LRI Children's Hospital

# Management of Children on Ketogenic Diet for Epilepsy

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|---|---|
| Staff relevant to: | Health professionals caring for children with epilepsy being managed on a ketogenic diet. |
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## Contents

## 1. Introduction and Who Guideline applies to

The ketogenic diet (KD) is a high-fat, low carbohydrate and adequate protein diet used in the management of childhood epilepsy. It is a therapeutic diet which has been shown to improve seizure control in patients with drug resistant epilepsy. [1]

**Related Documents:**
This guideline needs to be used in conjunction with relevant infection control and consent policies to ensure the child receives safe care and children and families are able to understand the reasons for care to facilitate co-operation.

The dietitian will work in line with the -

UHL C22/2017 - Clinical Guideline on the Dietary Management of Children with Intractable Epilepsy Treated with Ketogenic Diet. Ketogenic Diet for Children with Epilepsy UHL Dietetic Guideline

**How does the ketogenic diet work?**

Usually, the body uses glucose from carbohydrates found in foods like fruit, vegetables, sugar, bread, rice and pasta for its energy source. In the KD, the body's energy source comes from using fat instead of glucose. Ketones are made when the body uses fat as its source of energy. This is called 'ketosis'.
For some people with epilepsy, seizures are greatly reduced or prevented when the body makes ketones.

**There are different forms of KD regimes: [Appendix A]**

- The Classical KD
- The Medium Chain Triglyceride diet (MCT diet)
- The Modified Ketogenic Diet (MKD)

## 2. Ketogenic diet is indicated for:

See also (NICE 2022)

### 2.1 Children whose seizures fail to respond to at least 2 antiepileptic medications in therapeutic doses

**2.1a For certain epilepsy syndromes**
**Epilepsy syndromes and conditions where KDT is more beneficial (>70% seizure reduction than average) [2]**

- Dravet syndrome
- Epilepsy with myoclonic–atonic seizures (Doose syndrome)
- Febrile infection–related epilepsy syndrome (FIRES)
- Infantile spasms
- Ohtahara syndrome
- Super-refractory status epilepticus
- Tuberous sclerosis complex
- Formula-fed (solely) children or infants
- Angelman syndrome

**2.1b Conditions where KDT moderately beneficial (>50% seizure reduction) –** (arranged alphabetically) [2]

- Adenylosuccinate lyase deficiency
- CDKL5 encephalopathy
- Childhood absence epilepsy
- Cortical malformations
- Epilepsy of infancy with migrating focal seizures
- Epileptic encephalopathy with continuous spike-and-wave during sleep
- Glycogenosis type V
- Juvenile myoclonic epilepsy
- Lafora body disease
- Landau-Kleffner syndrome
- Lennox-Gastaut syndrome
- Phosphofructokinase deficiency
- Rett syndrome
- Subacute sclerosing panencephalitis (SSPE)

**2.2 For children with metabolic disorders:**

- Complex 1 mitochondrial disorders
- Glucose transporter protein 1 (Glut-1) deficiency syndrome (Glut1DS)
- Pyruvate dehydrogenase deficiency (PDHD)

**2.3 For children who have intolerable and/or severe effects from antiepileptic medication**

**2.4 Contraindications to the use of KDT [2]**

- Absolute
  - Carnitine deficiency (primary)
  - Carnitine palmitoyltransferase (CPT) I or II deficiency
  - Carnitine translocase deficiency
  - beta-oxidation defects
  - Medium/Long / Short-chain acyl dehydrogenase deficiency (CAD)
  - Long/Medium-chain 3-hydroxyacyl-CoA deficiency
  - Pyruvate carboxylase deficiency
  - Porphyria

- Relative
  - Inability to maintain adequate nutrition
  - Surgical focus identified by neuroimaging and video-EEG monitoring
  - Parent or caregiver noncompliance
  - Propofol concurrent use (risk of propofol infusion syndrome may be
  - higher)

**2.5 Adverse Effects of Ketogenic Diet [2] [Appendix B]**

## 3. Referral letters should include the following information

- The patient's present medical condition and medical history
- Seizure type, severity and frequency
- Previous medication tried
- Dosage of current medication
- Patients feeding ability and route for nutrition (oral or enteral tube)
- Information on recent investigations e.g. Electroencephalogram (EEG)

- If the patient recently had or is awaiting Vagus Nerve Stimulation (VNS)
- If the patient is a candidate for neurosurgery
- Meet basic standards of documentation as outlined by the Patient Health Records - Documenting UHL Policy (in all media)' Trust Ref B30/2006.

**New patient referrals**

New referrals are discussed in the monthly paediatric KD MDT meeting. If appropriate, Children are invited to a pre-assessment clinic with the Consultant Paediatric Neurologist, Senior Specialist Dietitian and Epilepsy Specialist Nurse.

The diagnosis is confirmed and if appropriate the ketogenic diet is offered as a treatment option.

The efficacy of ketogenic diet, possible side effects, routine monitoring and the practicalities of undertaking ketogenic diet are discussed in detail. Written information is provided to support this.

The Dietitian assesses the child and takes into consideration age, weight, height, activity level, other co-existing medical conditions, feeding issues, neurological deficits and psychological issues before formulating the KD[18].

The Dietitian regularly reviews the patient's progress via telephone, fine tuning the KD to maintain/improve ketosis and optimize the possibility for seizure reduction/cessation[18].

Once the child is established on an effective and appropriate KD, weaning of the other AEDs is considered.

For further information regarding this process and multidisciplinary roles, refer to the 'Clinical Guideline on the Dietary Management of Children with Intractable Epilepsy Treated with Ketogenic Diet'.

## Monitoring

Regular multidisciplinary follow up clinics are held and attended by the Consultant Paediatric Neurologist, Specialist Registrar, Senior Specialist Dietitian and the Epilepsy Specialist Nurse.

Children on the ketogenic diet are reviewed in this clinic three months after commencing ketogenic diet and then every six months (or sooner if necessary) while on ketogenic diet.

Blood monitoring and urinalysis is carried out before the diet is initiated and then as described below or more frequently as clinically indicated. [2, 3] (Please see following tables below and section 6 for condition specific guidance on frequency of monitoring)

**Table 1: Investigations & Monitoring**

| **Blood Investigation** | **Frequency of monitoring** |
|---|---|
| **Essential:**<br>• Full blood count<br>• Fasting cholesterol & triglyceride<br>• Ferritin, amino acid profile<br>• U&E, bicarbonate, lactate, albumin<br>• Urate<br>• Liver function tests<br>• Calcium, phosphate<br>• Magnesium<br>• Glucose<br>• Free and total Carnitine<br>• Acylcarnitine profile<br>• Vitamin A, D & E<br>• Zinc, Selenium, Copper<br>• Anti-convulsant level | Baseline, 3 months, 6 months and then every 6 months.<br>Additionally at 6 weeks for infants under 2 years old |
| • Clotting screen | Baseline only |
| **Recommended:**<br>• Blood ketones<br>• Free fatty acids | Baseline, 3 months, 6 months, and then every 6 months. |
| **Optional:**<br>• Folate<br>• Vitamin B12 | Baseline, 6 months, then every 6 months.<br>Baseline, then every 12 months. |
| **Urine Investigation** | **Frequency of monitoring** |
| • Calcium:Creatinine ratio | Baseline, 6 months, and then every 6 months. Additionally at 6 weeks for infants under 2 years old |
| • Amino Acids<br>• Organic Acids | Baseline only |

The Senior Specialist / Senior Paediatric Ketogenic Dietitian will aim to manage the biochemistry where possible through the use of food and dietary changes; and if necessary additional nutritional supplements or an increase in the vitamin and mineral preparation may be necessary.

Where dietary manipulation is not likely to be sufficient, the Consultant Paediatric Neurologist may need to arrange a prescription. This may include but is not limited to

- Iron and Vitamin D supplementation
- Potassium Citrate for raised urinary calcium:creatinine ratio, indicating an increased risk of renal stones.
- Carnitine supplementation. Carnitine is essential for the transport of Long chain triglyceride (LCT) fat to the cells to be broken down so Carnitine deficiency is theoretically more likely to occur on a classical or modified KD than on an MCT ketogenic diet.

## 4. Possible Side Effects of the Ketogenic Diet [2]

1. Vomiting, constipation, lack of energy, hunger and diarrhoea (these can generally be resolved with dietary manipulation).
2. Elevated serum lipids.
3. Excess ketosis and acidosis.
4. Long term vascular outcomes of KD are unknown.
5. Renal stones.
6. Impairment / delay in growth.
7. Compromised bone health. [17]

**Table 2: Additional Monitoring for Adverse Effects:**

| | |
|---|---|
| Consider DEXA scan | If on KD for >2y & 1 year later (if 1st scan is abnormal) |
| Renal USS | At 1 year on KD and annually thereafter |
| ECG (if family history of cardiovascular disease) | Before starting |

## 5. Principles of Management for Inpatient Admissions

**Inform Neurology team (by switchboard) and Specialist Dietitian (ext 15400)**

- Bloods *FBC, U/E, bicarbonate, blood gas, lactate, LFT, blood and urinary ketones, infection screen*
- Standard target ketones 2-5mmol/l. Some children will have their upper or lower ketone thresholds changed on review by the KD team due to individual response to ketosis. If individual ketone thresholds are unknown then a range of 2 – 5mmol/l should be used.
- Target blood glucose 2.5 mmol/l and above
- Choose appropriate IV fluids depending on ketone and blood glucose levels
- Do not start a non-ketogenic diet enteral feed, maintain on IV fluids until Dietitian reviews and calculates a suitable ketogenic feed recipe – there is no standard ketogenic feed for these patients.
- At evenings and weekends when a dietitian is not available parents/carers can order food from the Ketogenic/Metabolic Diet Loose Foods Menu to achieve their usual KD prescription. This is available via catering.
- Medications: Choose the lowest carbohydrate form possible (generally dissolvable/crushable tablets or powder preparations). Contact Pharmacists via dialling #6737
- Contact Medicines Information (LRI ext 16191/16491) to begin checking the carbohydrate content of medications

## 6. Inpatient Management of Children on Ketogenic Diet [5]

(Adapted from Ketogenic Diet in the management of Epilepsy; Clinical Guidelines. Great Ormond Street Hospital)

### 6.1) Gastrointestinal or Intercurrent Illness

- Medications: Choose the lowest carbohydrate form possible (generally dissolvable/crushable tablets or powder preparations) Contact Pharmacists via dialling #6737
- Medicine Information (LRI ext 16191/16491) to begin checking the carbohydrate content of medications
- If the child is unwell: medical assessment and urgent bloods to include *FBC, U/E, bicarbonate, blood gas, lactate, LFT, blood ketones, blood glucose, infection screen.*
- On admission refer to the specialist dietitian electronically via the ICE system.
- If the patient is fed solely via NGT or PEG order 1 x 400g tin of Polycal powder from pharmacy for treatment of hyperketosis and/or hypoglycaemia
- Check blood glucose and blood ketones 4 or 8 hourly (at discretion of clinician). Maintain blood glucose above 2.5 mmol/l
- Maintain blood ketones less than 5 mmol/l (refer to sections 6.2- 6.3 below) for treatment of hypoglycaemia and hyperketosis)
- Offer clear fluids as frequently as tolerated that are low in carbohydrate, e.g. water or sugar free squash. Dioralyte can be used if necessary but discuss with the Dietitian first as it contains glucose
- The Dietitian will arrange special meals or enteral feeds if required for the patient.
- If the child is usually enterally fed, Milk Kitchen will prepare the child's usual feed recipe.
- When symptoms (diarrhoea, vomiting) subside, the diet can be reintroduced at a quarter to half of all daily exchanges (parents will know their child's daily exchanges for fat, protein and carbohydrate). If this is tolerated the exchanges can be increased gradually as able. The medium chain triglyceride fat (MCT); Liquigen or MCT oil can be reintroduced slowly. The Dietitian will provide an individual plan for the patient. If at any stage the symptoms recur, there should be a return to the levels previously tolerated.

### 6.2) Hyperketosis (Ketones >5mmol/l)

**Target blood ketones 2-5mmol/l**

**Aim is to provide some carbohydrate to stop excess ketosis**
Occasionally ketones can become too high. This may occur after starting the diet, if the diet has recently been modified or during illness. Some children already established on the ketogenic diet may have had their carbohydrate treatment dose changed on review by the KD team due to individual response. If individual treatment doses are unknown then use doses suggested below.

**Signs of excess ketosis:**
- rapid, panting breath (Kaussmaul breathing)
- increased heart rate, facial flushing
- irritability
- vomiting

**Oral treatment**

A. **For Children older than 1 year and over 9kg:** Give 5g carbohydrate by giving 1 teaspoon of sugar or 2 teaspoons jam or 50ml 10% polycal solution (see below).

B **For infants under 1 year or under 9kg:** Give 2g – 4g carbohydrate[3] as 20 – 40ml 10% polycal solution (see below).

- Recheck ketone levels in 20 minutes, if there is inadequate response the same treatment can be repeated.
- Recheck ketone levels again in 20 minutes, if ketones are not back in the target range; IV fluids will be necessary – 5% glucose with 0.9% sodium chloride solution. See section 6.4 for further information.
- If oral fluids are not tolerated because of vomiting, intravenous fluids 5% glucose with 0.9% sodium chloride, given as maintenance fluids, are required. See section 6.4 for further information.
- If IV fluids are required to correct ketone levels then these children will require admission and bloods as listed in table1.

**Nasogastric tube (NGT ) or Gastrostomy (PEG) treatment**

Follow the steps above for oral treatment and use 10% Polycal solution as the source of carbohydrate, given as a flush via the NGT or PEG. If using a jejunostomy feeding tube then give the 10% polycal solution slowly and with caution.

**10% Polycal Solution**
- Prepare 10% polycal solution by making 1 level scoop of polycal (available via pharmacy) up to 50ml with water

**If ketones are below 2mmol/l. No immediate action required – Dietitian will adjust the diet if possible to optimise ketosis.**

### 6.3) Symptomatic Hypoglycaemia or Blood Glucose <2.5 mmol/l

**Target blood glucose: Above 2.5 mmol/l**

**Aim is to provide some carbohydrate to increase blood glucose levels**
Some children already established on the ketogenic diet may have had their carbohydrate treatment dose changed on review by the KD team due to individual response. If individual treatment doses are unknown then use doses suggested below.
Occasionally blood glucose levels drop below 2.5 mmol/l, usually as a result of illness.
Check Lab blood glucose and do a finger prick test every 2-4 hours.

**Symptoms of hypoglycaemia;**
- dizziness, confusion
- aggressive behaviour
- sweating, pallor
- cold and clammy

**Oral treatment**

A. **For Children older than 1 year and over 9kg:** Give 10g carbohydrate by giving one of the following; 2 teaspoons of sugar or 4 teaspoons of jam or 100ml 10% Polycal solution (see below) or
B. 1 tube of 40% Glucogel or Dextrogel (10g glucose per 25g tube) can be squeezed into child's mouth if the child is uncooperative or not able to take oral liquids.**For infants under 1 year or under 9kg:** Give 2g – 4g carbohydrate[3] as 20 – 40ml 10% Polycal solution (see below).

- Recheck blood glucose again in 20 minutes, if it remains below 2.5 mmol/l; IV fluids will be necessary – 5% glucose with 0.9% sodium chloride solution. See section 6.4 for further information.
- If oral fluids are not tolerated because of vomiting, intravenous fluids 5% glucose with 0.9% sodium chloride, given as maintenance fluids, are required. See section 6.4 for further information.
- If IV fluids are required to correct ketone levels then these children will require admission and bloods as listed in table1.
- For patients with reduced level of consciousness or seizures. Give 5-10ml/kg of 10% glucose intravenously according to UK Resuscitation Council guidelines.

**Nasogastric tube (NGT) or Gastrostomy (PEG) treatment**

- 

Follow the steps above for oral treatment and use 10% Polycal solution as the source of carbohydrate, given as a flush via the NGT or PEG. If using a jejunostomy feeding tube then give the 10% polycal solution slowly and with caution.

**10% Polycal Solution**

- Prepare 10% polycal solution by making 2 level scoops of polycal (available via pharmacy) up to 100ml with water

### 6.4) Choice of IV fluids if required

**Target blood glucose: Above 2.5 mmol/l  Target blood ketones 2-5mmol/l**

**If ketones and blood glucose are "within the target" range**

- Use 0.9% sodium chloride
- An infant should not be nil by mouth and without IV glucose for more than 6 hours.[3]
- Check ketones 2-4 hourly, if ketones are rising always check glucose (in addition to ketones) if on IV fluids (as likely ill, feed withheld etc.).
- If ketones are decreasing below the ideal range of 2-5 mmol/l – no immediate action required.
- Inform the Dietitian and check if any new medications introduced have high levels of carbohydrate and switch preparation to reduce the carbohydrate level if possible.

**If ketones are high (hyperketosis >5mmol/l) and/or blood glucose is low (hypoglycaemia < 2.5mmol/l)**

- Use 5% glucose with 0.9% sodium chloride solution
- Check ketones and blood glucose 2 hourly
- Once ketones have decreased to less than 4.0mmol/l and blood glucose is above 2.5mmol/l change IV fluids to 0.9% sodium chloride if IV fluids are still required otherwise return to previous KD plan. Otherwise ketosis may be lost and any positive effect of KD on seizure control will be lost. An infant should not be nil by mouth and without IV glucose for more than 6 hours.[3]

### 6.5) Sedation for Procedures and General Anaesthesia [6,7]

- Inform Paediatric Neurology team (via switchboard) and Specialist Dietitian (ext 15400)
- Medications: Choose the lowest carbohydrate form possible (generally dissolvable/crushable tablets or powder preparations) Contact Pharmacists via dialling #6737
- Contact Medicines Information (LRI ext 16191/16491) to begin checking the carbohydrate content of medications
- Ensure the patient is first on the morning surgical list to reduce the risk of hyperketosis and hypoglycaemia
- Test blood glucose and ketones 4 or 8 hourly (at discretion of clinician)
- Take bloods: FBC, U/E, bicarbonate, LFT, urinalysis, blood gas, glucose, lactate.
- For general anaesthetic, keep NBM for normal recommended time period
  (Food 6 hours and clear fluids for 1 hour)
- If IV fluids are required give 0.9% Sodium Chloride unless hyperketotic or hypoglycemic
- If anaesthetic is >3 hours monitor blood glucose and blood gas (PH and bicarbonate) 1-2 hourly.
- Consider Sodium bicarbonate if increase in acidosis.
- If fasting beyond 12 hours or blood glucose < 2.5 mmol/l use 5% glucose with 0.9% sodium chloride solution to maintain blood glucose between 2.5 and 4 mmol/L.
- Reintroduce normal ketogenic diet as soon as possible.

### 6.6) Children on Ketogenic diet admitted to PICU

- Inform the Specialist Dietitian on extension 15400 and the Paediatric Neurology team via switchboard.
- See section 6.4 for choice of IV fluids
- Monitor blood glucose levels and blood gas 1-2 hourly as appropriate
- Monitor ketone levels 4 hourly, excess ketosis and acidosis may require treatment with IV sodium bicarbonate
- A base excess of -10 indicates significant metabolic acidosis and should be half corrected over 4 hours with IV sodium bicarbonate.
    - If acidosis is explained by excess ketosis, glucose containing maintenance fluids would be appropriate.
    - If acidosis is not completely explained by excess ketosis i.e., high blood lactate this requires further advice from the Metabolic Team.
- Medications: Choose the lowest carbohydrate form possible (generally dissolvable/crushable tablets or powder preparations) Contact Pharmacists via dialling #6737
- Contact Medicines Information (LRI ext 16191/16491) to begin checking the carbohydrate content of medications
- Enteral feeding: Inform the Specialist Dietitian on extension 15400. If the child is usually gastrostomy or NGT fed the Milk Kitchen will provide the child's usual ketogenic feeds for you. It is essential that the parents or dietitian provide the latest dietary prescription to the milk kitchen to avoid using a previous plan. If the patient is usually orally fed and requires NGT feeding the Dietitian will calculate an appropriate ketogenic enteral feed recipe (note there is not a standard ketogenic enteral feed that can be used as a starter plan for these patients).

## 7. Formulation of Medication:

7.1 Levetiracetam Granules (Desitrend) are a low-Carbohydrate preparation for those children on Levetiracetam liquid formulation.

7.2 In case of emergencies, kindly give anti-epileptics / antibiotics IV formulation so Carbohydrate content of the medication does not become an issue at that time of emergency.

7.3 Paracetamol & Ibuprofen formulations (while child on Ketogenic Diet) **(See Appendix C)**

## 8. Education & Training

None

## 9. Monitoring Compliance

None currently identified

| What will be measured to monitor compliance | How will compliance be monitored | Monitoring Lead | Frequency | Reporting arrangements |
|---|---|---|---|---|
| | | | | |

## 10. Supporting References


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19. Clinical Guideline on the Dietary Management of Children with Intractable Epilepsy Treated with Ketogenic Diet (KD) V1 Approved by CSI Quality & Safety meeting on 10/05/2017 Trust Ref: C22/2017

UHL Intravenous policy B25/2010

UHL Hand hygiene policy B32/2003

UHL Personal protective equipment guideline B9/2004

UHL Sharps policy B8/2013

UHL Infection prevention policy B4/2005

## 11. Key Words

Blood Glucose, Dietitian, Hyperketosis, Hypoglycaemia, Ketogenic diet, Ketones, Epilepsy

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**The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.**
**As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.**

| Contact and review details | |
|---|---|
| **Guideline Lead:**<br>Dr Rajib Samanta FRCPCH(UK), MRCP(UK), DCH(UK), CCT (UK)<br>Consultant Paediatric Neurologist | **Executive Lead**<br>Chief Nurse |
| **Changes made during review;**<br>Page 4 – Urine investigations, amino and organic acids monitored once as baseline only rather than every 6 months.<br>Page 9 6.4 IV fluids – if ketones are rising, blood glucose testing changed from 'begin to check BG' to always check glucose (in addition to ketones) if on IV fluids. If hyperketosis and/or hypoglycaemia, monitoring/treatment changed to - Once ketones have decreased to less than 4.0mmol/l (previously 3-4mmol/l) and blood glucose is above 2.5mmol/l change IV fluids to normal saline – added, 'if IV fluids are still required otherwise return to previous KD plan.'<br>Updated references<br>Converted all references to dextrose to glucose, and normal saline now 0.9% sodium chloride in line with Trust recommendations.<br>Added preceding 1 to all UHL extension numbers<br>Removed appendix B – indications and contraindications for Ketogenic diet as in the main body of the guideline section 2<br>Added appendix D – Ketogenic diet bloods<br>Added appendix E – Clinic assessment proforma | |

## Appendix A - Types of Ketogenic Diet:

### CLASSICAL KETOGENIC DIET (KD)

The classical KD is calculated in a ratio of grams of fat to grams of protein plus carbohydrate. It is the strictest of all of the KDs, in that it allows the least amount of carbohydrates alongside prescribed amounts of fat and protein. The fat source is usually long chain triglycerides (LCT). Children who are exclusively enterally fed will have their diets calculated as a classical KD and therefore expressed as a ratio. It is also the recommended choice in infants because of the greater level of control over constituents of the diet.

### MEDIUM CHAIN TRIGLYCERIDE (MCT) DIET

This diet has up to 60% of energy derived from MCT fat. MCT fats are thought to yield more ketones per kcal of energy than LCT. This increased ketone potential allows less total fat to be used, and slightly more protein and carbohydrate than the classical KD. However, MCT fat can cause gastrointestinal discomfort in some children. This diet is also more complex for families in its calculations than other KDs.

### MODIFIED KETOGENIC DIET

Carbohydrate is restricted to 10-20g daily so generally a lower allowance than on the MCT KD. Uniquely, protein foods which are not sources of carbohydrate are not restricted and do not have to be weighed or measured making this the most liberal KD. A recommended number of fat choices are prescribed at UHL, although not all centres in the UK give specific advice on the quantity of fat to consume. Some centres simply encourage high fat foods at every meal. Quantified advice on fat is given at UHL to support parents to understand the very large amounts of fat required and to facilitate effective manipulation of the diet when required. MCT fats can be incorporated into the modified KD to increase ketones.

## Appendix B: Adverse Effects of Ketogenic Diet [2]

- Gastrointestinal system and are often seen during the initial few weeks of dietary therapy. Constipation, emesis, and abdominal pain may occur in up to 50% of children. These symptoms are usually mild and easy to correct with minimal interventions. When adequately managed and prevented, gastrointestinal side effects are rarely a reason to discontinue KDT.

- Hyperlipidemia is a well-known side effect of almost all KDT. Increased serum triglycerides and total and low-density lipoprotein (LDL) cholesterol levels have been reported in 14–59% of children on the classic KD. Hyperlipidemia can be seen as early as the first month of therapy. An early increase in serum lipids during the first months of KDT, this increase is usually temporary. In one study, 60% of those on the classic KD had hypercholesterolemia (>200 mg/dl). By 12 months, the serum lipid values often normalize and remain within normal limits. Strategies to prevent KD-induced hyperlipidemia include increasing consumption of MCT and olive oil, supplementing with omega-3 fatty acid or carnitine while decreasing the intake of trans fat, saturated fat, and cholesterol; decreasing the KD ratio; and excluding all fatty meats, egg yolk, cream, butter, animal fat, palm oil and coconut oil; and using a solely formula-based KD.

- Risk for coronary artery disease may increase with long-term elevations of cholesterol levels, previous paediatric studies showed no change in the carotid intima-media thickness compared to baseline at 6 and 12 months of therapy. Nevertheless, long-term vascular outcomes of this high fat diet are not known.

- Renal calculi occurs in approx. 3–7% of children on KDT. They typically do not require KDT discontinuation and lithotripsy is necessary only rarely. As previously stated, oral citrates appear to help prevent stone formation.

- Growth - There is mixed data on the effect of KDT on growth in children. However, all six studies with longer than 6 months duration indicate that the classic KD has negative effects on growth, and over time may cause a height deceleration. One retrospective review described 86% with slowed growth, and this effect was not related to age, KD duration, protein, or calorie intake. A prospective study of 237 children found that the while older children grew “almost normally,” younger children had more difficulties. A small change in protein, offered by the MCT diet, does not seem to result in better growth.

- Cardiac abnormalities have been reported in children on the KD, including cardiomyopathy and prolonged QT interval. The mechanism of these complications is not fully understood; one case was associated with selenium deficiency, but others were not. Routine ECG is not recommended at this time as a screening test.

- Pancreatitis has also been reported.

- Hepatic dysfunction may be more likely to occur in children who are on both valproic acid and KDT, with intercurrent viral illness furthering increasing the risk of elevated transaminases.

- Long-term complications in children maintained on KDT for >2 years;
  - Higher risk of bone fractures
  - Kidney stones
  - Decreased growth
  - Dyslipidemia is theoretically possible, but was not identified.

Conclusions:

- Like all medical therapies KDTs have potential adverse effects.
- Overall, the risk of serious adverse events is low;
- KDTs do not need to be discontinued for most adverse effects.
- Gastrointestinal complaints are often the most common but can be mostly remedied.

## Appendix: C – Paracetamol & Ibuprofen preparations

***PARACETAMOL:***

CALPOL SIX-PLUS (FASTMELTS) TABLET (250 mg)
Or **Crushable Paracetamol** tablet

……. Tablets to be dissolved in …… mls water.
…….. mls of that solution ( mgs) to be taken 4 (FOUR) times daily or as required.

***IBUPROFEN:***

NUROFEN MELTLET TABLETS (200mg)

…… Tablets to be dissolved in ……. mls water.
…….. mls of that solution ( ……mgs) to be taken 3 (THREE) times daily or as required.

The doses above will need to be reviewed as your child's age changes.

Parents might have these medications at home.

Hence need to remind the parents so they bring those special preparations from home.

These preparations are the preferable choice of Paracetamol and Ibuprofen to minimise the carbohydrate content from these medicines.

Additionally, these will provide a formulation which is dispersible and easy to administer to a child orally or via an enteral feeding tube.

## Appendix D: Ketogenic Diet Bloods

| **Form 1** : TEST Venous Blood | Sample Required |
|---|---|
| 3-OH BUTYRATE | 1 single YELLOW paediatric bottle |

| **Form 2** : TEST Venous Blood | Sample Required |
|---|---|
| Lactate | Both samples can be done from 1 single YELLOW paediatric bottle on ICE straight to lab |
| Glucose | |

| **Form 3** : TEST Venous Blood | Sample Required |
|---|---|
| Acylcarnitines | 1 single ORANGE paediatric lith hep bottle<br>(Nb free and total carnitine removed on advice from Elaine Maddox) |

| **Form 4** : TEST Venous Blood | Sample Required |
|---|---|
| Vit A<br><br>SE<br><br>Drug LEVEL eg sodium valproate, phenytoin if requested by Dr Samanta | ALL SAMPLES can be done from 3 BROWN paediatric bottles<br>White-topped plain gel-free serum tube (S-Monovette Serum, 4.9 mL, cap white) |
| Amino Acids ***AT BASELINE ONLY*** | 1 paediatric orange lith hep bottle |

| **Form 5** : TEST Venous Blood | Sample Required |
|---|---|
| INR ***AT BASELINE ONLY*** | 1 paediatric green bottle (1.4mls) |
| FBC | 1 paediatric red EDTA bottle |
| U & E, LFT, Bone Profile,<br>Fasting Chol/trig/HDL<br><br>Bicarbonate<br>Urate<br>Folate***AT BASELINE ONLY***<br>Ferritin<br>Vit D<br>Vit B12 ***AT BASELINE ONLY*** | <br>Take bloods 2 hours fasted<br><br>These could all be done out of 2 FULL brown bottles<br><br>If you have the possibility of getting an extra brown bottle here it would be good as VIT B12 and D require a good sample. |

| **Form 6** : TEST urine | Sample Required |
|---|---|
| ca:crea (request as Ca and Creatinine seperately)<br>Organic acids ***AT BASELINE ONLY***<br>Amino Acids ***AT BASELINE ONLY*** | Urine<br>*To be at lab within 1 hour of sample being taken |

State on Form 6 (under clinical details) which AEDs patient is on e.g. valproic acid, as these can affect levels in urine

**Ketogenic Diet Bloods**

- The bottles MUST be FULL.
- **The nature of the specimen should always be marked V.B or Venous blood not SERUM** as Sheffield lab will send back samples where forms are incorrectly labelled as SERUM.
- ALL on Combined CHEM PATH Request forms.

**Drug Levels:**

If patients are on the following anti-epileptic drugs add the drug name to Form 4 under other.

| Drug name | (Brand Names) | Drug name | (Brand Names) |
|---|---|---|---|
| Sodium valproate | Epilim | carbamazepine | Tegretol |
| Levetiracetam | Keppra | oxcarbazepine | Trileptal |
| Topiramate | Topamax | phenobarbitone | N/A |
| Lamotirigine | Lamictal | phenytoin | Epanutin |

## Appendix E: Assessment Clinic for Ketogenic Diet (Proforma)

Assessment Clinic for Ketogenic Diet (Proforma)

Keto Diet Started;……; Date of review;……..

| | |
|---|---|
| **Name:**<br><br>**DOB:**<br><br>**Hospital No:**<br><br>**Tel:** | **Weight:**<br><br>**Height:**<br><br>**OFC:**<br><br>**School:** |
| **Diagnosis / Epileptic syndrome /specific Clinical conditions** | **Past Medical History:** |
| **Complications:**<br>Drowsy / Lethargy<br>Irritable<br>Hyperactivity<br>Poor attention<br>Diarrhoea<br>Constipation<br>Vomiting | **Anti Epileptic Medications + Others** |
| **Compliance:** | **Last changes in Medication:** |
| **Sleep Hygiene** | |
| **Hyperketosis:** | **Medications used / stopped in the past** |
| **Hypoglycaemia** | |

**Current Seizure Descriptions**

| Seizure Type | Per Day | Per week | Per month | Per year |
|---|---|---|---|---|
| Tonic | | | | |
| TC | | | | |
| Myoclonic | | | | |
| Spasms | | | | |
| Atonic/Drop attacks | | | | |
| Head drops | | | | |
| Absences (Typical) | | | | |
| Absences (Atypical) | | | | |
| Complex partial Sz | | | | |
| Auras | | | | |
| | | | | |

**Semiology of each type of seizure:**

**MRI**

**EEG**

**Others Tests:**

**KD Therapy Annual Surveillance Tests:**
**RENAL USS date**

**Calcium : Creatinine Ratio:**

**Outcome of KD treatment:**

Seizure reduction:

Medication reduction

Cognition Behaviour change / improvement

Length of KD treatment at the assessment:

**Plan / Referral to other services**

**Keto Diet -** Weaned / Stopped / Continued

**Follow Up** - 3 month / 6 month,