Investigation and management of hypoglycaemia in children

Author: Dr Dunia Ismail / Dr Miki Lazner / David Annandale (prev additional authors Dr Amish Chinoy / Dr Dorothy Hawes)
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Background

- This guideline is for unexplained hypoglycaemia in children and does NOT cover the management of hypoglycaemia in children with Type 1 Diabetes Mellitus
- Once a diagnosis of the underlying cause of hypoglycaemia is made, a management plan should be followed for that condition

Persistent hypoglycaemia in the neonate, especially if associated with poor feeding / lethargy +/- fever – consider **disseminated herpes simplex virus (HSV) infection**. If high index of suspicion:
→ Take **blood** for HSV PCR and start aciclovir urgently. See **below** and the HSV guideline for further info

Definition

At RACH a **blood glucose <3.0mmol/l should be considered as hypoglycaemia** and requires further investigation and management.

Importance

In addition to the acute symptoms of hypoglycaemia, a low blood glucose can also cause neurodevelopmental problems in the long-term. **Thus the aim in managing hypoglycaemia is to prevent hypoglycaemic brain injury**.

Assessment

History
- Full birth history / issues in pregnancy or at birth / birth weight
- Any current illness / fevers?
- Relationship to fasting / feeding (How long after feeding? Relation to protein / carbohydrate feed? Relation to exercise?)
- Drug ingestion?
- Past medical history of prolonged neonatal jaundice or undiagnosed seizure disorder?
- Family history of unexplained deaths or consanguinity?

Examination
- Height and weight, genetic target for height
- LGA / SGA babies→ Consider Hyperinsulinism
- Dysmorphic features→ Consider syndrome associated with hypoglycaemia / hyperinsulinism
- Hyperpigmentation & hypotension → Consider adrenal insufficiency

- Hyperventilation → Consider metabolic acidosis (with respiratory compensation)
- Hepatomegaly, hypotonia → Consider inborn errors of metabolism
- Midline facial defects, microphallus → Consider pan/hypopituitarism
- Cataracts → Consider galactosaemia

Investigations – the "hypoglycaemia screen"

Blood samples must be taken at the time of hypoglycaemia (blood glucose < 3.0mmol/l).

Tests in **bold are the samples that **must** be taken for a hypo screen to be useful.
NB full screen costs £450 – please use sensibly

Blood

- Gas
- **Lab glucose** and lactate - fluoride oxalate sample, grey top *(if a lab glucose is not sent with the hypoglycaemia screen then the screen will be uninterpretable and therefore void)*
- U+E, LFT, CRP, FBC
- Ammonia (EDTA, purple top **on ice**)
- Blood culture, HSV PCR if suspicion of HSV infection (EDTA)
- **Insulin, C-peptide** *(for storage, only process if insulin undetectable or concerns regarding Munchausen's*) – clotted sample, yellow top **on ice**
- **BOHB (beta hydroxybutyrate**) – EDTA sample, purple top; **NEFA (non-esterified fatty acids**) – clotted sample, yellow top
- IGF-1, IGF-BP3 (clotted sample, yellow top)
- Cortisol, growth hormone (clotted sample), ACTH, glucagon (EDTA sample)
- Plasma amino acids (PAA) – Li Hep, green top
- Carnitines and Acylcarnitine (green Li Hep)
- Ethanol, sulphonylureas, salicylates (*only* if history suggests)

These bloods must be sent **immediately**, and **on ice**.
The laboratory (biochemistry) must be informed that these bloods have been taken, as some of them need to be processed urgently.

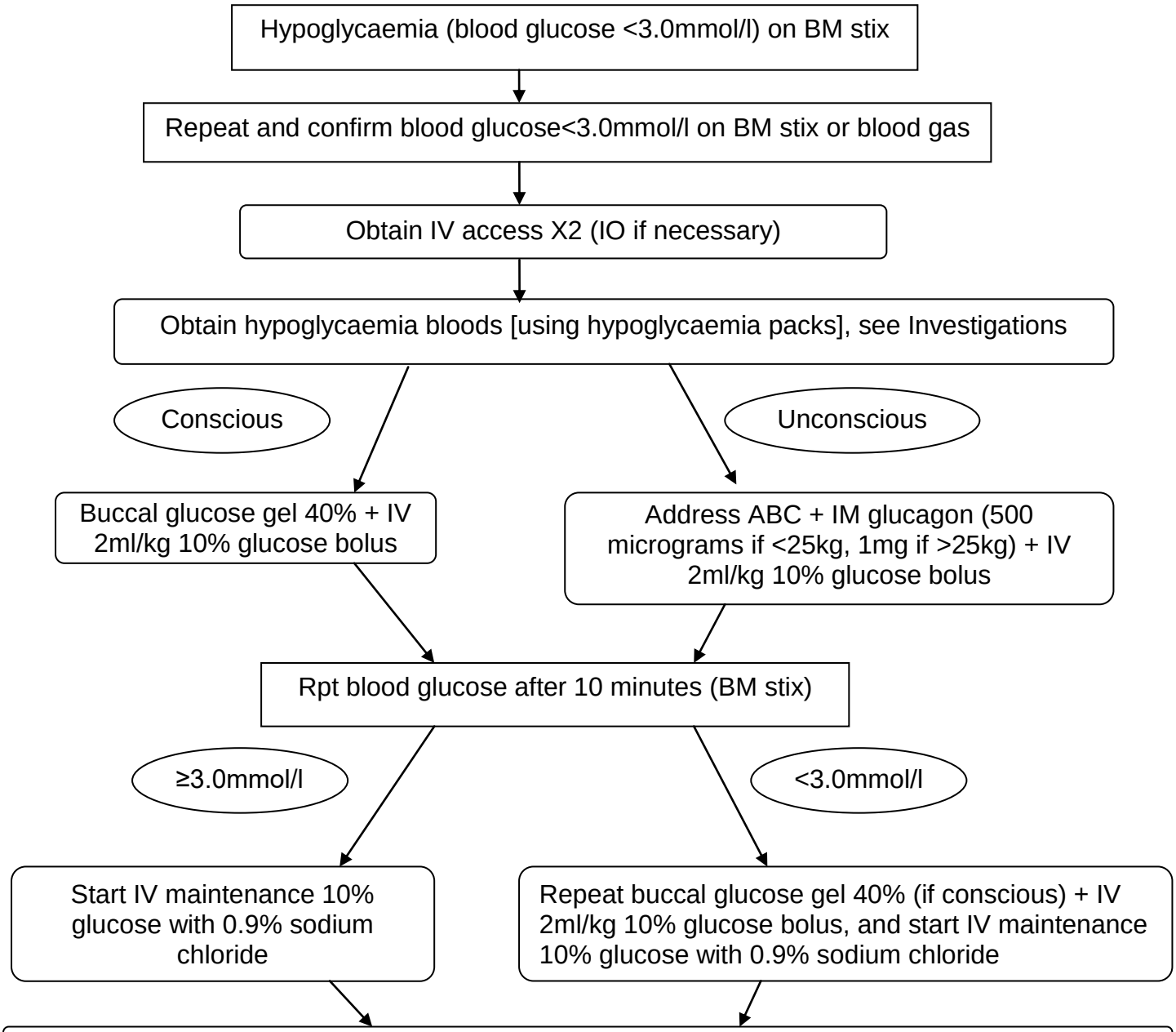
The volume of blood required depends on the size of bottle being sent.

Infants and young children (<12yrs of age): Use 1.3ml bottles **(Total volume = 15ml)**	√	Older children (>12yrs of age): Use adult bottles – if appropriate for child's size **(Total volume = 24ml)**	√
4 *full* yellow top bottles		3 *full* yellow top bottles	
4 *full* purple tops bottles		3 purple top bottles	
1 *full* grey top bottle		1 grey top bottle	
2 *full* green top bottle		2 green top bottle	

Urine (1st pass after hypoglycaemic episode – attach bag if difficulties):

- Organic and amino acids

Management



- Monitor blood glucose level for 24 hours
  - Hourly until three normal values have been obtained, then
  - Two-hourly until three normal values have been obtained, then
  - Four-hourly thereafter.
  - 30 minutes after any change in fluids.
- Aim to keep blood glucose ≥3.5mmol/l.
- If blood glucose <3.5mmol/l, increase rate of 10% glucose with 0.9% sodium chloride by 1ml/hr, up to a maximum of 120% of maintenance.
- After this, discuss with ward Consultant on-call regarding increasing the rate or concentration of glucose.

Glucose gel dose (0.3 g/kg)

Weight up to:	**10 kg**	**20 kg**	**30 kg**	**40 kg**	**50 kg**	**60 kg**
10 g (40%) **glucose gel** tube	½ tube	½ tube	1 tube	1½ tubes	1½ tubes	2 tubes

Calculation of glucose requirements:

Glucose Infusion Rate (mg/kg/min) = $\frac{\text{[Conc of glucose (\%) x Infusion rate (ml/hr)]}}{\text{[Weight (kg) x 6]}}$

Normal rate is <8mg/kg/min

- Maximum concentration of glucose to run peripherally is 10%
  - Risk of cutaneous and subcutaneous burns with higher concentrations if extravasation occurs.
  - Central access is needed for greater concentrations.

Switching to 5% glucose from 10% glucose:

- If BSL >10mmol/L on one occasion with a rising trend can switch to 5% glucose with 0.9% sodium chloride.
- BSL must then be checked 30mins post (as change in fluids) and if within normal limits, continue hourly for three normal readings, time interval then increasing as above.

Ongoing management

After 24 hours of treatment, if blood glucose levels are stable, monitoring can be 2-4 hourly.

Once BSL are stable, restart oral feeds. Regular monitoring of blood glucose levels is needed at that time.

Discussion with the appropriate speciality during working hours is needed whilst the child is an in-patient.

- For metabolic conditions, discuss with Dr Hildick-Smith or the Metabolic team at Evelina Children's Hospital
- For endocrine conditions and ketotic hypoglycaemia, or if the cause of hypoglycaemia is not clear or inconclusive, discuss with Dr Ismail (or Dr Kanumakala if Dr Ismail is unavailable).

Follow up

All children admitted with hypoglycaemia require follow up in Dr Ismail's endocrine clinic. **This includes those admitted to the short stay unit (SSU) with unexplained hypoglycaemia that resolves within 24 hours.**

Discharge with

1. **Locally approved Glucometer** – available from diabetes team or community nurses. Advise to check BSL during periods of illness
2. **SOS regime** – see **intranet guidelines**. Follow during next period of illness if BSL < 3.

If SOS not tolerated or BSL don't improve, advise parents to attend CED.

Notes

(Patho)Physiology

A normal blood glucose level depends on an intact endocrine system (insulin and counter-regulatory hormones), enzymes for glucose homeostasis, and an adequate supply of fat, glycogen and protein.
Therefore, hypoglycaemia occurs when there is an inappropriate presence of insulin, a deficiency of counter-regulatory hormones or too little glucose produced to match demand. It can occur during a period of fasting and/or intercurrent illness.

Symptoms & Signs

Autonomic: sweating, flushing, anxiety, palpitations, tremor, nausea and vomiting, tachycardia, pallor, peri-oral tingling
Neuroglycopaenic: impaired mental state, confusion, irritability, tiredness, poor feeding, behavioural change, hunger, drowsiness, lethargy, hypotonia, visual disturbance, bradycardia, apnoeas, seizures, coma, death

Differentials

Ketotic hypoglycaemia

This condition is the most common cause of unexplained hypoglycaemia in children. However, this is a diagnosis of exclusion (once other endocrine and metabolic conditions have been excluded). Children typically present between 18 months – 6 years of age during a period of fasting or intercurrent illness. The hypoglycaemic episodes tend to resolve over time, as the child develops greater reserves and therefore a greater fasting tolerance. The typical biochemical picture is a fasting hypoglycaemia in presence of undetectable insulin and raised NEFA (non esterefied fatty acids) and BOHB (beta-hydroxybutyrate).

Endocrine

- Hyperinsulinaemia - The typical biochemical picture is a fasting or postprandial hypoglycaemia in the presence of normal/raised insulin and suppressed NEFA (non esterefied fatty acids) and BOHB (beta-hydroxybutyrate), typically with glucose requirements >8mg/kg/min.
  - Congenital: Genetic defects in 8 (known) genes that regulate insulin secretion. However, identified genetic defects account for only 40% of cases of congenital hyperinsulinaemia
  - Transient: Can be caused by maternal diabetes, maternal beta-blockers, hypothermia, IUGR and birth asphyxia. The latter two can run a more prolonged course (up to 12 months), requiring medical treatment.
  - Exogenous: Accidental injection, or non-accidental (Munchausen's by proxy)
  - Insulin producing tumours (insulinomas): rare
- Adrenal insufficiency
  - Primary (Addison's disease, congenital adrenal hyperplasia)
  - Secondary (ACTH deficiency, pan/hypopituitarism – from tumours, head injury, congenital infections)
  - Iatrogenic (prolonged corticosteroid causing suppression of hypothalamic-pituitary-adrenal axis)
- Growth hormone deficiency: Usually due to pan/hypopituitarism

Metabolic

- Glycogen storage disorders (commonly type 1 – glucose-6-phosphatase deficiency)
- Galactosaemia
- Hereditary fructose intolerance
- Fatty acid oxidation defects (commonly MCAD)
- Defects in amino acid and organic acid metabolism

Others

- Sepsis, especially in malnourished children
- Malaria
- Poisoning with ethanol or salicylates
- Disseminated herpes simplex virus infection
  - Non-specific signs of neonatal sepsis. Jaundice or bleeding or hypoglycaemia. History of maternal genital herpes or contact with cold sore. Abnormal LFTs or clotting. May have normal CRP. **Send EDTA blood for urgent HSV PCR. Start I.V aciclovir if high index of suspicion**.