Management protocol for maple syrup urine disease
(Branched-chain ketoacid decarboxylase deficiency)

This version of the protocol has been anonymised prior to being put on the Metabolic Unit Online Handbook. There is at present only one patient with maple syrup urine disease in the Edinburgh area. Her outpatient care will continue to be provided in Glasgow, but she is a student at Edinburgh University, and this protocol is intended to provide guidance in the event that she needs in-patient care. If she requires admission she should bring with her a non-anonymised copy of the protocol which provides further contact details etc.

Background information

Maple Syrup Urine Disease (MSUD) is due to a deficiency of an enzyme common to an early step in the metabolism of the aminoacids leucine, Isoleucine and Valine. Special dietary measures are required at all times to minimise the body’s defence dependence on this non-functional metabolic pathway.

Patients with this disorder require nutritional therapy to restrict the dietary intake of these 3 aminoacids, and maintain blood levels of these aminoacids at about 2 to 3 times normal (400µmol/l for leucine). An adequate energy intake from carbohydrate is required at all times.

When well, this patient has normal blood levels of leucine, isoleucine and valine.

Illness will be episodic, and may be precipitated by intercurrent infections, fasting or an increase in the intake of natural protein from food. PROMPT ATTENTION TO MANAGEMENT AT THIS STAGE IS IMPORTANT SINCE IT CAN PREVENT DETERIORATION, WHICH CAN BE RAPID AND CATASTROPHIC. Without treatment blood concentrations of these aminoacids (particularly leucine) will rise to high and toxic levels (above 700µmol/l for leucine) and cause ataxia, drowsiness, vomiting and other signs of encephalopathy. There may be ketosis and dehydration. URGENT TREATMENT AS IN THIS PROTOCOL IS THEN REQUIRED.

Hypoglycaemia is unusual. Hyperammonaemia does not occur.
Management protocol

Day to day management
- Dietary protein is restricted to about 30g daily.
- Supplementary aminoacids are taken as 3 sachets per day of MSUD cooler, an aminoacid mixture containing all the significant nutrient aminoacids, except leucine, isoleucine and valine, and supplying the appropriate daily recommended vitamins and minerals.
- An energy supplement as 1 carton (200 ml) Maxijul liquid, providing 100 g glucose polymer.

MSUD cooler is supplied in ready mixed sachets to be shaken and drunk, and divided evenly through the day. Maxijul can be taken from the carton, or diluted and flavoured.

Blood levels of leucine, isoleucine and valine are measured regularly (ideally weekly) using dried blood spots on a card (Guthrie card) in the laboratory at the Royal Hospital for Sick Children, Glasgow.

The laboratory of the Royal Hospital for Sick Children, Edinburgh, will be able to analyse small liquid blood samples collected in a capillary tube, if required, or plasma from larger samples of blood.

Management during intercurrent illness, or if symptoms develop
- The intake of natural protein is stopped.
- MSUD cooler is continued, if possible taking 4 sachets instead of the usual 3. This may be sipped slowly through the day to minimise the risk of nausea and vomiting.
- Maxijul liquid (supplied as a 50% solution) can be diluted to a concentration of 15% - 20% and taken liberally. Other appropriate drinks can be taken freely, but should contain glucose or other from of sugar at 10-20% concentration, as, for example, apple juice, standard ribena, or standard lucozade. Laura should aim for a daily total fluid intake of up to 2 litres per day.

Most minor illnesses can be managed in this way at home, with gradual resumption of the intake of solid food and natural protein over about 48 hours.

Management of severe symptoms, or if anorexia or vomiting prevent an adequate intake of oral fluids
The patient will present herself to hospital if she cannot maintain an adequate fluid intake, or may present because of ataxia, confusion, reduced consciousness or even cerebral oedema.

Immediate care
Blood should be drawn for full blood count, urea and electrolytes and aminoacids. Test urine for ketones (acetoacetate) as resolution of ketosis is a good guide to the adequacy of energy and fluid replacement. Check a capillary blood gas (although severe acidosis is unusual). Discuss the aminoacid measurement with the laboratory as, depending on the urgency of the result you may have a choice of methods and sample requirements: (dried blood spots, blood in a capillary tube, plasma).

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It may not be possible to maintain an adequate intake by drinking or vomiting may prevent oral intake. If so:

- Ondansetron may be given as an antiemetic (up to 8mg IV as required: see BNF)
- A nasogastric tube should be passed. This can be used to provide 2 litres per day of “emergency regime enteral fluids”* (see below) PLUS 4 sachets per day of MSUD cooler.
- MSUD Cooler can be added to the emergency regime fluid, or can be given separately.

If vomiting prevents a large enough enteral intake, give intravenous fluids providing 10% glucose (this may be higher if a large central vein is used) and 37.5mmol/l NaCl and 20mmol/l KCl in each 500ml to provide approximately 2 litres per day (this amount will vary if there are deficits to be replaced, or ongoing losses).

Every effort must be made to continue MSUD cooler enterally, as IV (parenteral) aminoacid solutions which do not contain leucine, isoleucine and valine are obtainable only with great difficulty, and with several days delay. This may mean giving MSUD cooler by itself or with a little dilution continuously by an enteral feeding pump, while intravenous glucose-electrolyte solution is given in parallel.

**Ongoing care**
The 3 branch chain aminoacids should be measured on alternate days (lithium heparin tube to RHSC; turn-round time approximately 24hr during the week; special arrangements required at weekends). Watch out for a fall in Isoleucine and valine to under 50µmol/l when leucine is still high. She may then need supplements of isoleucine and valine (initially 200mg of each, perhaps more) added to her MSUD cooler: otherwise leucine may remain high.

Natural protein should not be reintroduced until the blood leucine level is falling and is approaching comfortably below 400µmol/l, oral fluid intake is adequate, and there is no acetoacetate in the urine.

This patient usually has leucine, isoleucine and valine levels in the normal range when she is well.

About 10g protein in food per day can be introduced initially, increasing over 2-3 days to her usual intake of 30g.

4 sachets a day of MSUD cooler should be taken until 30g natural protein is reached; the amount may then be reduced to her usual 3 sachets per day.

**Emergency regime fluids**

These are intended to replace fluids, electrolytes and provide some energy as glucose. Lucozade (19% carbohydrate) or Ribena in cartons at 15-20% carbohydrate concentration (not Ribena “lite” or sugar free Ribena) may be used in short-term but will not provide any sodium or potassium.

To replace sodium or potassium you may use oral rehydration solution provided Maxijul has been added to make the final glucose concentration to 15 – 20% - ask your dietitian.
Contact details

This patient’s outpatient management will continue to be provided in Glasgow. More information can be obtained from:

**Dr Peter Robinson**  
Consultant Paediatrician in Metabolic Medicine, RHSC, Glasgow, G3 8SJ  
Tel: 0141 201 0243 (sec)  
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Tel: 0141 201 0000 (switchboard) for home phone or mobile phone  
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**Mrs Carolyn Dunlop**  
Metabolic Dietitian, RHSC, Glasgow, G3 8SJ  
Tel: 0141 201 0163  
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**General practitioner in Edinburgh is:**  
**Dr JM Richardson**  
Edinburgh University Health Service, 6 Bristo Square, Edinburgh EH8 9AL

**Advice can also be obtained from:**  
**Dr Peter Rae**  
Consultant Clinical Biochemist, Royal Infirmary, Edinburgh, EH16 4SA  
e-mail: peter.rae@luht.scot.nhs.uk  
Royal Infirmary telephone number 0131 242 6853 (secretary 242 6870)  
Western General telephone number 0131 537 1890 (secretary 537 1895)  
Or (out of working hours) via switchboard (0131 536 1000). Ask for the person on call for clinical biochemistry who should be able to make contact via home phone, mobile or pager numbers.

If hospital admission is required this will ideally be arranged through Dr Richardson, Dr Robinson or Dr Schwahn. Admission will be under the care of the consultants at the Metabolic Unit at the Western General hospital in Edinburgh. Since there will have been a preceding period of intercurrent illness it should be possible to arrange this during the working day, but there are clear precedents for the admission of acutely ill patients to specialist units at the Western General at other times. There is at all times a duty metabolic registrar or an on-call metabolic consultant who can be contacted via switchboard (0131 536 1000). The main point of contact is **Dr Mark Strachan**, but the other metabolic consultants **Dr John McKnight** and **Dr Paul Padfield** are also aware of this arrangement. Contact via switchboard.

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