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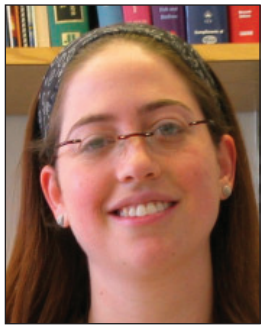
The Ketogenic and Atkins Diets: Recipes for Seizure Control



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Created in 1921, the ketogenic diet is a medical therapy used for children with difficult-to-control epilepsy. After decades of relative disuse, it has re-emerged in the past decade worldwide both clinically and in research studies. This high-fat, moderate protein, very low carbohydrate diet induces a ketotic state that theoretically leads to seizure reduction. Side effects may occur and include constipation, acidosis, kidney stones, dyslipidemia, and decreased growth. A modified Atkins diet may similarly lead to seizure reduction with less restrictiveness and is under investigation.

INTRODUCTION

Why do we need therapies for childhood epilepsy other than drugs? Unfortunately, approximately 1 in 5 children with epilepsy continue to have frequent, often daily, seizures despite trials of multiple anticonvulsant drugs. If surgery is a safe option and likely to lead to a cure, it is usually recommended, however many children are not ideal candidates or the risks are seen as too high. What options are then available?

For thousands of years before the recent development of anticonvulsant drugs in the 1900s, prolonged periods of fasting were commonly used to treat epilepsy with excellent reported results. Children were provided only clear fluids for as long as 2–3 weeks until their seizures improved. However, this was clearly not maintainable beyond the short term. At the Mayo Clinic in 1921, Dr. R.M. Wilder created a diet that could be continued for years and was designed to mimic the extensive biochemical changes that occur during fasting, acidosis, dehydration and ketosis (1). The diet provided was comprised of 10–15 grams of carbohydrates per day, 1 gram/kg of protein, and the remaining calories from fat. Calories were restricted to 75% of the daily allowance and fluids to 80%. Nearly a century later, the diet is almost identical in composi-

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Table 1
Typical day of food for a child on a 4:1 ratio, 1500 calorie ketogenic diet

Breakfast:	Egg with Bacon
	Egg 28g
	Bacon 11g
	36% heavy whipping cream 37g
	Butter 23g
	Apple 9g
Snack:	Peanut Butter Ball
	Peanut Butter 6g
	Butter 9g
Lunch:	Tuna Salad
	Tuna fish 28g
	Mayonnaise 30g
	Celery 10g
	36% heavy whipping cream 36g
	Lettuce 15g
Snack:	Keto Yogurt
	36% heavy whipping cream 18g
	Sour Cream 17g
	Strawberries 4g
	Artificial sweetener (e.g. Splenda™)
Dinner:	Cheeseburger
	Ground beef 22g
	American cheese 10g
	Butter 26g
	Cream 38g
	Lettuce 10g
	Green beans 11g
Snack:	Keto Custard
	36% heavy whipping cream 25g
	Egg 9g
	Pure vanilla flavoring

tion (2). For the next 20 years after its introduction, the diet became a popular treatment for seizures in both children as well as adults (3). However, after phenytoin (Dilantin™) was developed in 1938, followed by the now nearly 20 anticonvulsants on the market, the popularity of the ketogenic diet significantly decreased and was felt to be largely unnecessary. Very few hospitals continued using the diet and neurologists began characterizing it as a "holistic" or an "alternative" approach. In 1994, a 2-year-old boy with intractable seizures who failed multiple medications and surgery was started on the ketogenic diet (KD) after his father read about it in medical textbooks. He became seizure and medication-free, leading his father to create the Charlie Foundation, which exists today to help inform families and physicians about the KD (4). The diet is now well established in the medical community, performed in over 40 countries worldwide and reimbursed by nearly all insurance companies (5). Research has grown as well, and in the past decade, more than 200 articles have been published about the KD (2).

Although used predominantly for children with intractable epilepsy, it is occasionally used in adults and earlier in the course of treatment than ever before (6,7). In general, half of the children started on the traditional KD will have at least a 50% reduction in seizures within 6 months (2). Half of these will have >90% improvement; including approximately 15% seizure-free. Many families are able to successfully reduce or eliminate anticonvulsant drugs, and cognition is often improved as well (8,9). The KD can be maintained for years if successful, with no decreased efficacy typically noted over time (10).

INITIATION

The KD is calculated specifically for each child. An individualized menu plan is created, incorporating daily calories, fluid, and protein needs into a specific ratio of fat to protein and carbohydrates combined. Infants, young children and adolescents traditionally are started on a 3:1 ratio (fat: protein/carbohydrate), in order to provide increased protein and increased choices of food. Most other children ages 3–12 years, however, are started on a 4:1 ratio. However, while fine-tuning the diet, a patient may require anywhere from 2.5 to a 5:1 ratio.

Computer-generated meals are designed based on the child's food preferences. An example of typical foods used in the KD is provided in Table 1. A 3-day food record is obtained prior to starting the diet to ascertain these preferences and make the diet more

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Table 2
Ketogenic diet protocol at Johns Hopkins Hospital

Day prior to admission (Sunday)
- Reduced carbohydrates for 24 hours
- Fasting starts the evening before admission

Day 1 (Monday)
- Admitted to the hospital
- Fasting continues
- Fluids restricted to 60–75 mL/kg
- Blood glucose monitored every 6 hours
- Use carbohydrate-free medications
- Parents begin educational program

Day 2 (Tuesday)
- Dinner, given as "eggnog," providing 1/3 of calculated maintenance dinner calorie allowance
- Blood glucose checks discontinued after dinner
- Parents begin to check urine ketones periodically
- Education continues

Day 3 (Wednesday)
- Breakfast and lunch given as eggnog, providing 1/3 of maintenance breakfast and lunch calorie allowance
- Dinner (still eggnog), increased to 2/3 of maintenance dinner calorie allowance
- Education continues

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Day 4 (Thursday)
- Breakfast and lunch given as 2/3 of maintenance meal allowance
- Dinner is first full ketogenic meal (not eggnog)
- Education completed

Day 5 (Friday)
- Full ketogenic diet breakfast (calories) given
- Prescriptions reviewed and follow-up arranged
- Child discharged to home

palatable for each child. There are several factors to consider while calculating ratio, calories, fluid and protein needs, including age, weight, height, activity level and body mass index (BMI). On the classic KD, calories would be obtained by taking 75% of the Recommended Dietary Allowance (RDA) to meet total calories per day. However, since new Dietary Reference Intake (DRI) were established in 2000, a combination of food records, weight/height and Estimated Energy Requirements (EER) are used along with the DRI. The 3-day food record is also used to get a better understanding of how many calories per day the child is consuming. The goal is to provide adequate calories for growth, following the patients curve on their growth chart and attaining a BMI at the 50th percentile. Protein needs are based on specific requirements for age, stress factors, and kidney function. An alteration of the ratio may be necessary if protein needs are unable to be met. Fluids are classically restricted to 80% of calculated daily needs. However most children do not drink 80% of their estimated fluid needs before the diet is started, therefore the term "restriction" is often changed when counseling families to a requirement or allotment. Despite tradition, there is little evidence supporting the need to restrict calories and fluids to improve ketosis. In an immobile patient, a child with a history of kidney stones, or a patient on carbonic anhydrase inhibitor (e.g. topiramate, acetazolamide, or zonisamide), fluids are increased to 100% of their daily needs (11).

The specific protocol used at Johns Hopkins Hospital is described in Table 2. Children are admitted to the hospital for five days, during which time the KD is gradually advanced after a 24- to 48-hour fast. Side effects of fasting are minimal (transient hypoglycemia, vomiting, and occasional acidosis) and despite good evidence that long-term outcomes are equal in patients initiated without fasting, we have seen many occasions when a child has unique benefits attributable to fasting (12,13). For some children the initial fast can provide an immediate improvement in seizure control that can be motivating to the patient and the family. Most parents have a harder time with the fast than the child does!

Many centers do not require fasting to initiate the diet, but will still admit the child for several days to observe for any acute worsening on the diet as could be seen in a previously unrecognized metabolic disorder (e.g. pyruvate carboxylase deficiency and fatty acid oxidation defects) as well as to provide education. Also, an admission allows review of the patient's medications, ensuring that they are free of carbohydrates. We typically switch liquid medications to tablets, sprinkles, or orally ingested intravenous preparations,

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but will defer to pharmacies for up-to-date information on carbohydrate contents (14).

MAINTENANCE

The KD team, consisting of physicians and a dietitian, handle the management of children on the diet. We feel strongly that all aspects of their care while on this complicated dietary therapy should be handled by a center with trained personnel. All children are discharged home with prescriptions for daily multivitamin and calcium supplements, typically Unicap M™ and Calcimix™. Urine ketones are checked several times per week by parents with a goal of large ketosis (80–160 mg/dL). Adjustments to calories and macronutrient ratios are made as needed to maximize ketosis, prevent weight loss, and minimize hunger. Some centers have found it helpful to check serum beta-hydroxybutyrate levels at home with either a hand-held ketone meter or in the office setting. Weight, height, laboratory values (urine calcium and creatinine, urinalysis, fasting complete lipid profile, electrolytes, liver function tests, and a complete blood count), and anticonvulsant levels are typically checked every 3-6 months. Anticonvulsant medications are not changed immediately after starting the diet; however, if medication side effects are significant and efficacy is questionable, they can be safely tapered and discontinued even within the first month (9). Children are seen at 3, 6, and 12 months after the diet is started in a full-day KD clinic at our institution. In infants or children in whom the nutritional status is of higher concern, they may be seen monthly.

Increased seizure activity may occur while the patient is on the KD. It is important to ensure whether the patient has accidentally or intentionally received additional carbohydrates. Common causes are medications that are listed as sugar free but still may contain carbohydrates such as maltodextrin, sorbitol, starch or fructose. If ketones are not large or 80–160 mg/dL, then a 12- to 24-hour fast with clear liquids can rapidly improve ketosis. Illness is one of the most common reasons for increased seizures, even in children with epilepsy not on the ketogenic diet. If the child is ill, it may be advisable to make no changes and allow the infection to resolve. Rarely, antiepileptic medications can be adjusted or periodic benzodiazepines used.

SIDE EFFECTS

The ketogenic diet is not without side effects; however, they are less severe and fewer than reported in the literature for anticonvulsant drugs and surgery. Nonetheless, as with any therapy, the KD is a serious medical therapy with the potential to cause complications (15). Families are counseled that the KD is neither holistic nor all-natural.

Common side effects include constipation, lack of weight gain (as opposed to weight loss), low-grade acidosis, and hypoglycemia during the fasting period (15). Usually these side effects are easily managed and do not present significant problems or lead to diet discontinuation. Constipation can be easily alleviated with minor adjustments in the diet, stool softeners, and laxatives (Miralax™). Height, weight and BMI are obtained at each clinic visit and diet adjustments made accordingly to achieve appropriate height and weight gain. Most children on the diet have a low baseline acidosis, with HCO_3– of 12- to 18-mg/dL. Carnitine supplementation is controversial, and is usually only supplemented at our center if a patient has unexplained fatigue with optimal calories (16). Blood carnitine levels can be obtained and are usually reliable.

Occasional complications include kidney stones (seen in 5%–6% of children), dyslipidemia, and diminished growth (17–19). Kidney stones are more likely on the KD due to acidification of the urine as well as hypercalciuria. We routinely screen the urine calcium to creatinine ratio and begin oral alkalinization using potassium bicitrate at a dose of 2 mEq/kg/day divided twice daily if the ratio is higher than 0.2 (17). Unless there is a personal or family history of kidney stones, there is no evidence that anticonvulsants with carbonic anhydrase inhibition properties (topiramate, zonisamide, and acetazolamide) increase the risk of stones and should be avoided (11). Cholesterol may increase by an average of 30%, but tends to plateau over time (18). For significant dyslipidemia, the ratio can be lowered or polyunsaturated fatty acids substituted. Height may be adversely affected on the diet, and needs to be monitored, especially in young infants (19). Again, none of the aforementioned side effects automatically necessitate diet discontinuation; they can be treated with diet modifications or supplemental medications.

Table 3
Modified Atkins Diet Protocol (22)

- Copy of a carbohydrate counting guide provided to the family
- Carbohydrates described in detail and restricted to 10 grams per day for the first month
- Fats (e.g., 36% heavy whipping cream, oils, butter, mayonnaise) encouraged
- Clear, carbohydrate-free, fluids and calories not restricted
- Low-carbohydrate multivitamin (Unicap M™) and calcium (Calcimix™) supplementation prescribed
- Urine ketones checked semiweekly and weight weekly
- Medications unchanged for at least the first month, but changed if necessary to tablet or sprinkle (non liquid) preparations
- Low-carbohydrate, store-bought products (e.g., shakes, candy bars, baking mixes) discouraged for at least the first month
- Complete blood count, complete metabolic profile (SMA-20), fasting lipid profile, urine calcium, and urine creatinine obtained at baseline, 3, and 6 months

DISCONTINUATION

When should the diet be discontinued? The most common reason for discontinuation is inefficacy rather than restrictiveness (20). If it is unsuccessful, most families discontinue the diet by 3–6 months. Approximately half of the children started on the diet at Hopkins remain on it after one year (20). Children are maintained on the ketogenic diet for as long as it is beneficial, typically 1–2 years if it is successful. However, if medications have been considerably reduced or discontinued, the child is thriving, and seizures are controlled, it is not unusual to continue the diet, sometimes indefinitely.

Similarly to anticonvulsant drugs, the diet should not be stopped suddenly. In most situations, it is tapered over 1–2 months by lowering the fat to protein and carbohydrate ratio, then relaxing restrictions on weighing foods and measuring carbohydrate intake. For children in whom KD discontinuation is desired more rapidly, 36% heavy whipping cream can be changed immediately to whole, 2%, and eventually skim milk over several days.

Web Sites

Johns Hopkins Neurology web site, with information on the Epilepsy Division
www.hopkinsneuro.org/epilepsy/

The Charlie Foundation for Epilepsy
www.charliefoundation.org

A useful website created by a family of a child in our first pediatric Atkins study
www.atkinsforseizures.com

Recipes and advice
www.atkins.com

Just the Cheese™ snacks
www.specialcheese.com/bakedch.htm

High fat mayonnaise, very useful
www.dukesmayo.com

Information on KetoCal™, a ketogenic diet formula supplement
www.shsweb.co.uk/neuro/ketocal.htm

Information from the Epilepsy Foundation
www.epilepsyfoundation.org

American Epilepsy Society website
www.aesnet.org

Information about epilepsy in general
www.epilepsy.com

Makers of low carb products with plenty of fiber.
www.carbsense.com

Information on *The Doctor's Pocket Calorie, Fat & Carb Counter,* a helpful resource for patients on low-carbohydrate diets.
www.calorieking.com

THE MODIFIED ATKINS DIET

In 2003, the first case series of 6 children and adults started on a modified Atkins diet as an alternative to the traditional KD was published (21). Half had seizure

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reduction with associated large ketosis. Carbohydrates were restricted to 10–20 grams per day, and fats were encouraged. However, unlike the KD, these patients were neither admitted nor fasted, did not have calories or fluids restricted, nor were protein amounts limited.

Based on this preliminary success, a prospective study was recently completed of 20 children with intractable epilepsy started on a modified Atkins diet using 10 grams per day carbohydrates initially (22). The protocol used is listed in Table 3. Two-thirds had a >50% seizure reduction, and 9 were able to successfully reduce medications. Most children gained weight and none had kidney stones. Further studies, including adult patients, are underway at Johns Hopkins. We consider a modified Atkins diet approach in adolescents and adults, children with significant calorie or protein needs, and children with behavioral difficulties that would make the KD problematic. In young infants or patients with gastrostomy tubes, the ease of administration of an all-liquid KD formula makes a modified Atkins diet less advantageous (23). This can be provided as components (e.g. Ross Polycose™, Carbohydrate-Free™, and Novartis Microlipid™) or as a prepackaged 4:1 powder mix (SHS KetoCal™). Although easier than the KD, a modified Atkins diet has similar foods and requires family, neurologist, and dietitian commitment for any chance of success.

CONCLUSIONS

The dramatic increase in the use of dietary therapies for epilepsy over the past decade has broadened the therapeutic options for children with seizures. As the ketogenic and modified Atkins diets are both used and studied more worldwide, so will our understanding of how they work, how best to administer them, and what the long-term side effects might be. ■

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