

Cancer Association of South Africa (CANSA)



Fact Sheet and Position Statement on the Ketogenic Diet

Introduction

Dieting is the practice of eating food in a regulated and supervised fashion to decrease, maintain, or increase body weight. Dieting is often used in combination with physical exercise to lose weight, commonly in those who are overweight or obese.

[Picture Credit: Ketogenic Diet]

A study published in the American Psychological Association's journal *American Psychologist* found that dieting alone does "not lead to sustained weight loss or health benefits for the majority of people". However, other studies have found that the average individual maintains some weight loss after dieting. Weight loss by dieting, while of benefit to those classified as unhealthy, may slightly increase the mortality rate for individuals who are otherwise healthy.



The Ketogenic Diet

The ketogenic diet is a specific high-fat, low-carbohydrate diet that helps to control seizures in some children with epilepsy. It is prescribed by a physician and carefully monitored by a Registered Dietitian. The Ketogenic Diet requires careful measurement of kilojoules, fluids, and proteins.

- The name ketogenic means that it produces ketones in the body (keto = ketone, genic = producing). Ketones are formed when the body uses fat for its source of energy instead of carbohydrates.
- Usually the body uses carbohydrates (such as fruit; cereals such as oats; starchy vegetables such as potatoes, sweet potatoes, butternut, rice and pasta) for its fuel, but because the ketogenic diet is very low in carbohydrates, fats become the primary fuel instead.
- Ketones are not necessarily dangerous. They can be detected in the urine, blood, and breath. Ketones are one of the more likely mechanisms of action of the diet; with higher ketone levels often leading to improved seizure control. However, there are many other theories for why the diet will work (Epilepsy Foundation).

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Dip Audiometry and Noise Measurement; Diagnostic Radiographer; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

May 2019

Walczyk, T. & Wick, J.Y. 2017.

“Americans have embraced a large number of diets in an attempt to manage obesity, improve quality of life, and address specific health problems. Among diets developed to address health problems, the ketogenic diet has had a long and variable history. Developed in the 1920s by a faith healer to help children with epilepsy, this diet induces a state that mimics carbohydrate starvation. As medications became available and effectively addressed seizures, the diet fell out of favor. During the last few decades, researchers and clinicians have learned that it can be useful in children and adults with refractory epilepsy and a variety of other conditions. Once again, pharmacists may encounter patients who are employing dietary management of serious health problems. This very high-fat diet almost eliminates carbohydrates from the patient's food selection. The result is the substitution of ketone bodies as a source of energy. Today's ketogenic diet has been modified with scientifically proven adjustments to increase palatability and help with adherence. Effective for some forms of epilepsy, the ketogenic diet also seems to have some utility in Alzheimer's disease, Parkinson's disease, and glaucoma, and many Americans are using it to lose weight. Consultant pharmacists may field questions about this diet, its potential to correct or alleviate health conditions, and its limitations. The article discusses the ketogenic diet's strengths, limitations, potential mechanisms, and use in a number of conditions with an emphasis on the elderly.”

Rosenbaum, M., Hall, K.D., Guo, J., Ravussin, E., Mayer, L.S., Reitman, M.L., Smith, S.R., Walsh, B.T. & Leibel, R.L. 2019.

OBJECTIVE: The objective of this study was to measure changes in glucose, lipid, and inflammation parameters after transitioning from a baseline diet (BD) to an isocaloric ketogenic diet (KD).

METHODS: Glucose homeostasis, lipid homeostasis, and inflammation were studied in 17 men (BMI: 25-35 kg/m²) during 4 weeks of a BD (15% protein, 50% carbohydrate, 35% fat) followed by 4 weeks of an isocaloric KD (15% protein, 5% carbohydrate, 80% fat). Postprandial responses were assessed following mixed-meal tests matched to compositions of the BD (control meal [CM]) and KD (ketogenic meal).

RESULTS: Fasting ketones, glycerol, free fatty acids, glucagon, adiponectin, gastric inhibitory peptide, total and low-density lipoprotein cholesterol, and C-reactive protein were significantly increased on the KD. Fasting insulin, C-peptides, triglycerides, and fibroblast growth factor 21 were significantly decreased. During the KD, the glucose area under the curve was significantly higher with both test meals, and the insulin area under the curve was significantly higher only for the CM. Analyses of glucose homeostasis suggested that the KD insulin sensitivity decreased during the CM but increased during the ketogenic meal. Insulin-mediated antilipolysis was decreased on the KD regardless of meal type.

CONCLUSIONS: Switching to the KD was associated with increased cholesterol and inflammatory markers, decreased triglycerides, and decreased insulin-mediated antilipolysis. Glucose homeostasis parameters were diet dependent and test meal dependent.

Ketosis

‘Ketosis’ is a word one will most probably see when looking for information on diabetes or weight loss. It is a normal metabolic process, something one’s body does to keep working. When the body does not have enough carbohydrates from food for one’s cells to burn for energy, it burns fat instead. As part of this process, ketones are formed.

If one is healthy and eating a balanced diet, one's body controls how much fat it burns, and one will normally not make or use ketones. But when one cuts way back on kilojoules or carbohydrates, like going on a high-fat-low-carbohydrate diet, one's body will switch to ketosis for energy. It can also happen after exercising for a long time and during pregnancy. For people with uncontrolled diabetes, ketosis is a sign of not using enough insulin.

Ketosis can become dangerous when ketones build up. High levels of ketones lead to dehydration and changes in the chemical balance of one's blood.

In ketosis the patient's breath and urine usually smells like acetone.

There is often confusion as to the difference between ketosis and ketoacidosis.

Ketosis is the state whereby the body is producing ketones. In ketosis, the level of ketones in the blood can be anything between normal to very high.

Diabetic ketoacidosis, also known as DKA, *only* describes the state in which the level of ketones is either high or very high as a result of diabetes. In ketoacidosis, the amount of ketones in the blood is sufficient to turn the blood acidic, which is a dangerous medical state.

Ketosis will take place when the body needs energy and there is not sufficient glucose available for the body. This can typically happen when the body is lacking insulin and blood glucose levels become high.

Other causes can be the result of being on a low carbohydrate diet. A low level of carbohydrates will lead to low levels of insulin being produced, and, therefore, the body will produce ketones which do not rely on insulin to get into and fuel the body's cells.

A further cause of ketosis, less relevant to people with diabetes, is a result of excessive alcohol consumption.

The National Health Service (NHS) describes ketosis as a potentially serious condition, whereas a number of popular diets cite ketosis as being an essential part of weight loss. Ketosis is described as being potentially dangerous as very high level of ketones can make the blood acidic, a state known as ketoacidosis, which can lead to serious illness in a relatively short space of time.

The Typical Ketogenic Diet

The typical Ketogenic Diet, called the 'long-chain triglyceride diet', typically provides 3 to 4 grams of fat for every 1 gram of carbohydrate and protein.

A doctor or Registered Dietitian will recommend a daily diet that contains 10 093 to 12 881 kJ per day and 1-2 grams of protein for every kilogram of body weight. If this sounds complicated, it is! That is why one needs a dietitian's assistance.

A Ketogenic Diet Ratio is the ratio of fat to carbohydrate and protein grams combined. A 4:1 ratio is more strict than a 3:1 ratio, and is typically used for most children with uncontrolled epilepsy. A 3:1

ratio is typically used for infants, adolescents, and children who require higher amounts of protein or carbohydrate for some other reason.

The kinds of foods that provide fat for the Ketogenic Diet are butter, heavy whipping cream, mayonnaise, and oils (e.g. canola or olive). Because the amount of carbohydrate and protein in the diet have to be restricted, it is very important to prepare meals carefully.

In a typical Ketogenic Diet no other sources of carbohydrates can be eaten.

The Ketogenic Diet is supervised by a Registered Dietitian who monitors the child's nutrition and can teach parents and the child what can and cannot be eaten.

The Effects of the Ketogenic Diet on the Human Body

In essence, a ketogenic diet mimics *starvation*, allowing the body to go into a metabolic state called ketosis. Normally, human bodies are sugar-driven machines: ingested carbohydrates are broken down into glucose, which is mainly transported and used as energy or stored as glycogen in liver and muscle tissue. When deprived of dietary carbohydrates (usually below 50g per day), the liver becomes the sole provider of glucose to feed one's hungry organs – especially the brain, a particularly greedy entity accounting for ~20% of total energy expenditure. The brain cannot DIRECTLY use fat for energy. Once liver glycogen is depleted, without a 'backup' energy source, humanity cannot survive.

The 'backup' is ketone bodies that the liver derives primarily from fatty acids in the diet or body fat. These ketones – β -hydroxybutyrate (BHB), acetoacetate and acetone – are released into the bloodstream, taken up by the brain and other organs, shuttled into the 'energy factory' mitochondria and used up as fuel. Excess BHB and acetoacetate are excreted from urine, while acetone, due to its volatile nature, is breathed out (hence the characteristically sweet 'keto breath'). Meanwhile, blood glucose remains physiologically normal due to glucose derived from certain amino acids and the breakdown of fatty acids – and so, low blood sugar (blood glucose levels) is avoided!

Carbohydrate restriction induces the pancreas to 'tell' fat cells to release fatty acids, which get taken up by the liver and converted into ketones and released into blood. Once taken up by the brain, ketones enter the tricarboxylic acid cycle (TCA) cycle to generate energy. The TCA cycle is a series of enzyme-catalysed chemical reactions that form a key part of aerobic respiration in cells. This cycle is also called the Krebs cycle and the citric acid cycle.

Zhang, Y., Xu, J., Zhang, K., Yang, W. & Li, B. 2018.

BACKGROUND: Epilepsy is a syndrome of brain dysfunction induced by the aberrant excitability of certain neurons. Despite advances in surgical technique and anti-epileptic drug in recent years, recurrent epileptic seizures remain intractable and lead to a serious morbidity in the world. The ketogenic diet refers to a high-fat, low-carbohydrate and adequate-protein diet. Currently, its beneficial effects on epileptic seizure reduction have been well established. However, the detailed mechanisms underlying the anti-epileptic effects of ketogenic diet are still poorly understood. In this article, the possible roles of ketogenic diet on epilepsy were discussed.

METHODS: Data was obtained from the websites including Web of Science, Medline, Pubmed, Scopus, based on these keywords: "Ketogenic diet" and "epilepsy".

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Dip Audiometry and Noise Measurement; Diagnostic Radiographer; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

May 2019

RESULTS: As shown in both clinical and basic studies, the therapeutic effects of ketogenic diet might involve neuronal metabolism, neurotransmitter function, neuronal membrane potential and neuron protection against ROS.

CONCLUSION: In this review, we systematically reviewed the effects and possible mechanisms of ketogenic diet on epilepsy, which may optimize the therapeutic strategies against epilepsy.

Ketoacidosis in Breastfeeding Mom Who is on a Ketogenic Diet

A Swedish mother developed a dangerous condition called ketoacidosis as a result of a low-carbohydrate diet (LCHF) - or Banting diet - while she was breastfeeding.

In a medical report, published on 1 October 2015 in the *Journal of Medical Case Reports*, authors Louise von Geijer and Magnus Ekelund discuss the case of a 32-year-old woman who arrived at a Swedish hospital suffering from nausea, vomiting, heart palpitations, trembling and extremity spasms.

The woman, who was breastfeeding her 10-month-old son, had no family history of diabetes. She had started a strict LCHF diet (aka Banting diet), with an estimated carbohydrate intake of less than 20g per day, 10 days before admittance, lost 4 kilograms and had felt growing malaise.

Ketoacidosis normally affects people with diabetes and occurs when sugar cannot be used by the body because of a lack of insulin.

Fat is then used for fuel, and acidic waste products called ketones build up in the body. High levels of ketones in the body can be very poisonous and toxic.

Indications for Utilising the Ketogenic Diet

The Ketogenic Diet has the identified indications:

- Some children with epilepsy that standard antiepileptic drugs cannot control are candidates for the ketogenic diet. Although the diet can treat several seizure types effectively, it is not a first line treatment because it is difficult to implement and maintain, and the long-term effects are not well studied.
- Children with certain inborn errors of metabolism such as the glucose transporter syndrome and pyruvate dehydrogenase deficiency are also candidates.
- A third indication for utilising the Ketogenic Diet was proposed by Bueno, *et al.*, (2013), who found that otherwise healthy individuals on a diet with no more than 50g carbohydrates per day, achieved body weight reduction with low cardiovascular risk factor management when compared with individuals assigned to a conventional low-fat diet, i.e. a restricted-energy diet with less than 30% of energy from fat. They concluded that the Ketogenic Diet could be an alternative tool against obesity.

Some potential serious complications of extended utilisation of the Ketogenic Diet may include increased chance of kidney stones, gallbladder problems and bone fractures, especially in children. Menstrual irregularities often occur in women, with potential impact on

fertility. There are currently insufficient studies directly monitoring the side effects of ketosis, hence it is too early to conclude that the diet is completely safe for everyone.

deCampo, D.M. & Kossoff, E.H. 2019.

PURPOSE OF REVIEW: The ketogenic diet, a high-fat, low-carbohydrate therapy, has become an established treatment for pediatric epilepsy since 1921. There has recently been an increase in important studies on the ketogenic diet, and this review will highlight the most recent in order to provide a synthesis of where this field stands today.

RECENT FINDINGS: Clinical studies continue to support the use of ketogenic diets in epilepsy, with more recent trials supporting its use in adults. Clinical recommendations published in 2018 based on a decade of practice and research, guide implementation and management of the ketogenic diet in epilepsy. One of the most rapidly growing 'indications' includes the role of ketogenic diets in status epilepticus. An exciting new potential mechanism for how the ketogenic diet exerts its antiseizure effects is through changing the composition of the gut microbiome. Lastly, ketogenic diets are being applied to a range of neurological conditions from autism to Alzheimer's disease.

SUMMARY: The ketogenic diet is a versatile therapy, with growing clinical evidence and guidelines, widely used for the treatment of epilepsy. New indications include status epilepticus and neurological conditions other than epilepsy.

Contraindications for Utilising the Ketogenic Diet

While the Ketogenic Diet offers potential benefits in the treatment of children with epilepsy, a paediatric neurologist should carefully evaluate each child before recommending a trial on the ketogenic diet.

Individuals on the Ketogenic Diet should be directly supervised by a Registered Dietitian.

Medical contraindications to the ketogenic diet include:

- metabolic disorder
- defect in fat metabolism
- defect in ketone metabolism
- mitochondrial disorders
 - β -oxidation defects
 - primary and secondary carnitine deficiency
 - carnitine cycle defects
 - electron transport chain defects
 - ketogenic defects
 - ketolytic defects
 - pyruvate carboxylate deficiency
 - pyruvate dehydrogenase phosphatase deficiency.

Though the diet can exacerbate ketotic hypoglycaemia, this condition is not an absolute contraindication.

Some antiepileptic drugs can potentially exacerbate some of the adverse effects of the ketogenic diet, and these drugs require careful use when combined with the diet. These antiepileptic drugs include

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[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Dip Audiometry and Noise Measurement; Diagnostic Radiographer; Medical Ethicist]

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acetazolamide, topiramate, and zonisamide, which all can cause acidosis and kidney stones. Another antiepileptic drug requiring careful monitoring in children on the diet is valproate.

Finally, some children and adolescents are not candidates for the diet because they can get their own food and cannot understand the restrictions of the diet. These children and adolescents will not maintain the diet without constant supervision, which usually is not practical.

As the Ketogenic Diet uses lipids (fats) rather than carbohydrates as the primary energy source, it is essential that children are screened for disorders of fat metabolism, fatty acid transportation and oxidation, to avoid metabolic crisis. The absolute and relative contraindications and other pre-existing complications are listed:

Absolute Contraindications:

- Carnitine deficiency (primary)
- Carnitine palmitoyltransferase (CPT I or II) deficiency
- Carnitine translocase deficiency
- β -oxidation defects
- Medium-chain acyl dehydrogenase deficiency (MCAD)
- Long-chain acyl dehydrogenase deficiency (LCAD)
- Short-chain acyl dehydrogenase deficiency (SCAD)
- Long-chain 3-hydroxyacyl-CoA deficiency
- Medium-chain 3-hydroxyacyl-CoA deficiency.
- Pyruvate carboxylase deficiency
- Porphyria

Most of these conditions can be excluded on a routine urine metabolic screen and blood carnitine profile.

Relative contraindications:

- Inability to maintain adequate nutrition
- Surgical focus identified by neuroimaging and video EEG monitoring
- Parent or caregiver hesitance re: fussy eaters, diet and noncompliance with diet
- Bulbar dysfunction or Gastro-oesophageal disease -> aspiration risk
- Fat micro-aspiration – fat aspiration pneumonia -> severe complications

Most patients will require a risk assessment of aspiration as fat-aspiration can be lethal.

Other pre-existing complicating factors to be considered:

- Presence of kidney stones
- Dyslipidaemia
- Liver disease
- Failure to thrive
- Gastro-oesophageal reflux
- Poor oral intake
- Constipation
- Cardiomyopathy
- Chronic metabolic acidosis
- High carbohydrate content of current medications

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Kaira, S., Singla, R., Rosha, R., Sharma, S., Surana, V. & Kaira, B. 2019.

“This communication describes the aims and aspects of counseling prior to start of a ketogenic diet (KD). It uses a reader-friendly bio-psycho-social format to list and structure the various components of pre ketogenic diet counseling. These include strength mapping, risk and benefit explanation, and understanding the patient's selfcare responsibilities. This simple, yet practical discussion fills a major void in current literature, which seems to have ignored patient centred counseling strategies for KD in persons with obesity and diabetes.”

Hospital Admission Required

Children who are treated using the Ketogenic Diet will most likely have to stay in the hospital for up to 2 nights and 3 days unless there are complications. It may sometimes even be necessary for the child to stay a few days longer.

In order for the Ketogenic Diet to be effective, it is important that your child eats all of the food that is provided.

The following laboratory tests are carried out:

- Urine test for ketones
- Blood sugar levels by means of finger prick every six hours
- Blood ketone levels once a day by taking blood from a vein
- Vital signs every 4 to 6 hours – blood pressure, heart rate

Poelzer, K., Mannion, C., Ortiz, M.M. Bang, R. & Woods, P. 2018.

“The ketogenic diet (KD) is a nonpharmacologic treatment to reduce seizures with moderate to high success in pediatric patients with intractable epilepsy. Initiated in hospital, parents continue the treatment at home ensuring the ratio of high fat to low carbohydrate/protein is maintained to achieve metabolic ketosis. We conducted a systematic review to examine the quality of life (QoL) for families with a child using the KD for the reduction in epileptic seizures. A systematic review of the literature was conducted from 2007-2014 using key terms and combinations of: "epilepsy," "ketogenic diet," "children," "family," and "quality of life." We accessed CINAHL, Medline, PubMed, and PsycINFO. After removing duplicates, we screened 598 papers by title and abstract. Articles comparing alternate diets such as the Atkins diet to the KD, or those focusing on the KD and societal costs, were excluded. Eighteen articles remained, including 7 intervention studies (randomized controlled trial and quasiexperimental), 7 descriptive studies (retrospective), 2 observational studies, and 2 case studies. Most participants were diagnosed with epilepsy at the age of 5 y, and had a trial of antiepileptic drugs (AEDs) and had been using the KD after discharge from the hospital. QoL was infrequently reported as a primary variable and was defined in a variety of ways. We found recurring themes that could affect QoL: efficacy of seizure reduction, nutritional status, child growth and development, and child and family psychosocial impact. The dominant psychological factor was the need for counseling for parents and clear expectations on expected outcomes. Nonadherence and dropout rates were frequent, but unfortunately the reasons and timing were not well documented, and some of these could be associated with QoL. The success of the KD in seizure reduction addressed a primary parental concern. Further research should address KD adherence and dropout rates, and investigate factors of quality of life.”

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The Ketogenic Diet not Suitable for Adults

The Ketogenic Diet is usually not recommended for adults. Researchers at the Johns Hopkins Epilepsy Center states that dietary therapy by means of the Ketogenic Diet has been used to treat children with epilepsy for almost a century. However, this valuable treatment option has not been generally available to most adults with seizures. Johns Hopkins Epilepsy Center has introduced a modified Atkins Diet, which is a low carbohydrate, high fat alternative to the Ketogenic Diet for adults in 2002.

Recent studies have shown that the modified Atkins Diet lowers seizure rates in nearly half of adults that try it, usually within a few months. Unlike the Ketogenic Diet (used in children), there is no hospital stay involved, no fasting to get started, no food weighing, and no counting of calories or fluids. The diet is 'modified' from the traditional Atkins Diet where the intake of fats are encouraged.

CANSA's Position on the Ketogenic Diet

- The Cancer Association of South Africa (CANSA) believes that the Ketogenic Diet is a treatment option for children with epilepsy whose seizures are not adequately controlled by means of anti-epileptic drugs (AEDs).
- CANSA supports the use of the Ketogenic Diet to help to reduce the number or severity of seizures in children.
- CANSA accepts medical evidence that up to 70% of children with epilepsy could have their seizures controlled with AEDs. For some children who continue to have seizures, the ketogenic diet may help. However, the diet is specialised and should only be carried out under the care, supervision and guidance of specially trained medical specialists including monitoring by a Registered Dietitian.
- CANSA is also of the opinion that the Ketogenic Diet should not be utilised for any other purpose unless there is sufficient scientific evidence of its safety and efficacy
- CANSA advises that the ketogenic diet should only be utilised under direct supervision of a medical practitioner and/or Registered Dietician

Medical Disclaimer

This Fact Sheet and Position Statement is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation. Users should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Fact Sheet and Position Statement. So far as permissible by law, the Cancer Association of South Africa (CANSA) does not accept any liability to any person (or his/her dependants/estate/heirs) relating to the use of any information contained in this Fact Sheet and Position Statement.

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organisation wherever they shall be based, as a result, direct or otherwise, of information contained in, or accessed through, this Fact Sheet and Position Statement.



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