

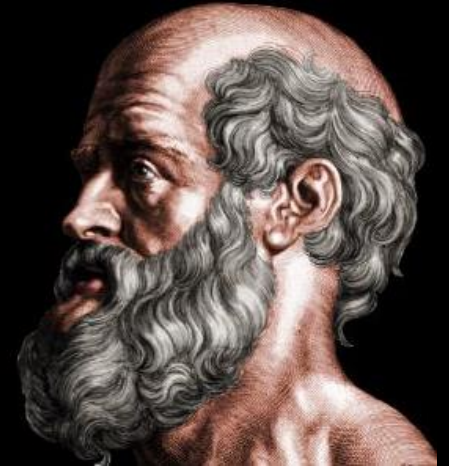
Ketogenic Diet Therapies In Adults With Epilepsy

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Some History...

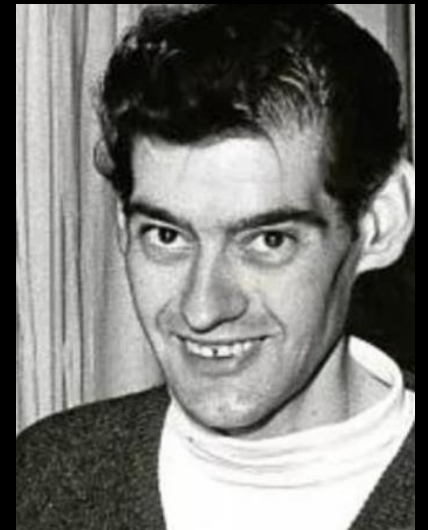
Epilepsy

- **Epilepsy** (“to seize, possess, or afflict”) was first documented in Mesopotamia 4,000 years ago, and viewed as a disease of divine (or demonic) spiritual possession for most of history.
- Around 400 BC, **Hippocrates** rejected these spirituals view of epilepsy, describing it as a treatable brain disorder.
- Regardless, spirits continued to be blamed for centuries, and people with epilepsy remained stigmatized and shunned (the witchcraft treatise **Malleus Maleficarum**, second only to the Bible from 1486 to 1678, described people with epilepsy).



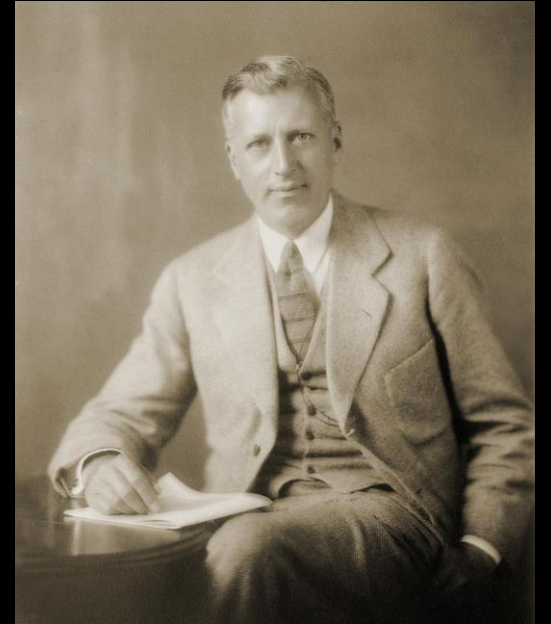
Fasting

- Hippocrates also advocated **fasting** in the treatment of epilepsy, for in addition to being a disease of spiritual possession, it was also known as a disease of “eating too much.”
- Although fasting was effective, **spiritual interventions** persisted as the predominant “therapies” for epilepsy.
- The likely reason may be that fasting had one Achilles’ heel - it could not be sustained indefinitely (the longest continuous fast in history is held by **Angus Barbieri** at 382 days, during which he lost 125 kg and continued about his daily business).



Ketogenic Diets

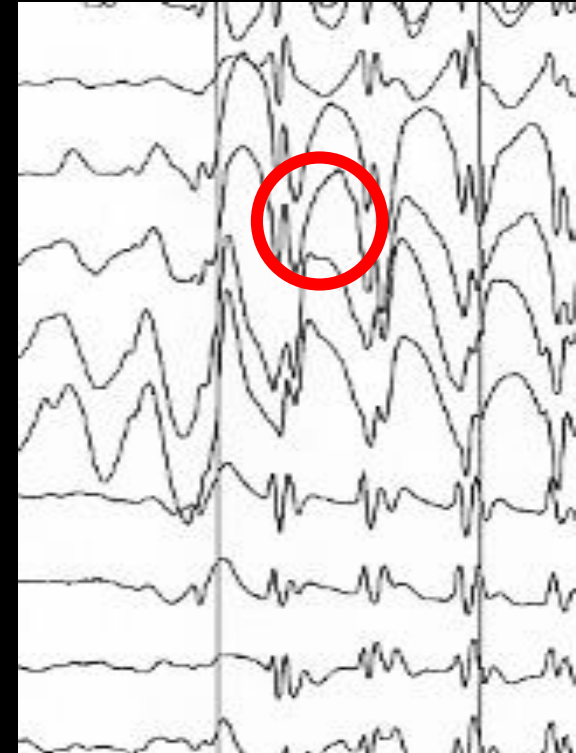
- In 1921, **Dr Russell Wilder** addressed this sustainability issue by developing a high-fat, low-carbohydrate diet designed to mimic the metabolic profile of a multi-day fast.
- The diet forced the body to **burn fat** - not carbohydrate - as the primary energy source (just like fasting), but it burned **ingested fat, not body fat** (unlike fasting); hence, the diet could provide adequate, sustained long-term nutrition.
- Since the liver converted much of the fat into organic molecules called **ketones**, Wilder coined the term “ketogenic diet.”



Seizures And Epilepsy

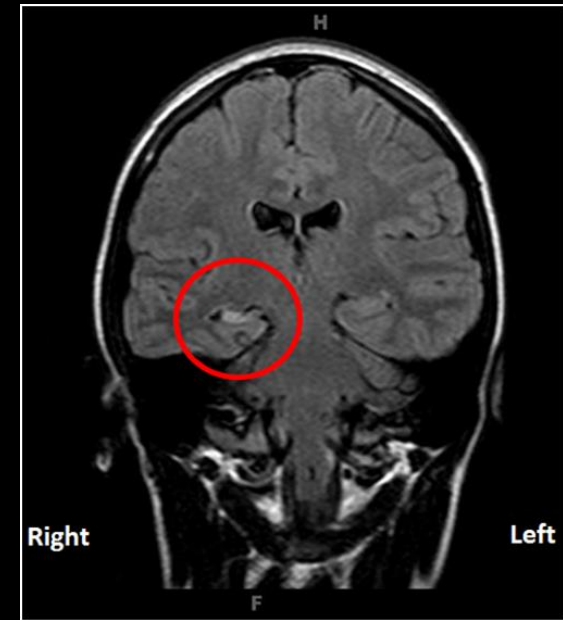
What Is A Seizure?

- A **seizure** is a transient period of signs or symptoms, ranging from brief and virtually undetectable events to prolonged episodes of vigorous shaking, that results from the abnormal, synchronous excitation of a group of neurons in the brain.
- A seizure may be **provoked** by a temporary event (such as head trauma, alcohol withdrawal, or sleep deprivation), or it may be **unprovoked**, occurring for no obvious reason.
- Thus, a seizure is a **single event** that can happen to anyone; a provoked seizure may never happen again.



What Is Epilepsy?

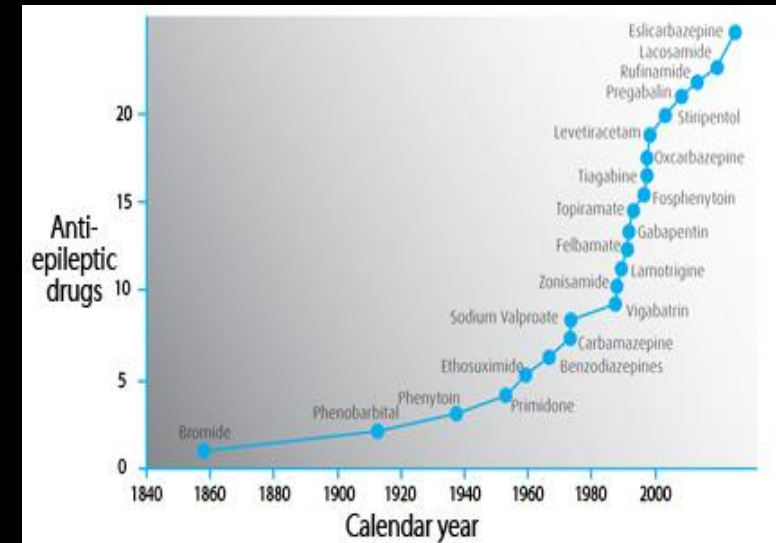
- **Epilepsy** is a disorder characterized by an enduring predisposition to generate seizures, usually diagnosed after a person has at least two unprovoked seizures, 24 hours apart.
- Sometimes, the **etiology** is known (such as a scar, tumour, head trauma, or stroke), but usually, epilepsy is “cryptogenic.”
- Thus, epilepsy is a **chronic disorder** that results in reduced quality of life due to loss of independence, social isolation, more injury, depression, and increased mortality.



Mesial temporal sclerosis
(brighter, smaller)

Current Epilepsy Treatments - Advantages

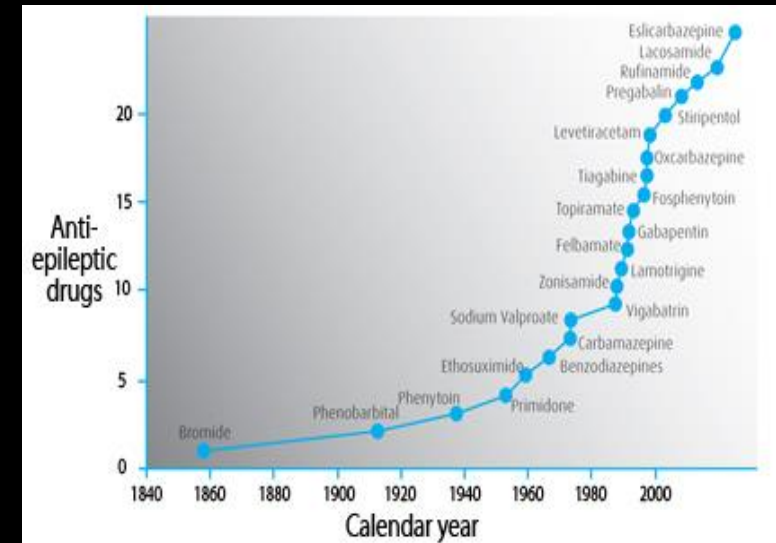
- Anti-epileptic **drugs** are the most common therapy for people with epilepsy (by far).
- Drugs can effectively control seizures in **two-thirds** of people with epilepsy.
 - The first drug will control the seizures in **50%** of people.
 - Adding a second drug will control another **12-13%** of people.
 - Adding a third drug will control another **2-3%** of people.
- Epilepsy **surgery** can also be effective, particularly in people with lesion-related epilepsy.



We have a lot of drug options now.

Current Epilepsy Treatments - Disadvantages

- Yet drugs and surgery have some major **disadvantages**.
 - Drugs produce noticeable adverse effects **50%** of the time; on average, **25%** of people will need to stop the drug.
 - Only **select** cases are eligible for surgery; many don't want it.
- Moreover, despite access to 30 different drugs as well as surgery, **one-third** of people with epilepsy continue to suffer from unrelenting, “drug-resistant” seizures.
- There is an under-utilized, highly effective third option that may benefit these people - **ketogenic diets**.



Despite all the drug options, they have not helped much.

Ketogenic Diets

What Is A Ketogenic Diet?

- In essence, a **ketogenic diet** is any high-fat, adequate-protein, low-carbohydrate diet that forces the body to burn ingested fat as the primary energy source.
- The liver produces detectable **ketones** from fat; there are three different types of ketones, but the primary blood ketone is beta-hydroxybutyrate (BHB).
- During a ketogenic diet, the blood BHB is elevated to **0.5-8 mmol/L**, constituting a state of “physiological ketosis” (as opposed to pathological ketoacidosis).



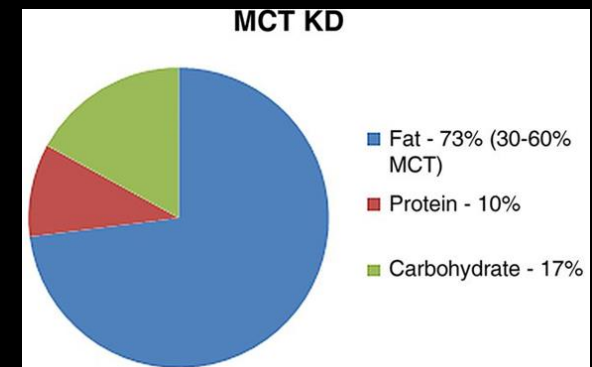
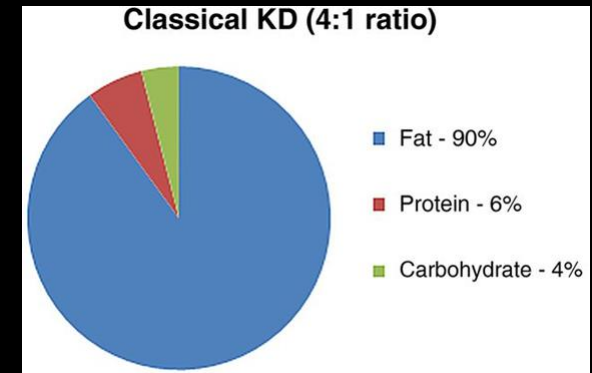
How Ketogenic Diets Work

- Ketogenic diets likely improve seizure control through a number of mechanisms (low glucose, high fatty acids, high ketones, etc) that **stabilize neurons** (so they stop firing abnormal discharges).
 - Enhancing neuron energy production.
 - Decreasing neuron hyperexcitability.
 - Increasing neuron seizure threshold.
- Since some aspects of these mechanisms are due to the ketones, there is interest in using **MCT oil** and **ketone esters** to confer part of the benefit of a ketogenic diet; however, it is not possible to confer all the effects of a ketogenic diet “in a pill.”



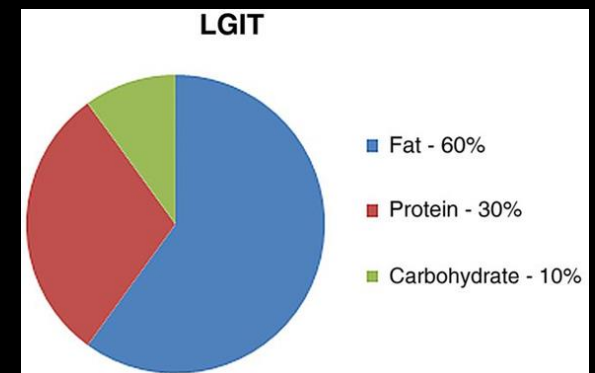
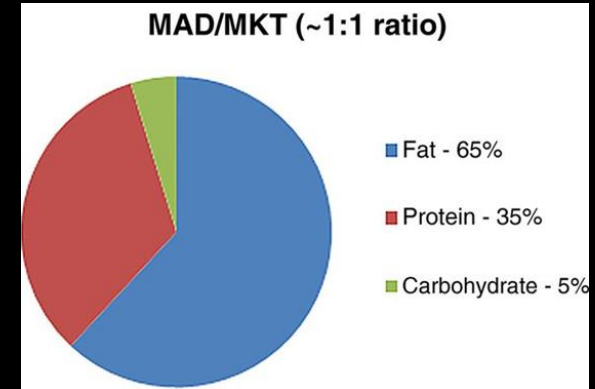
Conventional Ketogenic Diets

- Four **conventional** ketogenic diets are supported by evidence.
- (1) The **classic ketogenic diet** (CKD).
 - Created by Wilder in the 1920s; **90%** fat by calorie intake.
 - **Pros:** Most powerful conventional ketogenic diet, high ketone levels.
 - **Cons:** Most restrictive of the diets, potential adverse effects.
- (2) The **medium-chain triglyceride** (MCT) diet.
 - Created in the 1970s; **75%** fat by calorie intake, fat sourced from MCTs.
 - **Pros:** Less restrictive than CKD, allows more protein and carbohydrate.
 - **Cons:** Many people have MCT-related gastrointestinal adverse effects.



Conventional Ketogenic Diets

- (3) The **modified Atkins diet (MAD)**.
 - Shown to be effective for epilepsy in 2000s; **65-70%** fat by calorie intake.
 - **Pros:** Less restrictive than both CKD and MCT diet, no weighing of food.
 - **Cons:** Not as powerful as CKD or MCT diet, lower ketone levels.
- (4) The **low glycemic index treatment (LGIT)** diet.
 - Introduced for epilepsy in 2000s; **60%** fat by calorie intake, emphasizes carbohydrates with glycemic index less than 50.
 - **Pros:** Least restrictive conventional ketogenic diet.
 - **Cons:** Weakest of the diets.



Conventional Ketogenic Diets

Ketogenic Diet	Macronutrient Ratio (by Weight)	Macronutrient Ratio (by Calorie Intake)
CKD	Fat 80%	Fat 90%
	Protein 12%	Protein 6%
	Carbohydrate 8%	Carbohydrate 4%
MCT diet	Fat 60%	Fat 75%
	Protein 16%	Protein 10%
	Carbohydrate 24%	Carbohydrate 15%
MAD	Fat 50%	Fat 65-70%
	Protein 35%	Protein 25-30%
	Carbohydrate 15%	Carbohydrate 5%
LGIT diet	Fat 40%	Fat 60%
	Protein 45%	Protein 30%
	Carbohydrate 15%	Carbohydrate 10%

Non-Conventional Ketogenic Diets

- Many **non-conventional** ketogenic diets are also available; this is good, given that conventional ketogenic diets are rather old.
- **Pros:**
 - Non-conventional diets can be more easily tailored towards a person's food preferences and cultural tastes, making them less restrictive.
- **Cons:**
 - Some non-conventional diets provide inadequate nutrition, too much or not enough protein, too many processed foods.
 - Evidence for these diets is lacking (but that can be solved).



Not so restrictive.

Non-Conventional Ketogenic Diets

- Since there are so many non-conventional ketogenic diets and all are relatively new, it's hard to know which one to **trust**; most of the recipes from these sites are fine:
 - www.ruled.me
 - www.dietdoctor.com
 - www.ketogenicswitch.com
- Ultimately, **less restrictive, non-conventional ketogenic diets that are affordable and emphasize real food** likely represent the future of ketogenic diet therapies in epilepsy and other disorders.

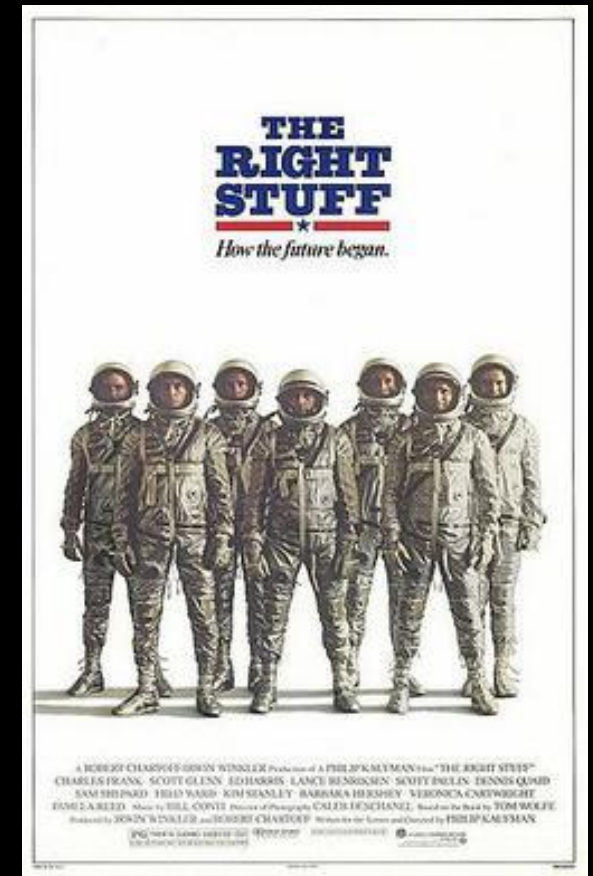


Must emphasize
real food.

Selecting The Right Person For A Ketogenic Diet

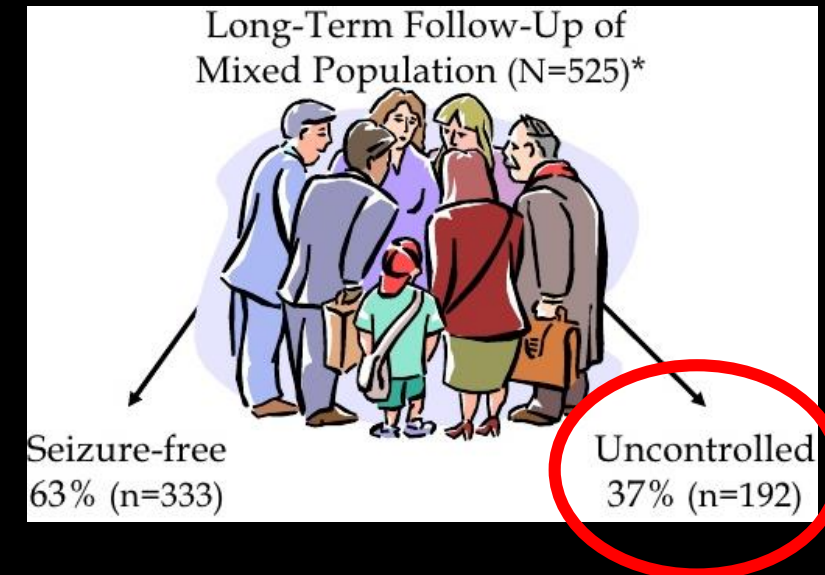
Who Is The Right Person?

- Probably more than anything, the right person is **self-motivated** and willing to embrace something new.
- Since ketogenic diets are usually utilized as “end of the line” options in epilepsy, most of the evidence comes from the **most difficult** epilepsy cases.
- Moreover, there is more evidence in children than in adults (since children don’t have much of a say as to what they eat); however, we will stick to **adults**.



Evidence For Ketogenic Diets


- In adults, solid evidence supports the use of ketogenic diet therapies in **several epilepsy disorders**.
- (1) **Drug-resistant epilepsy** (one-third of all epilepsy).
 - Defined as the failure of **two** appropriate, adequately-dosed drugs after 6 months.
 - Ketogenic diets confer a greater than 50% seizure reduction in **30-50% of people** with drug-resistant epilepsy by 3 months.
 - The evidence is good, but all studies are **single-arm**, so we still (desperately) need a randomized controlled study.
 - Nearly half of the participants in these studies withdrew by 3 months, largely due to **culinary and social restrictions**.



Evidence For Ketogenic Diets

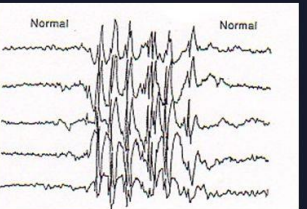
- (2) **Disorders of brain metabolism.**
 - Treatment of choice in GLUT1 DS and PDHD; ketogenic diets confer seizure freedom in **90% of people** with GLUT1 DS, and they are similarly effective in PDHD.
- (3) **Specific seizure disorders.**
 - Ketogenic diets confer a greater than 50% seizure reduction in **60-70% of people** with juvenile myoclonic epilepsy (5-10% of all epilepsy) by 3 months.
 - They are highly effective in Lennox-Gastaut syndrome, Rett syndrome, and many other specific seizure disorders.

Juvenile Myoclonic Epilepsy (JME)



Jerking of arms, shoulders, and head

EEG: bilateral generalized 4-6 Hz spike-wave or polyspike-wave activity



Normal Normal

Seizure types:

- myoclonic in AM
- "grand mal"
- absence

The slide features a dark blue background with a decorative grid of colored dots in the top right corner. It includes a medical illustration of a person with a seizure, EEG traces, and a list of seizure types.

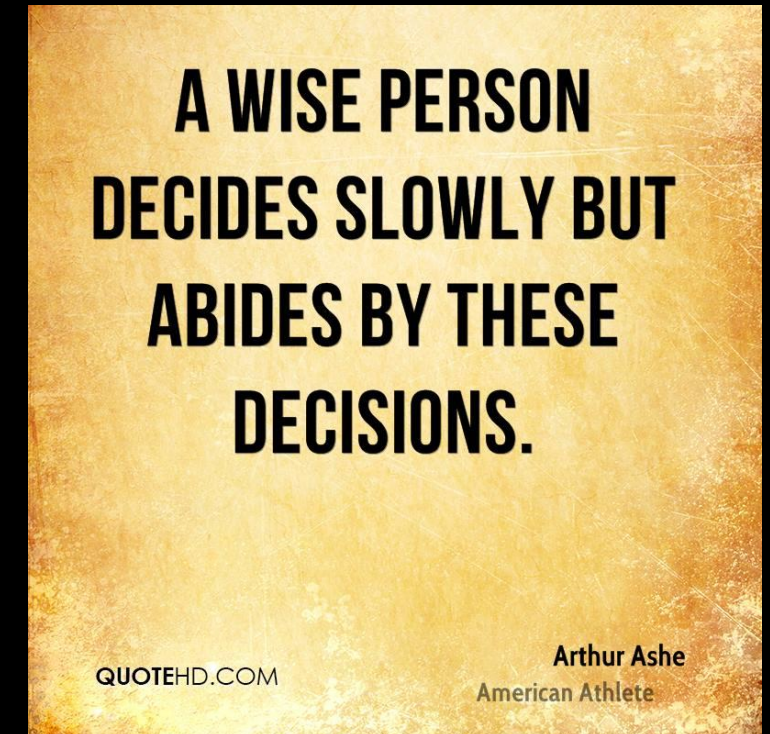
Ketogenic Diets - Indications In Adults

General Disorder	Specific Disorder
Drug-resistant epilepsy	2010 ILAE definition
Disorders of brain metabolism	GLUT1 DS PDHD
Specific seizure disorders	Juvenile myoclonic epilepsy Lennox-Gastaut syndrome Rett syndrome

Preparing For A Ketogenic Diet

What Is The Best Way To Prepare?

- Preparing by **learning about ketogenic diets** is a vital step before deciding to embark on the voyage.
- Once a person has elected to pursue a ketogenic diet, a **medical and nutritional evaluation** are indicated.
- Ideally, a cohabiting spouse or family member should accompany them to the evaluations (and consider **participating** in the diet, for support).



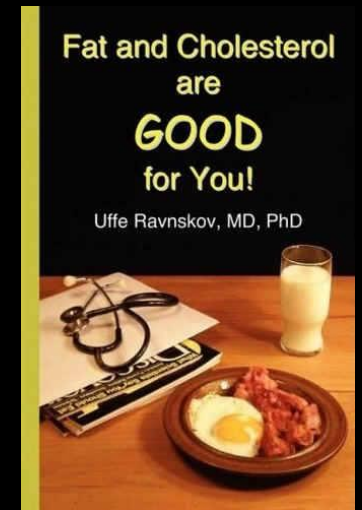
Medical Evaluation

- Basically, this is a check-list by the **neurologist** to ensure that there will be minimal complications on a ketogenic diet:
- (1) Assess the person's epilepsy and comorbidities.
 - Measure **current seizure control**, so response can be measured.
 - Make note of hyperlipidemia, low body weight, and type 1 diabetes.
- (2) Identify psycho-socioeconomic, cultural, religious factors.
 - Need to realistically appraise effects of personality traits, **alcohol intake**, income, culture, religion on the diet.



Medical Evaluation

- (3) Elucidate the person's level of commitment.
 - A ketogenic diet may involve a major change in lifestyle; anything less than a full commitment will probably fail.
 - Discuss how to manage mixed messages and emphasize other positive aspects of the diet, such as beneficial effects on **cognition, energy, and mood** (and weight loss, if desired).
- (4) Review anti-epileptic drugs and medications.
 - Anti-epileptic drug levels are **not usually altered** by the diet, so dose adjustments are rarely required.
 - However, some medications contain carbohydrates and may need to be altered.



Medical Evaluation

- (5) Provide a blood glucose and ketone monitor, and show how to use it.
 - The person needs a way to **monitor their ketones**, so they know how effectively they are achieving physiological ketosis.
 - Blood monitors are easier and more accurate than urine dipstick testing.
- (6) Order investigations.
 - These are largely done to **exclude contraindications**.
 - Routine bloods, plus a pregnancy test if relevant.
 - An EEG and MRI brain are standard in epilepsy.



Nutritional Evaluation

- Input and guidance from the **dietitian** helps a person choose a ketogenic diet, and learn how to do it.
- (1) Assess baseline physical parameters.
 - Measure baseline body weight, **body-mass index**, calorie and fluid intake.
- (2) Help the person select the ketogenic diet best for them.
 - The MAD, LGIT diet, and non-conventional ketogenic diets are the most suitable for adults.
 - Regardless of which is chosen, it is essential to **minimize culinary and social restrictions**.



Nutritional Evaluation

- (3) Provide a lists of foods for social settings.
 - Social activities are to be encouraged, but can jeopardize the diet.
 - A list of appropriate food options when **eating out** is wise.
- (4) Provide supplements.
 - A carbohydrate-free **multivitamin** is usually recommended.
- (5) Education.
 - Critical; the person must **understand** what is required for success!
 - A classroom-based format is best, with the dietitian showing how to identify appropriate (and inappropriate) foods.



Ketogenic Diets - Evaluations In Adults

Evaluation	Steps
Medical	Assess baseline epilepsy state and comorbidities
	Identify psycho-socioeconomic, cultural, and religious factors
	Elucidate level of commitment
	Review anti-epileptic drugs and medications
	Provide blood glucose and ketone monitor; show how to use
	Order investigations
Nutritional	Assess baseline physical parameters
	Select most appropriate conventional ketogenic diet
	If none appropriate, offer a non-conventional ketogenic diet
	Provide a list of foods for social settings
	Provide supplements
	Educate

Implementing A Ketogenic Diet

What Leads To Successful Implementation?

- If a person with epilepsy develops a sense of “ownership” over their ketogenic diet, it will confer a feeling of **empowerment** over their epilepsy.
- Therefore health professionals should **recommend and guide**, and resist the urge to dictate and prescribe.
- Implementation consists of three stages.
 - Initiation.
 - Maintenance.
 - Cessation.



Initiation



- This is usually straightforward:
- (1) Decide whether to initiate the ketogenic diet as an inpatient or outpatient.
 - Rarely, the diet is initiated in hospital (for example, if more time is needed for education).
 - Usually, it can be initiated **at home**, with clear instructions on how to do so.
- (2) If inpatient, decide whether an induction fast or graded approach are needed.
 - An **induction fast** is useful if a quick response is needed (for example, multiple daily seizures).
 - A graded approach may help adapt a person to the fat intake, but no evidence of benefit.

Maintenance



- Some troubleshooting will inevitably be required:
- (1) Self-documentation of seizure control and blood ketone levels.
 - A seizure diary is important; seizure control usually improves within the first few days.
 - No firm recommendations for blood BHB levels in epilepsy (but **aim for 2-4 mmol/L**).
- (2) Regular contact and review by neurologist and dietitian.
 - Monitor for adverse effects; in adults, most common are **hyperlipidemia** and **weight loss**.
 - With lipids, triglycerides decline and HDL rises (both good); LDL often rises, but as a result of increased LDL particle **size not number**, and LDL usually normalizes after 1 year.
 - Weight loss is usually **desired** (if not, dietitian can help keep it up).

Cessation



- May not be necessary (try to give the diet at least 3 months):
- (1) Decide whether to cease the ketogenic diet or not.
 - If the seizures improve and no serious adverse effects occur, can maintain **indefinitely**.
 - If seen as too restrictive, can be switched over to another type of ketogenic diet.
- (2) If to be ceased, decide on an abrupt versus gradual rate of cessation.
 - Usually, the diet can be stopped **abruptly** without any problems.

Ketogenic Diets - Stages In Adults

Stage	Steps
Initiation	Decide whether to initiate as inpatient or outpatient
	If inpatient, decide on induction fast and diet introduction
	If outpatient, provide clear instructions to caregiver
Maintenance	Adult self-monitors seizure control and ketone levels
	Review at 3 and 6 months, and 6-monthly after
	Monitor for adverse effects
	Document beneficial effects
Cessation	Identify when diet should be ceased (if ever)
	If to be ceased, consider switching to another ketogenic diet
	If to be ceased, decide on rate of diet cessation
	If relevant, consider diet cessation and driving

Ketogenic Diets Are Very Useful In Epilepsy

- Ketogenic diets are **proven therapies** for improving seizure control in adults with epilepsy; they frequently improve seizure control even in the most challenging epilepsy cases, when other therapies have failed.
- In many people, they have additional benefits on cognition, energy, mood, and overall **quality of life**.
- Adverse effects are often **overstated** (hyperlipidemia and weight loss in adults).
- They are **self-empowering**, providing a person with power over their epilepsy.

So Why Are Ketogenic Diets Not Used More?

- There is a **lack of knowledge** about ketogenic diets in general, not just in epilepsy (especially from health professionals, including neurologists and dietitians).
- The evidence in adults with epilepsy is still **not strong enough** (and what we have is from diets that are decades old); we need a randomized controlled trial of a less restrictive, non-conventional ketogenic diet in adults with epilepsy.
- Fat has been **vilified** for the last half-century; it continues to be unfairly vilified.
- No company can patent diet therapies involving real food; **no profit**.

The Last Reason...

- We live in an era of medicine that focuses on managing the **symptoms** of disease using medications and surgery; this is what we are taught.
- Managing the symptoms of disease is a **reactive** approach; which is fine if we just care about masking disease symptoms...but I think we want more than that.
- We need therapies that **prevent and cure** disease, using whatever means possible (such as dietary therapies); this is a health-promoting, **proactive** approach.
- I think, when the time is right, we'll get there...thank you.