2003a(15): Describe the physiological actions of thyroid hormones

General: Thyroid hormones include tri-iodothyonine (T₃) and thyroxine (T₄).

- Synthesised in thyroid gland within follicular cells
  - Iodination of tyrosine residues in thyroglobulin backbone
  - Synthesised hormones stored within thyroglobulin in colloid of follicular cells
- Synthesis and release stimulated by TSH released from anterior pituitary
- TSH release stimulated by TRH released from median eminence of hypothalamus via hypothalamic-hypophyseal portal system

**Release of T₃ and T₄**
- TSH binds to receptors on cell membrane of follicular cells
  - GPCR → ↑cAMP → ↑adenylyl cyclase
- Effect of TSH:
  - ↑I- uptake (active transport) into follicular cells → ↑iodine trapping
  - ↑synthesis of T₃ and T₄ via ↑iodination and ↑rate of coupling reactions
  - ↑proteolysis of thyroglobulin within follicular cells → liberate T₃ (7%) and T₄ (93%) for diffusion into circulation

**Physiological action of T₃ and T₄**

**Activity**
- T₃ and T₄: highly protein bound (>99%)
  - Bound predominantly to thyroxine binding globulin (TBG), albumin, thyroxine binding pre-albumin (TBPA)
- **t½**
  - T₃: 24hr
  - T₄: 7 days
- T₃ is **3-5 x more active** than T₄

**Effects:**
- **Cellular Effect:**
  - T₄ is de-iodinated to T₃ → binds intracellular receptors
    - ↑gene transcription → ↑protein synthesis, ↑mt activity
      (↑size, ↑numbers) →→ ↑cellular activity
  - **BMR:**
    - ↑Metabolic rate of cells
      - Excess T₃/T₄ → ↑BMR by 60-100%
      - ?2° ↑stimulation Na⁺/K⁺ ATPase → ↑Na⁺ and K⁺ transport through cells
    - ↑appetite / food intake
- **↑CHO Metabolism (T₄ and T₃):**
  - ↑absorption from GIT
  - ↑glycolysis, ↑cellular uptake, ↑gluconeogenesis
- **↑fat metabolism (1° T₄)**
  - ↑FFA release from adipose tissue
  - ↓plasma cholesterol, ↓plasma triglycerides, ↓phospholipids
  - Protein metabolism (T₃ and T₄) / muscles
    - Physiological amounts: Anabolic (↑protein synthesis)

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Excess amounts: Catabolic (↑muscle breakdown)
  - Excess: fine tremour 2° ↑excitability of spinal cord

- CNS:
  - Intra-uterine and neonatal brain development dependent on thyroid hormones
    - Deficiency: Mental retardation
  - Sexual function 2° direct gonadal effect and indirect negative feedback on anterior pituitary control of sexual hormones
    - Deficiency: ♂ → ↓libido
    - Excess: ♂ → erectile dysfunction

- Bones:
  - T₄ important in regulating bone growth

- CVS:
  - Direct: Positively chronotropic and ionotropic
  - Indirect (2° ↑BMR): ↑systemic blood flow → ↑CO
  - Nil effect on MAP (balanced by vasodilation (↓diastolic))
    - Excess: tachycardia, AF

- Resp:
  - Indirect (2° ↑BMR): ↑metabolic demand → ↑depth / rate respiration

- Thyroid Function:
  - Negative feedback (free thyroid hormones) on hypothalamus (inhibit TRH release) and anterior pituitary (inhibit TSH release)