)
Optional
Serum β-hydroxybutyrate (BOH) level
Zinc and selenium levels
Renal ultrasound
Bone mineral density (DEXA scan)
EEG

[a]Visits should be at least every 3 months for the first year of the KD.

Kossoff, et al. Epilepsia. 2009;50:304-17.

Follow-up

- Generally every 3 months for the initial year
  - Infants seen in 1 month
  - Labs at each visit
    - CMP, Fasting lipid panel, urinalysis, Vit D, selenium
- Medications usually not changed the first month
- Frequent phone and email contact in between clinic visits
- At our center, all management through the keto team from now on…

Summary

- Ketogenic diet involves time and dedication on the dietitians part
  - But not difficult
- Requires a team
  - Physician, RN, Pharmacy support…

References

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