# Thyroid and Parathyroid Disease in 30 minutes

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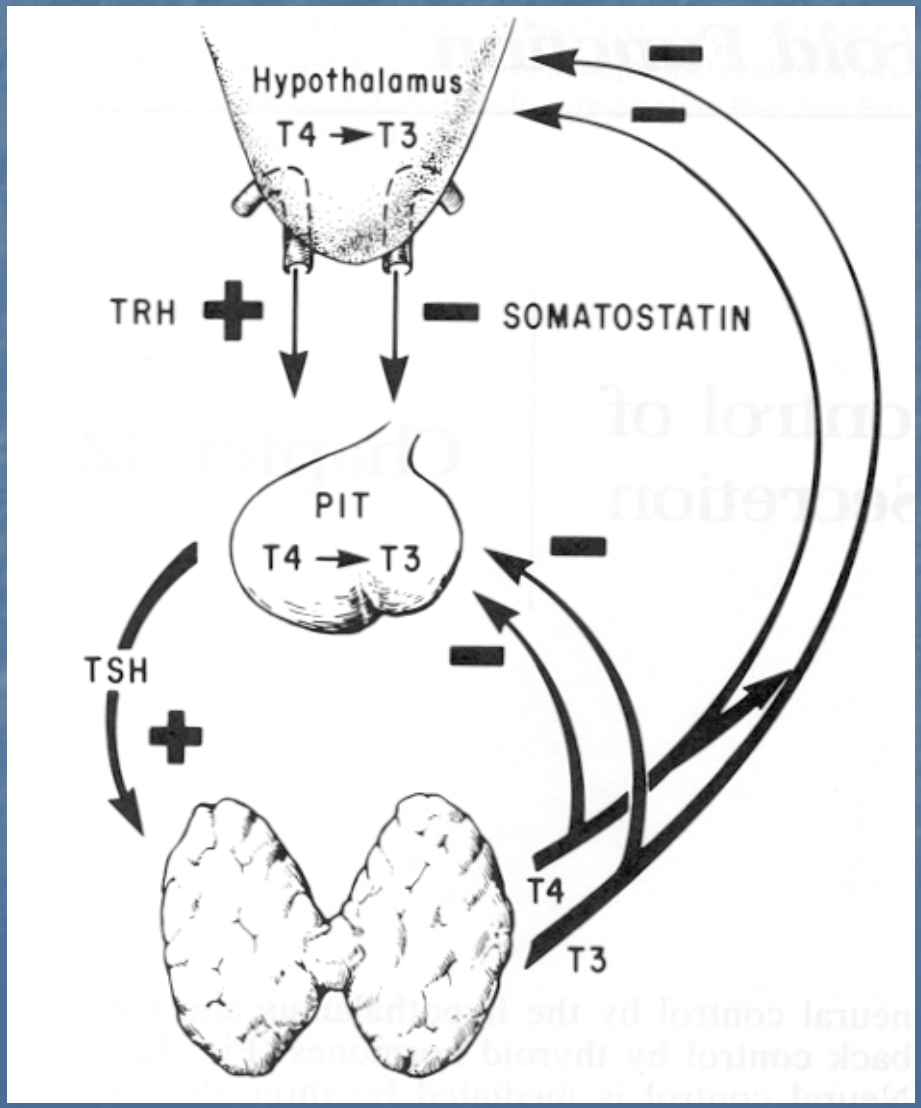
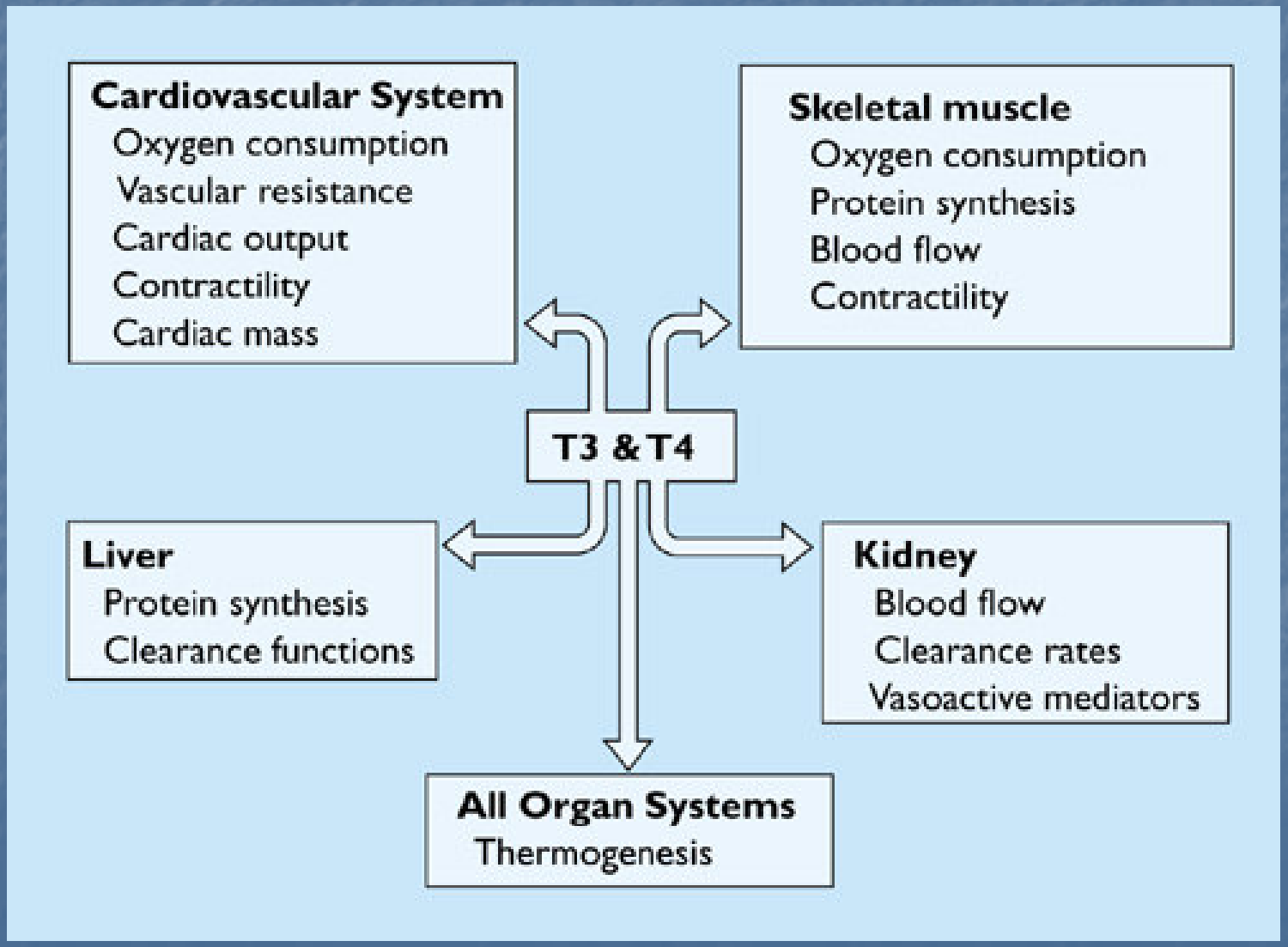
# Thyroid Disease

# A Bit of Endocrine Physiology

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

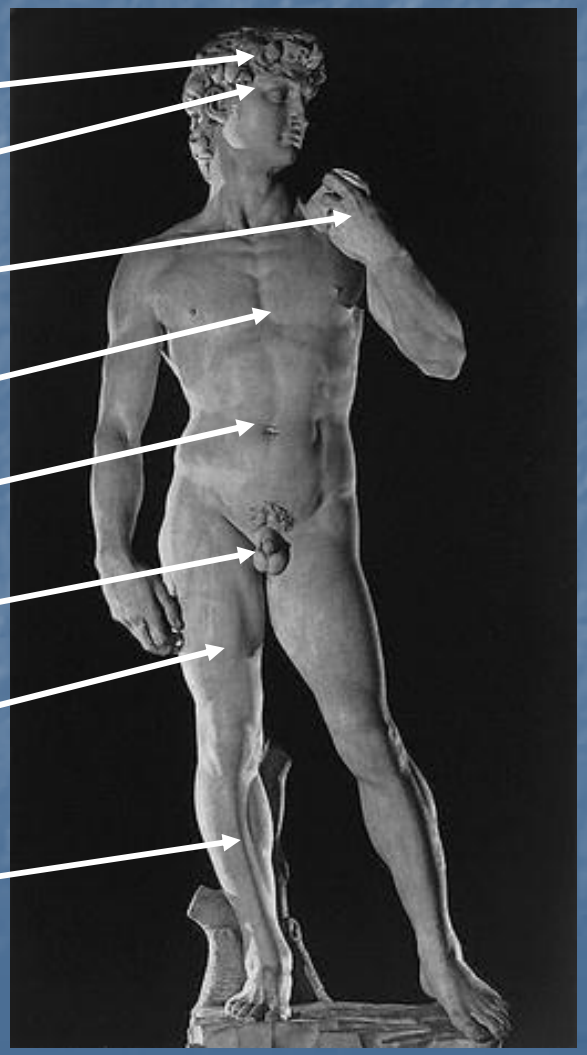


# What does Thyroid Hormone Do?



# 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

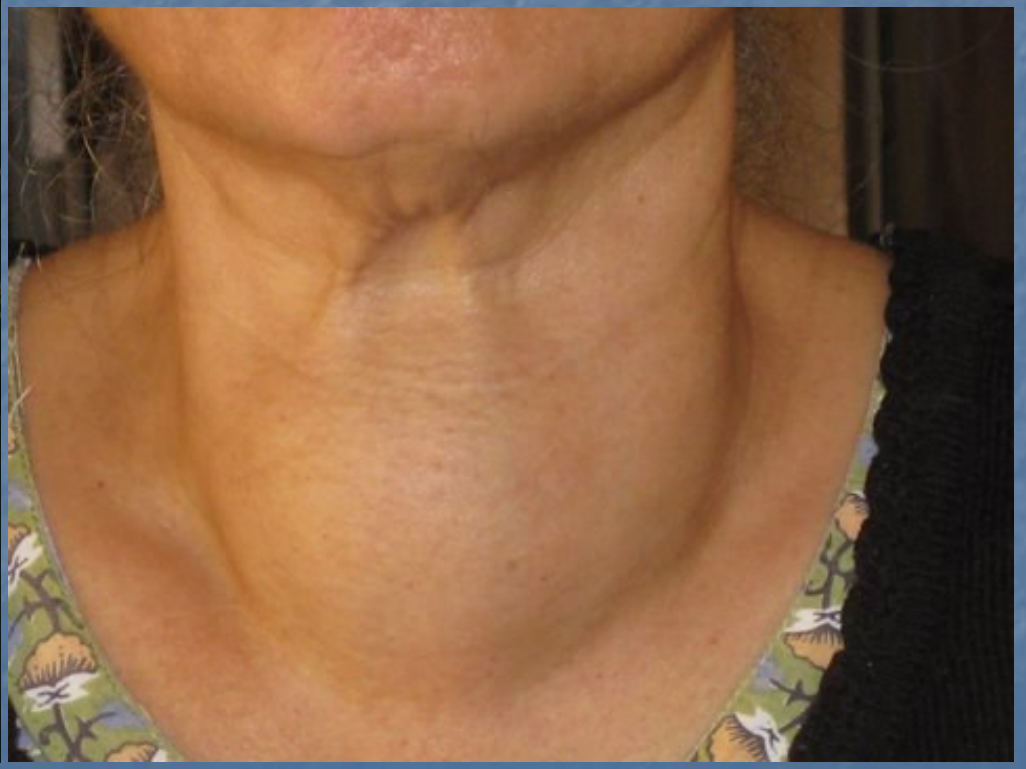
# Causes of Hypothyroidism

- 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 resistance, 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

- Measure TPO antibodies and 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

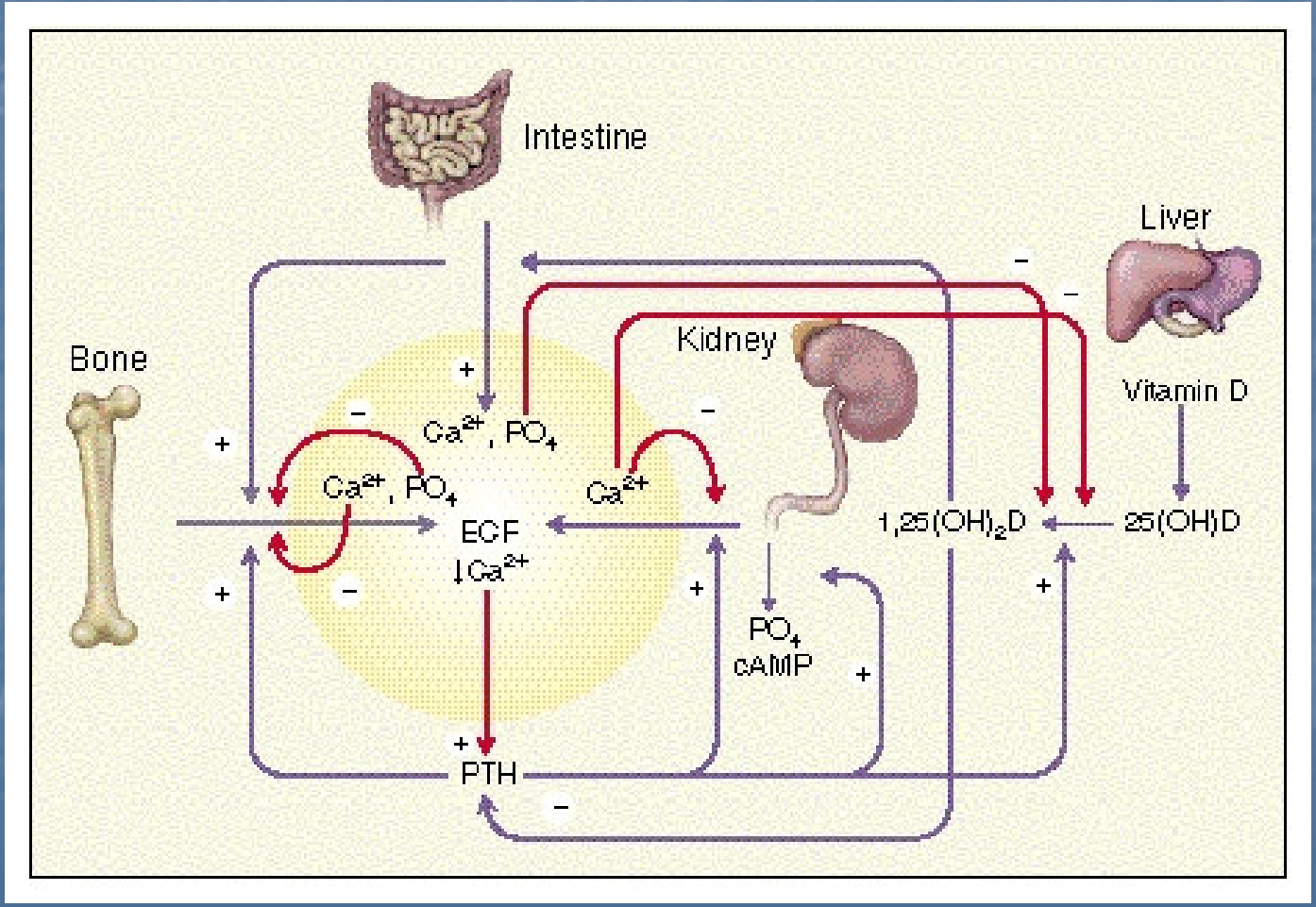
- Mild thyroid failure (subclinical hypothyroidism)
- Interfering (heterophile) antibodies giving misleading results
- TSH resistance

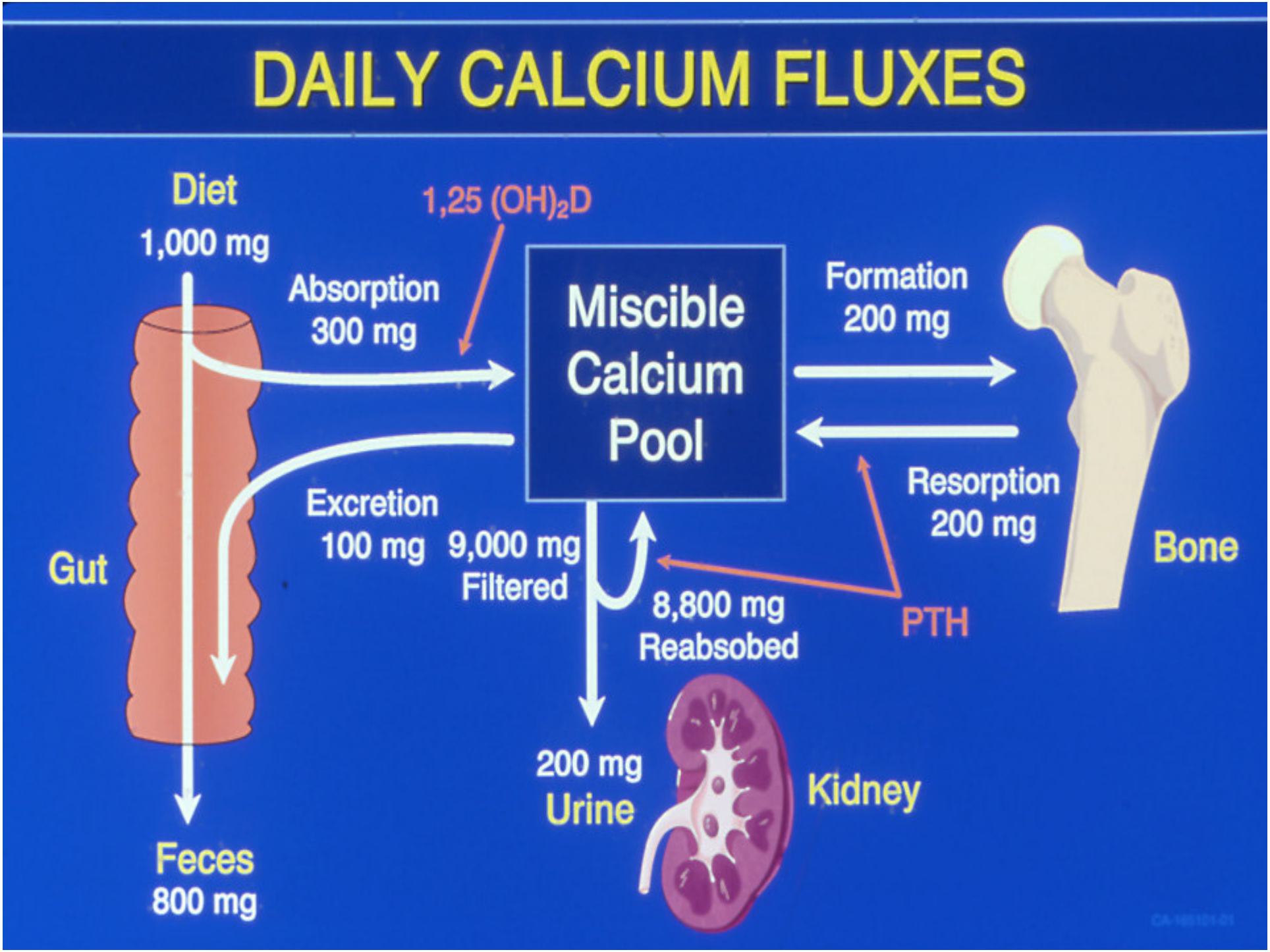
# Normal or High TSH, High fT4 or fT3

- 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

# Parathyroid Disease

# The Big Picture



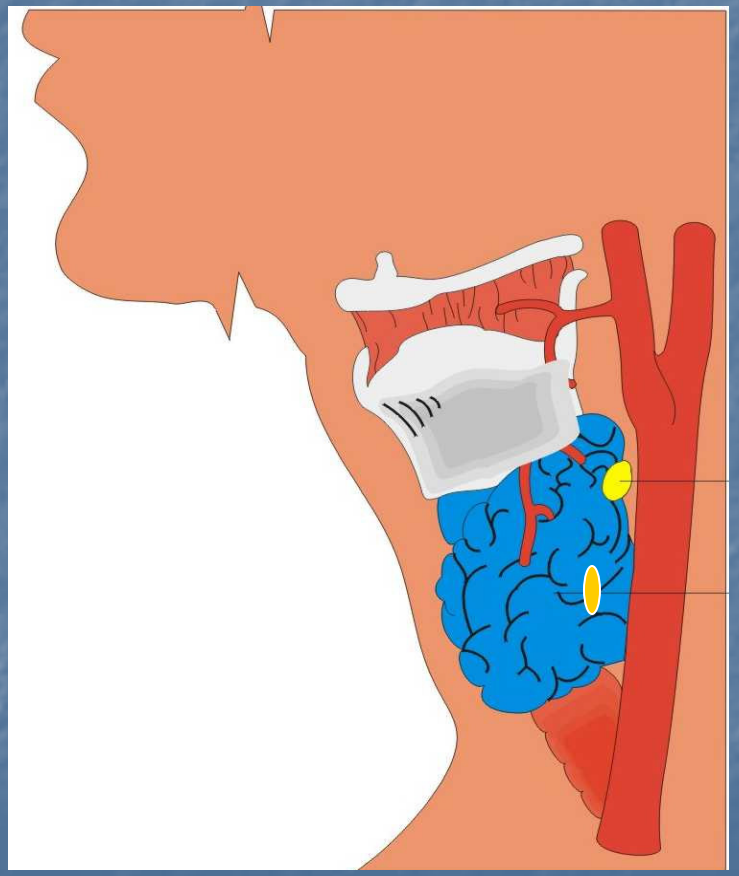

DAILY CALCIUM FLUXES
Diet
1,000 mg
1,25 (OH)2D
Absorption
300 mg
Miscible
Calcium
Pool
Formation
200 mg
Resorption
200 mg
Bone
Gut
Excretion
100 mg
9,000 mg
Filtered
8,800 mg
Reabsobed
PTH
200 mg
Urine
Kidney
Feces
800 mg

# Mineral Homeostasis - Why Care?

- Calcium
  - 99% bone/teeth mineral - hydroxyapatite
  - 1% ECF and soft tissues (neuromuscular stability)
- Phosphorus
  - 85% bone/teeth mineral
  - 15% ECF/soft tissues (cellular energy, intracellular messaging)
- Magnesium - cofactor, neuromuscular stability

# Parathyroid Glands

- Usually four glands (15% of people have 5 parathyroid glands)
- Usually posterior to/or imbedded in the thyroid gland (can be mediastinal, Thyro-oesophogeal groove)



# PTH - What does it do?

- PTH regulates serum calcium and phosphorus homeostasis
- Works in a concerted action with $1,25\ (OH)_2$ Vitamin D on three principal target organs:
  - intestine
  - kidney
  - bone

# PTH - No, really, what does it do?

- PTH ↑ calcium level in ECF by
  - Increasing reabsorption of calcium in kidney
  - Increasing intestinal absorption of calcium (indirectly via Vitamin D)
  - Liberating calcium from bone
- PTH ↓ phosphorus level in ECF
  - Inhibiting reabsorption of phosphorus in the kidney proximal tubule (increases renal excretion)

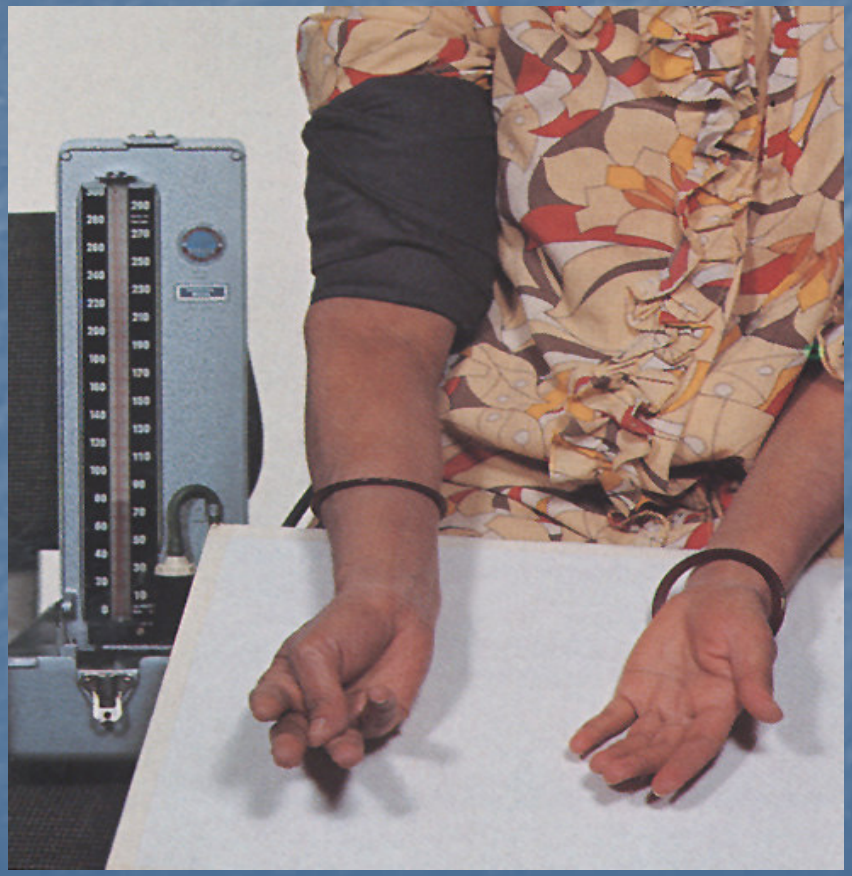
# Regulation of PTH - Calcium

- Acute hypocalcaemia causes PTH secretion from secretory vesicles (within seconds)
  - Intracellular degradation of PTH reduced within hours
  - Increased gene expression of PTH over hours to days
  - Enhanced proliferative activity of parathyroid cells over weeks to months
- Hypercalcaemia inhibits PTH secretion, gene expression, cellular proliferation

# Hypocalcaemia – Signs & Symptoms

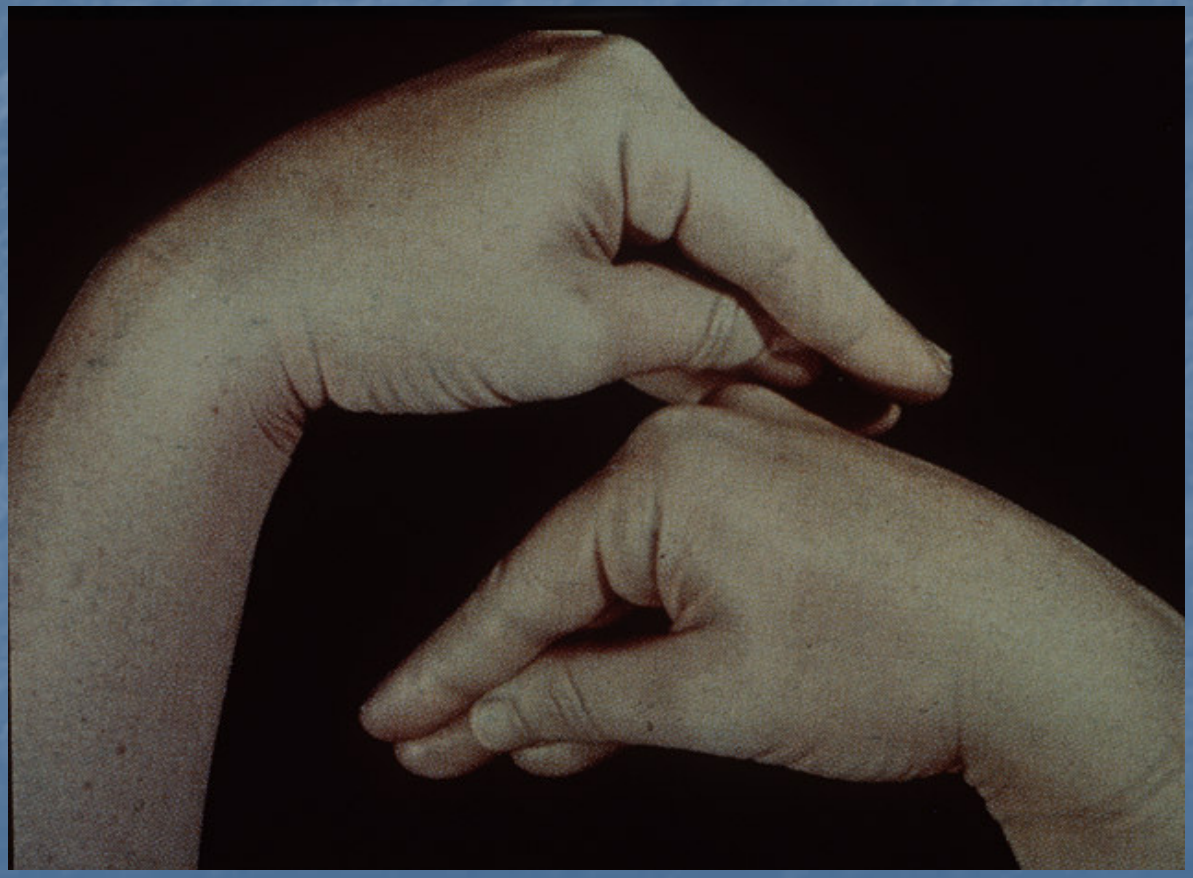
- Neuromuscular irritability
  - tetany (spontaneous tonic muscular contraction)
    - typically in the hands but can be any muscle
  - paraesthesias, fingers/toes/mouth
- Prolongation of QT interval, arrhythmias
- Disorientation
- Seizures
- Death

# Trousseau's Sign



- Neuromuscular irritability
- BP cuff above systolic pressure for 3 minutes
- Flexion of MCP joints, extension of IP joints
- Insensitive but fairly specific for hypocalcaemia

# Hypocalcaemia - Carpal Spasm



# Hypocalcaemia

- Failure to secrete PTH
- Failure to respond to PTH
- Deficiency of Vitamin D
- Failure to respond to Vitamin D

# Hypocalcaemia - Causes

- Hypoparathyroidism - failure to make PTH
  - Destruction of gland
    - surgery, autoimmune
  - Familial
    - some are probably activating mutations in CaR
  - Congenital
    - failure of chief cells to migrate to neck (22q11 AKA DiGeorge syndrome)

# Hypocalcaemia - Causes 2

- Pseudohypoparathyroidism - failure to respond to PTH
  - Target organ unresponsiveness to PTH
  - Type 1b – patients present with biochemical features of hypocalcaemia
  - Type 1a - in addition to biochemical features, a characteristic somatic phenotype consisting of short stature, short digits, round face.
    - loss-of-function of the G-protein of the PTH receptor - second messenger not signaled

# Vitamin D Deficiency

- Inadequate sunlight exposure
- Poor nutrition
- Fat malabsorption - gastrointestinal disease
- Renal failure
- Drugs
  - anticonvulsants interfere with 25 hydroxylation
  - interference with intestinal absorption

# Hypercalcaemia

- General mechanisms
  - Increased bone resorption
  - Increased intestinal absorption of calcium
  - Decreased renal excretion of calcium
- Symptoms of elevated calcium
  - Stones, bones, abdominal groans and psychiatric overtones or asymptomatic

# Hypercalcaemia - Causes

- Primary Hyperparathyroidism
  - Benign tumor making PTH disregards feedback
- Malignancy
  - Tumor making PTHrP (acts just like PTH)
- Extra-renal 1∝hydroxylase activity
  - Unregulated (not regulated by PTH)
  - Lymphoid tissue and macrophages, granulomas
  - Intestinal hyperabsorption of calcium

# Hypercalcaemia - Causes 2

- Familial Benign Hypocalciuric Hypercalcaemia
  - Inactivating mutation of CaR
  - Autosomal Dominant - lifelong
  - Typically mild hypercalcaemia and asymptomatic
  - Hypocalciuria as CaR is in distal nephron also
- Vitamin D intoxication
  - Oral ingestion
  - Doesn't happen with excessive sunlight. Why?

# Renal Failure

- Cannot make 1,25 $(OH)_2$ Vitamin D so serum calcium falls
- Can't excrete phosphorus so ↑ phosphorus
- ↑ PTH (secondary hyperparathyroidism)
- ↑ bone resorption - bone loss

Thank you for your attention