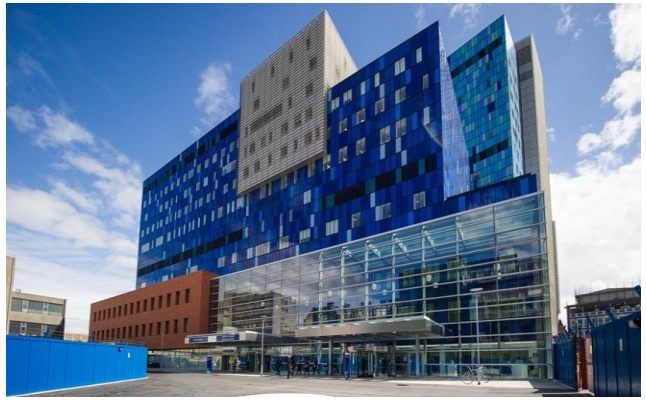
Managing Abnormal Thyroid Function Tests in Children



Dr Pratik Shah

Consultant Paediatric Endocrinologist and Honorary Senior Lecturer

Department of Paediatric Endocrinology and Diabetes

The Royal London Children's Hospital

Barts Health NHS Trust and Queen Mary University of London

Email: pratik.shah6@nhs.net

Physiology

- Thyroid hormones are essential for: Linear growth & pubertal development Normal brain development & function Calcium mobilization from bone

- **Normal Daily Thyroid Secretion Rate:**

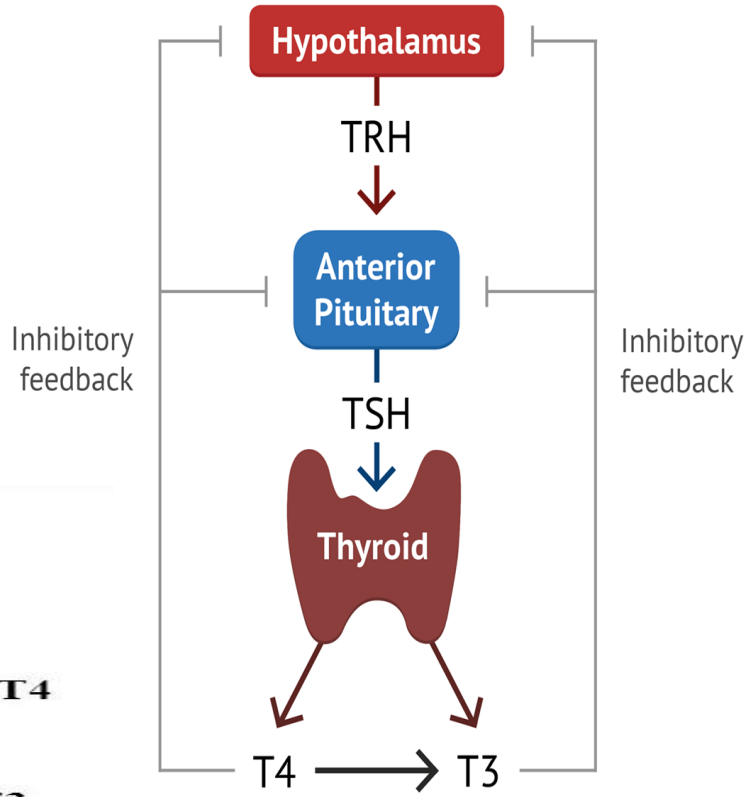
T4 = 100 ug/day
T3 = 6 ug/day
(ratio T4:T3 = 14:1)

T4 → **Protein binding** + **0.03% free T4**

↓ 85% (peripheral conversion)

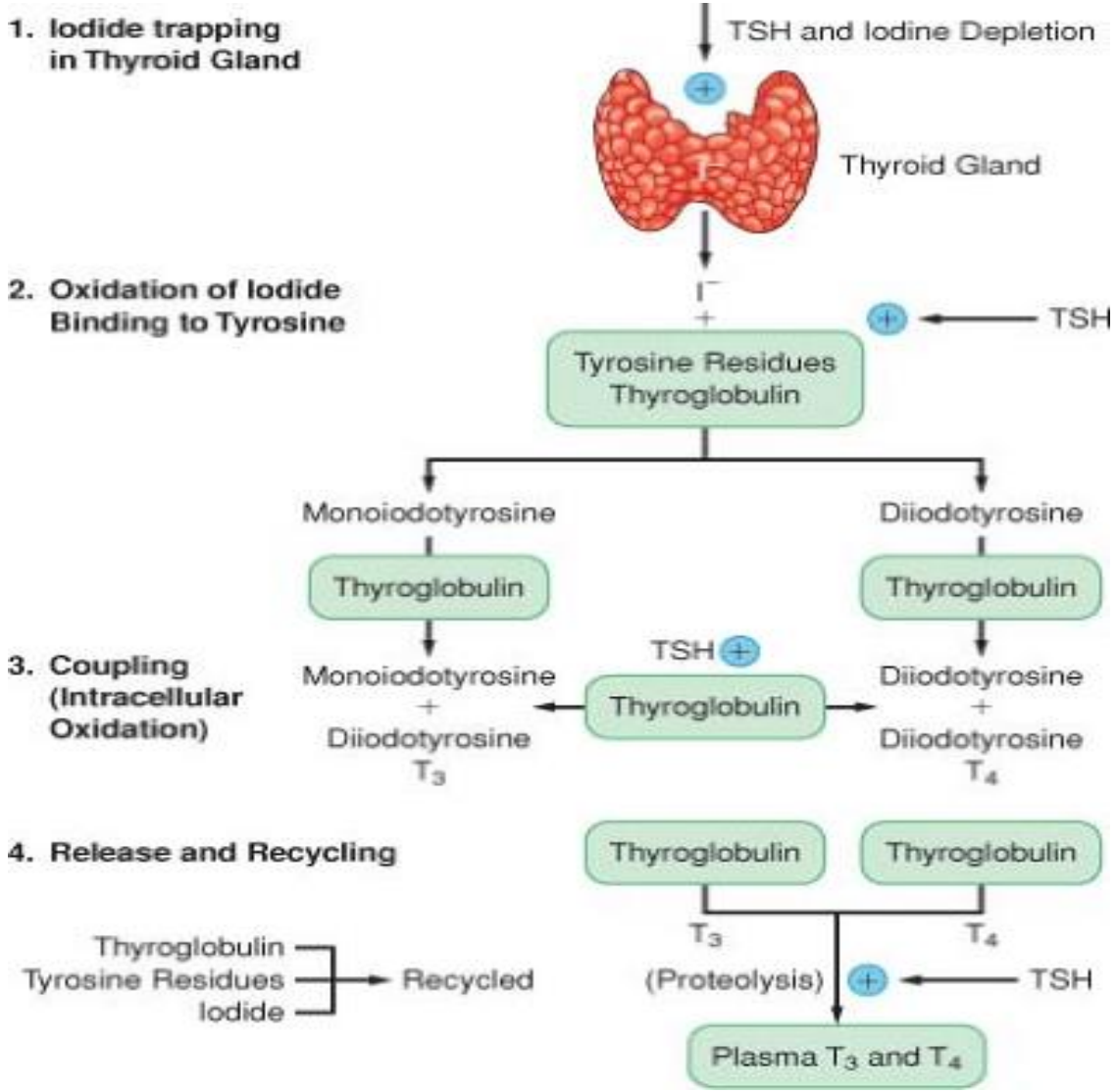
15% → T3 → **Protein binding** + **0.3% free T3**

(10-20x less than T4)



Bauer AJ, Wassner AJ. Thyroid hormone therapy in congenital hypothyroidism and pediatric hypothyroidism. Endocrine. 2019 Oct;66(1):51-62. doi: 10.1007/s12020-019-02024-6. Epub 2019 Jul 26. PMID: 31350727.

Physiology



Thyroid hormones are lipophilic so hard to dissolve in blood and so are transported bound to proteins - 70% by TBG (thyroxine binding globulin)
30% by albumin
Transported as T4
Converted by deiodinases to T3 to effect on the cells.

An understanding of the pathophysiology of endocrine function is important in the management of anesthesia for patients with disorders of the hormone-producing glands (Schwartz JJ, Akhtar S, Rosenbaum SH. Endocrine function. In: Barash PG, Cullen BF, Stoelting RK, Cahalan MK, Ortega R, Stock MC, eds. *Clinical Anesthesia*. Philadelphia: Lippincott Williams & Wilkins; 2013:1326–1355).

Effects of thyroid hormones

- Foetal brain & skeletal maturation
- Increase in basal metabolic rate
- Inotropic & chronotropic effects on heart
- Stimulates gut motility
- Increase bone turnover
- Increase in serum glucose, decrease in serum cholesterol
- Play role in thermal regulation

Dysfunction Thyroid Gland

Hypothyroidism - Decreased thyroid hormone levels Low T4
Possibly Low T3 too. Raised TSH (unless pituitary problem!)

Causes of hypothyroidism

Congenital (causes developmental delay)
Autoimmune (Hashimoto);
Iodine deficiency;
Subacute thyroiditis;
Drugs (amiodarone);
Irradiation;
Thyroid surgery;
Central hypothyroidism (radiotherapy, surgery, tumour)

Clinical features of Acquired hypothyroidism

Weight gain
Goitre
Short stature
Fatigue
Constipation
Dry skin
Cold Intolerance
Hoarseness
Sinus Bradycardia

Dysfunction Thyroid Gland

Hyperthyroidism Increased thyroid hormone levels High T4 +/- High T3
Low (suppressed) TSH

- **Causes of hyperthyroidism**

Graves Disease

Overtreatment with thyroxine

Thyroid adenoma (rare)

Transient neonatal thyrotoxicosis

- **Signs and Symptoms**

Heat intolerance, Hyperactivity, irritability

Weight loss (normal to increased appetite)
Diarrhoea
Tremor, Palpitations
Diaphoresis (sweating)
Lid retraction & Lid Lag (thyroid stare); Proptosis
Menstrual irregularity
Goitre
Tachycardia

Dysfunction Thyroid Gland

- **Treatment of Hypothyroidism**
  Replacement thyroid hormone medication: Thyroxine

- **Hyperthyroidism Treatment**

  Beta-blockers

  Carbimazole

  PTU (propylthiouracil)

  Radioactive iodine (in adults)

  Surgery - Thyroidectomy

Case 1

- Term baby born by normal vaginal delivery, girl
- Birth weight – 3.1kg
- Primigravida mum and no significant antenatal history
- Newborn screening TSH – 80 mu/L
- Brought in to the ward - FT4- 8 pmol/l (11-21 pmol/L) and TSH – 60mu/L, Thyroid antibodies – negative
- Management – Thyroid Technetium scan; Maternal TFT and antibodies
- Levothyroxine 10-15mcg/kg/day

<u>Clinical Features of Congenital Hypothyroidism</u>

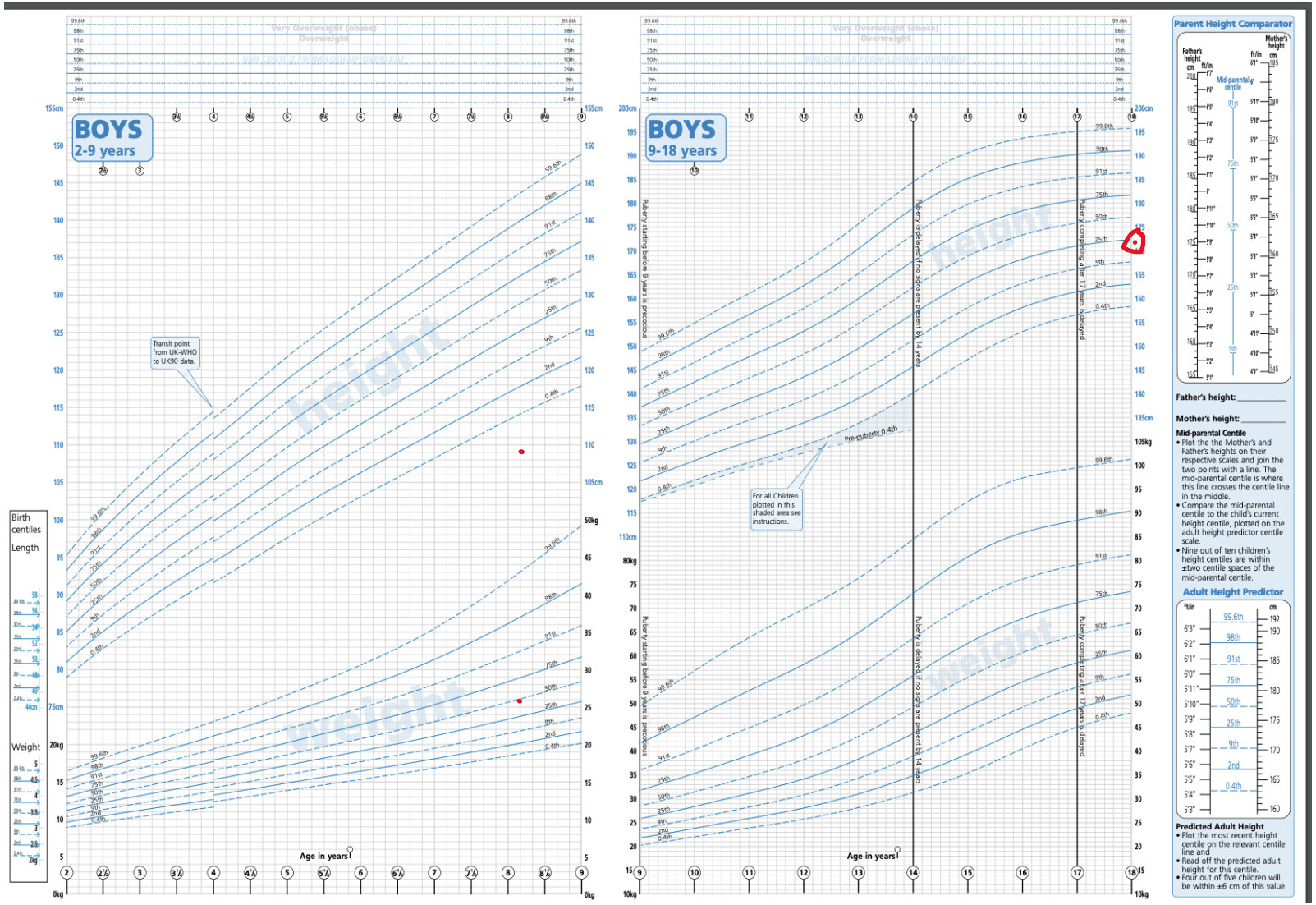
Lethargy 96%
Constipation 92%
Feeding problems 83%
Respiratory problems 76%
Dry skin, Thick tongue 67%
Hoarse cry, Umbilical hernia, Prolonged jaundice 12%
Goiter 8%

Peters C et al. *DUOX2*/*DUOXA2* Mutations Frequently Cause Congenital Hypothyroidism that Evades Detection on Newborn Screening in the United Kingdom. Thyroid. 2019 Jun;29(6):790-801. doi: 10.1089/thy.2018.0587. PMID: 31044655; PMCID: PMC6588112.

Case 2

- 8.2 year old boy
- HPC: Short stature – 2 years, tiredness – 1 year
- Past medical history /Family history– Not significant
- On examination:

Height – 110 cm (-2.8 SDS);
Weight – 26kg (0.3 SDS)
Mum's Height – 160cm, Dad's height – 170 cm;
MPH SDS - -2.27SDS



Case 2

- Investigations

TFT: FT4 – 8.1 pmol/l (11-21); TSH – 15mu/L (<4.5)
Thyroid peroxidase antibodies – 150KU/L (0-33); Thyroid receptor antibodies – negative

- Management
- Follow-Up

Case 3

- 10 year old girl, h/o increased sweating
- Past medical history /Family history– Not significant
- On examination: Height and weight – 50th centile, Systemic examination - unremarkable
- Investigations

TFT: FT4 – 13 pmol/l (11-21); TSH – 9 mu/L (<4.5)

Thyroid peroxidase antibodies /Thyroid receptor antibodies – negative

- Management/Follow-Up

(1) Idiopathic and mild Subclinical Hypothyrodism (SH) in children is generally a benign and self-remitting condition;

(2) long-term prognosis may be more severe in the cases with more elevated TSH levels at diagnosis (>10 mIU/l) and in those with underlying Hashimotos Thyroiditis (HT), especially if associated with Turner or downs syndrome;

(3) SH is often asymptomatic, but goitre and/or subtle proatherogenic metabolic abnormalities may be occasionally detected and might benefit from L-T4 treatment;

(4) such therapy is not indicated in asymptomatic children with mild and idiopathic SH, whilst it may be considered in children with -related SH and persistent TSH elevation.

Crisafulli G, Aversa T, Zirilli G, Pajno GB, Corica D, De Luca F and Wasniewska M (2019) Subclinical Hypothyroidism in Children: When a Replacement Hormonal Treatment Might Be Advisable. *Front. Endocrinol*. 10:109. doi: 10.3389/fendo.2019.00109

Case 4

- 36 weeks boy, Preterm, Birth weight – 2.8kg
- Maternal Graves Disease
- Systemic examination - normal
- Obs – stable and within normal limits
- Slightly floppy and poor feeding
- Treated for sepsis
- TFT (Day 3 of life) – FT4 – 80pmol/l (11-21) ; TSH - <0.01 mu/L (<4.5)
- Thyroid receptor antibodies (TRAb) – 17.8 IU/L (0-0.4); Thyroid peroxidase antibodies – 22 KU/L (0-33)
- Treatment:

Started on Carbimazole 750mcg/day in two divided doses
Monitoring TFT
Monitoring TRAb

- Progress

Case 5

- 15 years old girl
- HPC: Tiredness, palpitations, weight loss, neck swelling
- Family history: Maternal history of hypothyroidism
- On examination: Proptosis, Diffuse goitre

Temperature – 37 ^{0}C; Heart rate – 120/min, Resp rate – 22/min; BP – 110/70 mm of Hg
Weight – 42 kg (lost 8 kg in last 6 months); Height – 160 cm

On further questions: irregular periods last 12 months (menarche 12 years)

- Investigations:

FT4 – 78 pmol/l (11-21); TSH – 0.01 mu/L (<4.5); FT3 – 7.4 pmol/l (3-6)
Thyroid peroxidase antibodies – negative 20 KU/L (0-33); Thyroid receptor antibodies – 20 IU/L (0-0.4)

- Treatment:

Propranolol 250-500 mcg/kg 8 hourly
Carbimazole 30mg/day

- Monitoring and Follow-up

Ref: Wassner AJ. Pediatric Hypothyroidism: Diagnosis and Treatment. Paediatr Drugs. 2017 Aug;19(4):291-301. doi: 10.1007/s40272-017-0238-0. PMID: 28534114.

Conclusion

- **TFT – Free T4 and TSH** is recommended as the first line test for screening for thyroid disease. *To add Free FT3, TSH receptor antibodies and / or TPO antibodies when indicated.*
- **TSH with Free T4** is required for monitoring patients on thyroxine replacement for primary hypothyroidism. Review symptoms when when stabilising treatment of thyroid dysfunction
- Avoid requesting TFTs in **acutely ill patient or inpatients**. Check thyroid status 4-6 weeks after recovery from an illness.
- **TSH receptor antibody (TRAB)/Thyroid peroxidase antibodies** is valuable only in autoimmune hypothyroidism/hyperthyroidism. Children will need annual monitoring of TFT with normal TFT and positive antibodies
- Concomitant **drug therapy** with amiodarone, lithium, beta blocker, steroids, NSAIDs and anti-epileptics can interfere with thyroid hormone production and binding with transport proteins (e.g thyroid binding globulin).
- Uncertainty remains about the optimal management of mild subclinical hypothyroidism and monitoring of symptoms and TFT's is crucial
- **Referral to Paediatric endocrinology -** for complex cases, symptomatic children on treatment or worsening of mild subclinical hypothyroidism

Ref: Wassner AJ. Pediatric Hypothyroidism: Diagnosis and Treatment. Paediatr Drugs. 2017 Aug;19(4):291-301. doi: 10.1007/s40272-017-0238-0. PMID: 28534114.