

KETOGENIC DIET MANAGEMENT

BY

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Learning Outcomes

- Identify metabolic changes that occur with transition to a ketogenic diet and how they may impact health.
- Summarize disease states in which ketosis has been utilized or researched, and which may be benefited by the implementation of a ketogenic diet.
- Describe the basic implementation of the ketogenic diet, including determining who is a candidate, and when and how to start ketogenic diet.



Historical Background

Ancient Greece

“treating the disease by altering the patient’s diet”

Hippocrates

“epileptics can be purified through diet”

Erasistratus

“one inclining to epilepsy should be made to fast without mercy and be put on short rations”

Bible

“this kind can come forth by nothing but prayer and fasting”



Historical Background

Galen (2d century AD)

“dietary restriction and gentle purging to restore balance”

Caelius Aurelianus (5th century AD)

“if the patient was obese, weight reduction should be attempted”

Arnold of Villanova (13th century)

“the diet is the largest part of cure of epilepsy”

George Cheyne (1671-1743)

“strict diet”

Charles Radcliffe (1866)

“diet high in oil and fat”



Historical Background

American Medical Association (1921)

- Geyelin and H.W. Conkin –intermittent fasting to treat epilepsy with cure rates of 90% in children and 50% in adults
- Wilder: ketone producing diet-ketogenic diet

Talbot's *Treatment of Epilepsy* (1930)

- One small chapter on medications
- Half of book focused on the ketogenic diet

Lennox's *Epilepsy and Related Disorders* (1960)

- Single paragraph on ketogenic diet
- “For most patients, young and old, drug therapy is the kingpin of treatment”

History of the Ketogenic Diet

Ancient Times

- Fasting
- Ancient Greece
- Hippocrates
- Erasistratus
- Biblical

1921

- Ketogenic Diet
- "Mimic Fasting"
- Dr Woodyatt @ Rush
- Dr Wilder @ Mayo

2017

AND
Practice Paper

1986

- MCT Diet

2003

- Modified Atkins Diet
- Johns Hopkins

1938

- Discovery of phenytoin
- KD falls out of favor

2002

- Low Glycemic Index Treatment
- Mass Gen

1911

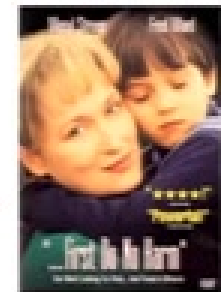
- Fasting
- Dr Geylin @ NY Presbyterian

Middle Ages

- Reports of fasting
- Diet of fat and oil

1994

- First Do No Harm
- The Charlie Foundation



Mayo Clin Bulletin. 1921. 2:307-308.
JAMA. 1938. 95(10): 707-709
J Child Neurol. 2009; 24(8):979-988.
JAO. 2017;1279-1292.

AND Ketogenic Diet Practice Paper – 2017



FROM THE ACADEMY

Practice Paper



Practice Paper of the Academy of Nutrition and Dietetics: Classic and Modified Ketogenic Diets for Treatment of Epilepsy



ABSTRACT

Ketogenic diet (KD) therapy is an established form of treatment for both pediatric and adult patients with intractable epilepsy. Ketogenic diet is a term that refers to any diet therapy in which dietary composition would be expected to result in a ketogenic state of human metabolism. While historically considered a last-resort therapy, classic KDs and their modified counterparts, including the modified Atkins diet and low glycemic index treatment, are gaining ground for use across the spectrum of seizure disorders. Registered dietitian nutritionists are often the first line and the most influential team members when it comes to treating those on KD therapy. This paper offers registered dietitian nutritionists insight into the history of KD therapy, an overview of the various diets, and a brief review of the literature with regard to efficacy; provides basic guidelines for practical implementation and coordination of care across multiple health care and community settings; and describes the role of registered dietitian nutritionists in achieving successful KD therapy.

J Acad Nutr Diet. 2017;117:1279-1292.

What is a ketogenic diet?

Any diet in which macronutrient composition would result in a ketogenic state of human metabolism.

Low Carbohydrate Diets

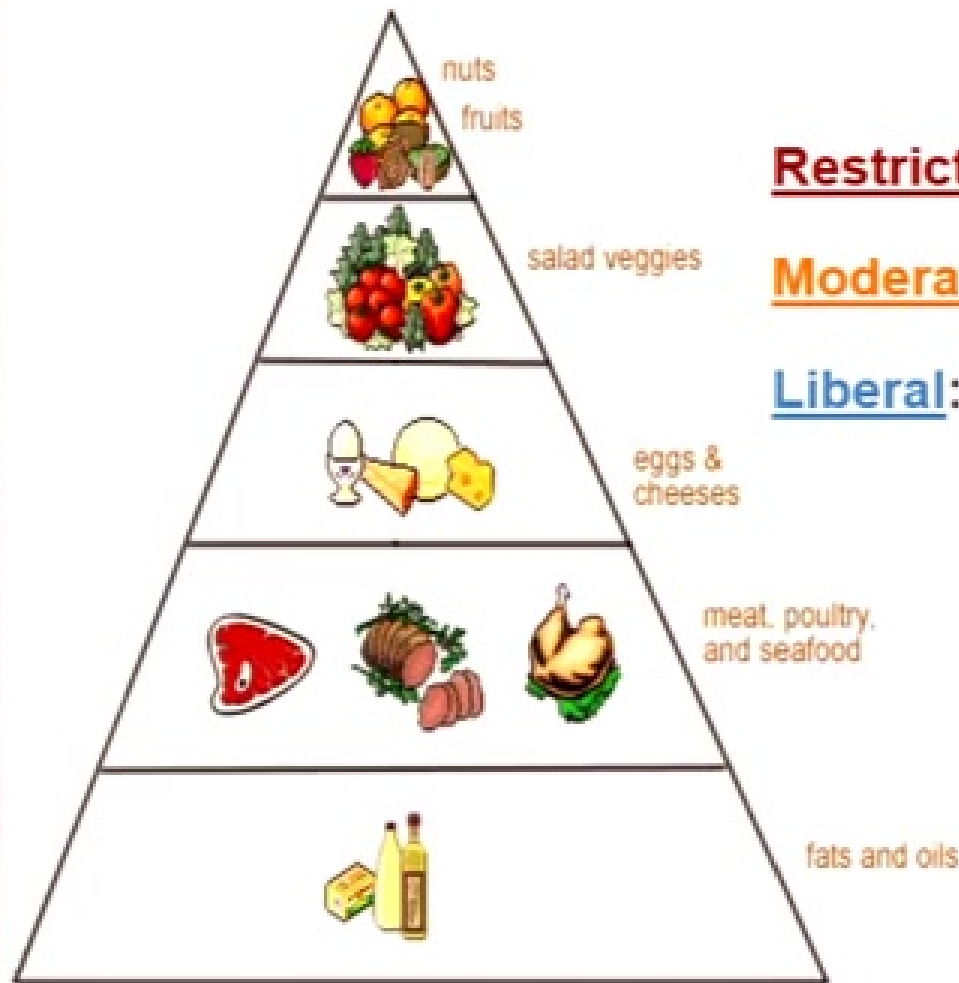
Restrict: processed foods, grains, desserts, sugar-sweetened beverages, starchy vegetables

Moderation: fruit, dairy, carrots & sweet potatoes, legumes, dark chocolate, red wine

Focus: Vegetables (all non-starchy), avocado, nuts, fats & oils, leafy greens, eggs, fish, meat, poultry



Ketogenic Diets



Restrict: carbohydrate (<60 g/day)

Moderation: protein (0.8-1.2 g/kg)

Liberal: fats (60-90% of total calories)



Types of Ketogenic Diets

Classic & Modified Ketogenic

- 1:1, 2:1, 3:1, 4:1 ratios
- Must count all intakes



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- 10-20 g net carb/day
- Encourage fat intake
- "adequate protein"



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Low-Glycemic Index

- 40-60 g net carb/day
- "Low-GI" carbs



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MCT

- 30-60% calories from MCT oil + other fats
- Can slightly more liberal in carbs



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MCT oil vs coconut oil



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**Restrict carbohydrate intake
15 – 60g/day**

**Typically induce ketosis
Restrict glycolysis**

MCT oil vs coconut oil

Ketogenic Diet Comparisons

Table 1. Comparison of macronutrient composition and initiation requirements between various ketogenic diets and the 2015-2020 Dietary Guidelines for Americans^a

Diet	Fat	Carbohydrate	Protein	Hospital admission
	range (%)			
2015-2020 Dietary Guidelines for Americans	20-35	45-65	10-35	No
Ketogenic diet ratio^b				
4:1	90	2-4	6-8	Yes
3:1	85-90	2-5	8-12	Varies ^c
2:1	80-85	5-10	10-15	Varies ^c
Modified Atkins diet (1:1 ratio^b)	60-65	5-10	25-35	No
Low glycemic index treatment (1:1 ratio^b)	60-70	20-30	10-20	No
Medium-chain triglyceride diet (1:1 ratio^b)	60-70	20-30	10	Yes

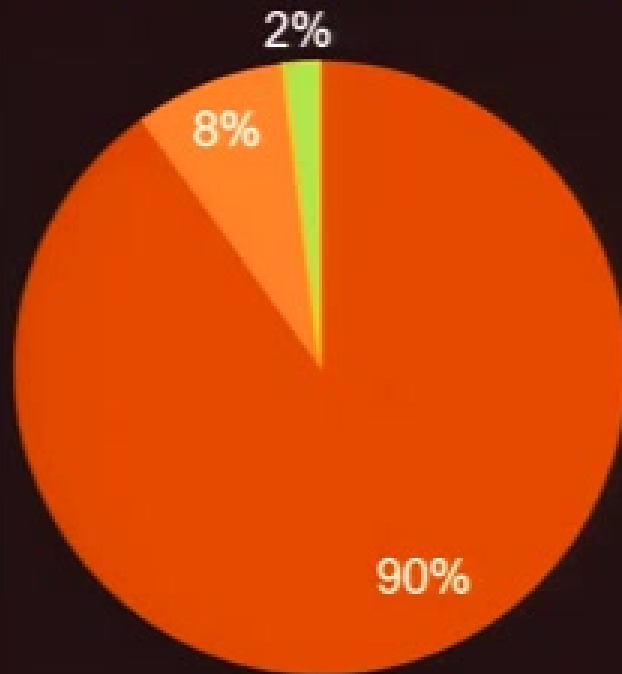
^aBased on data from The Charlie Foundation for Ketogenic Therapies²⁷ and US Department of Health and Human Services.²⁸

^bRatio refers to grams of calories from fat: carbohydrate+protein.

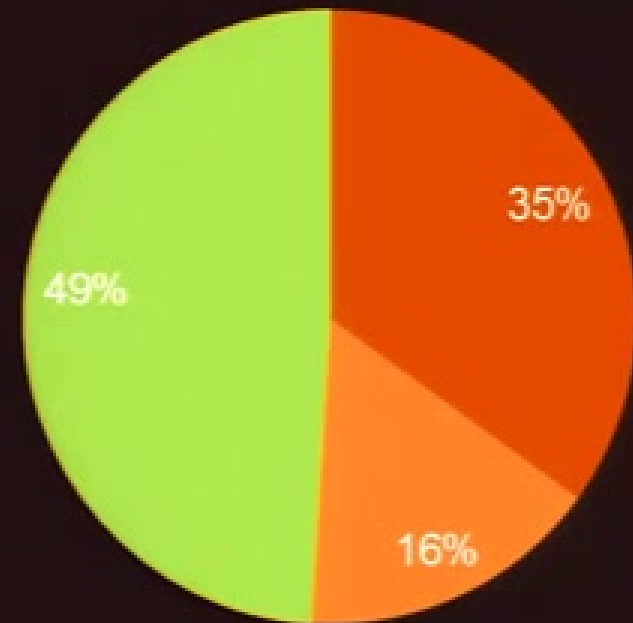
^cAdmission requirement may vary based on institution.

Diet Comparisons

Classic Ketogenic Diet



"American" Diet



Fat

Protein

Carbohydrate

Sample Menu – MAD

Table 3. Sample menu for the modified Atkins diet^a

	Grams net carbohydrate	Fat (in servings ^b)
Breakfast		
Egg Scramble (To prepare: Melt butter in frying pan; scramble all items together on medium heat.)		
2 large eggs	1	1
2 Tbsp heavy cream	1/2	1
1 Tbsp butter	0	1
1/4 cup feta cheese	2	1/2
1/2 cup spinach	1/2	0
1/2 cup mushrooms, chopped	1	0
Breakfast Subtotal:	5	3 1/2

JAND, 2017;1279-1292.

Sample Menu – MAD

Net carb = total g – g fiber

“fat serving” = 14 g fat

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Egg Scramble (To prepare: Melt butter in frying pan; scramble all items together on medium heat.)		
2 large eggs	1	1
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1 Tbsp butter	0	1
1/4 cup feta cheese	2	1/2
1/2 cup spinach	1/2	0
1/2 cup mushrooms, chopped	1	0
Breakfast Subtotal:	5	3 1/2

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Sample Menu – MAD

Table 3. Sample menu for the modified Atkins diet^a

	Grams net carbohydrate	Fat (in servings ^b)
Dinner		
Chicken and Zucchini “Pasta” (To prepare: Slice zucchini thinly into “noodles” and sauté in olive oil. Mix half the pesto into the zucchini and spread the other half on top of chicken.)		
1 medium baked chicken breast	0	0
1 cup sliced or spiraled zucchini	2½	0
1 Tbsp olive oil	0	1
2 Tbsp pesto	1	1
Dinner Subtotal:	3½	2

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Sample Menu – MAD

Table 3. Sample menu for the modified Atkins diet^a

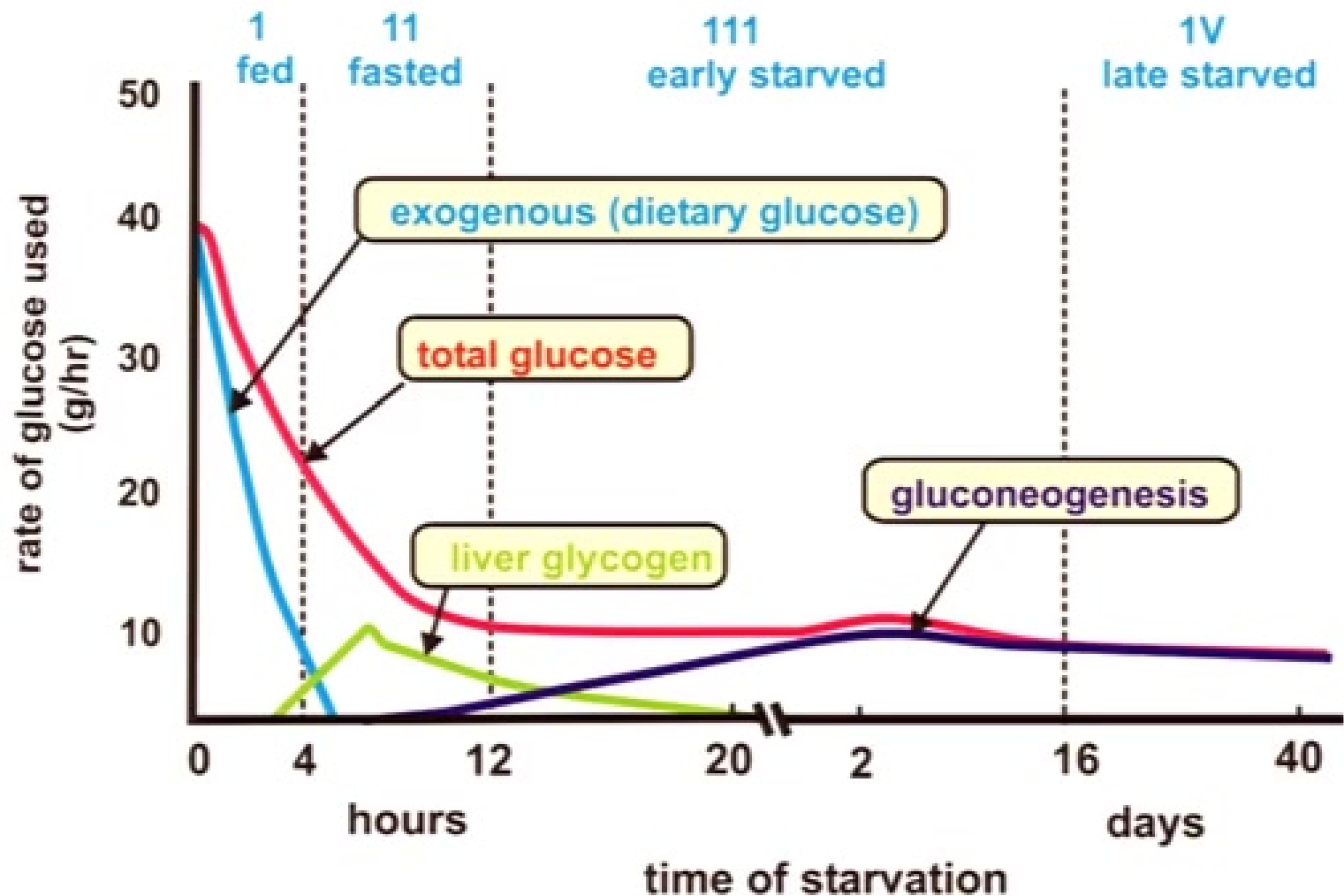
	Grams net carbohydrate	Fat (in servings ^b)
Snacks		
Celery & Cream Cheese		
1 stalk of celery, sliced	1	1
2 Tbsp full-fat cream cheese	2	0
Sugar-Free Gelatin, 1/2 cup	1/2	0
Snacks Subtotal:	3 1/2	1
Daily Total:	16 1/2	11 1/2

^aApproximate daily total: 1,700 kcal, 16 1/2 g net carbohydrate, 75 g protein, 150 g fat (11 1/2 servings).

^b1 serving=14 g of fat.

Metabolism & Pharmacokinetics

Fuel Sources & Starvation



Fuel Sources in Starvation (Ketogenesis)

Liver:

- Initial: glycogen degradation, gluconeogenesis
- Prolonged: fatty acids
- *Produces* ketones (cannot use)

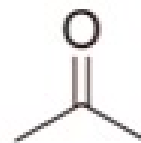
Doesn't the brain need 130 g/d of glucose to function?

Muscle:

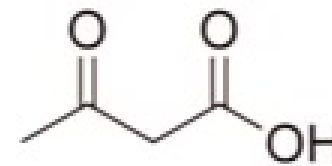
- Initial gluconeogenesis from proteolysis
- Prolonged: fatty acids, ketones

Brain:

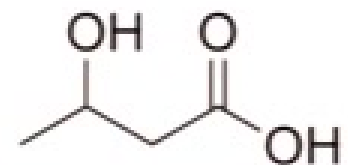
- Initial: glucose
- Prolonged: ketones



Acetone
(technically, a ketone)



Acetoacetic acid
(technically, a ketone)



Beta-hydroxybutyric acid
(technically, NOT a ketone)



Metabolic Changes with Ketogenic Diet

Mimic starvation without malnutrition

Induce a state of ketosis

- Lower blood glucose
- Lipolysis of exogenous (& endogenous) → ketone production and use for energy
 - β -hydroxybutyrate (blood)
 - acetoacetate (urine)
 - acetone (breath)
- *Gluconeogenesis can occur from exogenous protein intake if large amounts consumed*

JAND, 2017;1279-1292.

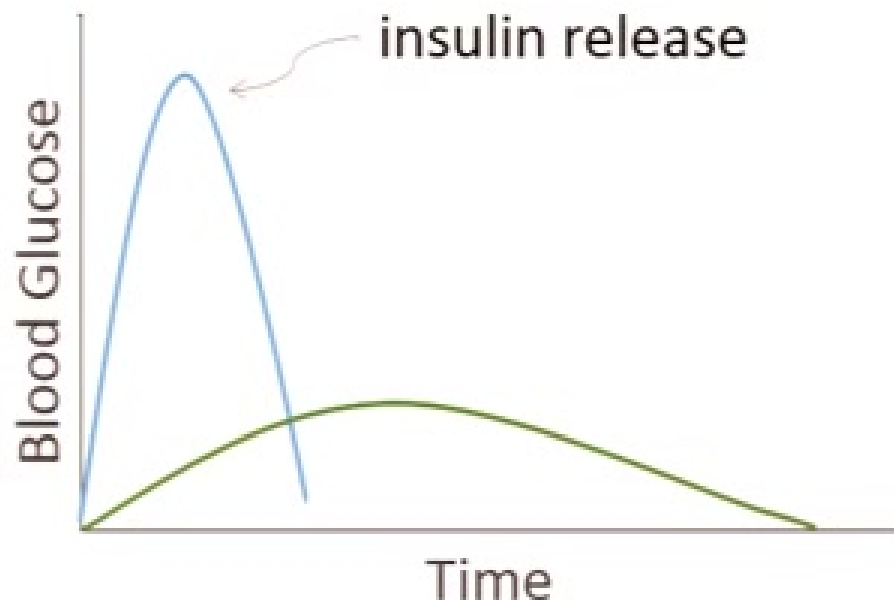
Ketosis \neq Ketoacidosis

Ketosis = shift in metabolism which relies on fat rather than glycogen as a primary fuel source

Table 1 | Blood levels during a normal diet, ketogenic diet, and diabetic ketoacidosis (Paoli et al., 2012).

Blood levels	Normal diet	Ketogenic diet	Diabetic ketoacidosis
Glucose (mg/dL)	80–120	65–80	>300
Insulin (μ U/L)	6–23	6.6–9.4	$\cong 0$
KB conc (mmol/L)	0.1	7–8	>25
pH	7.4	7.4	<7.3

Glycemic Index of Food



— = High glycemic index food

— = Low glycemic index food

High GI Foods

sugar, white flour, white grains, lower fiber fruits

Low GI Foods

vegetables, nuts, seeds, legumes, berries

**No need to check “GI”
if focus on high fiber,
overall low net
carbohydrate foods**

Fluctuations in Fuel Sources

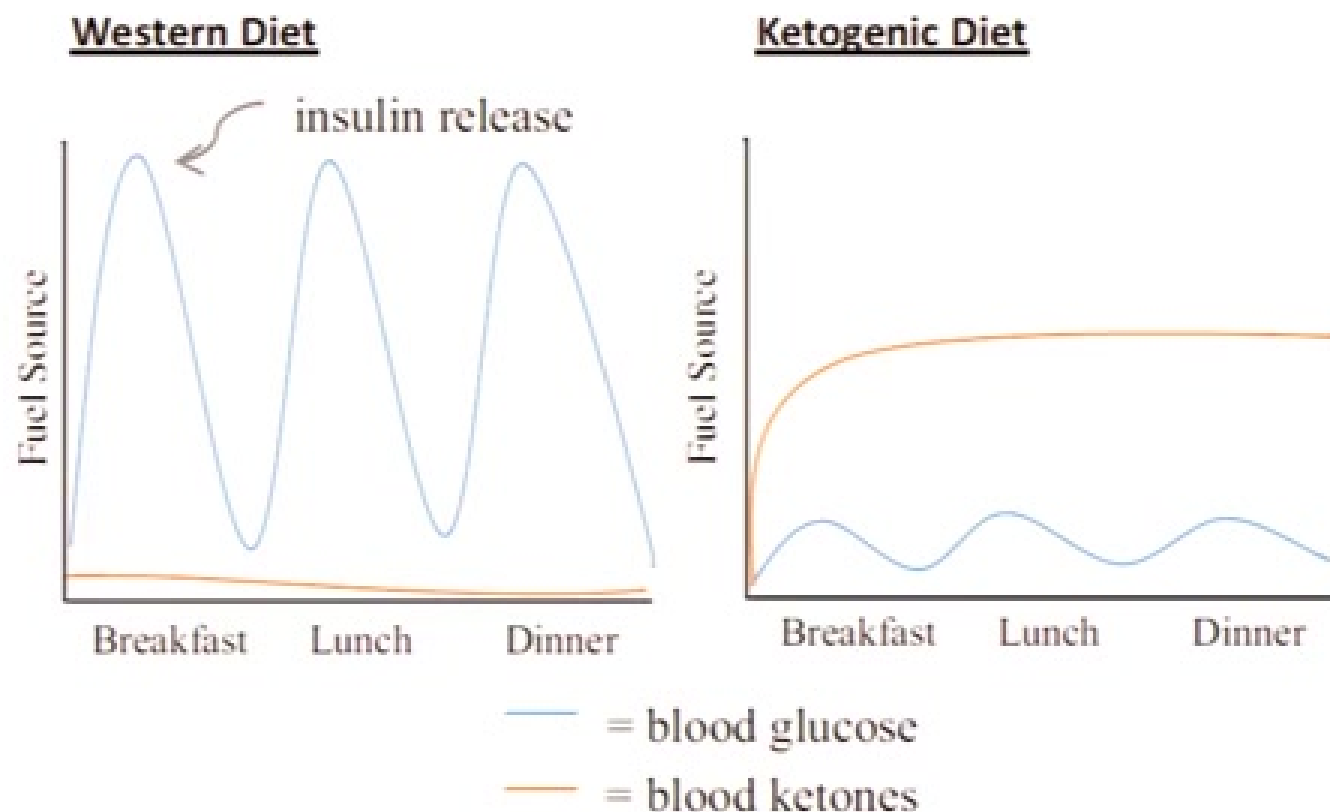


Figure 1. Variation in primary fuel source between a typical Western diet and a ketogenic diet. On a traditional Western diet, blood glucose rises after carbohydrate-rich meals (left), while on a ketogenic diet, carbohydrate intake is limited to only small quantities of those with low glycemic response, resulting in rises in serum ketone concentrations (right).

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Ketones & The Central Nervous System

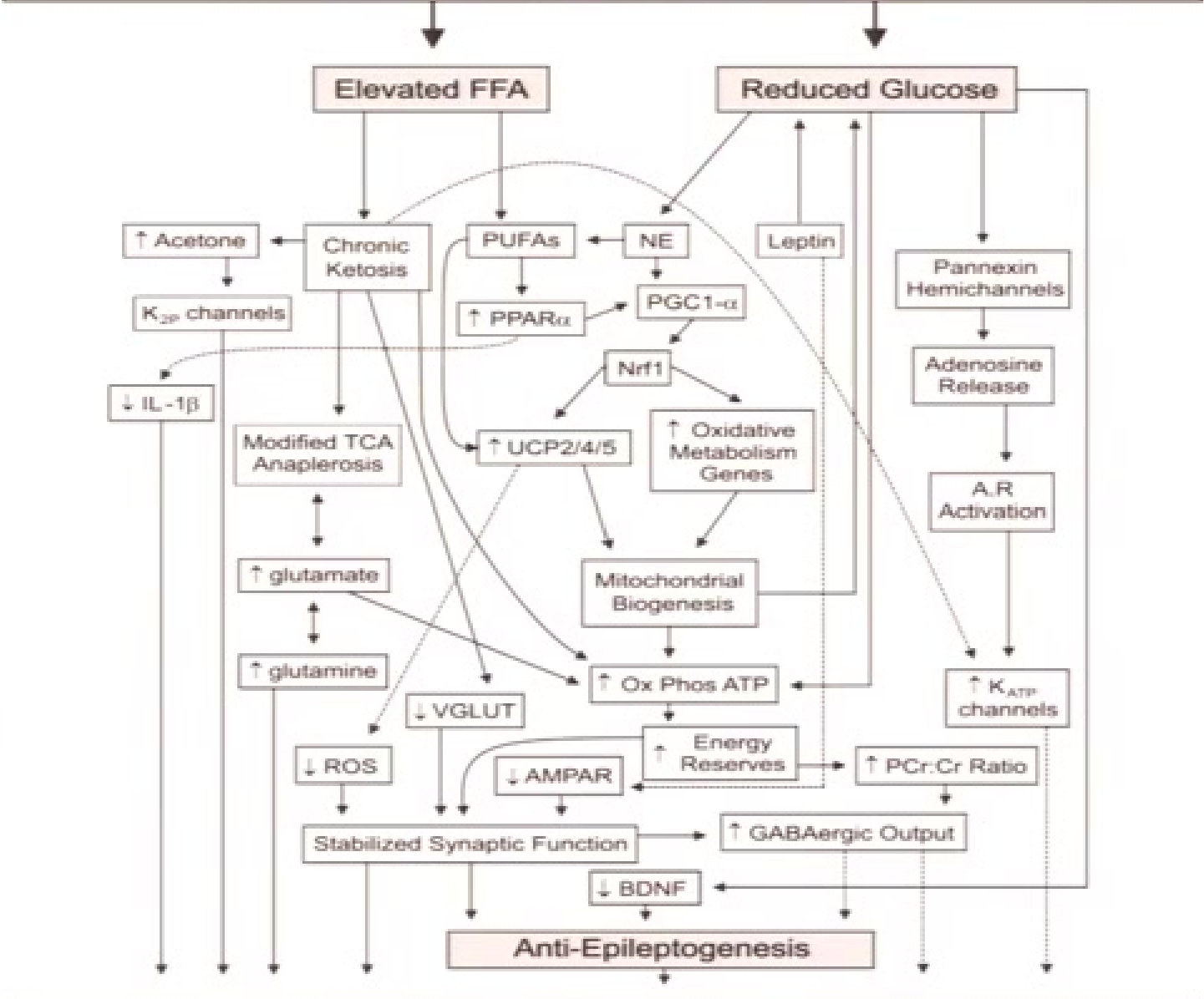
Brain cells can use and produce ketones

- Astrocytes (glial cell) is most abundant CNS cell
- Astrocyte ketogenesis may be cytoprotective
 - Decrease free radical production
 - Increase mitochondrial biogenesis
 - Stimulate brain-related antioxidant production
 - Block apoptosis of neurons

Brain-derived neurogenic factor (BDNF)

- Creates new neurons, protects existing neurons, promotes synapse formation

Ketogenic Diet



Anticonvulsant Action



Proposed Mechanisms

- **Alterations in Energy Metabolism**
 - Reduced gluconeogenesis, glycolysis
 - Enhanced lipolysis, ketosis
- **Alterations in Neurotransmitters & Hormonal Regulation**
 - Neurotransmitters & ion channels
 - Appetite, neuro modulation
 - Increased brain-derived neurotrophic factor (BDNF)
 - Microbiota (gut-brain axis)

J Clin Neurol. 2015;11:26-31. *J Lipid Res.* 2014;55:2211-2228. *Int J Biochem Cell Biol.* 2015;63:55-9. *J Biochem.* 2016;160:1-10. *Ann Gastroenterol.* 2015;28:203-209. *Neuroscience Letters.* 2017;637:4-10. *Frontiers in Neurology.* 2014;5:63. *J Clinical Investigation.* 2015;125:926-938. *J Neuroscience.* 2014;34:15490-15496. *Molecular Autism.* 2016;7:37. *Frontiers in Psychology.* 2015;6:27. *World J Gastroenterol.* 2014;20:16498-16517.

Areas of Research

Neurologic Conditions

Epilepsy, SE

Infantile spasms

ALS

Multiple Sclerosis

Parkinson's

Dementia

Sturge Weber Syndrome

Tourette Syndrome

Gangliosidoeses

Tay-Sachs

Sandoff disease

Other

Obesity & weight loss

Metabolic syndrome

Diabetes

Cardiovascular disease

Acute stroke & rehab

Changes in metabolism

Energy expenditure

Athletics & sports

Headaches/migraines

Cancer

Brain tumors

Pancreatic cancer

Head & neck cancers

Lung cancer

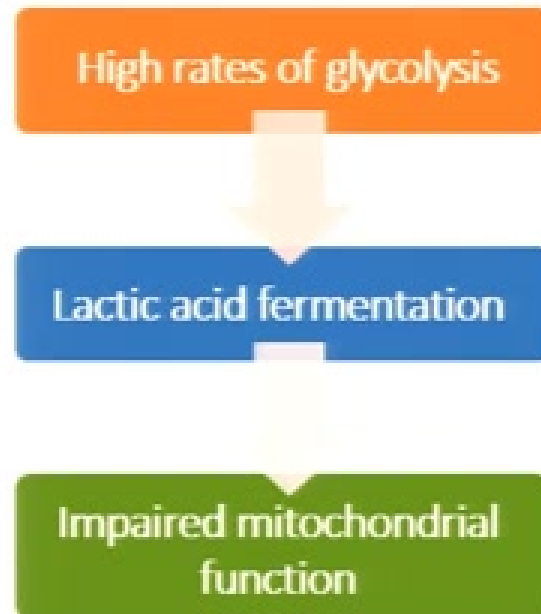
Malignant tumors

clinicaltrials.gov

Notable Theories – Ketogenic Diet

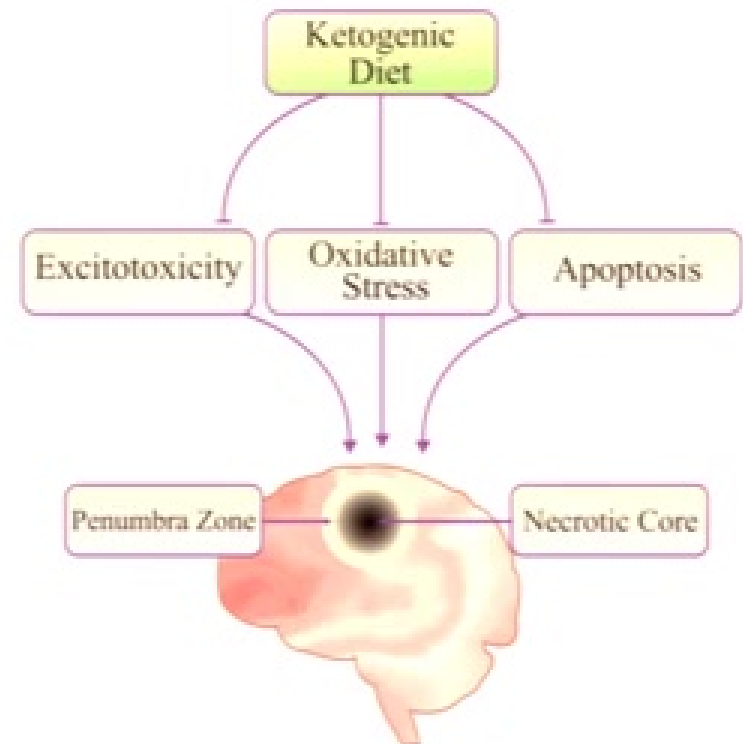
Cancer

Ketones = fuel for healthy
but not cancerous cells



Zucchi et al. *Nutrition & Metabolism*, 2010
Seyfried et al. *Nutr Metab*, 2010
Seyfried et al. *Nutr Metab*, 2008
Arismendi-Morillo et al. *J Electron Microsc*, 2008
Warburg et al. *J Gen Physiol*, 1927

Cell Injury



Giles et al. *J Neurochem*, 2011
Davis et al. *Neurosci Res*, 2008
Shahil S et al. *Adv Pharm Bull*, 2014;4:479-483
Offermann S. *Trends Molecular Med*, 2015;21:240-255.

WEIGHT LOSS *Benefits* IN KETOSIS



MORE FAT BURN

- Fat is utilized for energy instead of carbs
- Put the body into an extremely high fat-burning state.



REDUCED HUNGER

- Keto diet is high in fat, protein, and fiber
- Feel more satisfied and won't ever go hungry.



STABILIZED BLOOD SUGAR

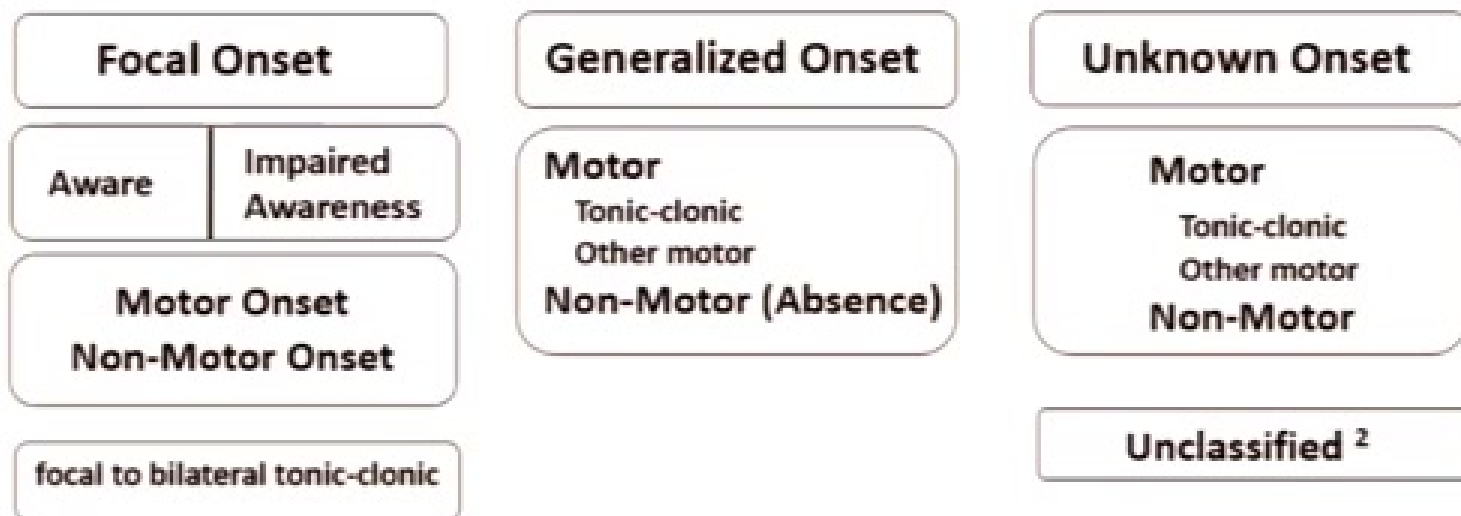
- Eating good sources of fat, protein, and veggies
- Eliminating sugar spikes caused by a carb-heavy diet.

Ketogenic Diet - Epilepsy

Epilepsy

A seizure is defined as “a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain.”²⁵ It is the clinician’s first task to determine that an event has the characteristics of a seizure and not one of the many imitators of seizures.²⁶ The next step is classification into a seizure type.

ILAE 2017 Classification of Seizure Types Basic Version ¹



¹ Definitions, other seizure types and descriptors are listed in the accompanying paper & glossary of terms

² Due to inadequate information or inability to place in other categories

Efficacy for Epilepsy

Pediatrics

- Cochrane Review – Levy 2012 (n=289)
 - 30-40% reduction in seizures (classic KD & Modified Atkins)
 - Children (classic KD) & Adults (MAD): efficacy similar to AEDs
- Cochrane Review – Martin 2016 (n=427)
 - Classic KD: 55% seizure freedom; 85% with seizure reduction
 - MAD: 10% seizure freedom; 60% with seizure reduction

Adults

- Meta-analysis – Ye 2015 (n=270)
 - $\geq 50\%$ improvement in seizure frequency
 - Classic KD: 52% (compliance 38%)
 - MAD: 34% (compliance 56%)
 - Combined efficacy: 42% (compliance 45%)

Levy et al. *Cochrane Database of Systematic Reviews*. 2012.3; CD001903.
Ye P et al. *J Clin Neurol*. 2015;15:26-35.
Martin et al. *Cochrane Database of Systematic Reviews*. 2016.2; CD001903

Status Epilepticus

A definition and classification of status epilepticus – Report of the ILAE Task Force on Classification of Status Epilepticus

*†‡Eugen Trinka, §Hannah Cock, ¶Dale Hesdorffer, #Andrea O. Rossetti, **Ingrid E. Scheffer, ††Shlomo Shinnar, ‡‡Simon Shorvon, and §§Daniel H. Lowenstein

Epilepsia, 56(10):1515–1523, 2015

doi: 10.1111/epi.13121

Status epilepticus is a condition resulting either from the failure of the mechanisms responsible for seizure termination or from the initiation of mechanisms, which lead to abnormally, prolonged seizures (after time point t_1). It is a condition, which can have long-term consequences (after time point t_2), including neuronal death, neuronal injury, and alteration of neuronal networks, depending on the type and duration of seizures.

Efficacy – Status Epilepticus




Neurocrit Care (2017) 26:267–272
DOI 10.1007/s12028-016-0312-4



ORIGINAL ARTICLE

A Practical Approach to Ketogenic Diet in the Pediatric Intensive Care Unit for Super-Refractory Status Epilepticus

Raquel Farias-Moeller¹  · Luca Bartolini¹ · Archana Pasupuleti¹ ·
R. D. Brittany Cines² · Amy Kao¹ · Jessica L. Carpenter¹

Neurology[®]

Phase I/II multicenter ketogenic diet study
for adult superrefractory status epilepticus



Neurology[®] 2017;88:938–943

Neurocrit Care. 2017;26:267–272.
Neurology. 2017;88:938–943.

Applications for Clinical Practice



Translating KD into Practice

- KD Team
- Determine Appropriateness
 - Indications/contraindications
 - Considerations for implementation
- Determine Diet Type
- Education & Initiate
- Follow Up & Weaning



KD Team Members

- **Must Have**
 - Neurologist
 - Registered Dietitian Nutritionist (RDN)
- **Should Also Include**
 - Registered Nurse
 - Social Worker / Case Manager
 - Nurse Practitioner
 - Pharmacists
 - Community RDNs
 - Family

Contraindications

- Primary carnitine deficiency
- Carnitine palmitoyltransferase I or II deficiency
- Carnitine translocase deficiency
- β -oxidation defects
 - Medium-chain acyl dehydrogenase deficiency
 - Long-chain acyl dehydrogenase deficiency
 - Short-chain acyl dehydrogenase deficiency
 - Long-chain 3-hydroxyacyl-CoA deficiency
 - Medium-chain 3-hydroxyacyl-CoA deficiency
- Pyruvate carboxylase deficiency
- Porphyria

Figure 3. Absolute contraindications to using ketogenic diet therapies. Based on data from Kossoff and colleagues.³²

Considerations for Implementation

Concern	Suggested Workup
Inability to maintain adequate nutrition or hydration <ul style="list-style-type: none">• Failure to thrive• Dysphagia• Gastrointestinal issues (chronic diarrhea, vomiting, reflux)• Not able to meet fluid goals• Extreme picky eating/limited food acceptance	<ul style="list-style-type: none">• Obtain gastrointestinal consult• Obtain swallow evaluation• Consider need for gastrostomy tube placement• Increase fat/kcal before initiation• Trial of 4:1 ketogenic formula• Provide recipes/foods to trial• Behavioral feeding consult
Concerning medical history <ul style="list-style-type: none">• Extreme dyslipidemia• Cardiomyopathy• Renal disease/renal calculi• Liver disease• Baseline metabolic acidosis	<ul style="list-style-type: none">• Obtain cardiology, nephrology, or hepatology consult for clearance• Adjust fluid minimums• Add citrate, consider bicitrate to alkalize urine, avoid/wean drugs like topiramate and zonisamide• Wean insulting medications if possible, increase fluid minimums, consider beginning with lower diet ratio
Social constraints <ul style="list-style-type: none">• Access to food and kitchen• Caregiver support and compliance• Multiple caregivers/unstable home environment	<ul style="list-style-type: none">• Connect family with social worker to discuss access to services, for example, but not limited to, durable medical equipment, Special Supplemental Program for Women, Infants, and Children, respite care, in home supportive services and/or formula company's assistance programs• Registered dietitian nutritionist can discuss meal/food options feasible for family

Figure 4. Considerations for determining appropriateness of initiation of ketogenic diet therapy and suggested further workup before diet initiation.

JAND, 2017;1279-1292.



Considerations for Implementation

Neurologic

- Seizure type, severity & frequency
- Baseline cognitive abilities

Nutrition

- Baseline food knowledge, preferences
- Ability to prepare meals, follow directions/recipes

Support & Investment

- Family and emotional support
- Patient investment (self-interest versus referral)
- Willingness & readiness to make diet changes
- *Potential* financial burden



Choosing the Diet Type

Classic Ketogenic Diet:

- Pediatric patients <2 years of age, G-tube feedings

Modified Atkins Diet:

- Medically intractable

Low Glycemic Index Diet:

- Medically intractable
- Medically non-intractable
- Limited cognitive abilities and/or those without family support



KD – Where to Initiate

Outpatient

- 2:1, 1:1 classic KDs (modified ketogenic)
- MAD, LGIT

Inpatient

- High risk for acute side effects
- MCT, 4:1, 3:1 classic KDs

Intensive Care Unit

- Emergent initiation for status epilepticus or refractory seizures
- Communication is key
 - Pharmacy
 - Nursing
 - Physicians
 - Kitchen



Considerations for Emergent Initiation

Enteral Nutrition

- Ketogenic formulas, protein modulars, MCT oil
- Flushes to maintain hydration
- Consider multivitamin with minerals and carnitine

Parenteral Nutrition

- Glycerol content of lipids = 0.11 g carb/1g lipid
- 4 g lipid/kg/day – may be infused over 24 hrs
- Check triglycerides after 72 hours

Transition to oral diet...

- Ensure kitchen can provide keto foods
- Monitor lab changes with transition



Determining KD Nutrient Requirements

Overweight/Obese (adjusted weight)

- 20-25 kcal/kg
- 0.8-1.2 g protein/kg
- 30-35 ml/kg

Normal/Underweight (actual weight)

- 25-35 kcal/kg
- 0.8-1.2 g protein/kg
- 30-35 ml/kg

Pediatrics (actual weight)

- Generally 40 kcal/kg, assess intake-diet recall
- 1-1.2 g protein/kg
- 35-40 ml/kg

Modified Ketogenic Diet Recommendations

Patient: Anne Example

DOB: 12/12/1964 (50 y.o. F)

Height: 65"

Weight: 83 kg

BMI: 30.4 kg/m² IBW: 57 kg (145% IBW) Dosing Weight: 64 kg (adjusted)

Your Individualized Diet: Modified Atkins Ketogenic Diet

25 kcal/kg
1.2 g pro/kg
35 ml/kg

~1.2:1 ratio

<i>Nutrient</i>	Daily Totals	
	<i>Grams per day</i>	<i>What does that mean?</i>
Fat	105 grams	8 servings
Net Carbohydrate	15 grams	15 grams
Protein	75 grams	11 ounces
Fluid	2250 mL	75 ounces
Calories	1300 calories	1300 calories

What Counts as a "serving" of Fat?

1 tbsp butter

1 tbsp any oil

1 tbsp coconut oil

1 tbsp MCT oil

2 tbsp heavy cream

1 tbsp fat = approximately 14 g of fat

Common Protein Serving Sizes:

7 grams protein = 1 ounce of protein

1 egg = 1 ounce of protein

'deck of cards' portion of poultry/fish/meat = 3 oz

1 ounce of cheese = 1 ounce of protein



KD – How to Initiate

Method 1:

- Day 1: 1/3 ketogenic, 2/3 standard diet
- Day 2: 2/3 ketogenic, 1/3 standard diet
- Day 3: full ketogenic

Method 2:

Increase ratio daily (or as tolerated)
1:1 → 2:1 → 3:1 → 4:1

Method 3:

- Start at goal ketogenic diet
 - ie: goal ratio, full MAD

Home Monitoring

Urine Ketones

- Aim for “small-large” ketones, little fluctuation
- Daily until positive
- Every other day once stable

Diet & Seizure Log

KETONE-Read at exactly 15 seconds.





Follow Up – every 1 to 3 months

Physician role

- Review changes in seizure frequency, severity, QOL, side effects, medications
- Repeat labs

Dietitian role

- Assess anthropometric changes
- Review vitamins
- Assess compliance through diet recall, ability to describe carbs/fats, urine ketones
- Provide suggestions to enhance compliance



Enhancing Compliance

- Individualized plan, adjustments
- Increasing time spent on between visit encouragement to maintain compliance
 - Phone/email contact with RD
 - Closer follow up (every 1-2 months) to improve compliance
 - Support groups, social networking support, newsletters, etc
- Family/social support
- Food record!



Enhancing Compliance

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- Family/social support
- Food record!

Consider following the diet yourself to enhance your credibility!



Weaning

When to stop the diet:

- Non-compliance
- Unintentional weight changes
- Uncontrollable hyperlipidemia
- No change in seizure or symptom control

Discontinuation:

- Increase carb intake by 5-10 g/day until >100 g/day/ketones neg
- If negative side effects noted, return carb intake to last tolerated and slowly increase protein/decrease fat

Length of KD Therapy --- varies by patient, institution



Potential Side Effects of KD

Risks

Gastrointestinal

- Dehydration

- N/V/C/D

- Pancreatitis

Kidney Stones

Lipid Abnormalities

Growth Concerns

Metabolic

- Low electrolytes

- Acidosis (excessive ketones)

- Carnitine deficiency

Benefits

- Improved seizure frequency

- Improved seizure severity

- Potential medication weaning


- Improved quality of life

 - Alertness

 - Mood

 - Sleep

JAND. 2017;1279-1292.
Nutrients. 2017;517;doi:10.3390/nu9050517
Nutrition. 2012;28:1016-1021.



The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

JULY 17, 2008

VOL. 359 NO. 3

Weight Loss with a Low-Carbohydrate, Mediterranean, or Low-Fat Diet “DIRECT” Trial

METHODS

In this 2-year trial, we randomly assigned 322 moderately obese subjects (mean age, 52 years; mean body-mass index [the weight in kilograms divided by the square of the height in meters], 31; male sex, 86%) to one of three diets: low-fat, restricted-calorie; Mediterranean, restricted-calorie; or low-carbohydrate, non-restricted-calorie.

CONCLUSIONS

Mediterranean and low-carbohydrate diets may be effective alternatives to low-fat diets. The more favorable effects on lipids (with the low-carbohydrate diet) and on glycemic control (with the Mediterranean diet) suggest that personal preferences and metabolic considerations might inform individualized tailoring of dietary interventions. (ClinicalTrials.gov number, NCT00160108.)

NEJM. 2008;359:229-241.

Effects of Low-Carbohydrate and Low-Fat Diets

A Randomized Trial

Lydia A. Bazzano, MD, PhD, MPH^{*}; Tian Hu, MD, MS^{*}; Kristi Reynolds, PhD; Lu Yao, MD, MS; Calynn Bunol, MS, RD, LDN; Yanxi Liu, MS; Chung-Shiuan Chen, MS; Michael J. Klag, MD, MPH; Paul K. Whelton, MD, MSc, MB; and Jiang He, MD, PhD

Participants: 148 men and women without clinical cardiovascular disease and diabetes.

Intervention: A low-carbohydrate (<40 g/d) or low-fat (<30% of daily energy intake from total fat [<7% saturated fat]) diet. Both groups received dietary counseling at regular intervals throughout the trial.

Measurements: Data on weight, cardiovascular risk factors, and dietary composition were collected at 0, 3, 6, and 12 months.

Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): a prospective cohort study



Methods The Prospective Urban Rural Epidemiology (PURE) study is a large, epidemiological cohort study of individuals aged 35–70 years (enrolled between Jan 1, 2003, and March 31, 2013) in 18 countries with a median follow-up of 7·4 years (IQR 5·3–9·3). Dietary intake of 135 335 individuals was recorded using validated food frequency questionnaires. The primary outcomes were total mortality and major cardiovascular events (fatal cardiovascular disease, non-fatal myocardial infarction, stroke, and heart failure). Secondary outcomes were all myocardial infarctions, stroke, cardiovascular disease mortality, and non-cardiovascular disease mortality. Participants were categorised into quintiles of nutrient intake (carbohydrate, fats, and protein) based on percentage of energy provided by nutrients. We assessed the associations between consumption of carbohydrate, total fat, and each type of fat with cardiovascular disease and total mortality. We calculated hazard ratios (HRs) using a multivariable Cox frailty model with random intercepts to account for centre clustering.

Interpretation High carbohydrate intake was associated with higher risk of total mortality, whereas total fat and individual types of fat were related to lower total mortality. Total fat and types of fat were not associated with cardiovascular disease, myocardial infarction, or cardiovascular disease mortality, whereas saturated fat had an inverse association with stroke. Global dietary guidelines should be reconsidered in light of these findings.



Cardiovascular and Metabolic Risk

Compared to low-fat, low carbohydrate, higher fat diets

- Significantly greater weight loss
- More favorable glycemic control
- More favorable lipid panel
- Cardiovascular risk factor reduction

Regarding dietary composition

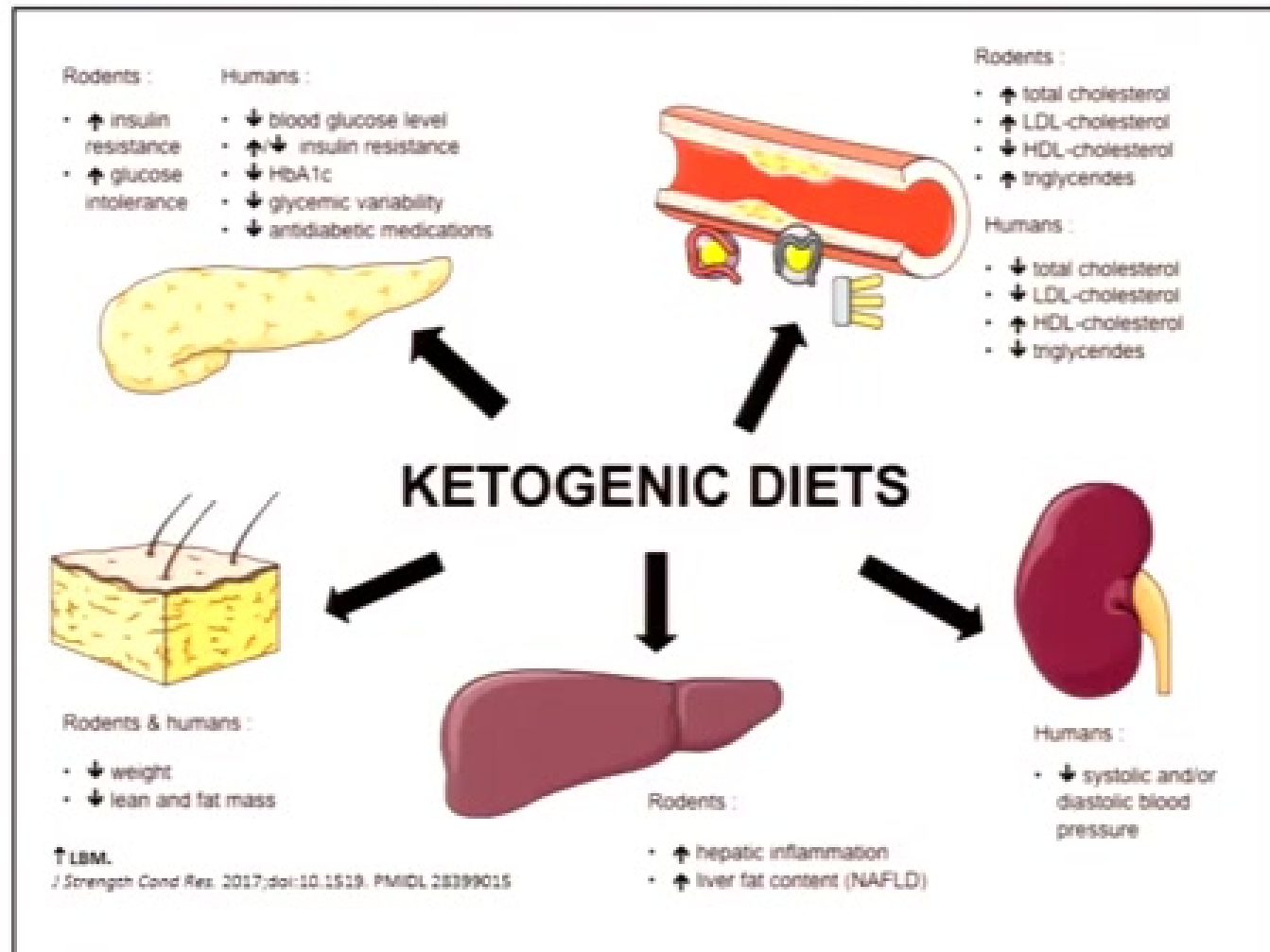
- High carbohydrate intake is associated with higher total mortality
- Total and individual types of fat:
 - Related to lower total mortality
 - Not associated with MI, CVD, CVD mortality
 - Inverse association with saturated fat and stroke

NEJM. 2008;359:229-241.

Ann Intern Med. 2014;161:309-318.

Lancet. 2017; doi: 10.1016/S0140-6736(17)32252-3

Cardiovascular and Metabolic Risk



Nutrients. 2017;517;doi:10.3390/nu9050517

Figure 1. Effects of ketogenic diets in rodents and humans.

Managing Side Effects

Side Effect	Treatment
Weight loss	Increase protein, carbohydrates
Weight gain	Reduce calories, ensure compliance
Constipation	Increase fiber & fluid consumption, pharmacologic
Acid reflux	Increase carbs, eliminate problematic foods, change eating patterns, pharmacologic
Hyperlipidemia	Ensure compliance, start carnitine, adjust types of fats consumed

Curr Opin Neurol. 2012;25:173-178.
Nutr Neurosci. 2014; epub. PMID: 2583724



Keys to Successful KD

- Keto Team must believe!
 - Diet changes are difficult, must market the diet!
- Buy-in from colleges (MDs, RDNs, RNs, etc)
 - Get them on board!
- Offer individualized therapy
 - Choose the right diet that does not cause stress
- Determine what “success” is – individualize!
 - Frequency reduction, severity, QOL, anti-epileptogenic potential

Keto References

- Academy of Nutrition and Dietetics Nutrition Care Manual: www.nutritioncaremanual.org
- Kossof EH, Turner Z, Doerr S, Cervenka MC, Henry BJ. *The Ketogenic and Modified Atkins Diets: Treatment for Epilepsy and Other Disorders*. 6th ed. New York: demosHEALTH; 2016.
- The Charlie Foundation for Ketogenic Therapies: www.charliefoundation.org
- Matthew's Friends: www.matthewsfriends.org
- Carson Harris Foundation: www.carsonharrisfoundation.org
- Carley Eissman Foundation: www.carleyeissmanfoundation.com
- Keto Hope Foundation: www.ketohope.org
- KetoDietCalculator: <https://ketodietcalculator.org>
- Nutricia: www.myketocal.com
- Cambrooke Therapeutics: www.ketovie.com

Figure 7. Ketogenic references for registered dietitian nutritionists (RDNs). These resources were determined to provide quality ketogenic recommendations by RDNs practicing ketogenic diet therapy.



Conclusions & Practice Applications

- Ketogenic diets have be utilized in a variety of populations, most notably – epilepsy and weight loss.



Conclusions & Practice Applications

- Ketogenic diets have been utilized in a variety of populations, most notably – epilepsy and weight loss.
- Research is underway, but much more is needed to fully understand potential benefits and risks in other populations.
- Ketogenic diet clinics must have a specially trained dietitian and a physician overseeing care with close follow up to optimize compliance.

Thank You!