## METABOLIC & ENDOCRINE DISTURBANCES

### Treatment of metabolic acidosis

in a haemodynamically stable baby:

where the base deficit ECF is >10 in a baby in whom there are no signs of hypovolaemia (such as increasing toe core gap, poor capillary refill) and no signs of hypotension;

where there is a base excess ECF of >10 the amount of bicarbonate which is given is a half correction which is calculated as folows:

**0.3 x base excess x baby's weight ÷ 2**

This is equivalent to the number of ml and half the number of millimoles of sodium bicarbonate that is required if 4.2% sodium bicarbonate is used (there is 0.5 mmol/ml of $Hco_3$ in 4.2%). This should be infused slowly at a rate of 1-2 ml/hr and no boluses of bicarbonate should be given over a period of <30 mins.

In small pre-term infants a figure of 0.4 is used because of the higher water content of the body (increased proportion of extra-cellular fluid).

1. Treatment of metabolic acidosis in a haemodynamically unstable baby:

   Differential diagnosis of metabolic acidosis in the pre-term include:

   a) hypoxaemia or ischaemia secondary to perinatal asphyxia

   b) severe lung disease

   c) volume depletion

   d) myocardial dysfunction caused by immaturity, sepsis or asphyxia

   e) severe acidosis caused by neonatal metabolic disorder is rare but must be considered.

   The most common causes in the haemodynamically unstable baby include hypovolaemia and hypotension.

   If there are signs of hypovalaemia - such as increasing toe core gap, worsening metabolic acidosis, poor capillary refill - the baby will need to be corrected with the appropriate fluid volume, blood if there is any anaemia (see transfusion protocol), or significant natural or iatrogenic blood loss, and possibly fresh frozen plasma if there is a coagulation defect and in very rare cases either albumin or normal saline solutions. If there is hypotension and there is no sign of hypovalaemia, it is possible that you may need to use ionotropes to counteract metabolic acidosis and hypotension (see hypotension protocol).

## Inherited Metabolic Disorder

SAMPLES TO COLLECT WHEN AN INHERITED METABOLIC DISORDER IS SUSPECTED IN AN ACUTELY ILL BABY/CHILD

The most useful samples are those taken at the time of admission, when acutely ill, and this opportunity should not be missed. If a non-metabolic diagnosis is made subsequently, samples for the special biochemical tests can always be discarded.

1) Samples for essential preliminary tests

Haematology: Full blood count, differential and platelets
Clotting studies if suspect liver damage (bleeding, jaundice, hepatomegaly)

Biochemistry:

**BLOOD** Arterial blood gases and acid-base status; biochemical profile, including electrolytes and liver function tests, plasma glucose and plasma amino acids.

**URINE** Must be saved for organic acids and amino acids. The best sample is the first urine passed at the time of acute admission. Diagnostic abnormalities often disappear quickly following intravenous glucose or other resuscitation. A urine bag should be applied at one and, if possible, at least 5 ml of urine collected. This should be placed in a sterile urine bottle. Smell it! Test it (on the ward) with a Multistix, or similar (note especially, pH, ketones, glucose) and with a Clinitest. Then send it straight to the laboratory or, if out-of-hours, freeze it (ice cream compartment of ward specimen fridge). The next sample of urine passed should be saved as well.

Other tests at the time of presentation may be indicated by the clinical features, e.g. plasma ammonium (unexplained intractable fitting; Reye's syndrome-like illness); plasma insulin, growth hormone, cortisol (hypoglycaemia).

2) Hypoglycaemia without obvious cause
- acute samples

(These do not apply to the majority of babies with 'common' neonatal hypoglycaemia!)

Blood for: glucose, insulin, growth hormone, cortisol, amino acids (with alanine quantification), 3-hydroxybutyrate, free fatty acids, liver function tests, lactate (if hepatomegaly). If possible, take 2 ml of 'spare' blood into a lithium heparin tube, which can be separated and stored for special tests (e.g. carnitine).

* The first urine passed must always be tested for ketones and stored for organic acid and amino acid analysis.

Urea and electrolytes and, perhaps, blood gas and acid-base status will be needed for management.

Plasma ammonium should be measured in cases with a Reye's syndrome-like illness. (Note: when the child has recovered from the acute episode, it may be very difficult to establish a diagnosis without recourse to a fasting test, with the associated risks.)

3) Children with suspected hyperammonaemia

Ammonium is measured usually when a urea cycle defect is a possible diagnosis. Ammonium should be measured in any <u>newborn</u> with unexplained lethargy, neurological disturbance, fits, vomiting or hyperventilation, especially if the baby was well initially, in the first 24-72 hours of life. (Significant values generally exceed 150 μmol/L).

**<u>Later</u>**, measurement is indicated in any child with a Reye's syndrome-like illness or unexplained coma, or with epijsodes of ataxia, vomiting, drowsiness, disorientation or bizarre behaviour, or severe epilepsy. (Significant values generally exceed 80 μmol/L).

* Samples should also be collected for the 'essential preliminary tests' (page 1).

4) Encephalopathic child with Reye's syndrome-like illness
Samples to collect

| | |
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| Features, typically: | effortless vomiting; increasing lethargy; irritability; drowsiness progressing rapidly to delirium and coma, sometimes with fits. |
| At presentation: | liver is usually enlarted; hypoglycaemia. A metabolic defect must <u>always</u> be considered: especially fat oxidation defects (e.g. MCAD deficiency); urea cycle defects; organic acid disorders. |

Blood for:
- ammonium
- glucose
- biochemical profile
- * 3-hydroxybutyrate and free fatty acids
- salicylate
- * carnitine
- lactate
- clotting studies

Urine for:
- ketones
- organic acids
- amino acids
- * orotic acid

* Analyses may be unnecessary after preliminary results available.

5) Acutely ill child who is dying
<u>in whom an inborn error is a strong possibility</u>
<u>Samples to collect</u>

1. Samples listed for essential preliminary tests (page 1). * Essential to collect

and freeze urine.

2. Consider need for plasma lactate: ammonium.

3. Take 2 or 3 ml of 'spare' plasma to be frozen, in case of need.

4. Also take 5 ml blood into an EDTA tube, to be saved for future DNA analysis. The whole blood (not to be centrifuged!) may be stored at $4^0$ C and sent as soon as possible to the local tissue culture laboratory. If forewarned, they will advise about, or supply, appropriate medium.

   In an emergency, skin biopsies may be kept overnight at $4^0$ C in a dry sterile container (tissue culture laboratories vary in their preference). **DO NOT FREEZE!**

   Sterility is of paramount importance in collecting biopsies, particularly post-mortem. Skin should be cleansed thoroughly with, e.g., Hibitane and then dried with an alcoholic swab.

   From a living baby - use local anaesthetic. The inner side of the forearm or the back of the arm, just above the elbow, are suitable sites.

   After death - collect two biopsies from different sites and place into separate bottle of media.

5. If non-ketotic hyperglycinaemia is a possibility, 0.5-1 ml of CSF should be frozen (plain tube). If a congenital lactic acidosis, 0.5-1 ml CSF into a fluoride tube.

6. In rare circumstances in which deficiency of a liver enzyme which is not expressed in fibroblasts is a strong possibility (e.g. some urea cycle defect; von Gierke's disease) liver biopsy should be collected. If to be collected immediately post-mortem, it is kinder to obtain parental consent before death.

Two or three needle biopsies of tissue should be taken, wrapped in aluminium foil, and snap frozen in liquid nitrogen or solid carbon dioxide. Samples should be stored frozen, as cold as possible ($-70^0$C, or in liquid nitrogen preferably).

If histology, electron microscopy, or cytochemistry are required, additional tissue should be placed immediately into appropriate preservatives.

6) Special biochemistry tests
Samples to collect

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| * Plasma ammonium: | 2 ml (minimum) blood into EDTA tube<br>Must reach the laboratory within 10 mins of collection |
| * Plasma lactate: | 2 ml (minimum) blood into fluoride tube (i.e. glucose tube)<br>Must be taken straight to laboratory |
| Plasma amino acids: | 1 ml blood into lithium heparin tube |
| Plasma free fatty acids: | 1 ml into fluoride tube |

Plasma for carnitine: 1 ml (minimum) into lithium heparin tube

CSF for glycine: 0.5-1ml into plasma tube

*CSF for lactate: 0.5-1ml into fluoride tube

Urine for organic and amino acids - at least 3 ml into a plain (MSSU) bottle. Send straight to laboratory during working hours. Freeze overnight if out-of-hours.
- if a dying child and very little urine, send whatever you can, however little!

Tissue culture fluid for skin biopsies - during working hours can be obtained from Histopathology, Level E, South Block.
- out-of-hours, put skin biopsies into a sterile (MSSU) bottle and keep at $4^0$C (**do not freeze**). Next day, contact the Cytogenetics laboratory at Guy's Hospital.

* These must only be sent after discussion with the laboratory, since they need imediate analysis.