Yorkshire and Humber
Neonatal Operational Delivery Network
Clinical Guideline

PAN-ODN

Hyperglycaemia

Author &/Or Working Group Name	**ODN Hyperglycaemia Working Group** **Updated by Marie-Anne Kelly Aug 2023**
Date Written/Reviewed	**Reviewed September 2023**
Date Ratified	**September 2023**
Next Review due Date	**September 2026**

This clinical guideline has been developed to ensure appropriate evidence based standards of care throughout the Yorkshire and Humber Neonatal Operational Delivery Network. The appropriate use and interpretation of this guideline in providing clinical care remains the responsibility of the individual clinician. If there is any doubt discuss with a senior colleague.

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To provide standardised, and evidence-based where possible, management guidelines for neonates with hyperglycaemia.

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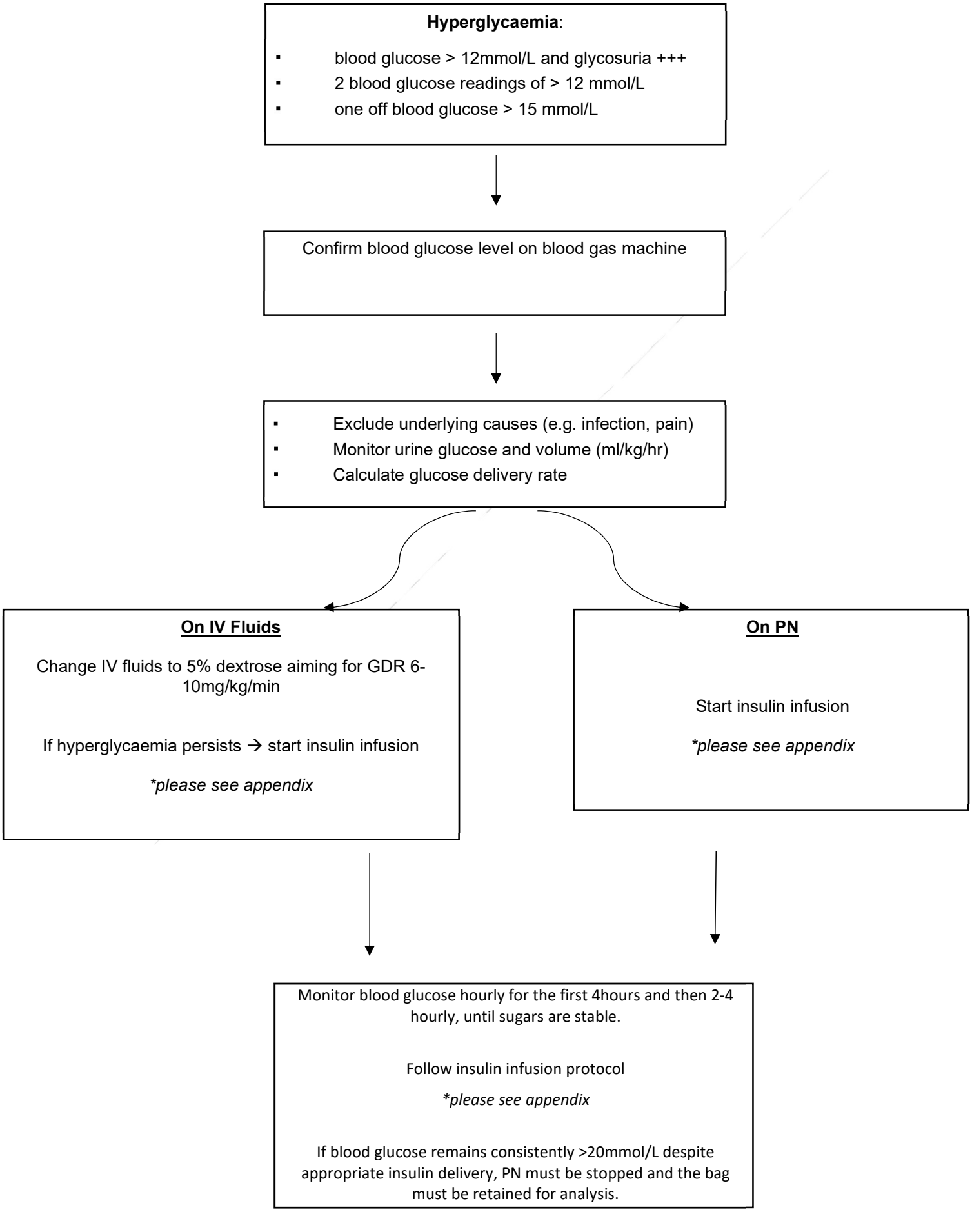

B Full Guideline & Evidence

1. Background

Hyperglycaemia is a common problem in the preterm infants (< 29 weeks) and very low birth weight infants (VLBW), estimated to occur in 45-80% of these infants, especially within the first 72 hours.

There are multiple factors contributing to hyperglycaemia. It can be in part a stress response, but also due to reduced islet cell function and relative insulin resistance. It is associated with significant morbidity and mortality, though the exact level of plasma glucose causing damage is unknown.

Hyperglycaemia is problematic both short term due to it causing an osmotic diuresis therefore hypernatraemic dehydration; but also, longer term is associated with NEC, ROP, IVH, prolonged periods of ventilation, late onset sepsis, BPD and prolonged hospital stay.

2. Aim

To provide standardised, and evidence-based where possible, management guidelines for neonates with hyperglycaemia.

3. Areas Outside of Remit

4. Evidence/Core guideline

4.1 Risk factors for hyperglycaemia

- Pain
- Stress
- Sepsis
- Hypoxia
- Drugs (Steroids, phenytoin, caffeine)
- Administration error

4.2 Definition of hyperglycaemia

There is no universal consensus on definition of neonatal hyperglycaemia, with values ranging from greater than 6.9 to greater than 12mmol/L. Definition used commonly, which would need treatment, is as below:

- Blood glucose > 12mmol/L and glycosuria +++
- 2 blood glucose readings of > 12 mmol/L
- One off blood glucose > 15 mmol/L

It is important to confirm diagnosis by repeating blood glucose on blood gas machine.

4.3 Management of hyperglycaemia

- Confirm the diagnosis by repeating blood glucose on the gas machine.

- Monitor urine for glycosuria and urine volume (ml/kg/hr) to ensure adequate fluid balance. If baby needs additional fluids to counter renal and extrarenal losses, consider using 5% glucose or 0.45% sodium chloride.

- Exclude risk factors of hyperglycaemia and act accordingly:
  - Pain
  - Stress
  - Sepsis
  - Hypoxia
  - Medications (Steroids, phenytoin, caffeine)
  - Maternal medication (diazoxide)
  - Administration error (Check the administration equipment and ensure that the fluid the baby has received is being administered at the correct rate and volume)

- If feeding is safe, start feeds as early as possible. It has been noted that even minimal enteral feeds induce insulin secretion.

- Calculate Glucose Delivery Rate (GDR)

$$\text{Glucose infusion rate (mg/kg/min)} = \frac{\text{rate of fluid (ml/kg/day)} \times \text{Glucose concentration (\%)}}{144}$$

Or use calculator found at: www.NICUtools.org

4.3.1 Babies on IV fluids

- If glucose delivery rate is >10mg/kg/min, consider weaning it gradually (by 1-2mg/kg/min every 2-4 hours) to 6 - 10mg/kg/min. It is more appropriate to reduce glucose concentration than overall rate as dehydration due to osmotic diuresis is a risk. (Reducing the glucose concentration of drug infusions should be prioritised).

- If glycosuria and hyperglycaemia persist despite an appropriate glucose infusion rate, commence insulin via separate venous access (peripheral or central).

4.3.2 Babies on PN

When babies are reliant on their intravenous infusions for nutrition there are additional considerations needed prior to reducing carbohydrate delivery. Not only does reducing the carbohydrates reduce overall calorie delivery, but it also changes the non-protein calorie lipid: carbohydrate ratio and reduces the body's ability to effectively utilise protein.

In these babies, insulin should be used preferentially prior to reducing carbohydrate delivery.

PN should continue unless the rates of insulin are >0.2units/kg/hr. A rate of >0.2units/kg/hr is suggestive of insulin resistance, and in these instances a reduction in the glucose delivery rate may be necessary. This should be discussed with the attending consultant, neonatal dietician and pharmacist and adjustments made to the PN prescription.

When the blood glucose is persistently >20mmol/l despite appropriate insulin administration consideration should be given to changing the PN bag and sending the bag for analysis. This should be a consultant decision.

4.3.3 Insulin management

Insulin should be used to treat hyperglycaemia as described above following the flow chart. It is recognised that there are different regimens for titrating insulin dosage to control blood glucose levels with limited evidence available to support one regimen over another.

Level 1/SCBU: Embrace or NICU advice should be sought if an insulin infusion is required for a baby being cared for in a level 1 unit.

The Neonatal ODN recommends use of the protocol in appendix 1 but is aware that there are other safe and effective protocols in practice within the region. An example insulin prescription chart for the protocol in Appendix 1 is provided in Appendix 2.

Infants needing more than 0.2 units/kg/hour of insulin is suggestive of insulin resistance, and a reduction in glucose delivery may be needed. It is also important if blood glucose is not falling as expected or the insulin infusion rate is 0.2 units/kg/hour or more to ensure appropriate insulin delivery e.g.:

- ensure iv access is working properly,
- check iv site,
- ensure no filter in the line,
- ensure drugs are compatible

If delivery is appropriate, further management should be discussed with the on-call consultant.

Monitor potassium and phosphate levels as insulin will cause reduction in serum concentration due to intracellular shift.

4.3.3.1 Special considerations when making up an insulin infusion:

- Ensure a dedicated insulin syringe is always used to draw up insulin, these are special syringes marked with graduations for the number of units of insulin- rather than the volume of drug in mls[15].
- Always draw up insulin from a vial, insulin should not be extracted from a cartridge or pen device[15,16].
- The term 'units' should be used in all contexts, abbreviations should never be used[15].
- Never use a filter when administrating insulin as the filter will ‘filter out’ some of the insulin, reducing the amount of insulin that is administered to the baby[14].
- Insulin can stick to the plastic in the giving set causing a decrease in the concentration of the insulin solution delivered. Due to this it is recommended the line should be primed prior to commencing the infusion. Prime the administration line with diluted insulin solution (as per prescription) and leave for 10 minutes then flush the line through with 5-20mL insulin solution before connecting to the patient. Repeat procedure when lines are changed[14,17].
- Low absorbing giving sets are in use in some units, they may reduce the amount of insulin that binds to the plastic. Some studies suggest there may still be a reduction in the expected delivery dose and units may choose to prime these lines too[13].
- IV insulin must be administered via a continuous syringe pump, to ensure an even supply and accurate administration of insulin.
- Ensure the correct strength of insulin is selected on guardrails/syringe driver and ensure this is double checked whenever a syringe is changed and at handover.

- Insulin infusions are usually run as 'extra', or in addition to the baby's total fluid volume. If the volume of the insulin infusion represents a substantial proportional of daily fluid intake the concentration of insulin should be increased, and volume decreased accordingly.

4.3.3.2 Choosing a line site

- Insulin should be administered via a line that will not need to be flushed (to avoid boluses)
- Monitor line sites closely and report any concerns immediately if glucose or PN administration is interrupted due to the risk of hypoglycaemia.
- Some areas may choose to run their glucose/PN in the same line as their insulin so that if a line stops working both are interrupted at the same time, this may result in fluctuations in insulin administration if the rate of maintenance fluid is altered.
- For compatibilities/incompatibilities see local formulary or discuss with pharmacist this information is also available via the Jessop wing formulary https://viewer.microguide.global/STH/OBGN#content,7f17c169-0460-4d74-bae1-a967cc45959d

5. Education Resources

None included.

6. Audit Criteria

Adherence to guideline recommendations.

7. Acknowledgements

With thanks to the working group members:
Dr Aoife Hurley, Neonatal grid trainee
Dr Fadi Maghrabia, Paediatric trainee
Dr Jo Preece, Consultant Neonatologist, Hull Royal Infirmary
Dr Cath Smith, Consultant Neonatologist, Jessop Wing Sheffield

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9. Appendices

Appendix 1 - ODN recommendation for Insulin Management.

Starting rate of insulin: 0.04units/kg/hour

Different strength insulin can be used, to allow concentration of insulin infusion and therefore reduce additional fluid intake on top of daily requirements.

Blood glucose to be documented, with current insulin dose and any changes to insulin doses, prescribed by a doctor or ANNP.

- If BG > 12 mmol/L and not reducing —> increase the rate of insulin by 0.02 units/kg/hr
- Check blood glucose within one hour of starting insulin infusion
- Increase by 0.02 units/kg/hr until blood glucose decreasing by at least 1mmol/l between blood samples
- If blood glucose not falling as expected, and/or an insulin infusion rate of 0.2units/kg/hour is required, ensure appropriate insulin delivery e.g. Check pump, check lines and iv site, ensure no filter, ensure compatible with other infusions
- Target blood glucose whilst on insulin is 7 to 12 mmol/L

- To prevent hypoglycaemia, if blood glucose is:
- **7-12 mmol/L and stable —>** keep the insulin running at **same rate**.
- **7-12 mmol/L and decreasing—> reduce** the rate of insulin by **0.02 units/kg/hr.**
- **4- 6.9 mmol/L** —> reduce insulin infusion rate by 50%,or stop if on lowest infusion rate
- **If BG < 4 mmol/L at any point —> stop insulin immediately.**
- Keep monitoring BG for 12 - 24 hours after stopping the insulin

Appendix 2

Insulin Infusion for Neonates

***** Do NOT use a filter***Use Low Sorbing extension sets*****

Before commencing insulin infusion ensure that **ALL** the following have been checked

1	Blood glucose >12mmol/L with glycosuria +++ or more
2	2 Blood glucose readings >12mmol/L
Or	Blood glucose ≥ 15 regardless of urine glucose
3	Glucose intake <10mg/kg/min

Glucose Conversion

mls/kg/day x % glucose / 144 = mg/kg/min

Name:

DOB:

(Affix Patient Label Here)

Hosp No:

Consultant:

Working weight: **kg**

If the volume of the insulin infusion represents a substantial proportional of daily fluid intake the concentration of insulin should be increased and volume decreased accordingly.

Single Strength Insulin Infusion	**0.1 unit in 1 mL**	Add 5 units of insulin to 50ml glucose
Double Strength Insulin Infusion	**0.2 units in 1 mL**	Add 10 units of insulin to 50ml glucose
Quadruple Strength Insulin Infusion	**0.4 units in 1 mL**	Add 20 units of insulin to 50ml glucose

- **When drawing up use a dedicated insulin syringe showing units not mls, Do Not use a filter, use a low sorbing set or prime set (see below)**
- **Commence infusion at 0.04 units/kg/hour**
- **Check blood glucose within one hour of starting**
- **Increase by 0.02 units/kg/hr until blood glucose decreasing by at least 1mmol/l between blood samples**
- **If blood glucose not falling as expected, and/or an insulin infusion rate of 0.2units/kg/hour is required, ensure appropriate insulin delivery e.g. Check pump, check lines and IV site, ensure no filter, ensure compatible with other infusions**
- **Target blood glucose whilst on insulin is 7 to 12 mmol/l**

Date and time	Strength of infusion	Amount of insulin required	Prescriber's Signature & Bleep No.	Batch number and expiry date of glucose 5%	Batch number and expiry date of insulin	Expiry date and time of infusion	Prepared by / Checked by
		units					
		units					
		units					
		units					

To prevent hypoglycaemia - If blood glucose is:

7 to 12 mmol/l and stable	- maintain infusion rate
7 to 12 mmol/l and decreasing	- reduce infusion rate by 0.02 units/kg/hr
4 to 6.9 mmol/l	- reduce infusion rate by 50% from present rate, or stop if on lowest infusion rate
<4 mmol/l	- stop infusion

Recheck blood glucose within 1 to 2 hours of reducing the dose, then check every 2 to 4 hours until stable

Priming the giving set

Prime the administration line with diluted insulin solution (as per prescription) and leave for 10 minutes then flush the line through with 5-20mL insulin solution before connecting to the patient. Repeat procedure when lines are changed.

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Appendix 3

**** Use Low Sorbing extension sets** **Do NOT use a filter****

To prevent hypoglycemia if blood glucose is:

7 to 12 mmol/l and stable - maintain infusion rate

7 to 12 mmol/l and decreasing - reduce infusion rate by 0.02 units/kg/hr

4 to 6.9 mmol/l - reduce infusion rate by 50% from present rate, or stop if on lowest infusion rate

<4 mmol/l - stop infusion

Recheck blood glucose within 1 to 2 hours of reducing the dose, then check every 2 to 4 hours until stable

Blood Glucose Monitoring

Date	Time	Blood Glucose (mmol/L)	Current Insulin Dose (units/kg/hr)	Updated Insulin dose (units/kg/hr)	Insulin rate prescription (signature and bleep)	Checked by

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10. Version Control Table

Version Control Table - Document History			
Date *(of amendment/ review)*	**Issue No**.*(e.g V1)*	**Author** *(Person/s making the amendment or reviewing the Guideline)*	**Detail** *(of amendment/misc notes)*
Feb 2021	V1	Working group	New guideline
Aug 2023	V1.1	Marie-Anne Kelly	Additions: Nursing care and management of insulin infusions including priming lines Consultant discussion if blood glucose persistently greater 20mmol/L despite insulin
May 2024	V1.2	Marie-Anne Kelly Charlotte Bradford	Formatting alterations & amendment to Appendix 2 ensuring all criteria visible in the preventing hypoglycaemia section