# Normal and Abnormal Thyroid Function (and How to Interpret Thyroid Function Tests)

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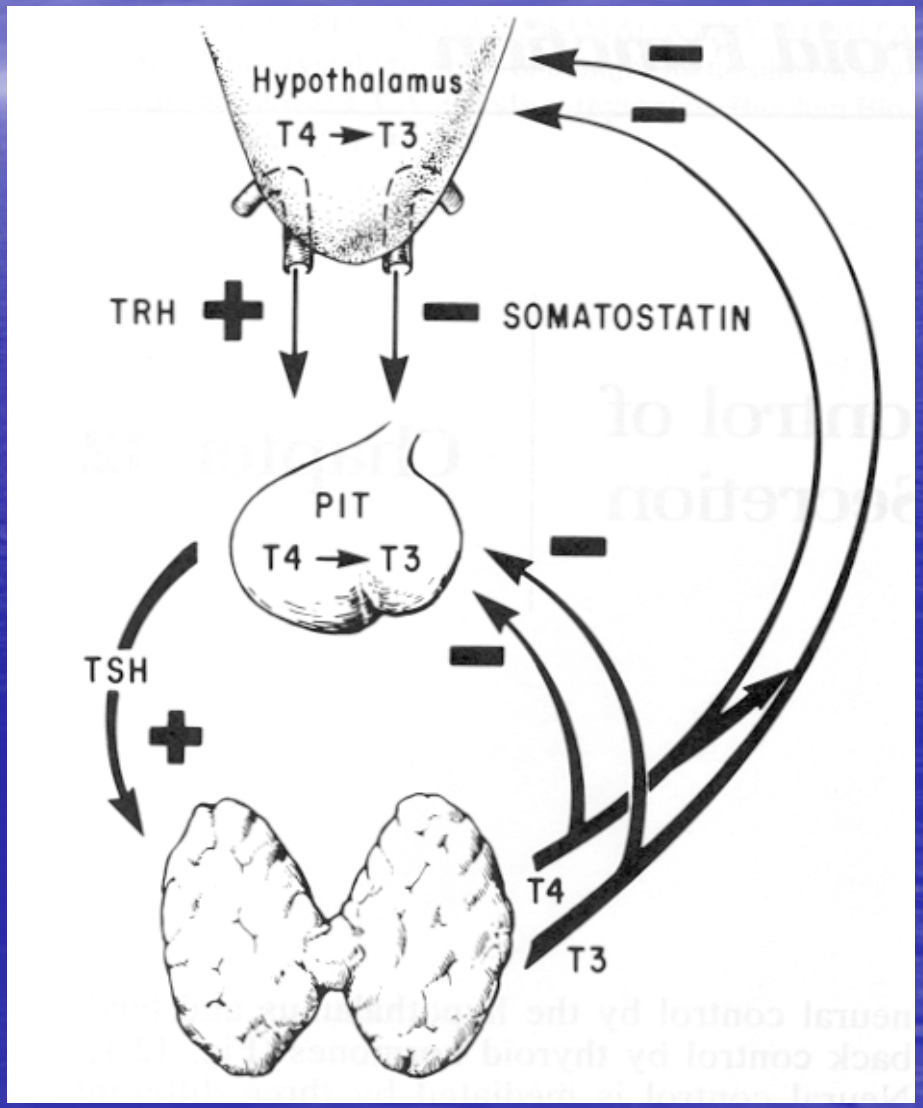
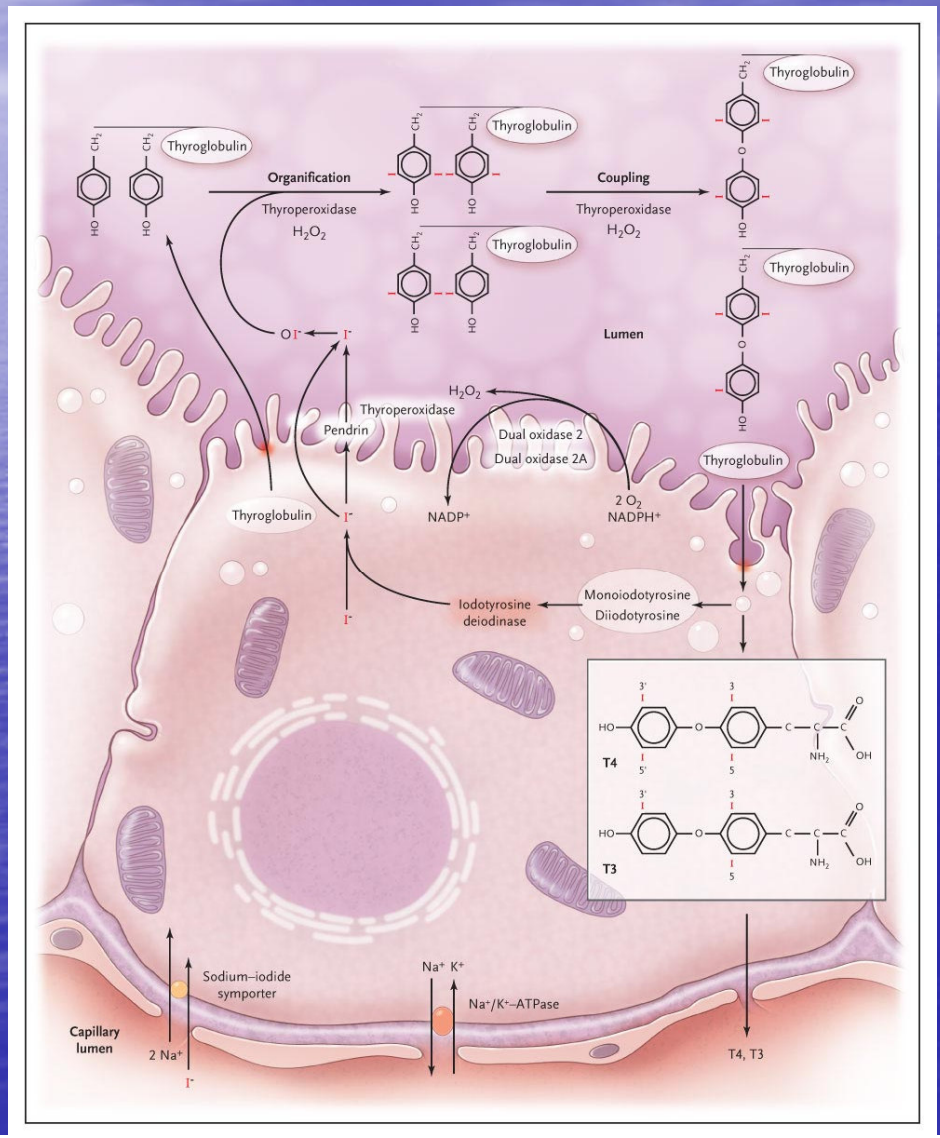
# A Bit of Endocrine Physiology

- The Hypothalamic-Pituitary-Thyroid axis is a classic feedback loop

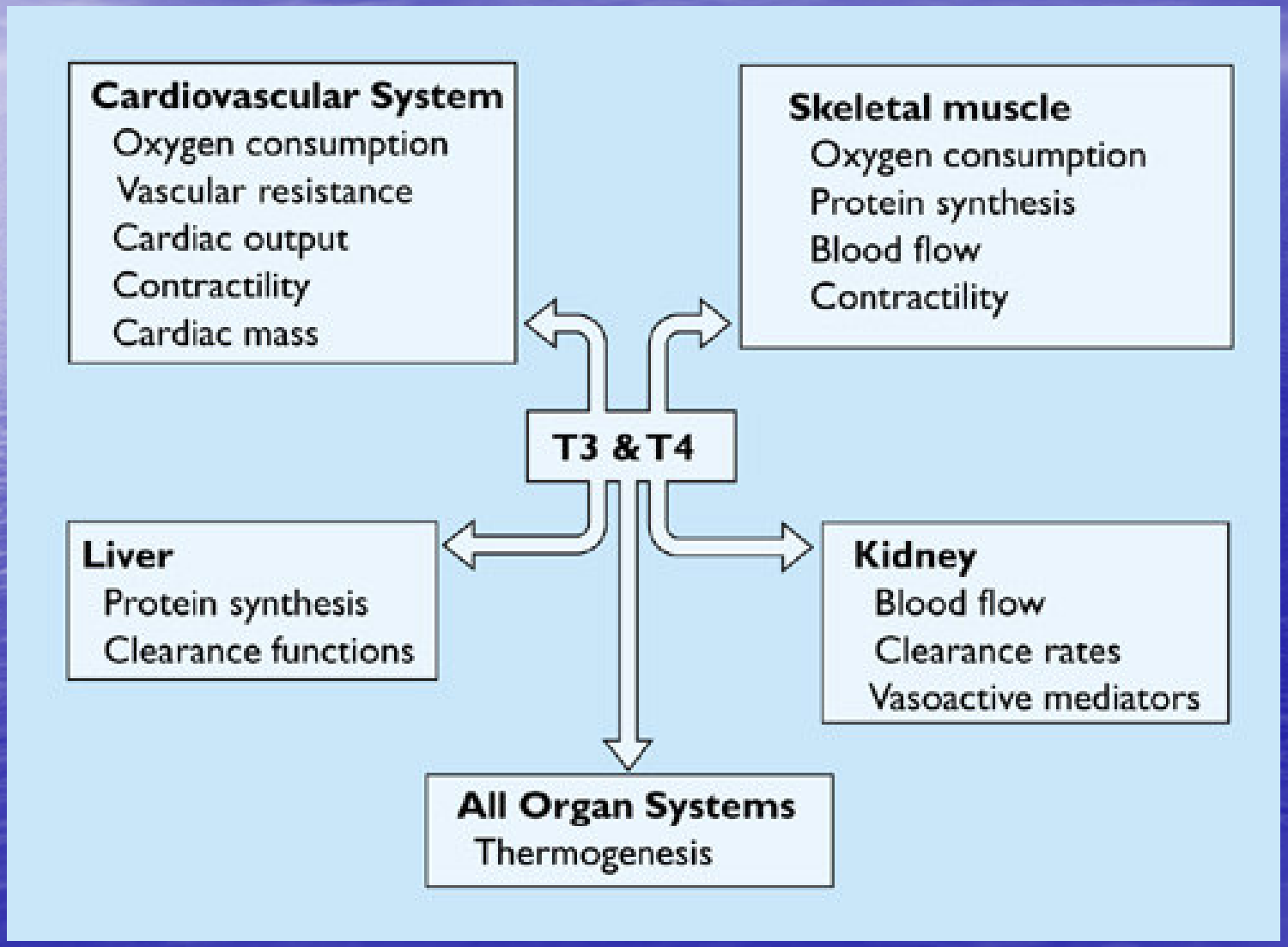


# Key Steps in Thyroid Hormone Synthesis



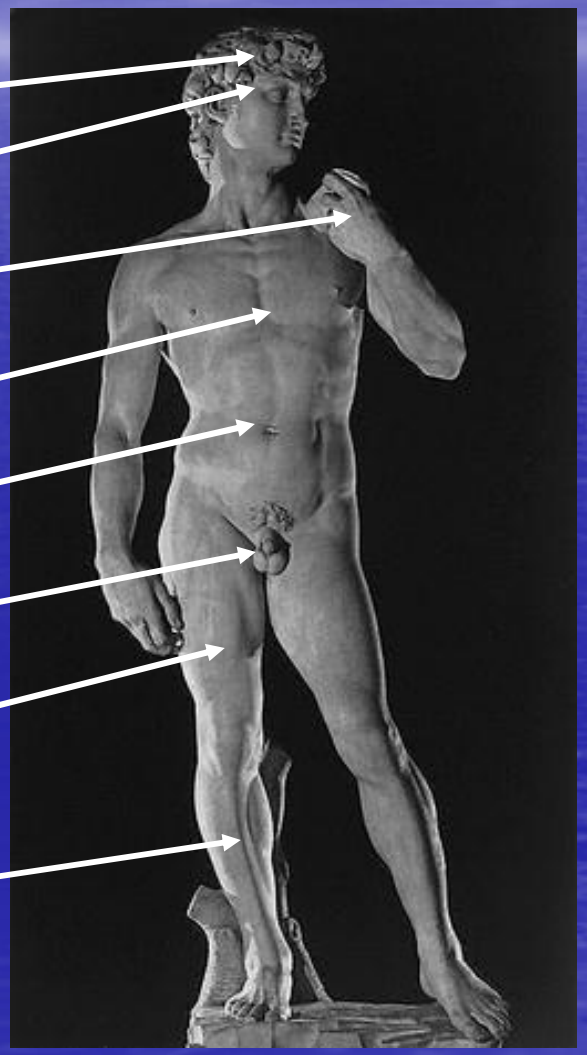

Kopp P. N Engl J Med 2008;358:1856-1859

# What does Thyroid Hormone Do?



# Symptoms of Hyperthyroidism

- Neuro-psychiatric
- Thermoregulatory
- Dermatological
- Cardio-pulmonary
- Gastroenterological
- Endocrine / reproductive
- Muscular
- Skeletal



# Symptoms of Hyperthyroidism

- Hyperactivity, irritability, altered mood (99%)
- Heat intolerance, sweating, (90%)
- Palpitations (85%)
- Fatigue, weakness (85%)
- Weight loss with increased appetite (85%)
- Diarrhoea (33%)
- Eye complaints (55%)

# Signs of Hyperthyroidism

- Sinus tachycardia (100%) or AF (10%)
- Fine tremor (97%)
- Warm, moist skin (97%)
- Goitre (100% in Graves')
- Palmer erythema, onycholysis, pruritus (35%)
- Alopecia
- Muscle weakness and wasting, proximal myopathy
- Lid lag and retraction (71%)
- Gynaecomastia (10%)
- Chorea, periodic paralysis, psychosis (<1%)

# Causes of Hyperthyroidism

- Graves' disease – TSH stimulating Ab's
- Hyperfunctioning nodule – autonomous adenoma
- Toxic MNG – multiple nodules
- Iodine load with underlying Graves'
- Hyperemesis gravidarium
- Hydatidiform mole
- Choriocarcinoma
- Pituitary adenoma

# Symptoms of Hypothyroidism

- Tired, lethargy, fatigue, weight gain
- Depression / low mood
- Cold intolerance
- Dry skin, hair / hair loss
- Constipation
- Cardiac failure
- Hypercholesterolaemia / vascular disease
- Hoarse voice
- Menstrual changes (menorrhagia)

# Signs of Hypothyroidism

- Dry skin, thin hair
- Cool peripheries
- Puffy face hands feet
- Yellow skin
- Bradycardic
- Peripheral oedema
- Slow relaxing reflexes
- Carpal tunnel syndrome
- Serous cavity effusions
- Galactorrhoea
- Ataxia, dementia, psychosis, coma

# Causes of Hypothyroidism

- Primary
  - Iodine deficiency
  - Autoimmune hypothyroidism (Hashimoto's)
  - Iatrogenic: $I^{131}$, thyroidecomy, DXT
  - Drugs: I containing contrast media, amiodarone, lithium
  - Congenital: absent or ectopic glands, or dyshormonogenesis, TSH receptor mutation
  - Destructive thyroiditis: postpartum, silent, subacute
  - Infiltrative disorders: amyloid, sarcoid, haemochromatosis, etc.

# Causes of Hypothyroidism

- Secondary
  - Hypopituitarism: tumours, trauma, surgery or DXT, infiltration, infarction
  - isolated TSH deficiency or inactivity
  - Hypothalamic disease: tumours, trauma, infiltration, idiopathic

# Goitre

# Causes of Goitre

- Endemic
  - Iodine deficiency
  - Goitrogens
- Sporadic
  - Simple, non toxic: diffuse of MNG (colloid)
  - Toxic MNG
  - Hashimoto's thyroiditis
  - Grave's disease
  - Destructive thyroiditis: Postpartum, silent, subacute
  - Goitrogens (including antithyroid drugs or kelp)
  - Genetic disorders: Dyshormonogenesis, thyroid hormone resistence, McCune – Albright syndrome, TSH receptor mutation

# Causes of Goitre

- Sporadic (continued)
  - Infiltration: Riedels, amyloid, sarcoid
  - Secondary: TSH secreting pituitary tumour, excessive stimulation from βHCG in pregnancy or choriocarcinoma

# Thyroid Function Tests

- About 90% to 95% of all thyroid problems can be diagnosed using measurements of Thyroid Stimulating Hormone (TSH), Free Thyroxin (fT4), and Free Tri-iodothyronine (fT3)

- Making a diagnosis is all about pattern recognition – but beware the pitfalls!

# Thyroid Function Tests

- If the TSH, fT4 and fT3 are within the normal range the likelihood of thyroid dysfunction can be excluded

# Low TSH, High fT4, and High fT3

- Primary hyperthroidism
  - Graves', MNG, toxic nodule

# Low TSH, Normal fT4 or fT3

- Thyroxine ingestion
- Subclinical primary hyperthyrodism
- High dose steroids
- Inotrope infusions

- Repeat TFT's about 6 weeks later

# Low/Normal TSH, Low fT4 or fT3

- Unwell patient with non-thyroidal illness
- Recent treatment for hyperthyroidism
- Secondary hypothyroidism (pituitary disease)
- Congenital TSH or TRH deficiency

- Important to exclude hypoadrenalism

# High TSH, Low fT4 or fT3

- Primary hypothyroidism

# High TSH, normal fT4 or fT3

- Mild thyroid failure (subclinical hypothyroidism)
- Interfering (heterophile) antibodies giving misleading results
- TSH resistance

# Normal or High TSH, High fT4 or fT3

- Usually artifactual
- TSH receptor mutations
- TSH secreting tumour
- Anti T4 or anti T3 antibodies interfering with the assay
- Amiodarone treatment
- Psychiatric disease
- Familial dysalbuminaemic hyperthyroxinaemia

# Amiodarone and the Thyroid

- Amiodarone is 37% iodine
- It is highly lipophilic and thus has a half life of months
- 10% is liberated as free iodine daily

# Amiodarone and the Thyroid

- Amiodarone inhibits type 1 and type 2 deiodinase
- Type 1 is found in the liver, muscle and other tissues
- This leads to
  - 10% increase in fT4
  - 60% decrease in fT3
  - 150% increase in reverse T3

# Amiodarone and the Thyroid

- Type 2 deiodinase inhibition in the pituitary leads to modest increases in TSH
- However, in the absence of autoimmune disease, the TSH usually remains within the reference range

# Amiodarone and the Thyroid

- Iodine loading also increases the plasma iodide concentration 50 fold
- And urinary iodine excretion increases by 30 fold
- But leads to a decreased radioactive iodine uptake

# Amiodarone and the Thyroid

- These changes can lead to either hyper or hypo thyroidism
- Which one will any individual will get is very difficult to predict

# Amiodarone Induced Hyperthyroidism

- 2 sorts of AIT
  - Type I
  - Type II
- Important to get the type correct as the management is different for the two
- More prevalent in Europe (15%) than USA (3%)

# Type I AIT

- Iodine induced thyrotoxicosis in people who often have pre-existing nodular goitres, most often in iodine deficient areas
- Highly vascular nodules lose the ability to self regulate the amount of iodine to trap, organify and incorporate into thyroid hormone

# Type II AIT

- Occurs abruptly without warning usually in individuals who do not have pre-existing thyroid disease due to the direct toxic effects of the drug
- Can start months or years after initiation of amiodarone treatment (av. 12 months)
- Weight loss, muscle weakness and AF occur commonly

# Type II AIT

- Thyroid gland may be a little enlarged and is non-tender
- Suppressed TSH, increased total T4 and fT3
- Histologically there is widespread disruption and follicular scarring – a unique finding
- Poorly vascualar

# Treatment of AIT

- Limited options due to the high iodine load, making targeted $I^{131}$ uptake reduced to only 1-2% - not enough to allow it to be used therapeutically
- However, in type I, the autonomous nodules may allow sufficient uptake to occur to treat them with RAI

# Treatment of AIT

- Anti-thyroid drugs may work less well due to the high iodine load
- Treatment is therefore clinically based
  - General state of the patient
  - Presence and degree of cardiac decompensation
  - Need for rapid reversal to a euthyroid state

# Treatment of AIT

- Considerations
  - Is it safe to stop the amiodarone?
  - If not then
    - Antithyroid drugs (better for type I than type II)
    - Glucocorticoids
    - Thyroidectomy
    - ?Potassium perchlorate

# Amiodarone Induced Hypothyroidism

- Higher in areas replete with iodine, e.g. USA
- Higher in people with autoimmune thyroid disease (therefore do an TFT and autoantibody level prior to starting amiodarone)
- Treatment is with thyroxine

# Are We Finished Yet?