LILY FOUNDATION

An Introduction to Ketogenic Diets

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What is a ketogenic diet?

- A **MEDICAL** treatment.
- Mimics fasting metabolism
- Alters fuel availability to brain- ketones rather than glucose
- An anticonvulsant in food form
- It can be effective for ALL seizure types.

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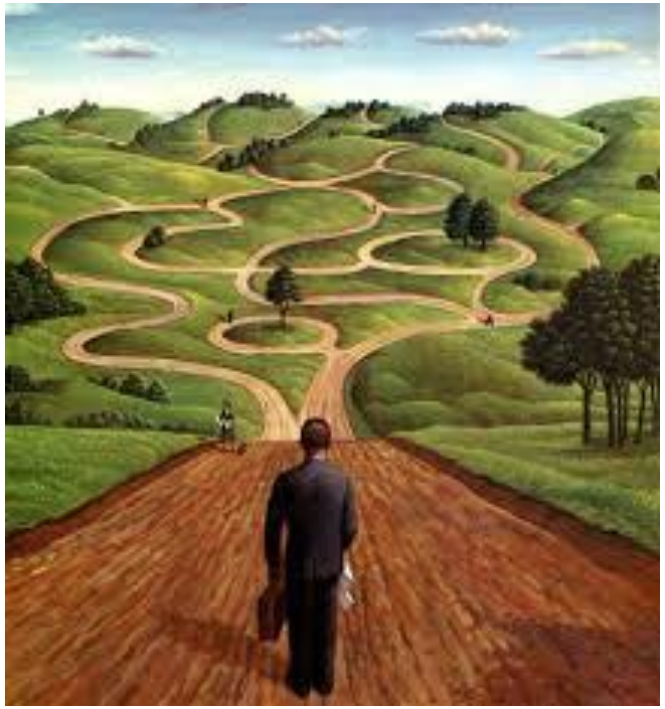
Each keto journey is different……



Prescribed and fine tuned around individual needs

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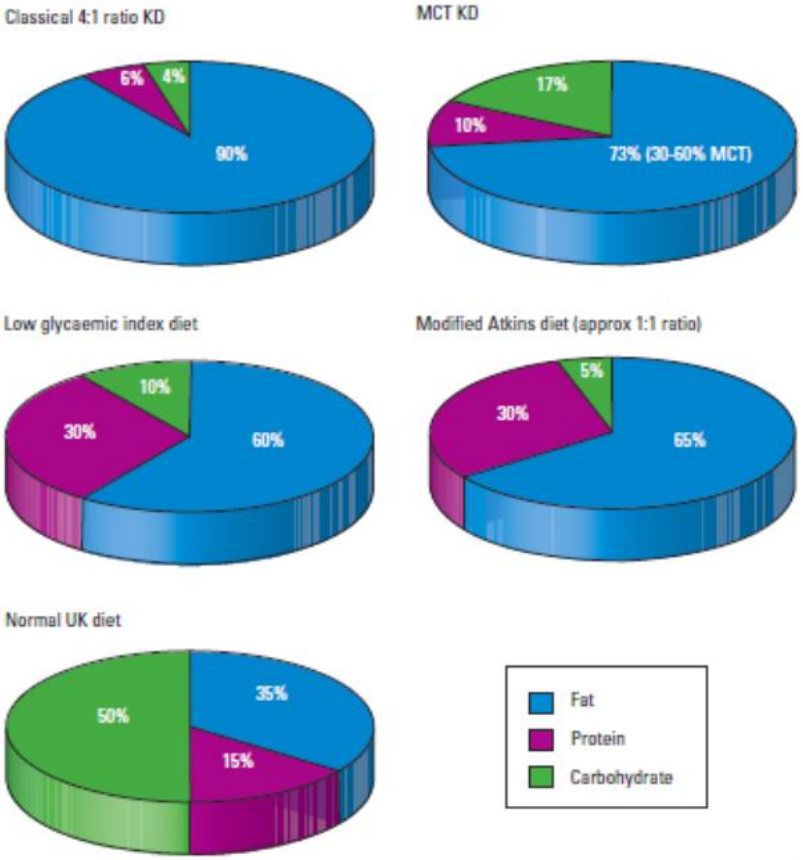
Ketogenic Diet …



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Carbohydrate reduction is the KEY!

Energy provision:

Carbohydrate 4-17%
+
Fat 60-90%
+
Protein 6-20%

- Classical Ketogenic Diet (LCT)
  - Control = Stable ratio of fat to protein & CHO
- MCT Ketogenic Diet
  - Control= % energy from MCT
- Modified Ketogenic Diet / MAD
  - Control = CHO counting & adequate fat
- Low Glycaemic Index Treatment
  - Control = CHO counting & adequate fat

……similar metabolic impact

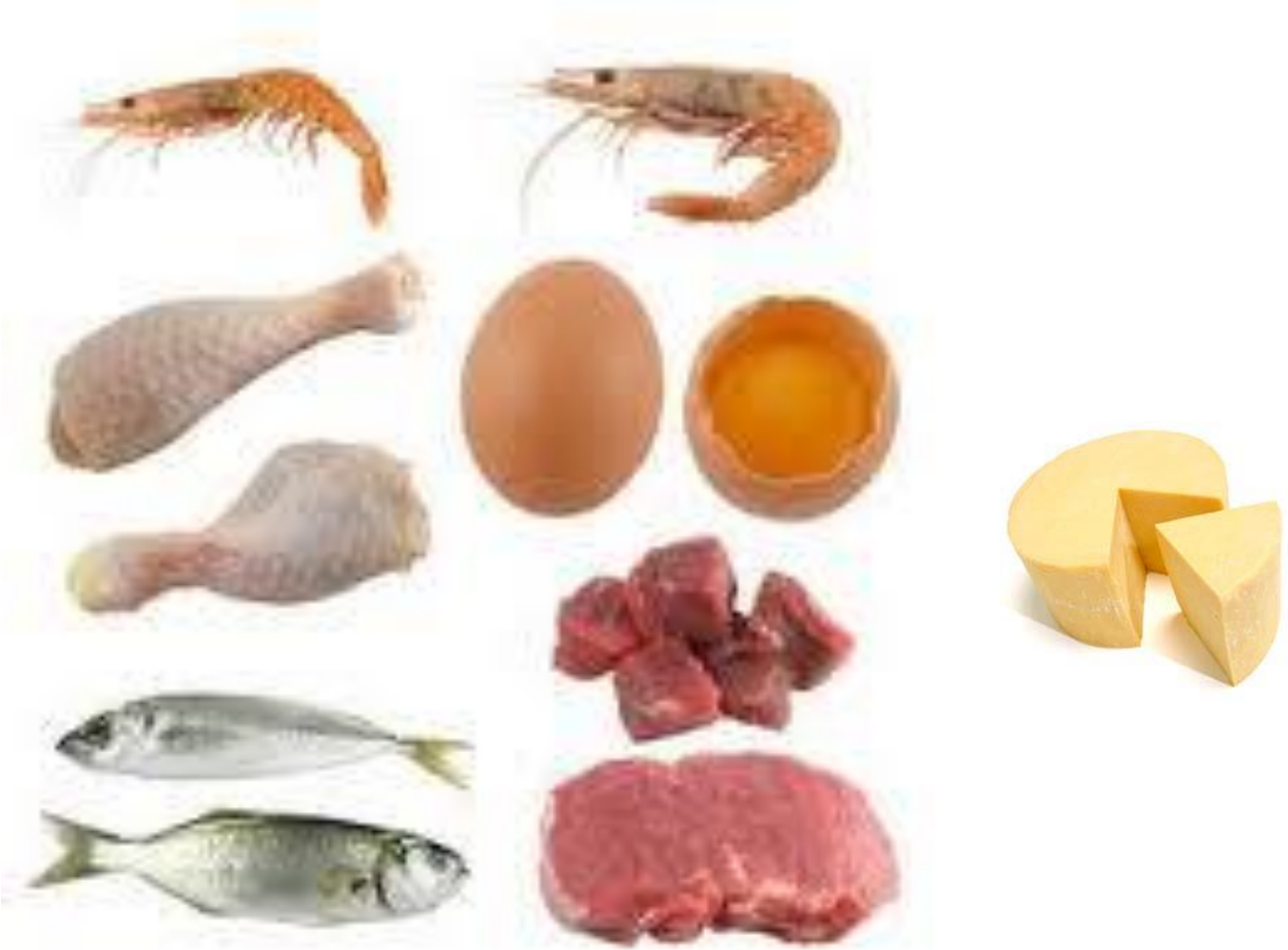
Carbohydrate foods ;

measured in ALL ketogenic regimes

FAT containing foods ;
measured in Classical & MCT (generous in Modified KD)

Protein containing foods ;

measured in Classical & MCT (moderate in Modified KD)



Food or Feed or both!

OR

What does a ketogenic meal look like?

The ketogenic effect?

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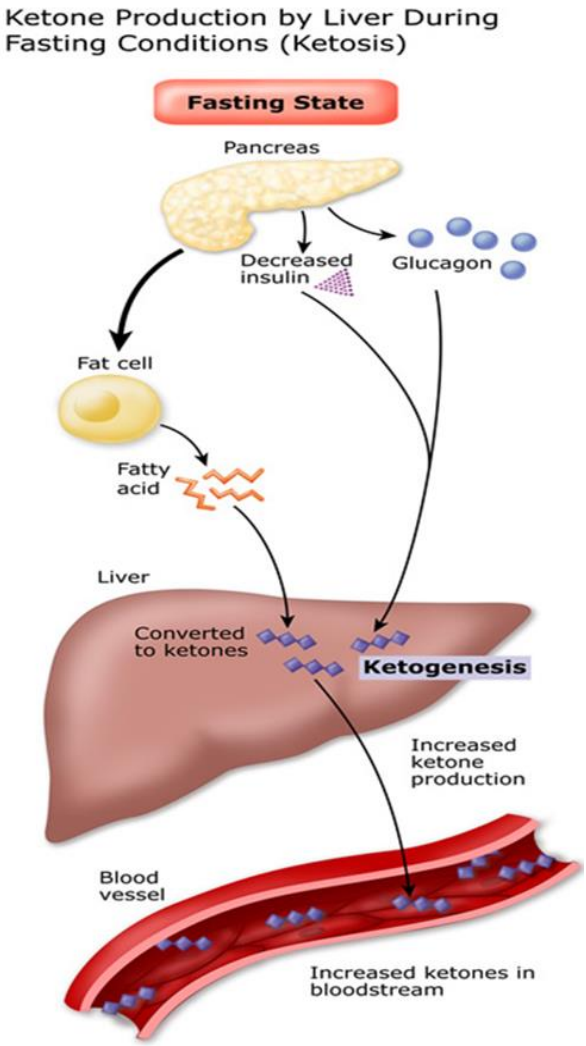
How does it work?



- Rise in blood ketone levels – stimulates mitochondria production
- Lower blood glucose levels & flatter profile
- Elevated free fatty acids & essential fatty acids
- Caloric control?

…….likely a combination of all the above

Use in the management of neurodegenerative disorders

frontiers in PHARMACOLOGY

REVIEW ARTICLE

The ketogenic diet as a treatment paradigm for diverse neurological disorders

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Dietary and metabolic therapies have been attempted in a wide variety of neurological diseases, including epilepsy, headache, neurotrauma, Alzheimer disease, Parkinson disease, sleep disorders, brain cancer, autism, pain, and multiple sclerosis. The impetus for using various diets to treat – or at least ameliorate symptoms of – these disorders stems from both a lack of effectiveness of pharmacological therapies, and also the intrinsic appeal of implementing a more "natural" treatment. The enormous spectrum of pathophysiological mechanisms underlying the aforementioned diseases would suggest a degree of complexity that cannot be impacted universally by any single dietary treatment. Yet, it is conceivable that alterations in certain dietary constituents could affect the course and impact the outcome of these brain disorders. Further, it is possible that a final common neurometabolic pathway might be influenced by a variety of dietary interventions. The most notable example of a dietary treatment with proven efficacy against a neurological condition is the high-fat, low-carbohydrate ketogenic diet (KD) used in patients with medically intractable epilepsy. While the mechanisms through which the KD works remain unclear, there is now compelling evidence that its efficacy is likely related to the normalization of aberrant energy metabolism. The concept that many neurological conditions are linked pathophysiologically to energy dysregulation could well provide a common research and experimental therapeutics platform, from which the course of several neurological diseases could be favorably influenced by dietary means. Here we provide an overview of studies using the KD in a wide panoply of neurologic disorders in which neuroprotection is an essential component.

Keywords: ketogenic diet, neuroplasticity, epilepsy, neurological disorders

Stafstrom CE Rho JM Frontiers in Pharmacology
April 2012 Vol3 Article 59

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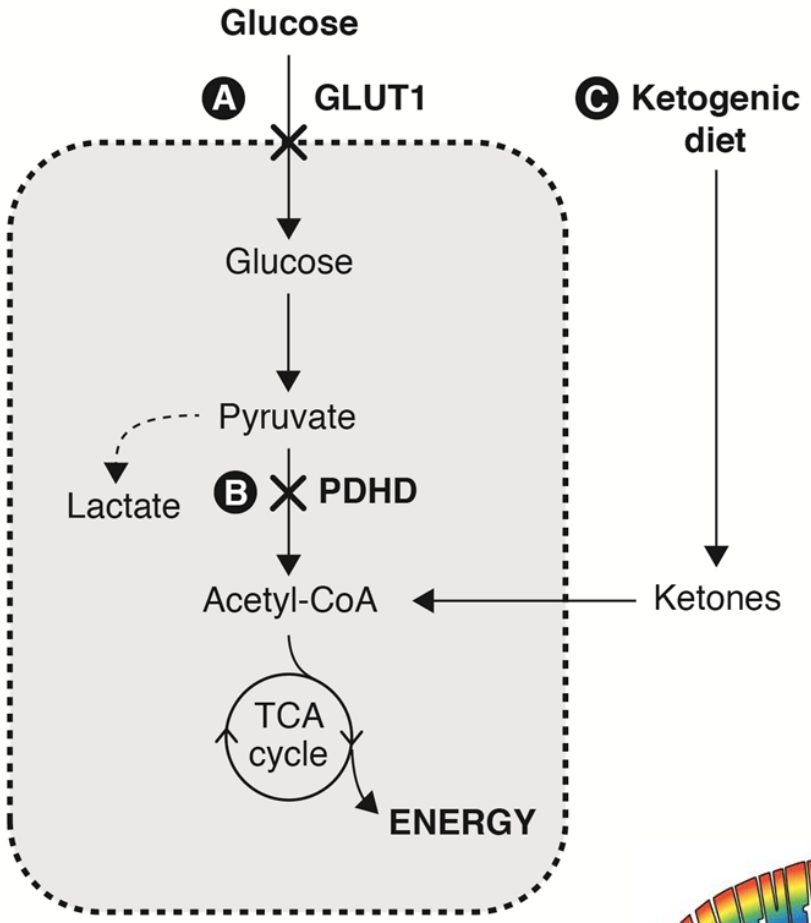
Current Research interest:

- Brain tumours – Astrocytoma / Glioblastoma Multiforme
- Alzheimer's disease
- Parkinson's disease
- Amylotrophic Lateral Sclerosis (ALS)
- Mitochondrial disorders
- Traumatic brain injury
- Post stroke care
- Autism
- Migraine
- Depression
- Aging

Could alterations in energy metabolism be the common theme?

Use in PDHD

Pyruvate dehydrogenase deficiency



A ketogenic diet

1. **Reduces lactate and pyruvate**
2. **Provides alternative 'fuel'; ketones**

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Longitudinal Study

DOI 10.1007/s10545-016-0011-5

ORIGINAL ARTICLE

Ketogenic diet in pyruvate dehydrogenase complex deficiency: short- and long-term outcomes

Kalliopi Sofou [1] · Maria Dahlin [2] · Tove Hallböök [1] · Marie Lindefeldt [2] · Gerd Viggedal [1] · Niklas Darin [1]

Received: 20 August 2016 / Revised: 8 December 2016 / Accepted: 12 December 2016 / Published online: 18 January 2017

Abstract

Objectives Our aime was to study the short- and long-term effects of ketogenic diet on the disease course and disease-related outcomes in patients with pyruvate dehydrogenase complex deficiency, the metabolic factors implicated in treatment outcomes, and potential safety and compliance issues.

Methods Pediatric patients diagnosed with pyruvate dehydrogenase complex deficiency in Sweden and treated with ketogenic diet were evaluated. Study assessments at specific time points included developmental and neurocognitive testing, patient log books, and investigator and parental questionnaires. A systematic literature review was also performed.

Results Nineteen patients were assessed, the majority having prenatal disease onset. Patients were treated with ketogenic diet for a median of 2.9 years. All patients alive at the time of data registration at a median age of 6 years. The treatment had a positive effect mainly in the areas of epilepsy, ataxia, sleep disturbance, speech/language development, social functioning, and frequency of hospitalizations. It was also safe—except in one patient who discontinued because of acute pancreatitis. The median plasma concentration of ketone bodies (3-hydroxybutyric acid) was 3.3 mmol/l. Poor dietary compliance was associated with relapsing ataxia and stagnation of motor and neurocognitive development. Results of neurocognitive testing are reported for 12 of 19 patients.

Conclusion Ketogenic diet was an effective and safe treatment for the majority of patients. Treatment effect was mainly determined by disease phenotype and attainment and maintenance of ketosis.

Introduction

The ketogenic diet (KD) was first introduced as an antiepileptic treatment, in 1921 (Wilder 1921), but it was not until 1976 that KD was shown to be beneficial in pyruvate dehydrogenase complex (PDC) deficiency (Falk et al. 1976). The biochemical rationale behind the metabolic effect of KD lies in the fact that this is a high-fat, low-carbohydrate diet that mimics the metabolic state of long-term fasting. In PDC deficiency, the glycolytic end product, pyruvate, is not optimally metabolized through the tricarboxylic acid cycle, leading to increased production of lactate and impaired production of

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Summary:

- 19 paediatric patients with PDHD
- 10 with epilepsy -50% became seizure free in a year
- Increased remission times, decreased severity and duration of ataxia
- Majority showed at least minimal improvement of neuro-cognitive development

Review- KD use in Mitochondrial Disorders

J Clin Med. 2017 Jun; 6(6): 56.
Published online 2017 May 26. doi: 10.3390/jcm6060056
PMCID: PMC5483866

Use of the Ketogenic Diet to Treat Intractable Epilepsy in Mitochondrial Disorders

Eleni Paleologou, Naila Ismayilova, and Maria Kinali*

Iain P. Hargreaves, Academic Editor

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Abstract

Go to:

Mitochondrial disorders are a clinically heterogeneous group of disorders that are caused by defects in the respiratory chain, the metabolic pathway of the adenosine tri-phosphate (ATP) production system. Epilepsy is a common and important feature of these disorders and its management can be challenging. Epileptic seizures in the context of mitochondrial disease are usually treated with conventional anti-epileptic medication, apart from valproic acid. However, in accordance with the treatment of intractable epilepsy where there are limited treatment options, the ketogenic diet (KD) has been considered as an alternative therapy. The use of the KD and its more palatable formulations has shown promising results. It is especially indicated and effective in the treatment of mitochondrial disorders due to complex I deficiency. Further research into the mechanism of action and the neuroprotective properties of the KD will allow more targeted therapeutic strategies and thus optimize the treatment of both epilepsy in the context of mitochondrial disorders but also in other neurodegenerative disorders.

Keywords: ketogenic diet, mitochondrial disorders, intractable epilepsy, treatment

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Conclusions:

- Improves cellular metabolism
- Makes cells more robust
- Seizure reduction often continues post Diet
- Diet appears to cause gene modification which may explain the permanent effect of the Diet
- Research interests centred around supplement replacements: “Ketogenic Pill”

Contraindications

Primary carnitine deficiency
CPT I or CPT II deficiency (Carnitine palmitoyltransferase)
Carnitine translocase deficiency
Fatty acid β-oxidation defects
MCAD deficiency (medium-chain acyl-dehydrogenase)
LCAD deficiency (long-chain acyl-dehydrogenase)
SCAD deficiency (short-chain acyl-dehydrogenase)
Long-chain 3-hydroxyacyl-CoA deficiency
Medium-chain 3-hydroxyacyl-CoA deficiency
Pyruvate carboxylase deficiency
Disorders requiring a high-carbohydrate diet treatment,
eg, acute intermittent porphyria
Hypoglycemia under investigation
Defects in ketoneogenesis or ketolysis
Severe liver disease

POSSIBLE contraindications
Familial hyperlipidemia
Dysphagia or significant GOR
History of renal stones
Diabetes mellitus
Medications that increase risk of acidosis
Steroid treatment

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Side effects?

☺Positive:

- Reduced seizure frequency
- Reduced seizure intensity
- More rapid recovery from seizures
- Feel sharper , brighter & more energy
- Ability to 'tune in' to the world

☹ Negative: mainly gastro……

- Constipation ….. occasionally diarrhoea reported.
- Lethargy / nausea / hypoglycaemia (if rapid introduction of regime)
- Raised lipids – often transient
- Increased risk of kidney stones (when combined with some medications)
- Growth retardation
- Possible increased risk of osteoporosis
- Increase in seizures …in some!

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Ketogenic therapy: team approach

Dietitian Patient/Carers Neurologist Biochemistry GP Epilepsy Specialist Nurse

Medical Referral to Ketogenic team
Medical & biochemical Screening

Pre-therapy Discussion: agreement?
Practical / possible
Realistic objectives?

Education: Food & monitoring
Nutrient sources / values
Making meals or feeds
Bloods / records

Diet Prescription
1: Classical prescription
Oral or via PEG or both

Support++ dietitian & keto diet assistant
Phone / e.mail / text

3 month follow up: neurologist & dietitian
Effective & managing well?
Wean drugs?

Ongoing treatment 6/12/18/24 month neuro/diet follow up
Wean ketogenic therapy?

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Biochemical screening

Blood investigation	Frequency of monitoring
Essential:	
Full blood count	Baseline, after 3 months, 6 months, then every 6 months
Clotting screen	Baseline, 6 months, then every 12 months
Renal profile (includes sodium, potassium, urea, creatinine, bicarbonate and albumin)	Baseline, after 3 months, 6 months, then every 6 months
Liver profile	Baseline, after 3 months, 6months, then every 6 months
Calcium, phosphate, Vitamin D	Baseline, after 3 months, 6 months, then every 6 months
Magnesium	Baseline, after 3 months, 6 months, then every 6 months
Glucose	Baseline, after 3 months, 6 months, then every 6 months
Lipid profile	Baseline, after 3 months, 6 months, then every 6 months
Free and acylcarnitine profile	Baseline, after 3 months, 6 months, then every 6 months
Thyroid Function	Baseline
Recommended:	
Vitamins A, E	Baseline, 6 months, then every 12 months
Zinc, selenium, copper	Baseline, 6 months, then every 12 months
Vitamin B12, folate	Baseline, 6 months, then every 12months
Ferritin	Baseline, 6 months, then every 12months

- **Note: Urine should also be checked every three months for haematuria and calcium-creatinine ratio.**

Initiation

- Generally at home
- No fasting
- Stepped in over a few days

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Home monitoring

- Blood ketones & glucose; initially test 2 times daily.
  - Blood Ketones aim 2-4mmol/l
  - Urine Ketones aim 4-16mmol/l
  - Blood Glucose 3.5-6.5mmol/l

- Seizures & symptoms

- More frequent monitoring when unwell or fine tuning or changing medication

Weekly monitoring reports

Weekly monitoring - NR

Week commencing...26/1/14..... **Weight at start of week 10stone 4lbs**

Date	Day	Number of seizures of each type							Blood or urine ketones		Blood glucose		Comments on any illness or changes to diet, activity or medication
		1	2	3	4	5	6	7	AM	PM	AM	PM	
26	Sun					1 (asleep)			3.7	2.8	4.1	4.8	N was very energetic and happy today.
27	Mon						1 x 11 mins cluster (h)		3.1	2.7	4.6	4.8	N did 20mins of horse riding. N was very interactive today, happy and chatty. N's period finished.
28	Tues						1 x 14mins (h) 1 x 50 secs(m)		2.6	3.6	4.4	4.2	2 x 15 mins walks. N was bright and chatty before her seizure. N had 0.5mls Buccal Midazolam.
29	Wed				1 x 30 secs(h)				3.2	1.3	3.7	5.3	N went swimming but had a seizure whilst there. N was tired and lethargic most of the day.
30	Thurs								2.3	1.9	4.9	5.9	N took part in 3 hours of on/off dancing. And did 2 x 15 mins walks. N was in great spirits all day.
31	Fri					1 x 1min(h)			1.8	2.3	5.8	4.8	N went bowling today. She was very tired today.
1	Sat		1 x 14min cluster (l)			1 x 23 secs(m)	1 x 4min 30secs (h)		2.1	2.7	5.6	4.8	N went swimming and had a seizure in the pool again. N was tired for the rest of the day.
Total		0	1 x cluster	0	1	3	3 +1 x cluster						

Thorough record keeping ….essential to support 'fine tuning' & optimisation

Fine tune to:

- **Optimise seizure and symptom control**
- Adjust level of ketosis
- Maintain stable blood glucose

Tuned In

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Clinic Monitoring; 3 / 6 / 12 Months

- Review seizure control and ketone levels
- General diet review (6 monthly nutritional analysis)
- Review medication
- Height and weight checks
- Head circumference & mid arm circumference
- Blood screen / urine if due
- General health and well being

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SUMMARY

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- Ketogenic therapy can be effective in the management of difficult epilepsy and associated symptoms.
- Can work for infants , children & adults
- Requires significant change to food choices and meals.
- It requires (experienced) dietetic & medical support to initiate and optimise outcomes.
- Treatment lasts 3 months – 2years
  …some longer

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Paleologou, Eleni, Naila Ismayilova, and Maria Kinali. Ed. Iain P. Hargreaves. *Journal of Clinical Medicine* 6.6 (2017): 56. *PMC*.

Thank you for listening!

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