Sgrinio Smotyn Gwaed Newydd-anedig Cymru
Newborn Bloodspot Screening Wales

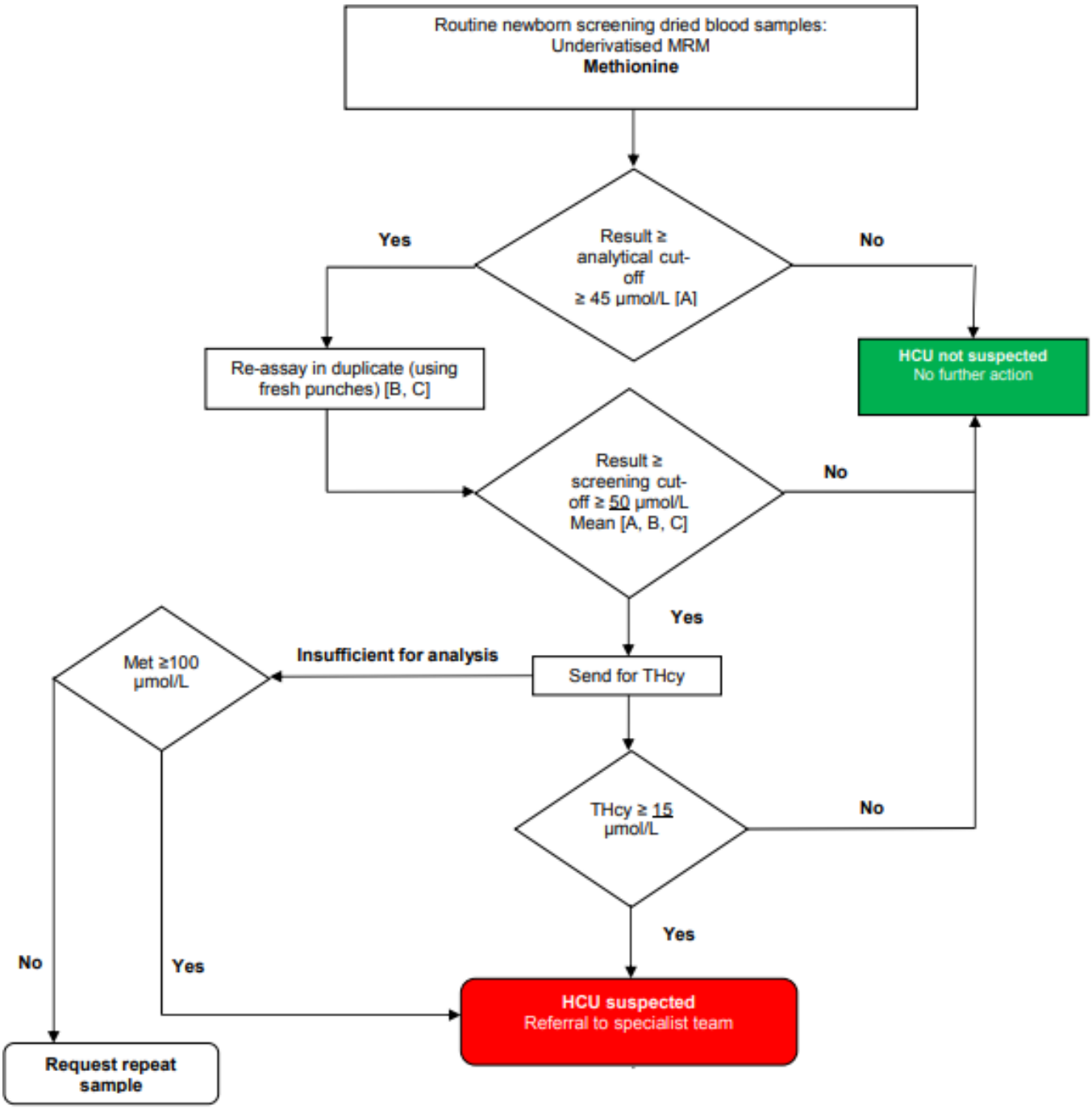
Homocystinuria (Pyridoxine unresponsive) (HCU) Clinical Referral Guidelines for Newborn Bloodspot Screening Wales

Based on the NHS Newborn Blood Spot Screening programme's: A laboratory guide to newborn blood spot screening for inherited metabolic diseases

[https://www.gov.uk/government/publications/newborn-blood-spot-screening-laboratory-guide-for-imds]

October 2020 Version 2

HCU newborn screening protocol



Key

THcy	Total homocysteine
Met	Methionine

Stage of Process	Guidelines
Defining a HCU suspected screening result:	If a sample from a baby is found to have a methionine concentration equal to or greater than 45 µmol/L, repeat tests should be performed in duplicate on the original bloodspot card. If the mean of triplicate results is equal to or greater than 50 µmol/L AND the total homocysteine is more than or equal to 15 µmol/L this is a presumptive positive screening result. If insufficient for total homocysteine analysis review methionine screening result. If methionine is equal to or greater than 50 µmol/L and less than100µmol/L request repeat for insufficient sample (for methionine). If methionine equal to or greater than 100 µmol/L this is a presumptive positive screening result.
Referral of babies with a positive ('HCU suspected') screening result:	**Betsi Cadwaladr UHB referrals will be to Manchester specialist metabolic team. For all other health boards in Wales the referrals will be to Cardiff and Vale UHB specialist metabolic team.** Wales Newborn Screening Laboratory notifies the local designated paediatrician AND the specialist metabolic team on the day of the result and also makes contact with the local laboratory to inform them. The clinical referral must be both verbally (by telephone) and by an email using a standard letter. The following information must also be emailed to the local designated paediatrician along with the standard letter. • 'HCU is suspected' leaflet • GP letter suspected HCU Note: For those babies with a screen positive result reported on a Friday, provision must be made to see the family face to face on the same day (Friday) or the next day as necessary.

	If a disorder other than HCU is suspected referral must be made to the specialist metabolic team.

First family contact	The local paediatrician will contact the family on the day that the screening result is available to inform them of the positive HCU screening result. And arrange appointment for the **next working day**. The family must be provided with the following information: • 'HCU is suspected' leaflet via email or web link • Contact numbers for the specialist metabolic team • The time and location for the appointment

First family face to face review with paediatrician (including diagnostic tests)	Pre-diagnosis management should include: • Explanation of the condition • Ensure family have received specialist metabolic team contact details and appropriate dietary guidelines When baby is seen with a positive screening result, specimens for the following tests should be collected to confirm diagnosis and exclude other possible metabolic disorders: • Plasma (lithium heparin) for amino acids • Plasma (EDTA) for total homocysteine • Liver function tests • Folate • Vitamin B12 Family to be given supply of pyridoxine 50mg bd and folic acid 5mg/day and shown how to administer and when to start if diagnostic tests confirm positive for HCU. Family to be contacted with the diagnostic results (these should be available within 5 working days of diagnostic sampling). If HCU diagnostic tests are negative, HCU is unlikely. Explanation of results given to the family and the baby discharged. If HCU is confirmed start pyridoxine 50mg BD and folic acid 5mg/day and arrange appointment with specialist metabolic team for 5-10 days. Local designated paediatrician to inform GP and send HCU GP letter via email. GP to inform health visitor.

Specialist metabolic team review (following positive diagnosis)	The first review with specialist metabolic team should ideally take place 5-10 days after starting pyridoxine. The specialist metabolic team must comprise of : • A consultant inherited metabolic disease paediatrician with relevant expertise • A paediatric dietician with metabolic expertise • A clinical nurse specialist with metabolic expertise Repeat plasma amino acids and total homocysteine will be taken and these results should be available within 2 working days. A fall in homocysteine <20% or <20µmol/L is unlikely to be significant. If there is no response, stop pyridoxine, continue folate and start a methionine-restricted diet (unless the baseline total homocysteine was <100µmol/L). If the plasma total homocysteine falls to <100µmol/L, continue pyridoxine and folic acid. The pyridoxine dose should be adjusted to the minimum that controls the homocysteine (ideally<10mg/kg/d). If the total homocysteine falls by >20% but remains >100µmol/L, consider monitoring the total homocysteine for longer, as it may take up to 6 weeks to see the full response. If the total homocysteine still remains >100µmol/L, reduce the pyridoxine dose to 10mg/kg/d & start a methionine-restricted diet.

Upon confirmation of diagnosis	Post diagnosis discussion should ensure the family have: • good understanding of the condition • support information • correct contact numbers for the specialist metabolic team • dietary treatment • Methionine-free formula. A specialist nurse should be available to provide advice and support. The specialist dietitian should make contact with the local dietitian if appropriate. Older siblings to be tested as appropriate. Families to be made aware of opportunities for early postnatal testing of subsequent siblings.