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Low Carbohydrate Diets In Elderly

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What Is a Low Carbohydrate Diet?

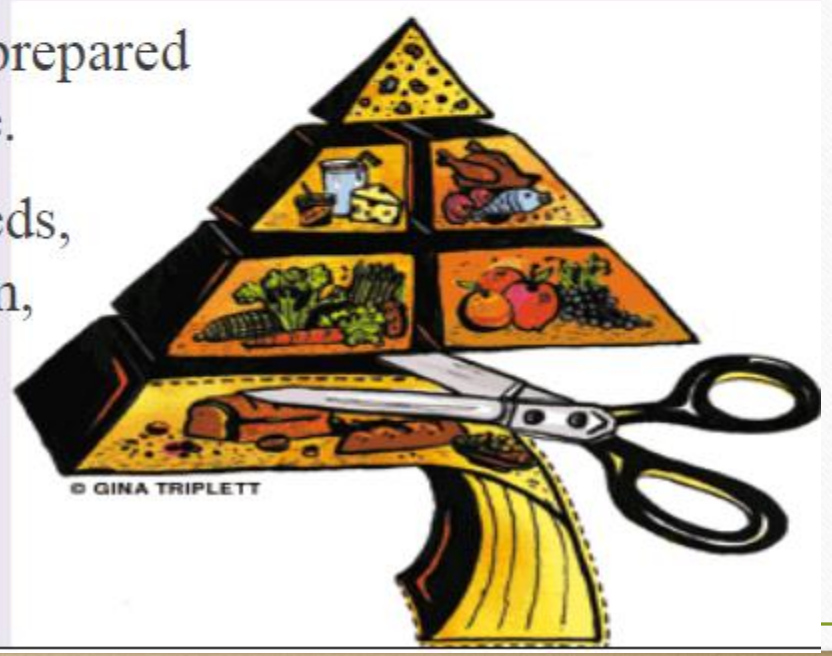
Table 1. Suggested definitions of different carbohydrate diets (Adapted from Feinman et al.) [23].

Description	Grams Per Day	Energy from Carbohydrate (%)
Ketogenic diet (very low carbohydrate diet)	<20–50 g	<10
Low Carbohydrate	<130 g	<26
Moderate Carbohydrate	130–230 g	26–45
High Carbohydrate	>230 g	>45

What is the Ketogenic Diet?

- High fat, low carbohydrate, and adequate protein diet
- Ketones become the primary fuel for the brain
- Started in the hospital

- All foods must be carefully prepared and weighed on a gram scale.
- Count the carb content in meds, vitamins, toothpaste, lip balm, sunscreen…*everything*!



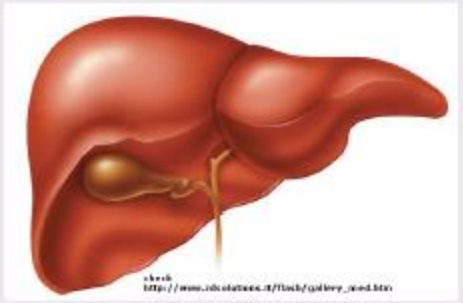
The Ketogenic Diet

How does it work?

Supplying the body with fuel in the form of fat with no carbohydrates

Eat high fat

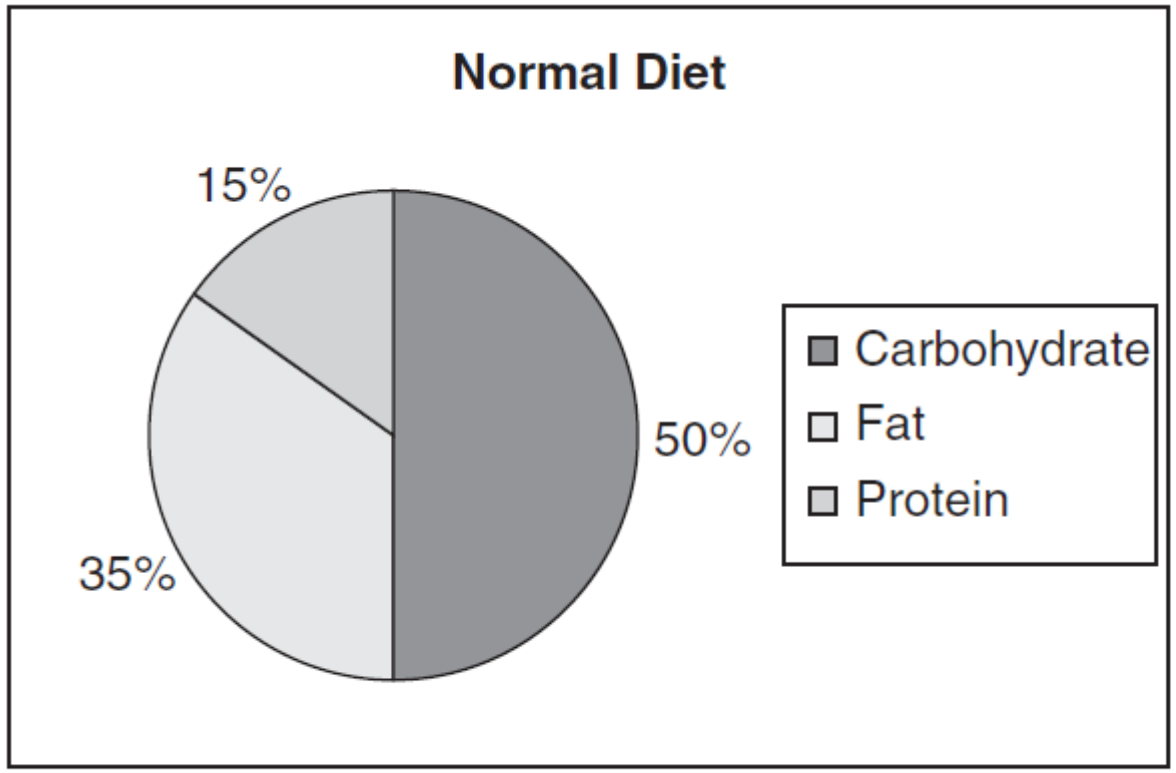
Fatty acids



Liver produces ketones from fatty acids

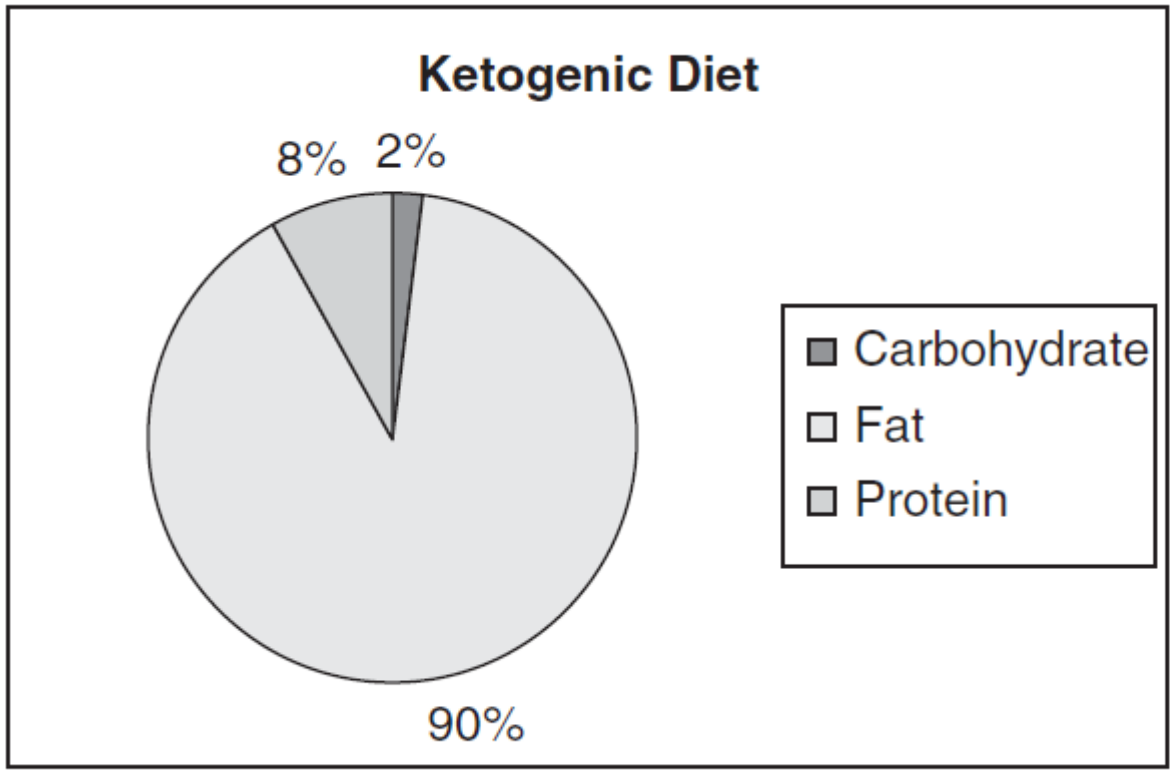
Ketogenic Diet
high fat, no carbs

When there is no glucose available, the brain uses ketones for fuel



Normal diet

Carbohydrate	50%
Fat	35%
Protein	15%



Classical ketogenic diet

Carbohydrate	2%
Fat	90%
Protein	8%

Ketogenic Diet

- The ketogenic diet (KD) is a nonpharmacologic treatment used worldwide for children with intractable epilepsy.
- It has been used to treat epilepsy in children since 1921 with little variation until recent years.
- The original protocol using a high fat, low carbohydrate diet was created at the Mayo Clinic, and popularized by the Johns Hopkins Hospital.
- The KD was traditionally started in the hospital after a 48-h fast followed by a gradual introduction of calories in the form of a KD over a 3-day period.
- Children were then seen periodically in clinic for medical and nutritional follow-up.

Specific diet selection and provision

- In the classic KD, fat is a LCT and obtained primarily from standard foods, protein is based on minimum requirements for growth, and carbohydrates are restricted.
- MCT oils yield more ketones per kilocalorie of energy than their long chain counterparts; they are absorbed more efficiently and carried directly to the liver.
- This increased ketogenic potential means less total fat is needed in the MCT diet, thus allowing inclusion of more carbohydrate and protein.

Specific diet selection and provision

- The classic KD is calculated in a ratio of grams of fat to grams of protein plus carbohydrate.
- The most common ratio is 4 g of fat to 1 g of protein plus carbohydrate (described as “4:1”).
- This means that 90% of the energy comes from fat and 10% from protein and carbohydrate combined.
- Sometimes it is necessary to provide the KD at a lower ratio to increase protein or carbohydrate intake.

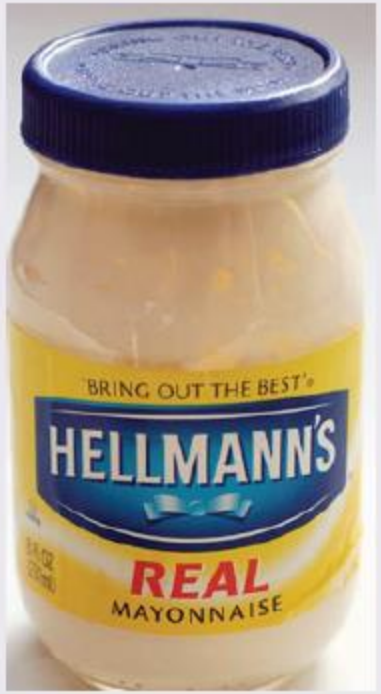
Modified Atkins Diet (MAD)

- MAD is more liberal. No gram scale. No calorie restriction.
- Count daily NET CARBS
- **Net Carbs** = Total Carbohydrate (g) – Dietary Fiber (g)
- **Max of 10 – 20 grams of net carbs per day**
- Increase fat intake!
- Very very low carb! Very high in fat.
- Less dietitian involvement in meal planning

Table 3. Modified Atkins diet protocol

Copy of *Dr. Atkins' New Diet Revolution* and a carbohydrate counting guide provided
Carbohydrates described in detail and restricted to 10 g/d for the first month (increase afterwards if child and family desire)
Fats (eg, 36% heavy whipping cream, oils, butter, mayonnaise) encouraged
Clear, carbohydrate-free fluids not restricted
Low-carbohydrate multivitamin and calcium supplementation prescribed
Check urine ketones semiweekly and weight weekly
Medications left unchanged for at least the first month, but changed if necessary to tablet or sprinkle (nonliquid) preparations
Low-carbohydrate, store-bought products (eg, shakes, candy bars, baking mixes) discouraged for at least the first month
Complete blood count, complete metabolic profile (SMA-20), urine calcium and urine creatinine, urinalysis, and fasting lipid profile at baseline, 3 months, and 6 months

Modified Atkins Diet: High Fat



Specific diet selection and provision

- The KD may be delivered as an all-liquid, formula based diet.
- Prescription of a formula-based KD is generally simpler for dietitians to calculate, requires less education of families and caregivers, and due to the ease of delivery of an all-liquid KD, ketosis is easily maintained as errors are less common.

KD LIQUID

KD POWDER

Ketogenic Diet Sample Meals

Breakfast:

40g 36% Heavy cream
32g Sausage links
24g Avocado
5g Canola oil

Lunch:

40g 36% Heavy cream
18g Sliced turkey breast
22g Raw cucumber slices and celery sticks
22g Mayonnaise

Dinner:

40g 36% Heavy cream
20g Baked cod
43g Roasted cauliflower
23g Butter

Diet initiation

- The KD initiation practices have their origin in the historical use of periodic fasting to treat seizures.
- **Fasting** is therefore part of the KD initiation in many centers worldwide.
- Because of concerns that fasting may result in hypoglycemia, acidosis, nausea, vomiting, dehydration, anorexia, lethargy, and a small risk for increase in seizures, most centers begin the KD in the hospital so that the patient can be closely observed, and medical interventions can be instituted if necessary.
- Hospitalization also provides the opportunity for intensive teaching of the caregivers on how to calculate, weigh, design meals, and manage the KD at home.

The main reasons for inpatient initiation include safety (management of acute medical side effects) and education of care providers.

Diet initiation

- The traditional method of initiating the KD involves a period of fasting, with no carbohydrate-containing fluids provided, and serum glucose monitored periodically.

- The duration of fasting varies from 12 h to "when urine ketones are large," which can be longer than 48 h.
- Children should not be fasted longer than 72 h.
- The meals are then typically advanced daily in one-third caloric intervals until full calorie meals are tolerated, while keeping the KD ratio constant.
- Another approach begins with full calories, but the KD ratio increases daily from 1:1, 2:1, 3:1, to 4:1 to allow the patient to acclimate to the increasing concentration of fat.

Fasting may be appropriate when a quicker time to response is desired, but is not necessary for long-term efficacy, and may have more immediate side effects.

Panel 2. Ketogenic diet protocol at Johns Hopkins Hospital

Day before admission

Low carbohydrate consumption for 24 h
Children examined in clinic the afternoon before admission
Fasting starts in the evening

Day 1

Admitted to the hospital
Fasting continues
Fluids restricted to 60–75 cc/kg
Blood glucose monitored every 6 h
Use carbohydrate-free drugs
Parents begin educational programme

Day 2

Dinner given as a third of calculated diet meal as "eggnog"
Blood glucose checks discontinued after dinner
Parents begin to check urine ketones periodically

Day 3

Breakfast and lunch given as a third of diet
Dinner increased to two-thirds (still eggnog)
Education programme completed

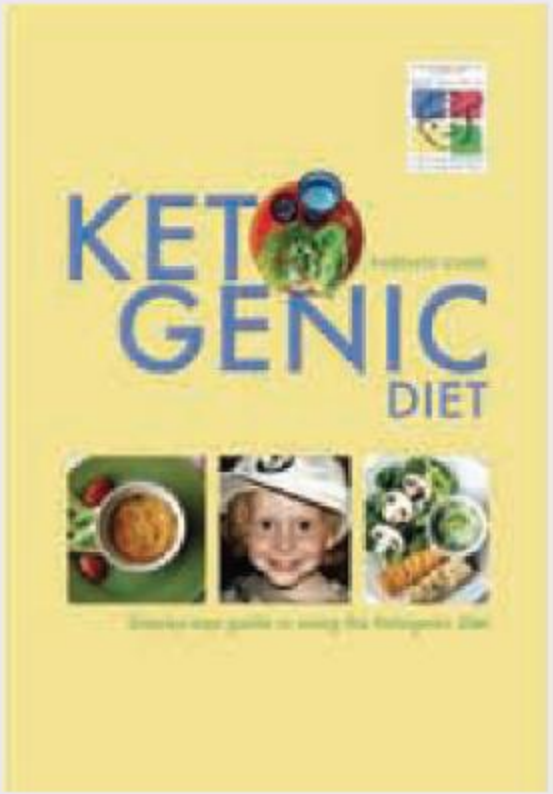
Day 4

Breakfast and lunch given as two thirds of diet allowance
Dinner is first full ketogenic meal (not eggnog)

Day 5

Full ketogenic diet breakfast given
Prescriptions reviewed and follow-up arranged
Child discharged to home

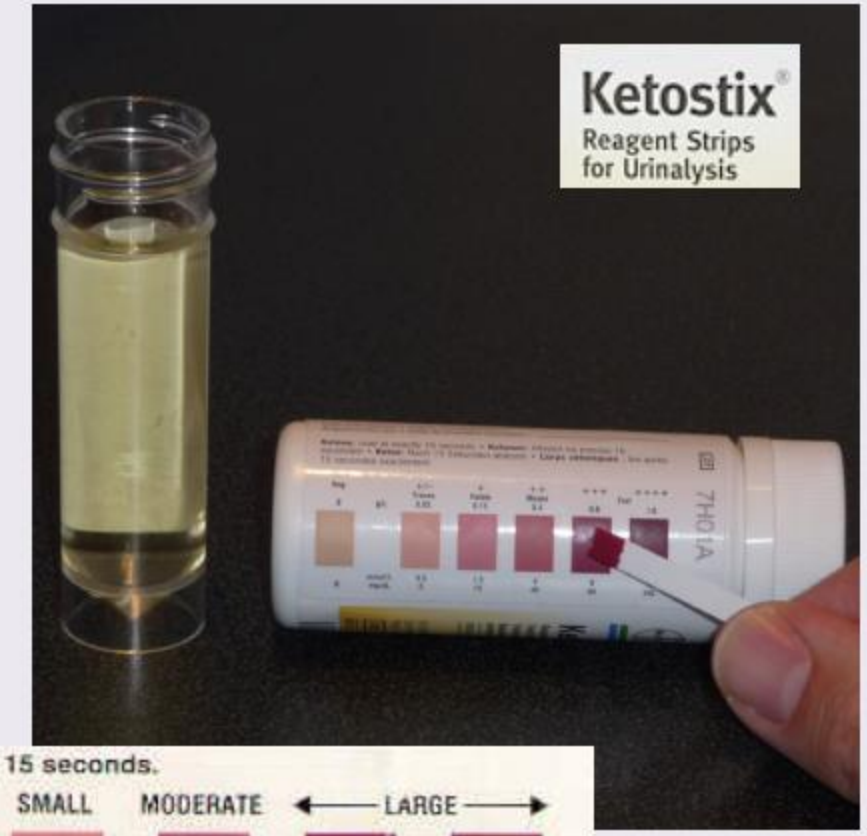
Starting the Ketogenic Diet



The Parents Guide to the Ketogenic Diet

Gram scale to weigh all meals

Urine ketones are checked regularly at home



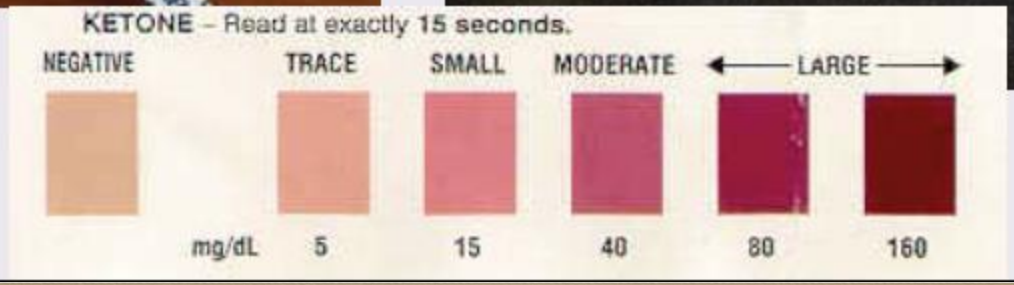


Table 4. Supplementation recommended for children receiving the KD

Universal recommendations

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

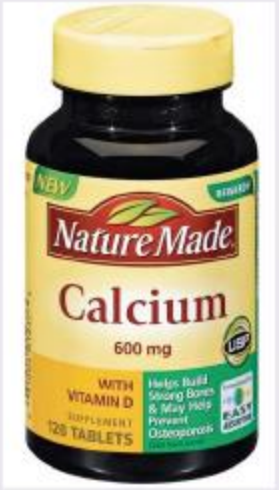
Optional extra supplementation

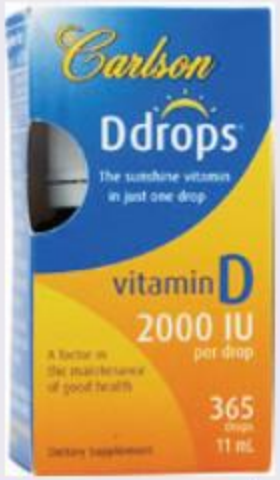
- Oral citrates (Polycitra K)
- Laxatives: Miralax, mineral oil, glycerin suppository
- Additional selenium, magnesium, zinc, phosphorus, vitamin D
- Carnitine (Carnitor)
- MCT oil or coconut oil (source of MCT)
- Salt (sodium to add to modular formulas if used for greater than age 1 year)

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

Vitamins & Supplements

Low-Carb





Adverse effects of the KD

- Like all medical therapies, the KD has potential adverse effects.
- Overall, the risk of serious adverse events is low, and the KD does not need to be discontinued for these reasons for most children.
- However, physicians need to be aware of these potential risks so they can properly counsel parents and monitor children for the development of these complications.

Potential side effects of the ketogenic diet

Table 4. Potential side effects of the ketogenic diet
Common
Lack of weight gain
Constipation
Hypoglycemia (with fasting)
Occasional
Gastrointestinal distress (medium chain triglyceride oil)
Dehydration/acidosis
Change in lipid profiles
Kidney stones
Growth retardation
Skeletal fractures
Rare
Pancreatitis
Cardiomyopathy
Prolonged QT syndrome
Basal ganglia injury
Vitamin and/or mineral deficiencies

Common

1. Lack of weight gain
2. Constipation
3. Hypoglycemia (with fasting)

Occasional

1. Gastrointestinal distress (medium chain triglyceride oil)
2. Dehydration/acidosis
3. Change in lipid profiles
4. Kidney stones
5. Growth retardation
6. Skeletal fractures

Rare

1. Pancreatitis
2. Cardiomyopathy
3. Prolonged QT syndrome
4. Basal ganglia injury
5. Vitamin and/or mineral deficiencies

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

Prediet Evaluation And Counseling

Table 3. Recommendations for pre-KD evaluation

Counseling
- Discuss seizure reduction, medication, and cognitive expectations
- Identify potential psychosocial barriers to the use of KD
- Review anticonvulsants and other medications for carbohydrate content
- Recommend family read parent-oriented KD information

Nutritional evaluation
- Baseline weight, height, and ideal weight for stature
- Body mass index (BMI) when appropriate
- Nutrition intake history: 3-day food record, food preferences, allergies, aversions, and intolerances
- Establish diet formulation: infant, oral, enteral, or a combination
- Decision on which diet to begin (MCT, classic, modified Atkins, or low glycemic index)
- Calculation of calories, fluid, and ketogenic ratio (or percentage of MCT oil)
- Establish nutritional supplementation products based on dietary reference intake

Laboratory evaluation
- Complete blood count with platelets
- Electrolytes to include serum bicarbonate, total protein, calcium, zinc, selenium, magnesium, and phosphate
- Serum liver and kidney tests (including albumin, AST, ALT, blood urea nitrogen, creatinine)
- Fasting lipid profile
- Serum acylcarnitine profile
- Urinalysis
- Urine calcium and creatinine
- Anticonvulsant drug levels (if applicable)
- Urine organic acids
- Serum amino acids

Ancillary testing (optional)
- Renal ultrasound and nephrology consultation (if a history of kidney stones)
- EEG
- MRI
- Cerebrospinal fluid (CSF) (if no clear etiology has been identified)
- EKG (echocardiogram) if history of heart disease

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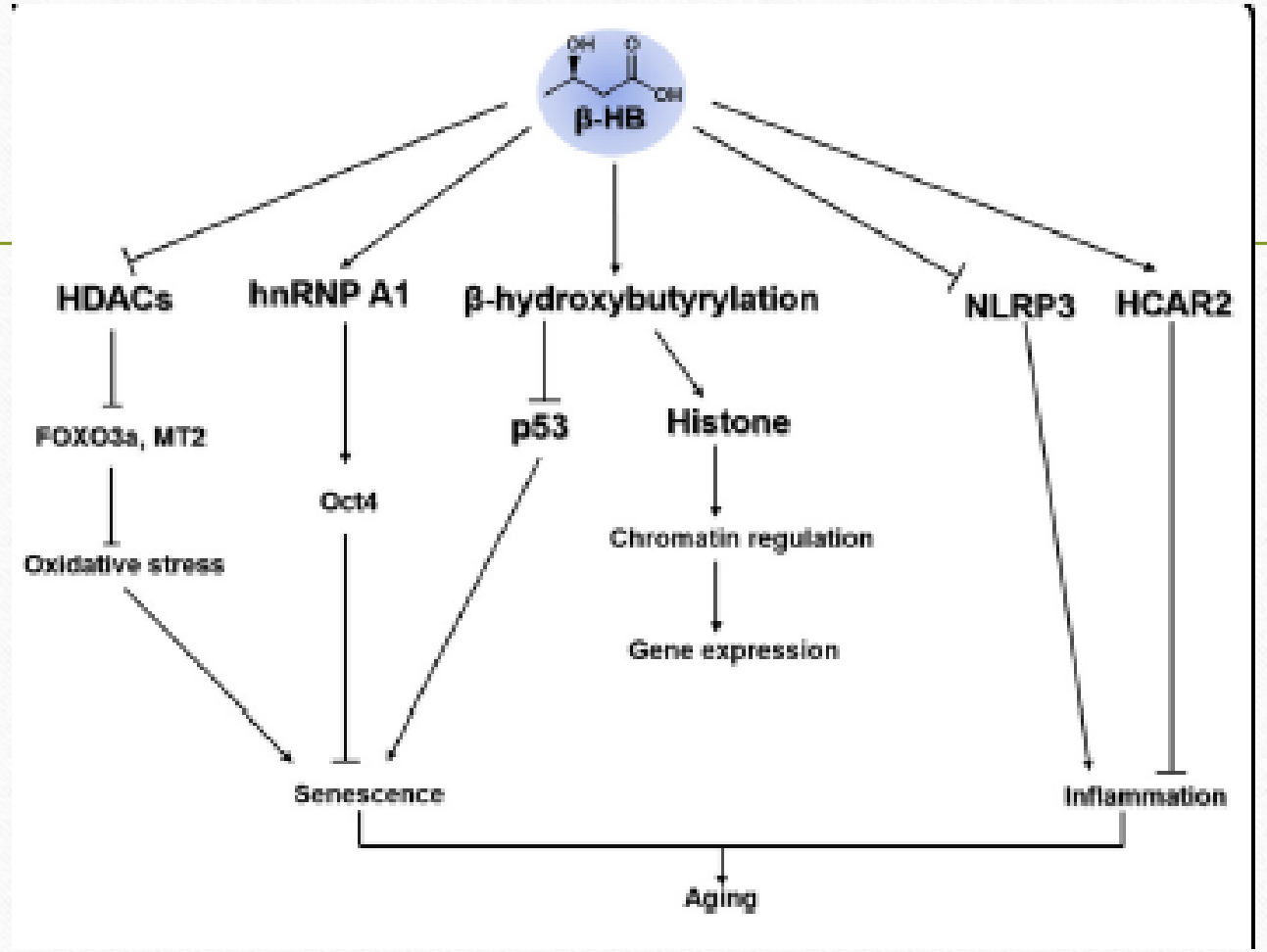
Introduction

- Aging, along with its associated ailments, including cardiovascular disease, cancer, arthritis, dementia, cataracts, osteoporosis, diabetes, hypertension, and Alzheimer's disease, is a primary health concern. Accumulating data demonstrate that a ketogenic diet elevates the levels of β-hydroxybutyrate (β-HB), improving many age-related diseases.

β-hydroxybutyrate and its metabolic effects on age-associated pathology

- Aging is a universal process that renders individuals vulnerable to many diseases. Although this process is irreversible, dietary modulation and caloric restriction are often considered to have antiaging effects. Dietary modulation can increase and maintain circulating ketone bodies, especially β-hydroxybutyrate (β-HB), which is one of the most abundant ketone bodies in human circulation. Increased β-HB has been reported to prevent or improve the symptoms of various age-associated diseases. Indeed, numerous studies have reported that a ketogenic diet or ketone ester administration alleviates symptoms of neurodegenerative diseases, cardiovascular diseases, and cancers.


β-HB
HDACs
hnRNP A1
β-hydroxybutyrylation
NLRP3
HCAR2
FOXO3a, MT2
Oct4
p53
Histone
Oxidative stress
Chromatin regulation
Gene expression
Senescence
Inflammation
Aging

Benefits of ketogenic diet on aging and associated diseases

- Aging
- Cancers
- Alzheimer's Disease
- Parkinson Disease
- Cardiovascular disease
- Epilepsy and Refractory Seizures
- Migraine Headache
- Motor Neuron Disease
- Diabetes

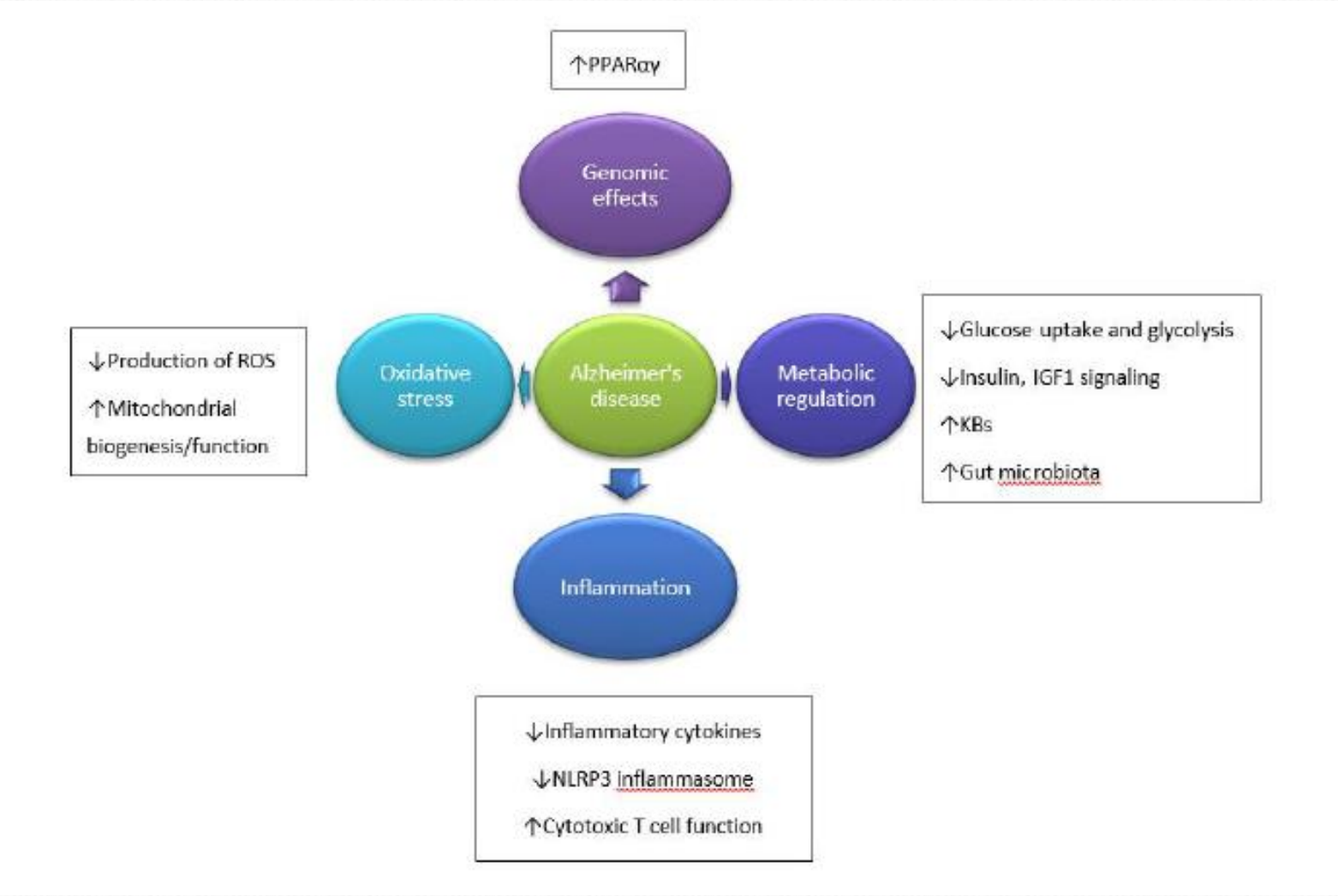
Mechanisms of Action of the Ketogenic Diet

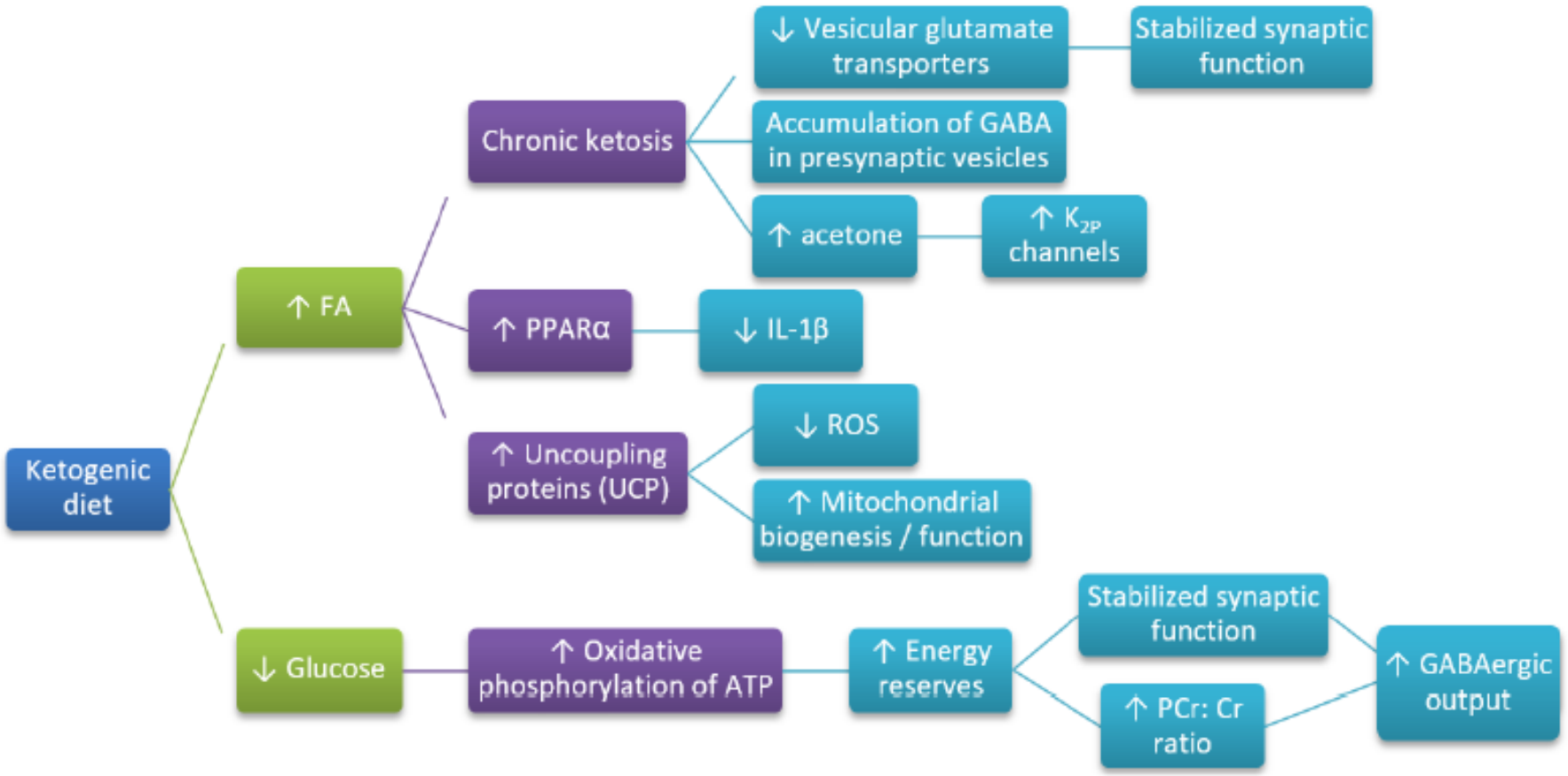
- Synaptic Transmission
- Antioxidant Effects
- Anti-inflammatory Effects
- Metabolic Regulation
- Genomic Effects

Table 1. Hypothesized mechanisms through which ketogenic therapies influence neurological disease.

Ketogenic Mechanisms	Epilepsy	Malignant Glioma	Alzheimer's Disease
Metabolic Regulation			
↓Glucose uptake & glycolysis	+	+	
↓Insulin, IGF1 signaling		+	+
↑Ketones/ketone metabolism	+		+
Altered gut microbiota	+		
Neurotransmission			
Altered balance of excitatory/inhibitory neurotransmitters	+		
Inhibition of AMPA receptors	+		
↓mTOR activation & signaling	+	+	
Modulation of ATP-sensitive potassium channels	+		
Oxidative Stress			
↓Production of reactive oxygen species	+	+	
↑Mitochondrial biogenesis/function	+		+
Inflammation/Neuroprotection			
↓Inflammatory cytokines	+	+	
NLRP3 inflammasome inhibition	+	+	
↑cytotoxic T cell function		+	
↓peritumoral edema		+	
↓amyloid-β levels			+
Genomic Effects			
Inhibition of HDACs	+	+	
↑PPARγ	+		
↓Expression of angiogenic factors in tumor cells		+	

AMPA—α-amino-3-hydroxyl-5-methyl-4-isoxazolepropionic acid; IGF1—insulin-like growth factor 1; HDACs—histone deacetylases; mTOR—mammalian target of rapamycin; NLRP3—NOD-like receptor protein 3; PPAR—peroxisome proliferator-activated receptor. ↓—decreased; ↑—increased; +—mechanism shown in *in vitro* or *in vivo* studies.


↑PPARαγ
Genomic effects
↓Production of ROS
↑Mitochondrial biogenesis/function
Oxidative stress
Alzheimer's disease
Metabolic regulation
↓Glucose uptake and glycolysis
↓Insulin, IGF1 signaling
↑KBs
↑Gut microbiota
Inflammation
↓Inflammatory cytokines
↓NLRP3 inflammasome
↑Cytotoxic T cell function


Ketogenic diet
↑ FA
Chronic ketosis
↓ Vesicular glutamate transporters
Stabilized synaptic function
Accumulation of GABA in presynaptic vesicles
↑ acetone
↑ K_{2P} channels
↑ PPARα
↓ IL-1β
↑ Uncoupling proteins (UCP)
↓ ROS
↑ Mitochondrial biogenesis / function
↓ Glucose
↑ Oxidative phosphorylation of ATP
↑ Energy reserves
Stabilized synaptic function
↑ PCr: Cr ratio
↑ GABAergic output

Questions