

METABOLIC DISORDERS

Learners Guide

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PRE READING

It's helpful for the learners to have read something about the basics of metabolic disorders before the session - these are some suggested resources for them to use

<https://dontforgetthebubbles.com/spotting-the-zebras/>

https://www.rch.org.au/clinicalguide/guideline_index/Hypoglycaemia/

https://www.rch.org.au/clinicalguide/guideline_index/Metabolic_disorders/

<https://www.peminfographics.com/infographics/the-anion-gap>

Additional learning material

<https://pemplaybook.org/podcast/the-undifferentiated-sick-infant/>

[Metabolic Disorders](#)

<https://www.rcemlearning.co.uk/foamed/metabolic-babies-in-the-ed-easy-as-1-2-3/>

<https://dontforgetthebubbles.com/low-can-go-neonatal-hypoglycaemia-hypoexit-trial/>

<http://www.emdocs.net/inborn-errors-of-metabolism/>

Also include your department / region's guidelines for managing children with suspected metabolic conditions and hypoglycaemia.

CASE SCENARIO 1

It's early morning in the ED and you are enjoying your coffee. You're called in to see a neonate with a history of irritability and seizures. You enter the room and are told the following: "Emma is a 3 day old, term baby who has been refusing feeds and crying excessively. There has been no history of fever or cough. At home she had seizure-like activity with tonic posturing".

First pregnancy, no antenatal or perinatal problems. Birth: Weight: 2950g, Apgar 9/10. Discharged home on day 2. Irritability since birth. Vomiting after feeds (mixed: breast and formula).

Examination: Awake, extremely irritable, upper limbs flexed, lower limbs extended, global hyperreflexia. No dysmorphic features. Otherwise no positive findings.

Weight: 3050g

Vitals: Temp 36.8°C, HR 155, RR 48, O2 sats 99%, BP wasn't checked.

What are the red flags in Emma's story?

What tests do you want to send?

You send some bloods:

FBC, CRP, U&E, LFTs - normal

Venous blood gas:

- pH: 7.33
- pCO₂: 3.1 kPa*
- HCO₃⁻: 14 mmol/L
- Na⁺: 142 mmol/L
- K⁺: 4 mmol/L
- Chloride: 100 mmol/L

Glucose: 5 mmol/L

Ketones: 2.1mmol/L

Ammonia 184

Urine: Ketones +2, and smells of sweaty feet.

Metabolic screen: plasma amino acids, urine organic acids, acylcarnitine profile sent

***1kPa = 7.5mmHg**

What do you think about these results?

What treatment will you start in the ED?

For bonus points - can you suggest a diagnosis?

CASE SCENARIO 2

The next baby you see is remarkably like Emma but with a subtle difference. Lucy is a 3 day old baby, presenting with poor feeding, irritability and seizures at home. There has been no fever, cough, coryza, or sick contacts.

Examination: Awake, extremely irritable, upper limbs flexed, lower limbs extended, global hyperreflexia. No dysmorphic features. You notice that she seems tachypnoeic, although lungs are clear.

Vitals: Temp 36.8°C, HR 155, RR, O2 sats 98%, BP wasn't checked.

Glucose = 5 mmol/L Ketones = 0.1 mmol/L

VBG: respiratory alkalosis

Venous blood gas:

- pH: 7.48
- pCO₂: 3.1 kPa*
- HCO₃⁻: 24 mmol/L
- Na⁺: 135 mmol/L
- K⁺: 4 mmol/L
- Chloride: 99 mmol/L

*1kPa = 7.5mmHg

What are the key differences between Lucy's and Emma's presentations?

What is the anion gap?

What does a respiratory alkalosis make you suspicious of?

The lab phones you with Lucy's ammonia result. It's 1250.

Why does Lucy have a respiratory alkalosis?

What do you think the diagnosis is?

What treatment do you want to start in ED?

CASE SCENARIO 2.1

Jane, 14 years old, is brought in by ambulance unconscious after a generalized tonic clonic seizures at home lasting at least 20 minutes. While doing the standard resuscitation steps, you talk to her mother. You learn that she has been a healthy child with no chronic conditions, no history of drug abuse, no acute illness. She's a vegetarian and enjoys dancing. It's the Coronavirus pandemic, so she has been at home for the last 3 weeks. She's started a new 'intermittent fasting diet' and yesterday, hadn't eaten since brunch. She went to bed early and this morning her mother was woken early by strange sounds coming from Jane's room and found her seizing on the floor.

Physical exam: GCS 10/15, hyperreflexia. No dysmorphic features .
You notice that she seems tachypneic, although lungs are clear.

Vitals: Temp 37.4°C, HR 112, RR 30, O2 sats 100% on supplemental oxygen (started at the ambulance), BP 110/70 mmHg.

You send some bloods:

Glucose = 5 mmol/L Ketones = 0.1

VBG: respiratory alkalosis

Ammonia = 650 (normal <40)

Anion gap = 15 (normal)

LFTs: slightly above reference levels

FBC, U/E, CRP normal

What are your differential diagnoses?

What key points in this case point you towards a metabolic disorder?

CASE SCENARIO 3

It's 11am on Easter Monday in Dublin. Ellie-Mae is a 6 day old baby, born at 37 weeks via SVD, in Wales while her mother was visiting some friends.

When Ellie-Mae was 3 days old her mother returned to Ireland to stay with her own mother, for some early baby support. Since day two of life Ellie-Mae has been vomiting after feeding. She is bottle fed and since yesterday she has only been accepting half of each bottle, but mother thought it was tiredness from the long trip.

Ellie-Mae's mother brought her to the ED this morning because she has been quiet, hasn't been crying as usual with nappy changes and seemed too sleepy to take this morning's bottle.

Pregnancy: Mother 21 years old, G1P1, no problems.

Birth: SVD at 37/40, BW 2.9kg, no resus, no NICU. She was jaundiced on the second day of life, but below phototherapy levels.

Family history: healthy parents from the Irish Traveller Community.

Physical exam: Weight 2.45kg (16% below birth weight), jaundiced, lethargic.

Anterior fontanelle is sunken, and Ellie-Mae looks dehydrated. You can palpate the liver 2 cm below the right costal margin. No spleen palpable. Otherwise no positive findings.

Vitals: Temp 37°C, HR 185, Capillary refill time 3 seconds, RR 55, BP systolic = 102 mmHg (crying), O2 sats 97%

What are the red flags in Ellie-Mae's case?

You take some bloods:

Glucose 2.0mmol/L

Ketones = 6 mmol/L

VBG metabolic acidosis - hyperchloremic

Venous blood gas:

- pH: 7.32
- pCO₂: 4 kPa
- HCO₃⁻: 20 mmol/L
- Na⁺: 135 mmol/L
- K⁺: 3.5 mmol/L

• **Chloride: 95 mmol/L**

When you see Ellie-Mae's low glucose level you send a hypoglycaemia screen. You also send FBC, U&E, LFTs, clotting, ammonia and blood culture

LFTs: AST 70U/L, ALT 75U/L, Bilirubin total 255 µmol/L, direct 60µmol/L, Alkaline phosphatase 270U/L

INR 1.8

Ammonia 47

How do you investigate hypoglycaemia?

What treatment do you want to start in ED?

Do these tests make you suspicious of any diagnoses?

CASE SCENARIO 4

Liz is a 3 year old girl from the countryside, who is visiting her grandmother in the city. She has been having diarrhea since yesterday and started vomiting last night. In the last 3 hours she hasn't been able to tolerate anything orally. There has been no fever or respiratory symptoms and she is passing urine as normal. Her 5 years old cousin has similar symptoms.

Her Grandmother informs you that Liz has MCAD deficiency and her emergency plan was tried at home, without success. Liz is not usually treated at your hospital and you don't have her chart. Unfortunately Liz's grandmother didn't think to bring the plan to hospital.

Physical exam: Liz looks tired and is mildly dehydrated, but smiles at you.

Her heart sounds are normal and her chest is clear. She has increased bowel sounds, a soft abnormal with mild diffuse pain on deep palpation and no masses or organomegaly.

Vitals: Temp 37°C, HR 165, capillary refill time 3 seconds, RR 32, BP systolic = 104mmHg, O2 sats 97% in air.

Glucose 2.5 mmol/L, Ketones 0.4 mmol/L

What is the priority in Liz's treatment?

Is her ketone response appropriate to the degree of hypoglycaemia?

Liz's grandmother told you Liz has MCAD Deficiency, but what is it?

Where can you find resources to help you manage Liz?

CASE SCENARIO 5

Mike is 12 years old, presenting to the ED with cough and fever. He has been coughing for 10 days, worse progressively in the last five and febrile in the last 3 days. Since yesterday he just wants to sleep and even when afebrile he looks unwell. Appetite is poor and he has been “sipping some apple juice”. You learn from his mother that he has a condition called Mucopolysaccharidosis (MPS) type I and is on treatment with “the enzyme”. Every now and again, “he is chesty and needs to come to hospital”.

Physical exam: Pink, hydrated, but looks sick. You notice that he is shorter than an average 12 year old boy, has hand contractures and coarse facial features. Cardiovascular: systolic murmur, +2/+6. Good pulse volume. Respiratory: creps and rhonchi on the right side. Abdominal exam: mild hepatomegaly. Umbilical hernia.

Vitals: Temp 37.5°C, HR 132, RR 30, BP systolic = 112mmHg, O₂ sats 88% in air.

What is Mike’s clinical diagnosis and what treatment do you want to start in the ED?

MCQS

Question 1.

A neonate presents with extreme irritability and vomiting. Which laboratory tests can be most helpful in identifying an underlying inherited metabolic condition?

- A** Ammonia
- B** Glucose
- C** LDH
- D** Coagulation profile

Question 2.

Hypoglycaemia with low ketones are an _____ response, it can lead us to think of _____ diagnosis.

- A** Appropriate, sepsis
- B** Appropriate, diabetes
- C** Inappropriate, diabetes
- D** Inappropriate, fatty acid oxidation disorders.

Question 3.

Which tests are part of the investigation of hypoglycemia?

- A** Insulin and GH
- B** Amino acids (plasma)
- C** Ketones
- D** All the above

Question 4.

Extremely high ammonia can be usually found in which condition?

- A** Hyperinsulinism
- B** Phenylketonuria
- C** Urea Cycle disorders
- D** MSUD

Question 5.

Which of the following is incorrect regarding Anion Gap (AG)?

A

The AG is the difference between primary measured cations and the primary measured anions.

B

Potassium (K⁺) is the most important cation for AG calculation.

C

Commonly measured anions are Chloride and Bicarbonate.

D

AG is useful in understanding causes of metabolic acidosis.

Take home tips

- 1** Common is common. Treat for common diseases while looking for rare differential diagnoses.
- 2** You don't need to make a specific diagnosis in the emergency department but don't forget metabolic conditions while investigating sick patients. The early symptoms are often non-specific and initially, therefore, the diagnosis is easily overlooked.
- 3** Have a low threshold for sending basic metabolic investigations: plasma amino acids, urine organic acids and acylcarnitines. The ammonia result will be back quickly and will help you manage the child acutely.
- 4** Hypoglycemia requests immediate action in children. Collect relevant samples and treat as soon as possible.
- 5** Atypical smells can help you with the differential diagnosis. You don't need to remember the specific condition; suspecting a metabolic disorder and collecting relevant samples is enough.
- 6** Do not panic. Patients with diagnosed metabolic disorders usually carry an emergency plan. If not, reliable online resources can help. Also, the opposite is true: patients with some metabolic disorders might not require any different acute treatment from other children with a similar presentation.

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