

Scottish Paediatric Endocrine Group (SPEG)

Management of Congenital Hypothyroidism Guideline

NOTE

This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined based on all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.

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Purpose of guideline

- To guide the management of infants referred with an elevated thyroid stimulating hormone (TSH) concentration on Guthrie blood spot screening
- To give guidance on the initial investigations for infants diagnosed with congenital hypothyroidism
- To give guidance for ongoing management and monitoring of infants and children with congenital hypothyroidism

Who should use this guideline?

- General paediatricians
- Neonatologists
- Paediatricians with an interest in paediatric endocrinology
- Paediatric endocrinologists

Patients to whom this guideline applies

- Infants in Scotland with an elevated TSH on Guthrie blood spot screening

Summary

Diagnosis

- A screening test is performed on a newborn blood spot sample for the measurement of thyroid stimulating hormone (TSH). A high TSH suggests hypothyroidism
- Confirmatory tests
 - Pre-treatment thyroid function tests (TSH and free thyroxine fT₄)
 - Quantitative thyroglobulin (TG)
- Optional confirmatory tests may include:
 - Thyroid imaging (ultrasound and/or radio-isotope scans of the neck, sub-lingual and upper chest area)
 - Thyroid autoantibodies (thyroid peroxidase and TSH receptor antibodies) in the infant (and if indicated in the mother)
 - Maternal TFTs
- Genetic testing

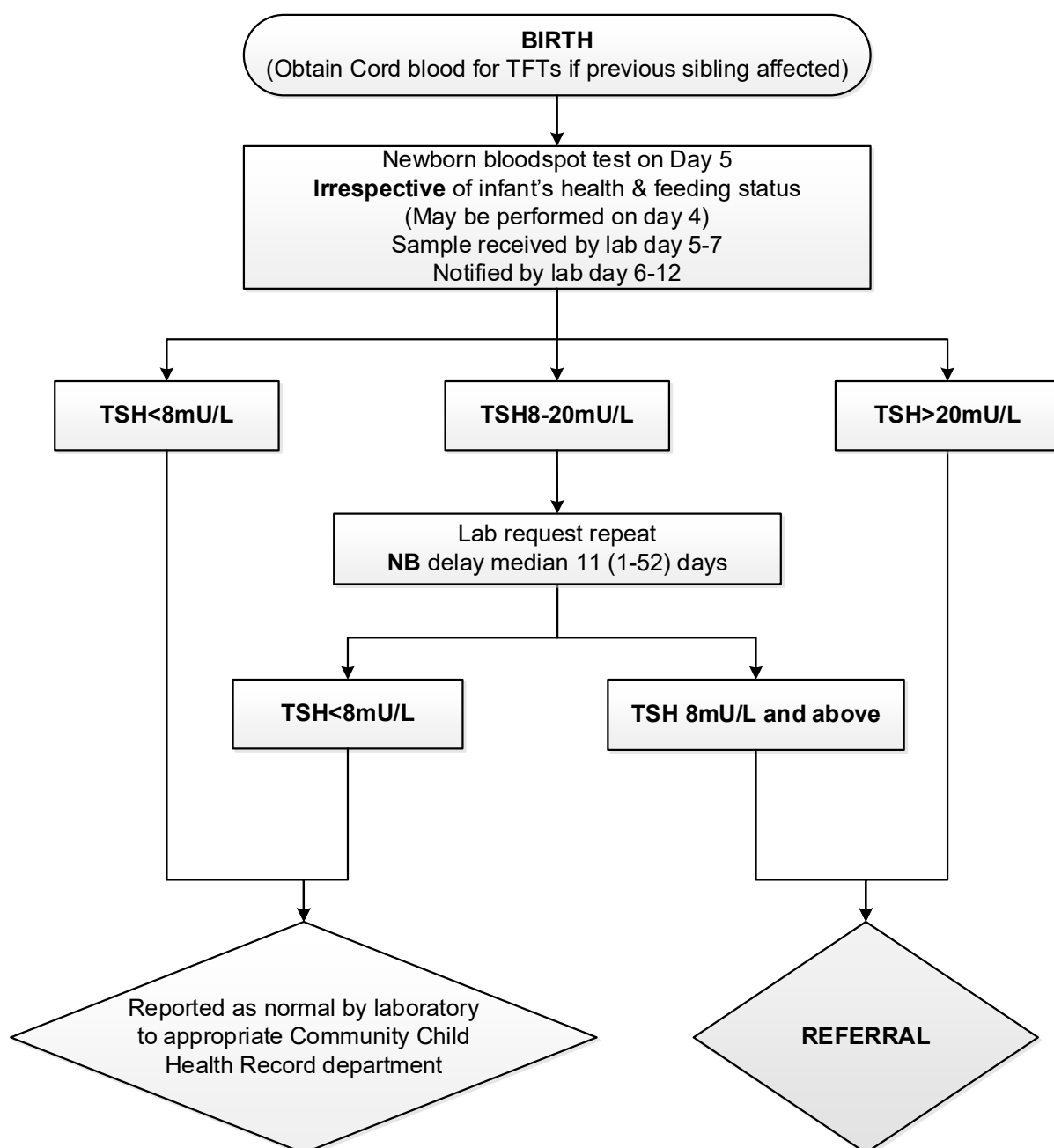
Treatment

Replacement therapy with levothyroxine (thyroxine, L-thyroxine, LT₄)

Clinical aims

- To bring thyroid function into the normal range as rapidly as possible while avoiding adverse effects
- To maintain ft_4 in the upper quartile of the normal reference range and concurrent TSH in the normal range
- To diagnose the cause of congenital hypothyroidism following positive screening

Screening Laboratory Notification Protocol



Laboratory Notification List

Referral procedure by laboratory

Laboratory staff notifying an abnormal result **must speak directly** to a consultant paediatrician. Either one of the two named paediatricians shown in the table below **or** the on-call paediatrician for the maternity unit.

NB all results are notified simultaneously to the person managing the Scottish CHT Register at Royal Hospital for Children, Glasgow.

Table 1 – Named Paediatricians for Notifications Of Raised TSH

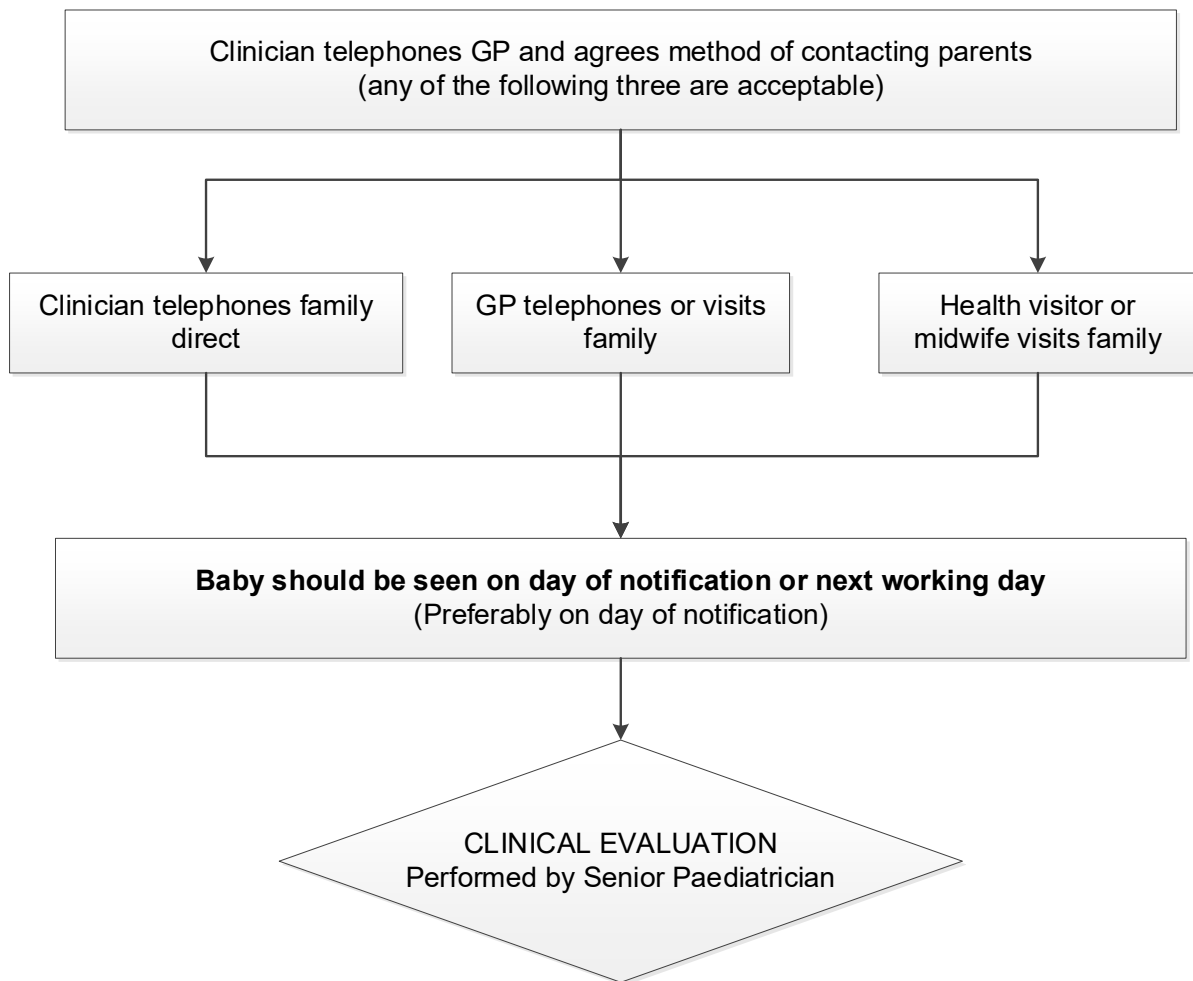
Centre	1 st Named Paediatrician	2 nd Named Paediatrician	Default
Ayrshire	Scott Williamson	TBC	On-call paediatrician in maternity / neonatal unit
Borders	Graeme Eunson	Andy Duncan	
Dumfries	Rajendran Shyam	On call consultant	
Fife	Anthony Tasker	Jo Watt	
Forth Valley	Sabine Grosser	On call consultant	
Glasgow	Guftar Shaikh	Avril Mason	
Grampian	Amalia Mayo	Craig Oxley	
Highland	Stuart Henderson	Alan Webb	
Lanarkshire	Ian Hunter	Shubhangi Shewale / Padma Rajagopal	
Lothian	Via Paed. Endo. Secretary	Endocrine Consultant of week	
Tayside	Nicky Conway	Clare Webster	

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Table 2 – Telephone Numbers

Centre	Hospital	Main contact number(s)	Switchboard
Ayrshire	Crosshouse, Ayr	-	01563 521133
Borders	Borders General, Melrose	01896 826892	01896 826000
Clyde	Royal Alexandra, Paisley	-	0141 887 9111
Dumfries	Dumfries General	01387 241732 01387 241963	01387 246246
Fife	Victoria Hospital, Kirkcaldy	-	01592 643355
Forth Valley	Forth Valley Royal, Larbert	01324 567202 (Bleep 1812) 01324 567692 (on-call paediatrician)	01324 566000
Glasgow	Royal Hospital for Children	0141 451 6548 0141 451 5799	0141 201 0000
Glasgow	Princess Royal Maternity	-	0141 211 5400
Grampian	Children's Hospital	01224 550125	0845 456 6000
Highland	Raigmore, Inverness	01463 705324	01463 704000
Lanarkshire	Wishaw General	01698 366481	01698 361100
Lothian	Royal Hospital for Children and Young People, Edinburgh	-	0131 536 1000
Lothian	Royal Infirmary, Edinburgh	-	0131 536 1000
Tayside	Ninewells, Dundee	-	01382 660111

Clinician Procedure following Notification of Congenital Hypothyroidism



Clinical evaluation

HISTORY – to include:

- Whether a sibling is affected
- A family history of thyroid illness / problems
- A history of thyroid disease or anti-thyroid therapy in the mother
- Any symptoms of hypothyroidism (e.g. poor feeding, sleepiness, jaundice, constipation, cold peripheries, hoarse cry)

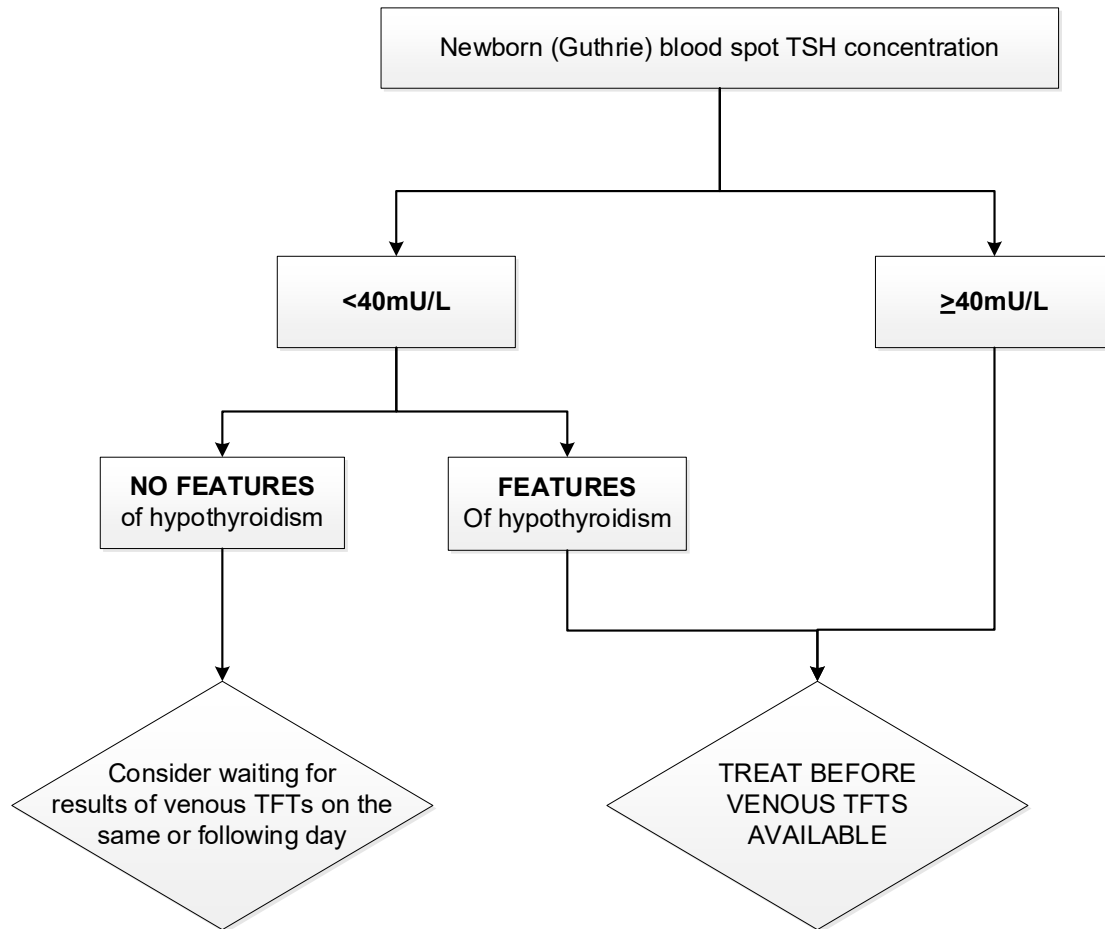
EXAMINATION – to include:

- Measurement of weight, head circumference and length
- Measurement of (c.f. reported) parental heights
- Presence or absence of goitre
- Signs of hypothyroidism (e.g. coarse facies, hoarse cry, umbilical hernia)

INITIAL INVESTIGATION

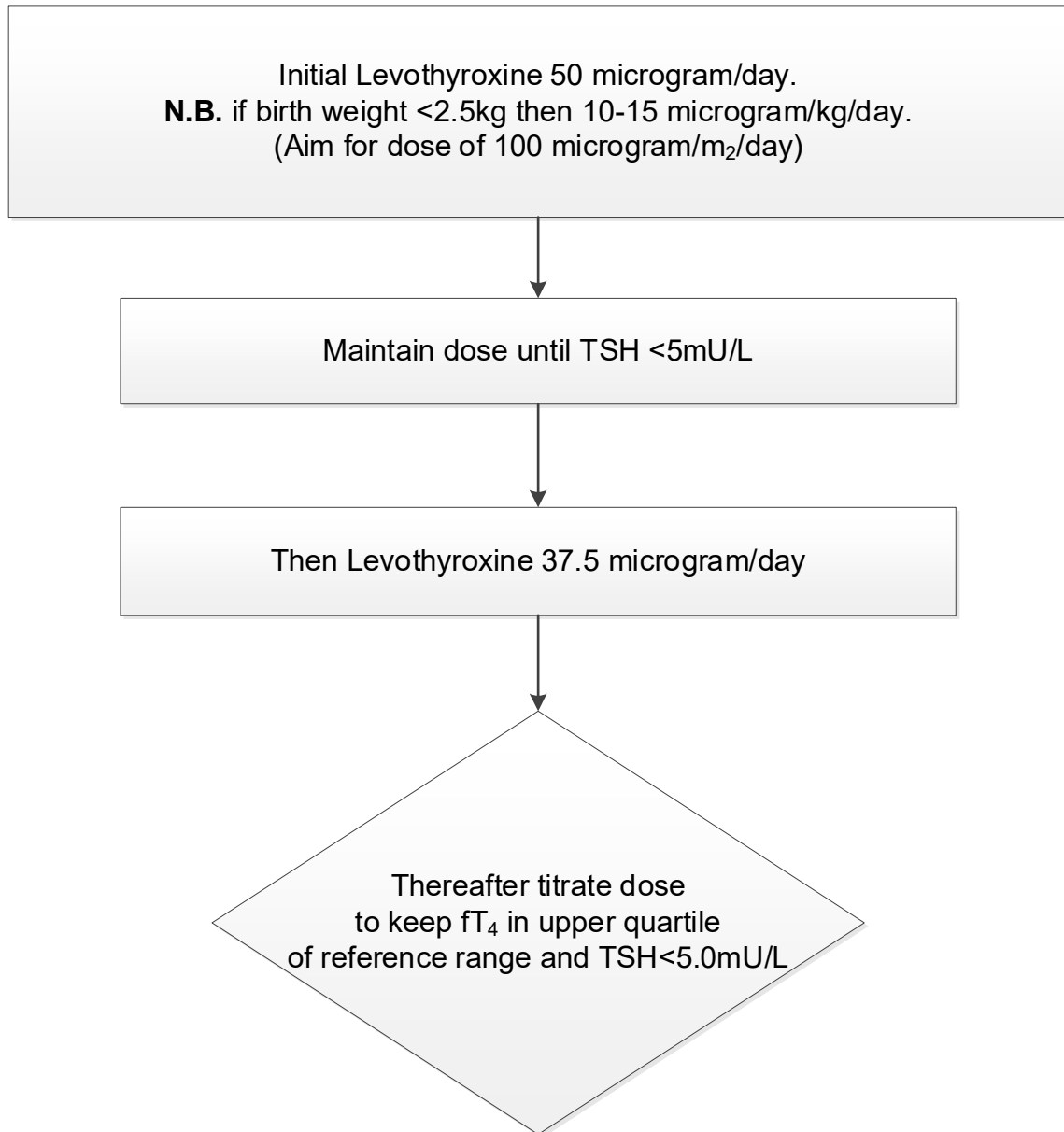
- **A minimum of 1 mL of blood for TFTs** in heparinised bottle or paediatric heparin tube (be prepared to make several attempts in order to get sufficient blood)
(It is vital that sufficient blood is taken)
- 1 mL clotted blood for quantitative thyroglobulin
- Blood for genetics if sufficient blood is available (sample can be stored for use later)

Clinician Treatment Decision Tree in Management of Congenital Hypothyroidism



This decision tree is based on referenced evidence (1: 2)

Dosage Schedule for Infant with Elevated TSH (If Treatment Is Recommended - See Decision Tree)



Preparations of Levothyroxine

Written instructions on how to give thyroxine should be available and supplied to the parents.

Levothyroxine tablets

- Available as 12.5microgram, 25 microgram, 50 microgram, 75 microgram or 100 microgram strength
- The tablets should be crushed and mixed with a small volume (less than 5ml) of liquid (formula, expressed breast milk or boiled and cooled water)
- If necessary, a tablet cutter for halving tablets should be supplied to the family
- The first dose should be given by parents under the supervision of a nurse or pharmacist

SPEG does not recommend using any of the liquid forms of thyroxine which are available including syrups, solutions and suspensions.

Tablets have been used extensively and successfully in the management of congenital hypothyroidism and therefore SPEG recommends the use of tablets, in accordance with European Society for Paediatric Endocrinology guidelines (ESPE) (1). Tablets are also much cheaper to use than other preparations.

Initial counselling and management

ESSENTIAL INFORMATION TO GIVE AT THE INITIAL VISIT

- Thyroid hormone is vital for normal brain development and somatic growth
- The thyroid gland is either absent, too small or not producing thyroid hormone properly
- It is likely to be permanent, or there is insufficient evidence to determine whether or not it is permanent
- With treatment, it has a good prognosis
- Adherence to treatment is crucial, especially from birth to 3 years of age when the brain is developing most rapidly
- The treatment is easy to administer, but should be given with care
- Verbal and written instructions should be given on how to give medicines

It is important to give the family written information about congenital hypothyroidism.

Scottish Paediatric Endocrine Group (SPEG) Management of Congenital Hypothyroidism

There are several excellent leaflets and booklets available (National Newborn Screening, British Society for Paediatric Endocrinology and Diabetes (BSPED):

- [Congenital Hypothyroidism \(CHT\) suspected](#)
- [CHT further information for families](#)
- [Hypothyroidism in childhood](#)
- [How to give Thyroxine to babies and children](#)

Thyroid Imaging

ESPE consensus statement (1) on congenital hypothyroidism recommends thyroid imaging for all babies with suspected congenital hypothyroidism because:

- It is more informative than blood tests alone
- It will aid in guiding options for genetic counselling
- With the results, it is possible to determine the likelihood of lifelong treatment if permanent congenital hypothyroidism is proven
- It provides a useful additional guide as to thyroxine dose (agenesis is likely to require larger doses)

Isotope scans should be performed by day 5 of the start treatment (5) to ensure the avoidance of false negatives, due to TSH suppression (it is advisable to check thyroid function on the day of scans to confirm the reliability of results).

Currently, if imaging is to be performed, the Royal Hospital for Children, Glasgow is currently the only site that is able to perform these scans. If scanning is to be considered, there should be early discussion with a paediatric endocrinologist.

- Imaging should never be allowed to delay the initiation of treatment

Mutation analysis in suspected cases of dyshormonogenesis

If thyroid imaging suspects that the cause of the hypothyroidism might be due to an enzyme defect in the function of the thyroid gland, there is a mutation analysis service available in Scotland. This is based in the genetics laboratories of Queen Elizabeth University Hospital, Glasgow.

The service offers analysis for the three most common mutations responsible for dyshormonogenesis in Scotland, namely mutations in thyroperoxidase (TPO), thyroglobulin (Tg) and the TSH receptor (TSHR) genes.

For genetic testing, a sample of blood in an EDTA bottle is required. The lab requires at least 1ml volume.

Samples should be obtained from the infant, and also from both parents. This can be performed at a subsequent follow up visit as it may be difficult to obtain sufficient blood samples at the initial diagnostic visit.

The service is managed by Therese Bradley who can be contacted on therese.bradley@ggc.scot.nhs.uk or by telephone 0141 354 9330. If unavailable the duty scientist can be contacted on geneticlabs@ggc.scot.nhs.uk

Subsequent Monitoring & Follow-up

- **1st visit after screening result occurs by day 11 of life.**
- **2nd visit:** Subsequent visit should be within 7 to 10 days after starting treatment. At this visit:
 - Carry out thyroid imaging if applicable (isotope scan needs to be performed before this visit).
 - Ensure that fT4 is in the normal range.
 - Ensure that the family is managing OK.
 - Provide further counselling.
- **3rd visit:** Next visit should be 7 to 10 days.

Suggested follow-up intervals after one month of age provided thyroid function tests have normalised		
From (age)	Until (age)	Suggested interval
1 month	6 months	2 to 4 weeks
6 months	1 year	4 to 8 weeks
1 year	5 years	3 to 6 months
5 years	Completion of growth	6 to 12 months (if reasonable compliance)

N.B. We would always suggest additional clinic visits following dosage alteration or when there are problems with poor adherence.

At puberty / rapid growth or weight gain, more frequent monitoring is recommended.

What to do at each visit

1. Calculate the optimal dose and adjust dosage **pre-emptively**, using Thyroid Function Tests to confirm adherence.
2. Assess growth:
 - Weight measurement
 - **Supine** length measurement until 2 years, then height measurement
 - Head circumference measurement until 3 years
3. Development assessment:
 - i. Consider pre-school formal audiology (for subtle hearing impairment due to congenital hypothyroidism (1))
 - if aged <4-5 years, developmental progress
 - aged over 4-5 years, school progress
 - ii. Consider neurodevelopmental assessment
4. Education:
 - From secondary school onwards ensure the patient has reasonable knowledge of CH
5. Adult transfer:
 - Boys to GP
 - Girls to GP, give pre-pregnancy counselling

Transfer to primary care for 6-12 monthly monitoring of TFT's

Aim for: fT₄ in the upper quartile of reference range and TSH <5.0 mU/l (but avoid undetectable TSH).

Re-evaluation of Thyroid Axis

This may be required if no cause has been identified for the hypothyroidism in the neonatal period and should be considered after the age of 3 years.

Re-evaluation should be considered in patients with a normally sited thyroid gland and / or those who have had no increase in thyroxine requirement since infancy.

This can consist of either:

- An initial reduction in thyroxine dose followed by monitoring of thyroid function and further reductions in thyroxine dose and monitoring of thyroid function if results remain normal, until thyroxine is discontinued
- Discontinuation of thyroxine with thyroid function assessment in 4-6 weeks

If the TSH is elevated, hypothyroidism is confirmed, and treatment should be recommenced as soon as possible.

Re-evaluation is not indicated if there has been a rise in the TSH in the first year, if there is a genetic cause or if there is an abnormal gland on imaging.

References

1. Leger J, Olivieri A, Donaldson M, Torresani T, Krude H, van VG, Polak M, Butler G: European Society for Paediatric Endocrinology consensus guidelines on screening, diagnosis and management of congenital hypothyroidism. *Horm Res Paediatr* 2014;81:80-103
2. Pokrovska T, Jones J, Shaikh MG, Smith S, Donaldson MD: How well does the capillary thyroid-stimulating hormone test for newborn thyroid screening predict the venous free thyroxine level? *Arch Dis Child* 2016;101:539-545
3. Jones JH, Gellen B, Paterson WF, Beaton S, Donaldson MD: Effect of high versus low initial doses of L-thyroxine for congenital hypothyroidism on thyroid function and somatic growth. *Arch Dis Child* 2008;93:940-944
4. Selva KA, Harper A, Downs A, Blasco PA, Lafranchi SH: Neurodevelopmental outcomes in congenital hypothyroidism: comparison of initial T4 dose and time to reach target T4 and TSH. *J Paediatr* 2005;147:775-780
5. Perry RJ, Maroo S, Maclennan AC, Jones JH, Donaldson MD: Combined ultrasound and isotope scanning is more informative in the diagnosis of congenital hypothyroidism than single scanning. *Arch Dis Child* 2006;91:972-976