



Proceedings of Ketogenic Diet Therapies Symposium

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The Charlie Foundation for Ketogenic Therapies

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WHITE PAPER

■ THE FOCUS OF THIS MEETING WAS ON ADMINISTERING KETOGENIC THERAPY TO INDIVIDUALS WITH UNIQUE OR CHALLENGING NEEDS AND THOSE WITH COMPROMISED HEALTH.

The objective of this two-day health professionals' symposium was to share and discuss ketogenic diet (KD) practices for neurological disorders and cancers with the goal of broadening the application of therapy and improving clinical skills. The focus of this meeting was on administering KD therapy to individuals with unique or challenging needs and those with compromised health. Health professionals in southern California with existing KD therapy centers were the primary speakers for this meeting. This paper is a summary of the speakers presentations.

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SECTION I

■ SUCCESSFUL USE OF KETOGENIC THERAPIES IN PEOPLE WITH MORBIDITIES, SUCH AS IN SOMEONE WHO HAS BOTH EPILEPSY AND DIABETES, HAS OPENED THE DOOR TO THE APPLICATIONS OF THE DIET BEYOND EPILEPSY.

Evidence classification for the application of KD therapies

Ketogenic diets have been in existence since the 1920s. A 2015 Cochrane Report has validated the use of KD therapy in medication-resistant epilepsy based on numerous published studies. Those who maintain ketogenic diets (typically a short-therapy) may receive long-lasting benefits beyond their tenure on the diet. Animal research has shown that ketogenic diets have disease-modifying effects in a broad range of neurological disorders. Enhanced energy use in neuronal cells has been a common theme in these studies. Successful use of ketogenic therapies in people with morbidities, such as in someone who has both epilepsy and diabetes, has opened the door to the applications of the diet beyond epilepsy. This list of beneficial applications of KDs in humans is based on current evidence.

Level I

Evidence (randomized controlled trials)
Epilepsy – medication resistant; pediatrics

Level II

Evidence (prospective or retrospective studies)
Dravet syndrome
Epilepsy – medication resistant; adults
Infantile spasms
Lennox-Gastaut syndrome
Myocloic-astatic epilepsy (Doose syndr.)
Tuberous sclerosis complex

Level III

Evidence (studies with no control groups, case studies, and anecdote)

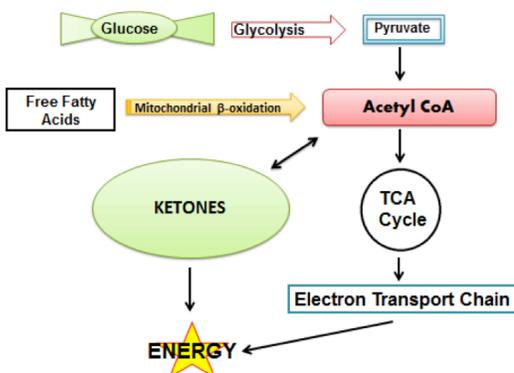
Adenylosuccinate lyase deficiency
Alpers-Huttenlocher syndrome
Alzheimer's disease – early onset
Argininosuccinate lyase (ALS) deficiency
Amyotrophic lateral sclerosis
Autism
Cancers
Diabetes mellitus
Dravet syndrome
Glycogenoses and glycogen storage diseases
Glucose-1 transporter deficiency syndrome (Glut-1DS)
Lafora body disease
Landau-Kleffner Syndrome
Lennox Gastau
Metabolic Syndrome
Migraine
Mitochondrial disorders – Complex I, II, IV
Mitochondrial encephalopathy w/ lactic acidosis & stroke (MELAS)
Nonketotic hyperglycinemia
Obesity
Otahara syndrome
Parkinson's disease
Phosphofructokinase deficiency
Polymerase gamma related disorders (POLG)
Pyruvate dehydrogenase deficiency
Respiratory chain defects
Rett syndrome
Subacute sclerosing panencephalitis
Succinic semialdehyde dehydrogenase deficiency
Traumatic brain injury

Ketogenic diet therapies for epilepsy

Although there is a growing array of anticonvulsant medications, 30-40% of people with epilepsy continue to experience seizures despite standard treatment. As early as the 5th century B.C., there are references to abstinence from food leading to healing from epilepsy. Following a series of studies demonstrating that fasting can reduce seizures, Dr. Wilder of Mayo Clinic first proposed the concept of a ketogenic diet (KD) in 1921 which could recapitulate the biochemical changes induced by fasting—ketogenesis in the wake of a hypoglycemic state. By restricting carbohydrate intake, the ketogenic diet limits glucose supply, and muscle and other tissues progressively switch to using free fatty acids as an energy source. Free fatty acids are converted to ketone bodies in liver mitochondria through beta-oxidation. Subsequently, these ketones are used as an alternative fuel with proven, but not completely understood, anticonvulsant properties in neurons (Figure 1). Contraindications to KD therapy include defects in the transport or oxidation of fatty acids, lipid myopathies, primary or acquired carnitine deficiency, pyruvate carboxylase deficiency, acute intermittent porphyria, and some organic acidurias (Figure 2).

Figure 1

Schematic of the metabolism of carbohydrates in comparison to fat. In both routes of metabolism there is energy production.



Glucose which is derivative from food-based carbohydrate is broken down through glycolysis to produce pyruvate which is converted to acetyl-CoA in the mitochondria by pyruvate dehydrogenase. Acetyl-CoA then enters the tricyclic acid cycle (Kreb’s cycle) for complete oxidation. The cofactors then enter the electron transport chain and are reconverted to produce energy. The high-fat KD provides ample lipids which process into free fatty acids and subsequently undergo mitochondrial beta-oxidation to produce acetyl-CoA which is reconverted to produce ketones (specifically, beta-hydroxybutyric acid). Ketones cross the blood brain barrier to produce energy for the brain (as an alternative to glucose) (*1).

Today, there exists a spectrum of diets which can be tailored, depending on clinical and nutritional goals (Table 1). The classic 4:1 ratio ketogenic diet provides about 90% of total daily calories from foods containing long-chain fatty acids, a 3:1 diet provides 87% fat, 2:1 provides 82% fat and 1:1 provides 70% fat. The MCT is also approximately 70% fat however its main fat source is medium-chain tryglicerides which are highly ketogenic. [This diet requires a source of long-chain fat to meet essential fatty acid requirements.] The Modified Atkins diet allows approximately 60% of total calories from fat and is very low carbohydrate with moderate protein. The Low Glycemic Index Treatment (LGIT) is also 60% fat and allows moderate carbohydrates from low glycemic index sources, and moderate protein. Further differences in these diets are displayed in Table 1.

A primary factor used in determining the appropriate diet is the age of the candidate. Children under the age of 5 years are typically the best candidates for the most restrictive diets (4:1 and 3:1). Infants are also excellent candidates for these higher fat diets. One could argue that infants are programmed for a ketogenic diet as the first milk that nursing mothers produce (colostrum) is 60% fat. Patients who are

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■ TODAY, THERE EXISTS A SPECTRUM OF SUCH KETOGENIC DIETS WHICH CAN BE TAILORED DEPENDING ON CLINICAL AND NUTRITIONAL GOALS.

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fed via an enteral feeding tube are also candidates for restrictive KDs

Older children, adolescents and adults who are independent of a constant care-giver or companion may find the more liberal diets easier to maintain. A precept to a very-low carbohydrate, high-fat KD may be trialed initially. The Charlie Foundation has designed a Whole Foods Diet; sugar-free, gluten-free, and with healthy fats. This (free) publication is intended to introduce the user to some of the restrictions of KDs but without ketosis. This “pre-KD” could be trialed while waiting for an appointment to receive formal KD instructions. It can also serve as a tool to determine compliance before attempting a KD and it may even reduce seizure burden.

The first prospective, multi-center trial to investigate the efficacy of the classic ketogenic diet across the U.S. was published in 1998. Seven epilepsy centers prospectively enrolled 51 children with intractable epilepsy and found that 10% were seizure free and 40% achieved a >50% decrease in baseline seizure frequency at one year of follow-up (*2). A pivotal, randomized controlled trial later revealed a significant reduction in the mean percentage of baseline seizures after 3 months for patients receiving the classic ketogenic and MCT diets when compared to the group on a regular diet. (*3). A meta-analysis of combined data found a similar drop-out rate across studies of about 50%, with the majority of subjects discontinuing the diet due to perceived ineffectiveness or its restrictiveness (*4). Common but manageable side effects reported across studies include constipation, vomiting, lack of energy, and hunger.

These and other studies have demonstrated the effectiveness of ketogenic diets across the age spectrum, for a variety of both primary generalized and focal-onset epilepsies, with an evolving role in refractory status epilepticus. The ketogenic diet is the treatment of choice in individuals with GLUT-1 Transporter Defect and Pyruvate Dehydrogenase Deficiency. There is published and significant efficacy as well for several epileptic encephalopathy syndromes associated with both symptomatic and asymptomatic etiologies. Clinicians and families also report improved cognition and behavioral profiles in patients, with an added ability to taper antiepileptic drugs in almost all diet responders. Such data and continued clinical experience have validated the importance of the ketogenic diet in many forms of intractable epilepsy.

Due to the multiplicity of factors associated with ketogenic therapies, a multi-disciplinary medical team is necessary to provide safe and effective services. The timeline of therapy includes a pre-diet biochemical evaluation, initiation of therapy and follow-up throughout the course of therapy. The spectrum of diet therapies displayed in Table 1 offers a range of options to optimize compliance. Nutritionists, nurses, pharmacists, hospitalists, food service personnel, pediatric and family physicians, and neurologists must communicate to safeguard the individual against the common error of providing exogenous carbohydrate (such as in intravenous dextrose). Intensive care teams need to be educated if the diet will be used for status epilepticus.

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Table 1. Spectrum of diet therapies for epilepsy

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Questions	Ketogenic Therapies	MCT Oil	Low Glycemic Index Treatment	Modified Atkins
Is medical supervision required?	Yes	Yes	Yes	Yes
Is diet high in fat?	Yes	Yes	Yes	Yes
Is diet low in carbohydrate?	Yes	Yes	Yes	Yes
What is the ratio of fat to carbohydrate & protein?	4:1, 3:1, 2:1, 1:1	Approximately 1:1	Approximately 1:1	Approximately 1:1
How much carbohydrate is allowed on a 1000 Calorie diet?	8gm carb on a 4:1 16gm carb on a 3:1 30gm carb on a 2:1 40-60gm carb on a 1:1	40-50gm	40-60gm	10gm adolescents or 15gm adults for 1 month 20gm afterwards
How are foods measured?	Weighed	Weighed or measured	Measured or Estimated	Estimated
Are meal plans used?	Yes	Yes	Yes	Optional
Where is the diet started?	Hospital	Hospital	Home	Home
Are calories controlled?	Yes	Yes	Yes	No
Are vitamin and mineral supplements required?	Yes	Yes	Yes	Yes
Are liquids (fluids) restricted?	No	No	No	No
Is a pre-diet laboratory evaluation required?	Yes	Yes	Yes	Yes
Can there be side-effects?	Yes	Yes	Yes	Yes
What is the overall difference in design of these diets?	This is an individualized and structured diet that provides specific meal plans. Foods are weighed and meals should be consumed in their entirety for best results. The ratio of this diet can be adjusted to effect better seizure-control and also liberalized for better tolerance. This diet is also considered a low glycemic therapy and results in steady glucose levels.	An individualized and structured diet containing Medium Chain Triglycerides (MCT) which are highly ketogenic. This allows more carbohydrate and protein than the classic ketogenic diet. A 2008 study showed that both diets are equal in eliminating seizures. A source of essential fatty acids must be included with this therapy.	This is individualized but less structured diet than the ketogenic diet. It uses exchange lists for planning meals and emphasizes complex carbohydrates. The balance of low glycemic carbohydrates in combination with fat result in steady glucose levels. It is not intended to promote ketosis.	This diet focuses on limiting the amount of carbohydrate while encouraging fat. Carbohydrate may be consumed at any time during the day as long as it is within limits and should be consumed with fat. Suggested meal plans are used as a guide. Protein is not limited but too much is discouraged.

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Candidate evaluation and preparation

During the initial consult, it is important to understand the safe implementation of the ketogenic diet to prevent adverse events. Practitioners should be aware and screen for absolute contraindications as well as relative contraindications. The absolute contraindications include patients who have trouble breaking down fats, problems with carnitine, pyruvate carboxylase deficiency, and porphyria (*1) (figure 2). Relative contraindications may also complicate the administration of the ketogenic diet therefore patients should be evaluated thoroughly (*1) (figure 3).

Figure 2

Absolute Contraindications

Absolute Contraindications

PROBLEMS WITH FAT METABOLISM

- ▶ 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

PROBLEMS WITH CARNITINE

- ▶ Primary carnitine deficiency
- ▶ Carnitine palmitoyltransferase (CPT) I or II deficiency
- ▶ Carnitine translocase deficiency

PYRUVATE CARBOXYLASE DEFICIENCY

PORPHYRIA

Figure 3

Relative Contraindications

Relative Contraindications

CARDIOVASCULAR

- ▶ Hyperlipidemia
- ▶ Arrhythmia
- ▶ Cardiomyopathy

GASTROINTESTINAL

- ▶ Failure to thrive
- ▶ Dysphagia
- ▶ Unresolved GI symptoms

RENAL

- ▶ Renal calculi

MUSCULOSKELETAL

- ▶ Osteopenia

Thus, the following screening labs are suggested for pediatric patients to be drawn prior to initiation of any KD therapy (Figure 4). In particular, the urine organic acids, plasma amino acids, plasma acylcarnitine, free and total carnitine are comprehensive tests in detecting for absolute contraindications of fat metabolism and primary carnitine deficiency. Other laboratory tests (complete metabolic panel, complete blood count, platelet, fasting lipid panel, prealbumin, ionized calcium, magnesium, phosphorus, selenium, zinc, vitamin D 25-OH, routine urinalysis, spot urine calcium and urine creatinine) will help to identify patients who have any other problems or complications which may need to be corrected prior to initiation of the diet. A beta-hydroxybutyric acid (BHB) level may be significant if the patient has already initiated a KD on his/her own. This level may also be helpful in evaluating abnormal urine organic acids.

Figure 4
Pre-diet Screening and Baseline
Laboratory Tests

URINE

Urine organic acids
Routine urinalysis, microscopic
Urine calcium
Urine creatinine

BLOOD

Plasma amino acids*
Plasma acylcarnitine*
Serum free and total carnitine*
Complete metabolic panel
Complete blood count
Fasting lipid
Prealbumin
Ionized calcium
Magnesium
Phosphorus
Selenium
Zinc
Vitamin D 25-OH
Beta-hydroxybutyrate level**

* Tests to screen for absolute
contraindications with fat metabolism and/or
primary carnitine deficiency

** Test when there is a high suspicion or
probability that a patient may already be
producing ketones

Upon referral, prospective patients are
given a pre-diet packet to complete prior to
their initial diet therapy consult. The packet
includes a fact sheet, sample meal plans,
helpful websites, brief health history, and a
three-day diet record.

The diet history seeks pertinent information
regarding meal patterns, food allergies,
intolerances, likes/dislikes, feeding
difficulties, fluid intake, chewing or
swallowing difficulties, and past or present
use of enteral modes of nutrition. Additional
information may include where meals are
consumed (i.e. daycare, home, school,
restaurants) and ability to self-feed. Social
factors impacting diet are also reviewed
including cultural and religious preferences,
who buys and prepares food, food retailers
they frequent, other siblings at home, and if
food and economic constraints exist.

A medical history is obtained including
baseline seizure activity, medications,
dietary supplements and anthropometrics.
History of kidney stones, elevated lipids or
familial hyperlipidemia are noted. Accuracy
is necessary when obtaining baseline height
and weight, particularly with children.
Recent changes in weight (unintentional
vs. intentional), history of failure-to-thrive,
and usual energy expenditure (i.e. ventilator
dependent, sports) is obtained as this
impacts energy and macronutrient goals. A
digestive history including nausea, vomiting,
gastro-esophageal reflux and bowel
regularity are also requested on the intake.

Caregivers are involved with the selection
of ketogenic therapy (Classic or modified
KD, LGIT, Modified Atkins) intended to
achieve optimal compliance and therefore
maximize effectiveness. Individualization
of the selected diet therapy is essential for
compliance.

Prior to starting diet therapy, eliminating
sugar, juices and sweetened beverages
as well as processed foods is advised. A
two-page guide, “Does What I Eat Affect
my Epilepsy”, is available through the
Charlie Foundation and concisely explains
these goals. This document introduces the
candidate to carbohydrate restriction and
also provides the health professional with a
tool to determine further ability to comply
with a KD therapy.

Screening for feeding difficulties

Feeding difficulties are common in patients
with neurological impairments therefore it
is essential to screen candidates during the
initial evaluation. Screening questions will
help to identify red flags that may inhibit
successful diet tolerance (*2, *3) (Table 2).
These questions may uncover a concern
and warrant a feeding evaluation, a swallow
study, and possible gastrostomy tube
placement prior to starting the KD. If enteral
feeding support is placed, administering the
KD using a combination approach of oral
and enteral feeds can be designed. There are
a variety of approaches to feeding described
in Table 3. Most importantly, it's essential
to customize the feeding plan. If a swallow
study or feeding therapy is necessary
while on a KD therapy, diet adjustments

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■ INDIVIDUALIZATION OF THE DIET THERAPY IS ESSENTIAL FOR COMPLIANCE.

may be made to maintain ketosis. For example, the barium solution used during swallow studies contains carbohydrate. The nutritionist should communicate with the feeding therapist to adjust the patient's next meal to accommodate for the additional

carbohydrate load in the solution. The nutritionist should also maximize the feeding therapy session by including a variety of textures (i.e. pureed, mechanical soft) if appropriate.

Table 2. Pediatric screening questions to identify potential feeding difficulties

Screening Question	Red Flags
1. What does your child eat on a typical day?	Limited food repertoire (less than 10-15 foods), liquid diet, inability to progress to age appropriate foods and textures, food rigidities
2. How long do mealtimes last?	Mealtime duration >1 hour, grazing, lack of mealtime structure, developmentally inappropriate feeding methods (bottle, syringe, spoon-feeding of liquids)
3. Where do meals take place?	Distracted eating, sleep eating, inability to self-feed, does not participate in family-style meals
4. Does your child express hunger?	Constipation, grazing, filling up on liquids at meals, turning head away from caregiver when food is presented on utensil
5. Was your child born prematurely or with other health problems?	Delayed feeding milestones, frequent respiratory infections/pneumonia
6. How is your child's development, especially speech?	Delayed milestones, autism spectrum disorder, speech apraxia
7. Does your child walk on grass and sand?	Sensory integration dysfunction, problems with smells, wet or messy food, not able to brush teeth
8. Does your child choke, gag or vomit with feedings?	Vomiting frequency, decline in participation during mealtimes, multiple swallows to get food down, congestion or wet vocal quality after eating
9. Fussy or irritable only during feedings?	Any signs of reflux, food allergies, Eosinophilic Esophagitis (EoE)
10. Any pocketing of foods in cheeks/mouth?	Lack of endurance to chew, extended mealtimes, overstuffs mouth, requires liquid to get food down

Table 3. Examples of combinations of oral and enteral feeding plans

Feeding Regimen	Example
All meals are equal. Oral and enteral are equal in value, therefore, interchangeable depending on patient's tolerance and abilities.	4:1 ratio, 6 feeds of 150 kcals per day of which 4 feeds via g-tube and 2 feeds oral.
Patient primarily formula fed, able to provide pureed meals equal to 100 ml formula equivalents.	4:1 ratio, 600 ml formula per day. Subtract 100 ml formula for each pureed meal. Replace formula volume with water.
Oral meals and formulas are at different ratios due to tolerance. Average the ratios.	Average 3.25:1 ratio, 3 formula meals at 3.5:1 ratio and 3 pureed meals at 3:1 ratio.
Provide carbohydrates oral and gavage remaining ingredients.	Gerber Pears by mouth, with calculated amount of ketogenic formula 4:1 via g-tube.
Blend entire recipe together, spoon feed, then gavage remaining portion of meal.	Blend Beechnut Chicken with Chicken Broth, Gerber Carrots, Liguigen, olive oil, offer by mouth, then gavage remainder via g-tube.
Use ratios of oral intake to determine amount of formula to provide via g-tube.	If patient takes <50% of the pureed meal, then provide 100 ml Ketogenic formula 4:1.

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Initiation of KDs: inpatient & outpatient

In the early 1920s, Dr. Wilder and colleagues at Mayo Clinic, agreed that a ketogenic ratio was necessary for the efficacy of the ketogenic diet (KD). However, Dr. Wilder did not necessarily fast all patients at the onset of the diet (*1). Over time, fasting followed by initiation of ketogenic meals in the hospital setting became the most popular method known as the Hopkins Fasting Protocol by Livingston and Freeman (*2). Two subsequent studies have compared the effects of fasting versus non-fasting (*3,*4). Both have concluded that non-fasting results in fewer adverse events and is tolerated better overall while maintaining the efficacy of classic fasting protocol. The method of diet initiation should be determined based on the patient's diet prescription, type of epilepsy, concurrent conditions, age, and parent and caregiver's needs. For example, arresting an acute exacerbation of seizures may be achieved with fasting as with status epilepticus (discussed later). Those who have confounding morbidities and are receiving multiple medications are at higher risk for diet intolerance or adverse effects and may benefit from a gradual, non-fasting initiation.

Outpatient KD initiation is a less common method that is receiving more attention in the past few years. Screening, assessment and follow-up care remain the same for both inpatient and outpatient initiations. With outpatient initiation, the KD diet is initiated at a low ratio, and goal calories are adjusted every 7-14 days (*5). The transition to ketosis occurs with less adverse effects.

Outpatient initiation at a 1:1 ratio with full (goal)calories (and fluids) can be implemented all at once in children older

than age 3. The diet can be advanced weekly in ratio increments such as 2:1, 3:1 etc. The diet is not advanced if there are tolerance issues or seizure control is already improved(*5,6,*7). Using the same number of meals and snacks as their previous diet helps in the transition to the new diet. There appears to be less frequency of diet intolerance, dehydration, hypoglycemia, and excessive ketosis with a gradual transition to the diet, however, close monitoring of the diet is still necessary. The parent or caregiver should initially monitor and record daily urinary ketones, hydration, bowel movement and seizures. The dietitian should monitor the patient weekly in clinic or at minimum on the phone.

After one week on the 2:1 ratio, ketosis is usually consistent and follow-up ketogenic diet labs are ordered and evaluated similar to the Classic KD. The patient is seen in clinic every 3 months during the first year and every 6 months thereafter. The main advantage of outpatient initiation is that the diet training is completed prior to starting therapy. This training takes place in an office setting without distraction of hospital routines. Differences between the outpatient and inpatient initiation method are compared in Table 4. Outpatient initiation can be a viable option for initiating the KD. It is a slower method to transition into ketosis and diet advancement is based on seizure control, not an arbitrary ratio. This method typically results in lower ketogenic ratios which are associated with fewer adverse effects such as excessive ketosis, nausea, vomiting, acidosis, and constipation.

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■ IN 2005, BERGQVIST AND COLLEAGUES PUBLISHED A CLINICAL TRIAL TO COMPARE THE EFFICACY OF FASTING VS GRADUAL KETOGENIC DIET INITIATION. THEY CONCLUDED THAT A GRADUAL INITIATION RESULTS IN FEWER ADVERSE EVENTS AND IS TOLERATED BETTER OVERALL WHILE MAINTAINING THE EFFICACY OF CLASSIC FASTING KD PROTOCOL.

SECTION II

■ WHILE THE BENEFIT OF DIETARY TREATMENT IN CHILDREN WITH MEDICALLY INTRACTABLE EPILEPSY HAS BEEN ESTABLISHED, LIMITED DATA IS AVAILABLE AMONG THE ADULT POPULATION.

Table 4. Comparison of Ketogenic Diet initiations

Inpatient	Outpatient
Most Common Method	Evolving New Method
2-5 day admission	3-4 week initiation
Rapid transition to ketosis	Slower transition to ketosis
Use an arbitrary goal ratio	Seizure control can be achieved with lowest ratio
Diet adjustments every 18-24 hours	Diet adjustments every 7-14 days
Limited food available in the hospital	Variety of foods available at home
Acute metabolic fluctuations may occur	Less occurrence and severity of metabolic fluctuations

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Diet therapy for adults – a retrospective review

Summary report on a retrospective study performed at Rush University Hospital, 2014.

While the benefit of dietary treatment in children with medically intractable epilepsy has been established, limited data is available among the adult population. The aim of this retrospective study was to evaluate the efficacy and tolerability of Modified Atkins Diet (MAD) and Low Glycemic Index Treatment (LGIT) among adults with medically intractable epilepsy as a complimentary treatment modality.

The medical records of 34 adults with medically intractable epilepsy treated with MAD or LGIT were retrospectively reviewed. All patients were seen and treated at the Dietary Treatments of Epilepsy Clinic at the Rush Epilepsy Center by an epileptologist and a registered dietitian. After an education session, either the MAD or LGIT was initiated, based on clinician recommendation and patient preference. Treatment outcomes included:

1. self-reported improvement of seizure control, defined as >50% improvement in seizure frequency from pre-diet;
2. self-reported improvement of quality of life, reported as subjective improvement in mood and/or alertness; and
3. side effects, including weight loss, defined as >5% loss from pre-diet, constipation, and elevated total cholesterol (TC), defined as TC >200 mg/dL.

Outcomes were assessed after three months of MAD or LGIT treatment.

A total of 34 patients with medically intractable epilepsy were reviewed, of which 27 patients (79%) were females; ages ranged from 18 to 70 years (mean 38 years). A total of 27 patients followed MAD (79%), while 7 patients followed LGIT (21%). A total of 15 patients (44%) reported >50% improvement in seizure frequency. Of those reporting >50% seizure frequency, 12 patients (80%) were on MAD, and 3 patients (20%) were on LGIT.

Among the 34 patients, quality of life was improved in 27 patients (79%). The most common side effects included weight loss in 19 patients (56%), and constipation in six patients (18%). Only minimal changes in TC were noted. Of the 20 patients with TC values available at follow up, seven patients (35%) had TC >200 mg/dL; however, only two patients (10%) with normal pre-diet TC had TC >200 mg/dL at follow up.

This retrospective study suggests that both MAD and LGIT are well tolerated and may be effective in improving seizure control and quality of life among adults with medically intractable epilepsy with minimal side effects. Future prospective controlled studies are necessary to further evaluate the benefit of these dietary treatments.

Modifications in ketogenic therapies

Although most people who require ketogenic therapies are able to consume an oral diet, liquid versions of the diet are needed for infants and for those who require an enteral feeding tube. Formulas are simple to design and calculate and options include a growing variety of commercial products and a multitude of options for blender formulas.

Liquid formula for infants

The use of ketogenic diet in infants can be administered safely with established protocols (*1). Breast feeding may be continued while on the K according to retrospective studies and have demonstrated marked reduction in seizure frequency (Table 5) (*2).

At this writing a ketogenically balanced, FDA approved infant formula is not available. Designer formulas using expressed breast milk along with carbohydrate-free formula (such as RCF) plus supplemental fat modulars (emulsified LCT or MCT oils) is commonly used. Adapting whey-based commercial ketogenic formulas such as KetoVie 4:1 (Cambrooke) or KetoVolve 4:1 (Nutrevolution) are other options that have been used in infants; however, these are not designed for infants and, therefore, require micronutrient comparison to Recommended Dietary Intakes to evaluate age-appropriate nutrition.

SECTION II

- THE USE OF KETOGENIC DIET IN INFANTS CAN BE ADMINISTERED SAFELY WITH ESTABLISHED PROTOCOLS.

SECTION II

Table 5. Efficacy of ketogenic diets in children under two years of age.

Patient	Gender	Age at Diet Initiation	Baseline Seizure Activity	% Seizure Reduction	Time on Diet While Breastfeeding
A	M	10.5 months	9-11/day	>90	9 months
B	M	8 months	30-100/day	>90	6-8 weeks
C	M	55 days	Several/day	>90	10 weeks
D	M	14 months	1/3-4 weeks	50-90	4 months
E	M	19 months	50-80/day	>90	1 month

Successful seizure control in infants receiving a KD can be optimized by adjusting calories (to support normal growth) and ratio to optimize ketones. Hypoglycemia is noted to be more common in infants than older children during diet initiation; therefore, blood glucose monitoring is advised. Recommendations for advancing to solid foods may include calculated small KD feedings initially such as pureed meats and vegetables with whipped heavy cream.

A range in volume of formula is typically advised for bottle-fed infants such as 20-24 ounces daily to accommodate on-demand feeding. Infants fed enterally typically require routinely scheduled feedings of equal volume. Due to the rapid growth that occurs in the first year of life, monitoring protocols should include weekly growth parameters of weight and length plus monthly head circumference, and laboratory surveillance including electrolytes, glucose and ketones.

Enteral feedings

Multiple ketogenic formula choices exist for those with enteral feeding tubes. The goals for the enteral diet are to optimize tolerance, minimize cost, and facilitate ease of administration. Formula may be provided as a bolus or as continuous feedings (necessary for jejunal feedings). Many families are now seeking an alternative to the commercial formulas typically designed for tube feedings and are requesting blended tube feedings using whole foods. A Pureed by Gastrostomy Tube (PBGT) Diet is an option that closely resembles a solid food diet and is easy to prepare. This modification in feeding texture is uniquely helpful for those with previous formula intolerance and feeding issues. Benefits of the PBGT include the following:

- ▶ Decrease and eliminate gagging and retching
- ▶ Decrease frequency or length of feedings and/or transition off of drip feedings
- ▶ Meet nutrient and fluid goals
- ▶ Improve weight gain, growth and nutritional status
- ▶ Encourage opportunity for oral intake (*3, *4, *5)

Preparation of Ketogenic PBGT diets include the use of commercial stage 2 infant foods including meats with broth, plus fruit or vegetables. Stage 2 infant foods are ideal for promoting consistency in the viscosity of the ketoenic PBGT formula. Since small quantities of solid food is typical for ketogenic therapy, purchasing commercial Stage 2 foods is usually affordable and also eliminates the need to use a blender. Emulsified long and short chain fats provide additional thickness to the formula and prevents fat from separating out and floating to the top. The benefits of the ketogenic PBGT diet over a diluted commercial ketogenic formula include:

- ▶ Small, calorically dense boluses given 4-5 times/day requiring only 5-10 minutes to administer
- ▶ Eliminates the need for a feeding pump; fluid goals are met as separate boluses
- ▶ Abides with hospital feeding policies; no hang time is required and uses safe, sterile foods
- ▶ No costly blender is required; accommodates ease when traveling
- ▶ Easy preparation method and storage guidelines (*5)

Due to the high-fat and low-fluid content of the ketogenic PBGT formula, the gastrointestinal transit time may be delayed resulting in constipation, therefore, it is crucial to include additional fluids between feedings. A PBGT diet is a viable alternative to commercial ketogenic formulas particularly for when diet or feeding intolerances exist.

In addition to the PBGT, families are requesting to be able to blenderized whole food into KD formula. This can be done effectively and requires a high-powered blender to liquify foods completely to prevent clogging of feeding tubes. Sufficient water is needed to ensure the correct viscosity and to separately as boluses to meet individual fluid requirements.

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What to feed when NPO (nothing by mouth)

Individuals on the ketogenic diet should be able to fast during times of acute illness; however, certain criteria exist for the management of these patients while NPO to maintain ketosis and seizure control. Intravenous fluids should be initiated to maintain hydration and they should be dextrose-free. Glucose monitoring is recommended every 2-4 hours during periods of fasting to monitor for hypoglycemia(*1). Once a patient is tolerating diet advancement and normoglycemic for 24 hours, glucose monitoring can be liberalized to every 4-6 hours, and discontinued once on full strength ketogenic meals or formula. (*1). A daily basic metabolic panel should be obtained until diet advancement to monitor for acidosis.

Certain complications may arise while maintaining a patient NPO including hypoglycemia and metabolic acidosis. If a patient develops hypoglycemia (blood glucose <40 mg/dL), it may be treated by providing 0.25 g/kg dextrose as a D10W bolus. (*1) Blood glucose should be

rechecked in 30 minutes and repeated as necessary until BG >40 mg/dL. Persistent hypoglycemia (3 episodes of BG <40 mg/dL within the previous 24 hours) should be treated with a D2.5-D5W continuous infusion at maintenance fluid requirements should be considered (*1). [Note that some centers use <50mg/dL in consideration of the potential drop in glucose during the time to retrieve the rescue dextrose]. The goal of glucose management should be within the range of 50-80 mg/dL. Once feedings are resumed, sufficient calories should prevent hypoglycemia. During stressed states such as illness, surgery or procedures, cortisol is released which causes an increase in glucose; therefore, hypoglycemia is not common and ketogenic patients typically do not require glucose infusion.

Metabolic acidosis may occur during NPO management with a CO₂ <20 mmol/L. It is important to evaluate for excessive ketosis or hypoglycemia. Patients on carbonic anhydrase inhibitors such as topiramate and zonisamide, are at increased risk of acidosis and should be monitored closely (*2). Oral bicarbonate supplementation should be

SECTION II

■ DURING STRESSED STATES SUCH AS ILLNESS, SURGERY OR PROCEDURES, CORTISOL IS RELEASED WHICH CAUSES AN INCREASE IN GLUCOSE THEREFORE HYPOGLYCEMIA IS NOT COMMON AND KETOGENIC PATIENTS TYPICALLY DO NOT REQUIRE GLUCOSE INFUSION.

SECTION II

■ FUTURE

CONSIDERATIONS FOR PATIENTS WHO PRESENT WITH SUBOPTIMAL KETOSIS AND WEIGHT LOSS DESPITE SERIAL INCREASES IN CALORIES SHOULD INCLUDE IDENTIFYING THE SOURCE OF SUBOPTIMAL CALORIE UTILIZATION WHILE ON THE KD.

initiated at 1-2 mEq/kg/day divided 2-3 times daily. If CO₂ remains <20 mmol/L with supplementation and/or the patient remains symptomatic, supplementation should be increased to replace 50% of the calculated deficit using the following equation; (HCO₃ mEq) = 0.3 x weight (kg) x base deficit (mEq/L). Consider advancing to continuous parenteral infusion of sodium acetate if low CO₂ persists. If the IV solution also contains NaCl, the total sodium content should not exceed 154 mEq/L, which is the concentration of normal saline.

Malnutrition and refeeding syndrome

There are multiple adverse effects related to the ketogenic diet (KD) reported in the literature; however, refeeding syndrome has not been reported. The occurrence of severe malnutrition with resulting refeeding syndrome during a ketogenic wean has been observed.

Prior to initiating a KD, metabolic screening labs are obtained to ensure appropriate metabolism on a high fat diet. These include serum amino acids, urine organic acids, serum acylcarnitine profile, lactate, and ammonia(*1). The starting calories on a KD can match the previous calories for enterally fed patients, (if those calories were sufficiently supporting growth). However, at one institution there has been an observed trend in hypocaloric patients (receiving <75% of calculated WHO), who have demonstrated weight loss on the KD receiving equivalent calories to their pre-ketogenic regimen. Furthermore, these patients required significantly more calories to support adequate growth.

One patient also demonstrated severe refeeding syndrome during the weaning of the KD. This patient had suboptimal betahydroxybutyrate ranging from 7.8-27.5 mg/dL (0.75-2.64-mmol/L) on a 3:1 and 4:1 ratio. Persistent weight loss was also

present resulting in severe malnutrition (22% weight loss x 6 months on diet), despite serial increases in calorie provisions to 1.5 times pre-KD calories (*2). Other causes of suboptimal ketosis and calories were ruled out, which included absence of diarrhea or vomiting, normal free and total carnitine. As a result the patient was weaned off the KD after six months during a hospital admission. Enteral feedings were initiated at 20% of current regimen with a standard pediatric formula. Serum phosphorus was obtained the following morning at 1.3 mg/dL, (normal range 4.5-5.5 mg/dL). Intravenous supplementation of phosphate was provided at 0.2-0.4 mEq/kg/dose for replacement (*3). Transition to oral phosphorus was completed prior to discharge. Feedings were not advanced until phosphorus levels were maintained at >4 mg/dL. Feedings were advanced stepwise to provide 65% of calories from previous KD regimen prior to discharge. Upon follow up 1.5 weeks post discharge, the patient regained 2.2 kg.

A potential temporary or long-term support therapy for individuals who are struggling with digestion of fats is the use of pancreatic enzymes. Enzyme therapy has been helpful in improving weight gain, reducing triglycerides and allowing continuation of KD therapy when seizure control is beneficial. (*4)

Future considerations for patients who present with suboptimal ketosis and weight loss despite serial increases in calories should include identifying the source of suboptimal calorie utilization while on the KD (Table 6). Patients who are malnourished should be monitored for refeeding syndrome during KD weaning and prophylactic phosphorus supplementation should be considered.

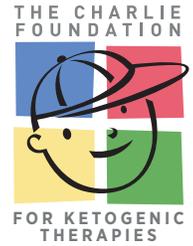


Table 6. Sources of potential suboptimal calorie utilization

Assessment	Description
MCT oil dosing	Provide MCT as a bolus when on pump feedings due to oil separation unless using an emulsified oil or if the formula has an emulsifier (such as in KetoVie, KetoCal, KetoVolve)
Acylcarnitine & UOA	Mild and intermediate forms of metabolic disorders may be missed pre-diet when not actively metabolizing fats & protein
Carnitine, free & total	Esterified/free carnitine ratio may not be accurate on ketogenic diet therapy therefore use free carnitine >20 uMol/L (free carnitine is that which is available vs. bound (acyl)).
Free fatty acids	When fat is metabolized, TG are broken down into glycerol & 3 FFA; the level of FFA can determine which substrate is being metabolized
Stool studies	Fecal fat to assess absorption; stool elastase to assess pancreatic sufficiency

MCT = medium chain triglycerides; UOA = urine organic acids;
 KD = Ketogenic Diet; TG = Triglycerides;
 FFA = free fatty acids

SECTION II

■ KETOGENIC RATIOS ABOVE 2:1 MAY NOT BE ACHIEVABLE WITH PN DUE TO THE LIMITATION IN PROVIDING ADEQUATE PROTEIN WITH LOWER THAN USUAL CALORIES.

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Ketogenic parenteral nutrition

Parenteral nutrition is used for conditions when the gut requires digestive rest. Ketogenic parenteral nutrition (PN) may be used when enteral nutrition is not tolerated for a prolonged period or is inadequate to sustain appropriate nutrition. The goal of ketogenic PN is to maintain or induce ketosis and seizure control, while preventing acidosis and hypertriglyceridemia. Ketogenic ratios above 2:1 may not be achievable with PN due to the limitation in providing adequate protein. It is important to note that full calories will not be achievable on ketogenic PN due to maximum lipid infusion rates; therefore, enteral feeds in combination with PN should be considered for long-term management.

Lipids may be initiated at 2-3 g/kg, advancing by 0.5 g/kg/day as tolerated to a maximum of 4 g/kg/day (*3, *4). Lipids should infuse over 24 hours to improve tolerance. Triglycerides should be monitored closely during initiation and advancement and should be maintained below 300 mg/dL. However, some centers may allow up to 1,000 mg/dL(*5). Carnitine supplementation can improve fatty acid metabolism and henceforth ketosis. Carnitine can effectively reduce tryglicerides and higher doses may be necessary during PN than with an oral KD.

It is important to consider that lipid products contain 2.25-2.5% glycerol which is a carbohydrate and should be accounted for (Table 7). Other IV products may also contain carbohydrate or additional calories and may affect ketosis (Table 8).

SECTION II

■ MULTIPLE CASE
REPORTS AND ONE
RETROSPECTIVE STUDY
CONCLUDE THAT
KETOGENIC PN APPEARS
TO BE EFFECTIVE IN
MAINTENANCE OR
INDUCTION OF SEIZURE
CONTROL AND KETOSIS
EVEN AT LOWER
KETOGENIC RATIOS OF
1:1 OR 2.

Table 7. Example calculation of ketogenic parenteral nutrition

Base solution	Ordered items	Volume (mL)	Kcal	Fat (g)	Pro (g)	CHO (g)	Ratio
Dextrose 70%	2.4%	24.7	59	-	-	17.3	
Travasol 10%	1 g/kg	113	45	-	11.3	-	
20% IL	3 g/kg	169.5	339	33.9 (+2) ^b	-	3.8	
			47% ^a				1.1:1
MCT oil (EN)	5 mL q 4 hr	30	231	25.7	-	-	
			73% ^a				1.9:1

Parenteral nutrition provided at 45 mL/hr x 16 hr (720 mL); IL over 24 hr. Reference weight of 11.3 kg. ^aPercent of goal calories; ^bEgg phospholipid. IL = Intralipid; MCT = medium chain triglycerides; EN = enteral nutrition

Table 8. Carbohydrate, fat and alcohol content of common intravenous products (*6)

Intravenous product	Strength	Carbohydrate	Fat	Alcohol
Phenobarbital	130 mg/mL	Propylene glycol 702 mg	-	79 mg
Diazepam	5 mg/mL	Propylene glycol 414 mg	-	79 mg
Lorazepam	2 mg/mL	Propylene glycol 753 mg	-	-
Phenytoin	50 mg/mL	Propylene glycol 414 mg	-	79 mg
Pentobarbital	50 mg/mL	Propylene glycol 414 mg	-	79 mg
Famotidine	10 mg/mL	Mannitol 20 mg	-	-
Propofol	10 mg/mL	22.5 mg Glycerol	100 mg Soybean oil	-
			12 mg Egg lecithin	

Note: A compounding pharmacist may be able to prepare intravenous medications without carbohydrate additives.

It is recommended that 1.5 g/kg/day protein be provided during stress for children greater than 2 years old. (*7) However, 0.5-0.8 g/kg/day may be more realistic during short-term PN therapy to maximize the ketogenic ratio. (*4)

Dextrose limits are determined by each institution, as some centers may have limitations based on the compounding system used. To decrease the dextrose infusion, PN may be cycled over 12-16 hours, while providing dextrose free fluids during the remaining hours to provide maintenance fluid requirements. It is possible to provide dextrose free PN solution and maintain adequate osmolarity >280 mOsm/L. Furthermore, the glycerol content from the lipid emulsion will provide minimum requirements to preserve glycolysis.

Trophic feeds using a ketogenic formula should be considered to maintain gut

integrity. Supplementation of MCT oil provided as a bolus should also be considered to increase the ketogenic ratio and provide calories. Starting at 2.5-5 mL every 4 hours and increasing stepwise as tolerated has been implemented.

There is limited research published on the safety and efficacy of the use of ketogenic PN. Multiple case reports and one retrospective study conclude that ketogenic PN appears to be effective in maintenance or induction of seizure control and ketosis even at lower ketogenic ratios of 1:1 or 2:1. (*5, *8-12) Side effects of ketogenic PN include transient elevated triglycerides, cholesterol, liver function tests, and pancreatic enzymes, which appear to resolve after PN is discontinued. Table 9 lists laboratory monitoring recommendations while on ketogenic PN.

Table 9. Ketogenic parenteral nutrition laboratory monitoring (*4)

Laboratory assessment	Frequency
Comprehensive metabolic panel, magnesium, phosphorus	Daily until stable, then weekly
Triglycerides, amylase, lipase	Daily until stable, then weekly
Serum betahydroxybutyrate	Daily until stable, then weekly
Carnitine, free & total	Baseline, then every 2 weeks
Zinc & Selenium	Every 2 weeks (if supplementing)
Urine ketones	Every void

SECTION II**Treating status epilepticus with enteral ketogenic nutrition**

The ketogenic diet is an alternative, non-pharmacologic treatment for refractory status epilepticus. Uncontrolled status-seizures carry a high risk of morbidity and mortality. Patients with refractory status epilepticus are typically treated with multiple anticonvulsants and/or anesthetic agents. Unfortunately a significant subset of these patients does not respond to the agents and are therefore placed into a medication-induced coma. Recent clinical reports show that status seizures treated with ketogenic therapy are typically arrested within 2 weeks. One of the confounding difficulties in establishing ketosis is the excessive carbohydrate provided in intravenous medications (Table 8). Significant carbohydrate can interfere with development of ketosis, thereby limiting the effectiveness of therapy.

Additional considerations for this unique population include providing ketogenic

formula via an enteral feeding tube. The comatose patient is in a compromised nutritional state with limited caloric expenditure. Traditional methods of initiation include starting formula at a high ketogenic ratio (5:1 up to 6:1) with the inclusion of MCT oil (which is more ketogenic than long-chain-fat) and at 50% of maintenance energy needs then graduating calories as sedation is removed. Glucose is the best biomarker for gauging energy intake and should be used as a guide to determine if more or less calories are needed. Intravenous carnitine supplementation is advised to support fatty acid conversion to ketones at the cellular level. Surveillance for the presence of acidosis is important particularly with the concomitant use of carbonic-anhydrase inhibitors (i.e. topiramate). Parenteral nutrition delivery is a more difficult approach to achieve ketosis due to the limitation of the liver to process a continuously high intravenous lipid-load. (*13)

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SECTION III

■ ALTHOUGH THE EXACT MECHANISMS OF ANTIEPILEPTIC ACTION CONTINUE TO REQUIRE CLARIFICATION, THE GENERAL INTENT WHEN INITIATING THE KD IS TO TRANSITION THE BODY AWAY FROM PREFERENTIAL GLUCOSE METABOLISM TOWARDS BURNING FAT AND KETONE BODIES FOR ENERGY.

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Non-epilepsy applications

In recent years, there has been growing interest in potential applications of the ketogenic diet (KD) for neurologic diseases other than epilepsy. Although the exact mechanisms of antiepileptic action continue to require clarification, the general intent when initiating the KD is to transition the body away from preferential glucose metabolism towards burning fat and ketone bodies for energy. Thus, conditions in which glucose metabolism is either impaired or undesirable may potentially benefit from KD implementation.

In Alzheimer's disease (AD), metabolic changes are known to occur, and fluorodeoxyglucose-positron emission tomography (FDG-PET) studies of elderly adults with and without dementia have shown a 17-23% reduction in cerebral glucose metabolism, and furthermore the degree of cognitive impairment correlated with the rate of glucose utilization (*1). Acute treatment with a medium chain triglyceride (MCT) oil emulsified drink was associated with a small improvement in certain cognitive tests in apolipoprotein E4- negative patients with AD or mild cognitive impairment (MCI). The Food and Drug Administration has approved a MCT oil product, Axona, as a medical food for use in mild/moderate Alzheimer's disease.

However, further studies are required to definitively assess the ability of this product to provide sustained cognitive improvement in AD or MCI.

Gliomas and other primary brain tumors are well-known to exhibit exuberant hypermetabolism on FDG-PET imaging. Glioma cells avidly metabolize glucose, and furthermore have been shown to lack the ability to switch to most non-glucose metabolic substrates. Currently, the treatments for brain tumors often include corticosteroids to reduce vasogenic edema; the associated hyperglycemia may also inadvertently provide an ideal nutritional environment to support the survival of glioma cells. Implementing the ketogenic diet may selectively target cancer cells;

1. by substantially lowering the availability of glucose,
2. reducing lactic acid in the tumor microenvironment which in turn reduces inflammation, and
3. inhibiting the mTOR pathway associated with tumor progression.

Adjacent normal brain tissue is able to utilize ketone bodies as a primary energy source. Clinical trials are ongoing here and abroad.

Traumatic brain injury (TBI) is associated with a hallmark physiologic response known as “hyperglycolysis,” consisting of a transient increase in cerebral glucose metabolism, followed by a more prolonged depression. Thirty-five to 45 day old rats (analogous to an adolescent age group) who are placed on a KD following TBI demonstrate decreased contusion volume and improved cognitive performance in comparison to control animals who maintain a standard diet. (*3, *4)

The KD is currently not a standard treatment for any of these conditions. More definitive clinical trials are needed in the future to validate the feasibility, safety and efficacy of the ketogenic diet in these disparate situations.

Cancer specific application

Speculation that a ketogenic diet can ameliorate cancer is driven by the observation that cancer thrives on the fermentation of glucose even in the presence of oxygen (the Warburg Effect) (*1). It is also well understood that fermentation produces high levels of lactic acid in the tumor microenvironment, a known contributor to inflammation and subsequent disease progression.

Severely restricting carbohydrate intake reduces the glucose/insulin spikes that in turn limit movement of glucose across cell membranes. Beneficial downstream effects of lower insulin also include a decrease in IGF-1, a hormone that fosters cancer cell proliferation. Carbohydrate restriction should be the primary path to facilitate the shift to ketosis. Most normal tissue quickly adapts to the utilization of ketones but cancer cells are not as metabolically flexible (*1).

Recently, therapies have targeted molecular pathways that impact cancer cell metabolism. Many of these pathways are similarly impacted by adoption of a ketogenic diet (*2). Preclinical data supporting the use of ketogenic diets for cancer include mouse model research (*3, *4), case reports (*5, *6), literature reviews (*7) and peer-reviewed research based on safety and feasibility trials (*8, *9). There is also evidence that maintaining high levels of ketones during radiation treatment is neuroprotective for normal brain tissue while

compromising survival of tumor tissue (*10). New Clinical Trials are ongoing (*11).

Professionals involved in implementing the diet for cancer should undertake a careful risk/benefit analysis on a case-by-case basis. A qualified healthcare professional should take the lead in providing a testing protocol that identifies absolute and relative contraindications to the diet (as outlined in a consensus statement for the use of the ketogenic diet for epilepsy) (*12). A well-designed intake provides information on comorbidities, impediments to lowering glucose levels and predicts challenges associated with side effects of standard therapies. Other considerations include incorporation of food preferences, assistance in meal planning, assessment of the ability to follow dietary guidelines and evaluation of caregiver support.

A nutrition professional experienced in implementing ketogenic diets should prepare a preliminary diet prescription based on client demographics and assessment of current nutritional status. Protein intake may need to be adjusted to accommodate for systemic damage due to disease progression or side effects of prior or concurrent therapies. The carbohydrate allowance should keep glucose low and steady while simultaneously maintaining a ketogenic state. Finally, fat grams are calculated to meet anticipated energy needs. Information on glucose/ketone levels, lab results and changes in body weight are used to periodically update the diet prescription. The diet may be implemented with or without caloric restriction though there is some pre-clinical evidence suggesting that caloric restriction may enhance outcomes in cancer (*1, *3).

The ketogenic diet for cancer is quickly gaining acceptance as a viable, feasible and safe adjunct to conventional cancer care. Much of the information and practices found in evidence-based protocols for epilepsy are now applied for cancer as well. Research focus must expand to include studies that aim to identify best-practice guidelines for this special application of the diet.

SECTION III

■ THE KETOGENIC DIET
FOR CANCER IS QUICKLY
GAINING ACCEPTANCE
AS A VIABLE, FEASIBLE
AND SAFE ADJUNCT
TO CONVENTIONAL
CANCER CARE.

SECTION III

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A growing need for ketogenic practitioners

There is a recent surge of public interest in the use of ketogenic diets for epilepsy and other metabolic disorders. With that interest comes the need for experienced nutrition professionals willing to work outside the clinical setting. These professionals may be poised and ready to commit to private practice or may opt to test the waters first by working with a number of clients before making a commitment to a full-time practice. A part-time practice is another option, offering the flexibility to working hours. An important first step is to research the licensing requirements set by the State.

The Limited Liability Corporation (LLC) is the Gold Standard for a start-up private nutrition practice. Establishing an LLC allows collection of payments for services, establishment of a business checking account and purchase of low-cost professional liability insurance. The simplest LLC entity is Single Member. Registration requirements, including payment of filing fees, can be completed online through the Secretary of State's office. Annual requirements are minimal and self-employment income flows through to federal taxes. Nutrition professionals are responsible for complying with all federal, state, and local sales tax reporting requirements. All business-related income and expenses need to be tracked and recorded.

The Small Business Administration (SBA) and State economic development office offer business start-up information. Many communities also offer support for business development. The business plan should include (at a minimum) a summary, mission statement and list of any products and all services. The business model should reflect not only your passion, but also details on how to price and deliver services, receive reimbursement, maintain professional affiliations and stay connected to colleagues.

A website is essential and should include a disclaimer that describes the limits of the practice and profession. Social media to promote your business should remain professional and keep your message consistent across all platforms. This extends to interviews, blogs and commentaries.

Confidentiality is required for all client information and data. E-mail communication must remain secure and private. The practice must keep within the boundaries set by the license and credentials. HIPPA regulations must be followed by those who work with patients (as opposed to those who work with clients). In all cases, personal information cannot be shared without explicit written permission.

SECTION IV

- THERE IS A RECENT SURGE OF PUBLIC INTEREST IN THE USE OF KETOGENIC DIETS FOR EPILEPSY AND OTHER METABOLIC DISORDERS.