Hereditary Tyrosinaemia type 1 (HT1) Dietetic Management Pathway

Presumptive positive screen for HT1
Refer to: "HT1 Clinical Management Guidelines" (www.bimdg.org.uk)

On same day
Admission to local hospital or metabolic specialist centre
Liaise with local dietitian and team, as necessary
Initial investigations and assessment will determine if infant is managed as "presumed affected" or "presumed unaffected"

1. Presumed Affected

Dietary treatment of HT1 is a restricted tyrosine and phenylalanine diet. The aim is to maintain blood tyrosine in the target treatment range and phenylalanine within the normal reference range, for local laboratory.

1.1 Initial treatment:

- Baby may initially be nil by mouth (NBM) and on IV 10% dextrose with electrolytes or if clinically appropriate can give 10% glucose polymer orally
- If breast feeding mother should be supported to express and store breast milk
- Aim to re-introduce natural protein (standard infant formula/breast feeds) within 24-48hours, as advised by medical team
- Start restricted tyrosine, phenylalanine feed plan as:

    1. Breast milk/expressed breast milk or infant formula to provide natural protein
    2. Tyrosine, phenylalanine-free infant formula

- **The volume of each feed should be based on diagnostic blood tyrosine results; if:**

    - > 600 μmol/L, give tyrosine, phenylalanine-free infant formula only for 24 - 48 hours
    - 400 - 600 μmol/L, give 1g natural protein/kg/day from breast feed/infant formula plus tyrosine, phenylalanine-free infant formula to provide remainder of daily fluid allowance
    - 200 - <400 μmol/L, give 1.5g natural protein/kg/day from breast feed/infant formula plus tyrosine, phenylalanine-free infant formula to provide remainder of daily fluid allowance
    - < 200 μmol/L, give 1.5 - 2g natural protein/kg/day from breast feed/infant formula plus tyrosine, phenylalanine-free infant formula to provide remainder of daily fluid allowance

- Monitor blood tyrosine /phenylalanine every 2 days. Continue to adjust natural protein provided by breast feeds or infant formula until tyrosine is maintained in treatment reference range **(refer to sections 1.2, 1.3)**
- Each formula should be given in a separate bottle and not mixed together
- Give both feeds at each feed time and divided evenly across 24hours, if practical
- To limit natural protein intake from breast feeds, give tyrosine, phenylalanine-free infant formula first
- Tables 1 and 2 give practical examples of bottle and breast-feeding plans **(refer to section 5.1)**
- Once stabilised on diet and in early infancy expect to provide around:

    - 1.5-2g/kg/day of natural protein from infant formula or breast feeds or expressed breast milk
    - 1-1.5g/kg/day of protein equivalent from tyrosine, phenylalanine-free infant formula
    - Combined total protein intake (natural and protein equivalent of 2.5-3g/kg/day).

Other considerations

- If in acute liver failure, fluid may be restricted and necessitate a reduced feed volume
- If problems with low blood glucose levels, give feeds 2 to 3 hourly. If necessary, add glucose polymer to feeds to a maximum of 10% carbohydrate (CHO)
- If inadequate oral intake, top-up feeds via NG
- If high conjugated bilirubin and cholestasis, consider need for extra fat-soluble vitamins and change to infant formula with medium chain triglyceride (MCT)

1.2 Initial and long-term biochemical monitoring of diet:

- Monitor blood spot or plasma tyrosine and phenylalanine every 2 days until stabilised. Ideally same or next day turnaround time is required. Once discharged monitor weekly
- Diet monitoring blood should be done at the same time every day and ideally before a feed is due in the morning
- Adjust natural protein from breast feeds or infant formula based on blood tyrosine and phenylalanine results **(refer to section 1.3)**

1.3 Guide for blood tyrosine and phenylalanine levels, interpretation of results, and feed adjustments:

- **Recommended level for blood spot tyrosine is 200 – 400 µmol/L (this is above the normal reference range)**
    - If tyrosine < 200 µmol/L, increase natural protein by 0.5-1g/day from infant formula. If breast feeding decrease the volume of tyrosine, phenylalanine-free infant formula, so more breast milk is taken*
    - If tyrosine is > 400 µmol/L, decrease natural protein by 0.5-1g/day from infant formula. If breast feeding increase the volume of tyrosine, phenylalanine-free infant formula, so less breast milk is taken*.

  * **Note:** breast milk provides 1.3g protein/100ml (~ 75 mL = 1g protein)

- **Recommended level for blood spot phenylalanine is normal reference range**
  Phenylalanine deficiency has been documented in HT1. Regular monitoring is essential.
    - If phenylalanine is less than or at lower end of normal reference range on two consecutive occasions and tyrosine level is within target treatment range increase natural protein by 1g from infant formula. If breast feeding, decrease the volume of tyrosine, phenylalanine-free infant formula, so more breast milk is taken*
    - If phenylalanine is less than or at lower end of reference values on two consecutive occasions and tyrosine is above or close to 400umol/L give an L-phenylalanine supplement of 50mg/day (~ 10-15mg/kg/day).

1.4 Succinylacetone and NTBC blood spot monitoring and aims

- Monitor succinylacetone and NTBC on dried blood spot. Frequency to be determined locally
- Aim for undetectable dried blood spot succinylacetone <0.3µmol/L. If detectable check compliance with NTBC and consider if dose needs to be increased
- Recommended level for dried blood spot NTBC - 20-40µmol/L.

1.5 Practical Examples of Feeding plans

Table 1: Example of a bottle-feeding plan for a 3.3 kg infant, age 3 weeks old

***Aim*: 1.5g natural protein/kg/day and 2.5 – 3g total protein/kg/day**

Total fluid intake 170 mL/kg/day = 560 mL daily = 70 mL x 3 hourly x 8 feeds

Natural protein requirement: 1.5g/kg/day x 3.3kg = 5g protein/day

SMA First Infant Milk provides 1.24g protein per 100ml

= 8 × 50 mL SMA First Infant Milk = 400 mL daily

Total fluid requirement = 560 mL

- Fluid from SMA First Infant Milk = 400 mL
- Fluids from tyrosine, phenylalanine-free infant formula = total fluid volume - SMA First (560 mL – 400 mL) = 160 mL = 20 mL x 8 feeds

Feed plan at each 3 hourly feed give:

50 mL of SMA First Infant Milk followed by

20 mL of tyrosine, phenylalanine-free infant formula (more can be given if still hungry)

(some centres give tyrosine, phenylalanine-free infant formula first if small volume)

Nutrient composition	**Energy**		**Protein** (g)	**Carbohydrate** (g)	**Fat** (g)	**Fluid** (mL)
	kcal	kJ				
400 mL SMA First Infant Milk *	268	1344	5.0 (natural)	30	14.4	400
160 mL Tyr Anamix Infant **	112	468	3.2 (PE)	12	5.6	160
Total	380	1812	8.2	42	20.0	560
Intake per kg/day	115	549	2.5 8.6% energy	44% energy	47% energy	170
Requirement/aim per kg/day	96 - 120	403 - 504	2.5 - 3			

Manufacturer :* SMA Nutrition, ** Tyr Anamix Infant (Tyrosine, phenylalanine-free infant formula), Nutricia UK.

Table 2: Example of a breast and bottle-feeding plan for a 3.3 kg infant, age 3 weeks old

***Aim*: 1.5 g natural protein/kg/day and 2.5 - 3g total protein/kg/day**

Total fluid intake 170 mL/kg/day = 560 mL daily = 70 mL x 3 hourly x 8 feeds

Natural protein requirement: 1.5 g/kg/day x 3.3kg = 5g protein/day

Breast milk provides 1.3g protein per 100ml

- Fluid from breast milk to provide 5g protein = 390 mL
- Fluids from tyrosine, phenylalanine-free infant formula = total fluid volume – breast milk (560mL – 390 mL) = 170 mL = ~ 20 mL x 8 feeds

Feed plan at each 3 hourly feed give:

20 mL of tyrosine, phenylalanine-free infant formula followed by breast feed on demand

Nutrient composition	**Energy**		**Protein** (g)	**Carbohydrate** (g)	**Fat** (g)	**Fluid** (mL)
	kcal	kJ				
390 mL breast milk	269	1130	5 (natural)	28.4	16.0	390
160 mL Tyr Anamix Infant	112	468	3.2 (PE)	12	5.6	160
Total	381	1598	8.2	40.4	20.6	550
Intake per kg/day	115	484	8.6% energy	43% energy	49% energy	167ml/kg
Requirement/aim per kg/day	96 - 120	403 - 504	2.5 - 3			

* Tyr Anamix Infant (tyrosine, phenylalanine-free infant formula), Nutricia UK.

2. Presumed unaffected

A baby referred as "condition suspected" from initial screening but who has normal clotting and liver function tests will be managed as "presumed unaffected":

- continue normal infant formula or breast feeding
- refer to "**HT1 Clinical Management Guideline**" for ongoing monitoring.

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