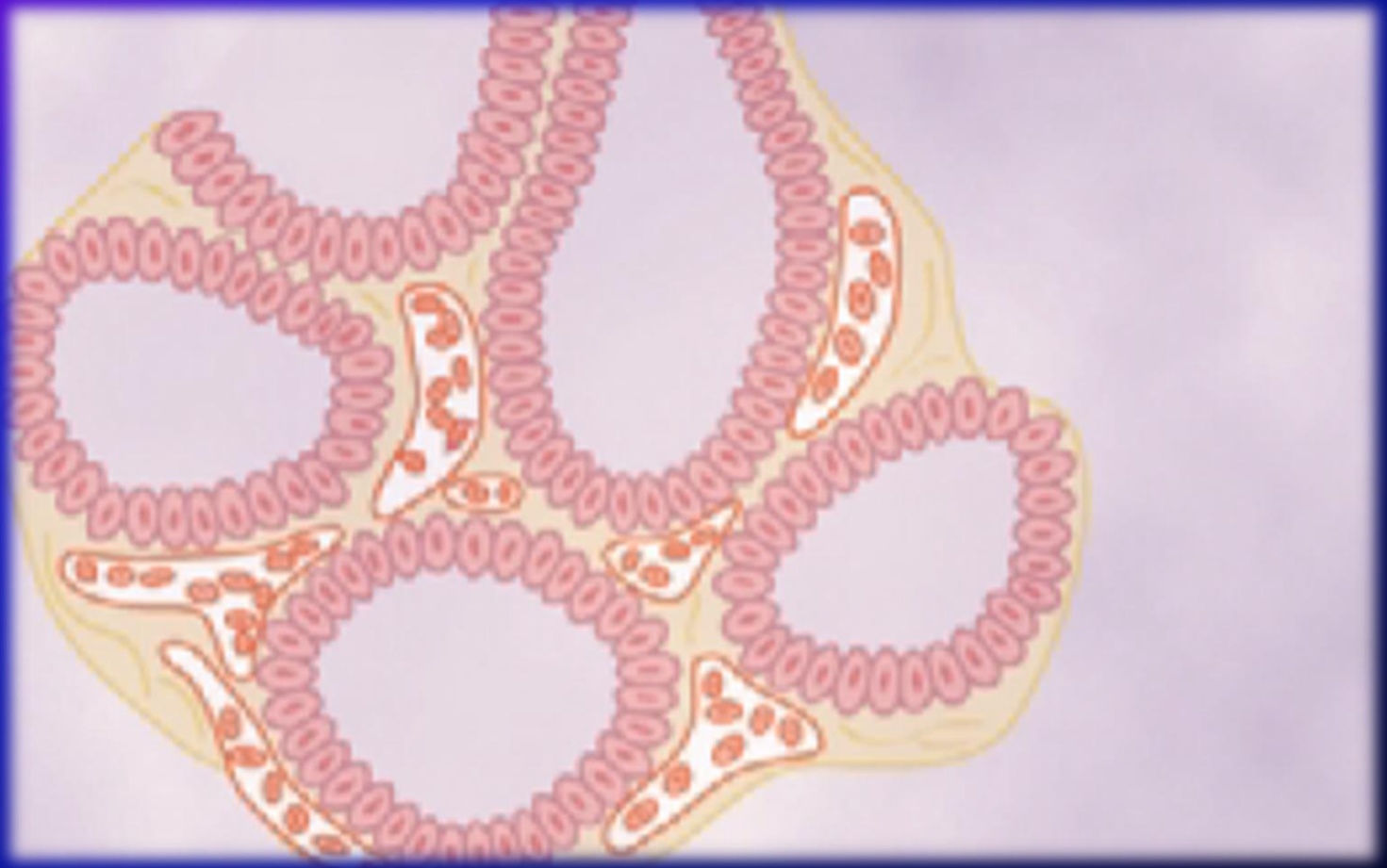
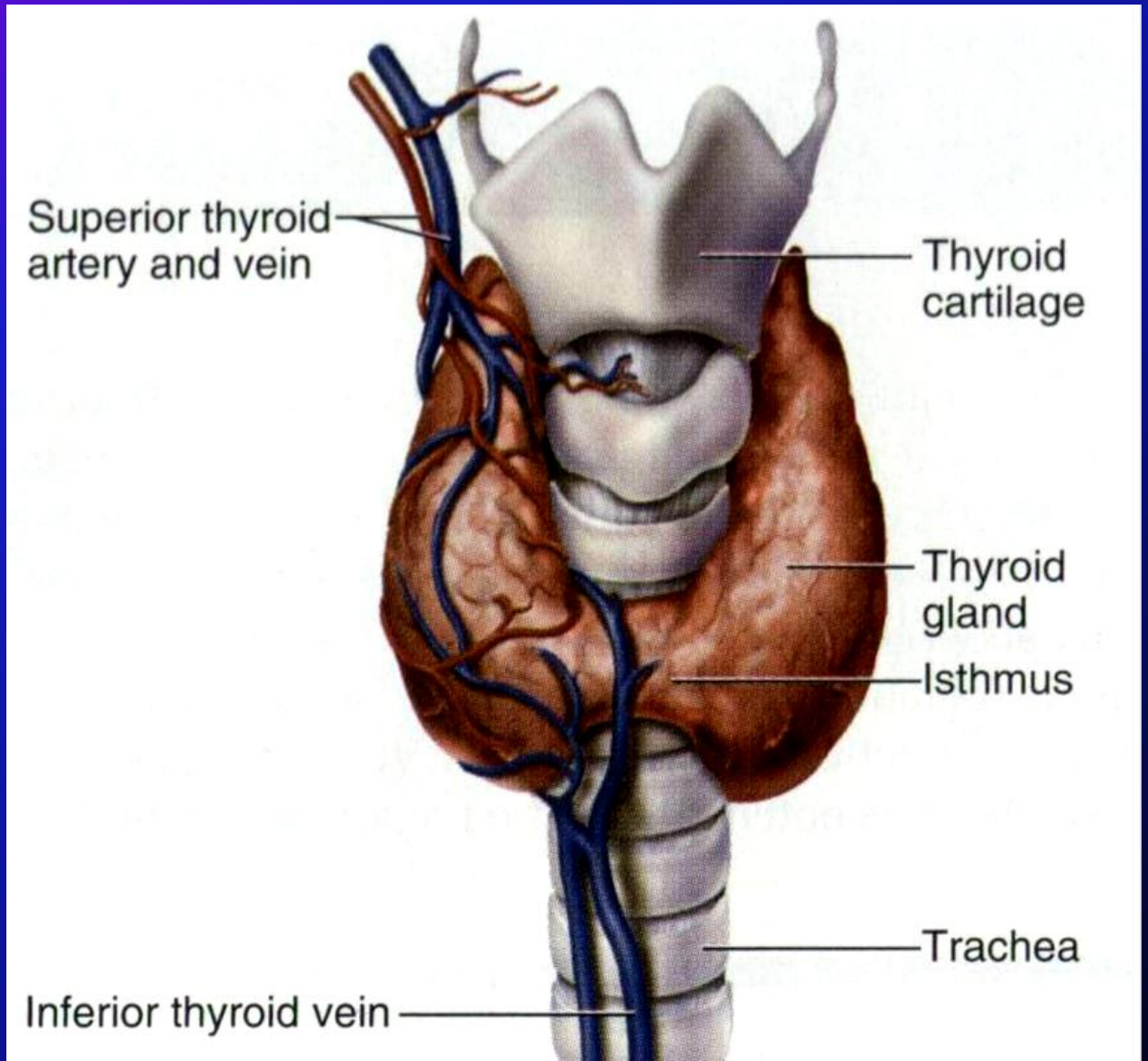
Thyroid Hormones



Thyroid Gland - Anatomy



Thyroid Gland - Histology

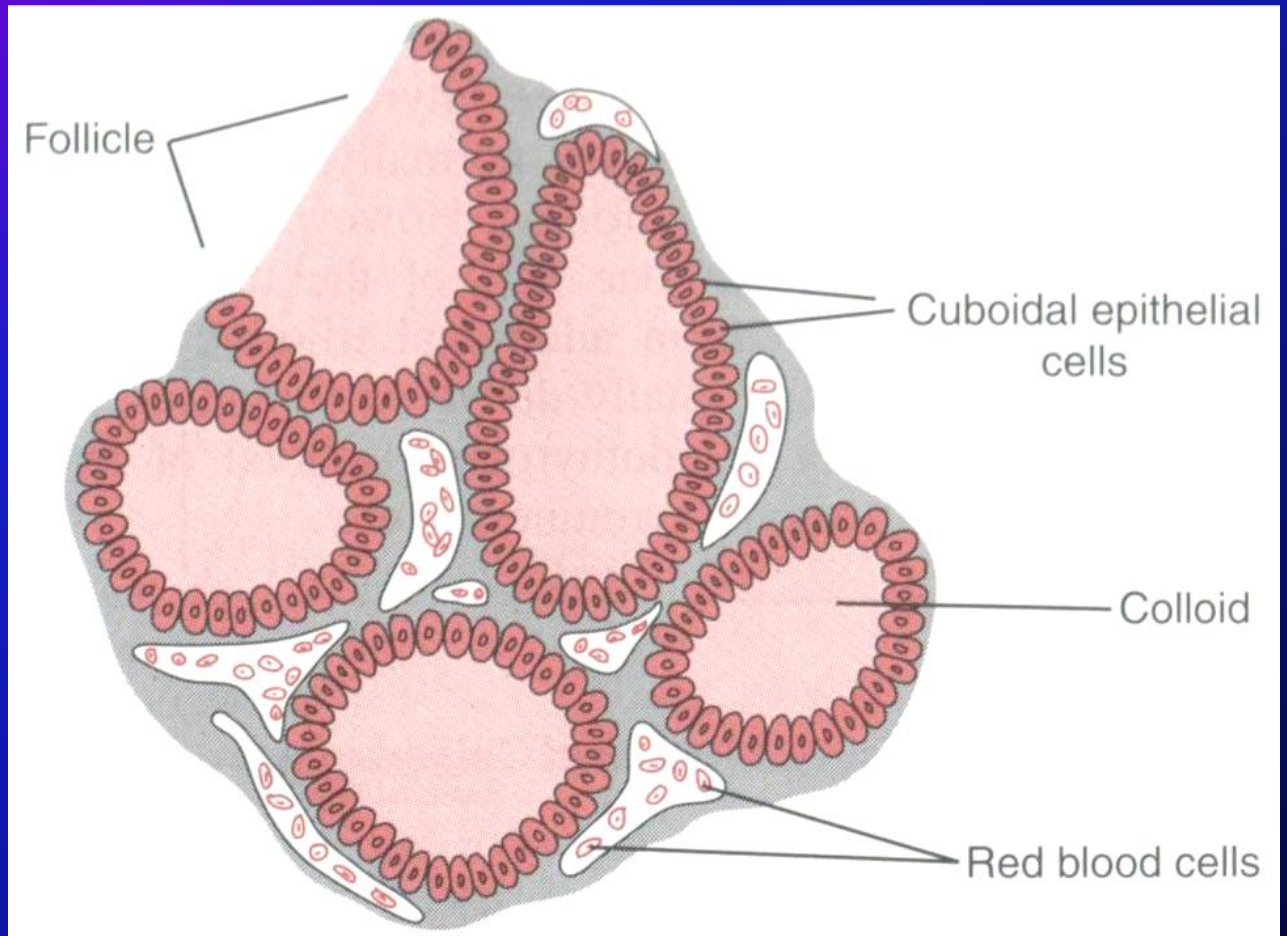
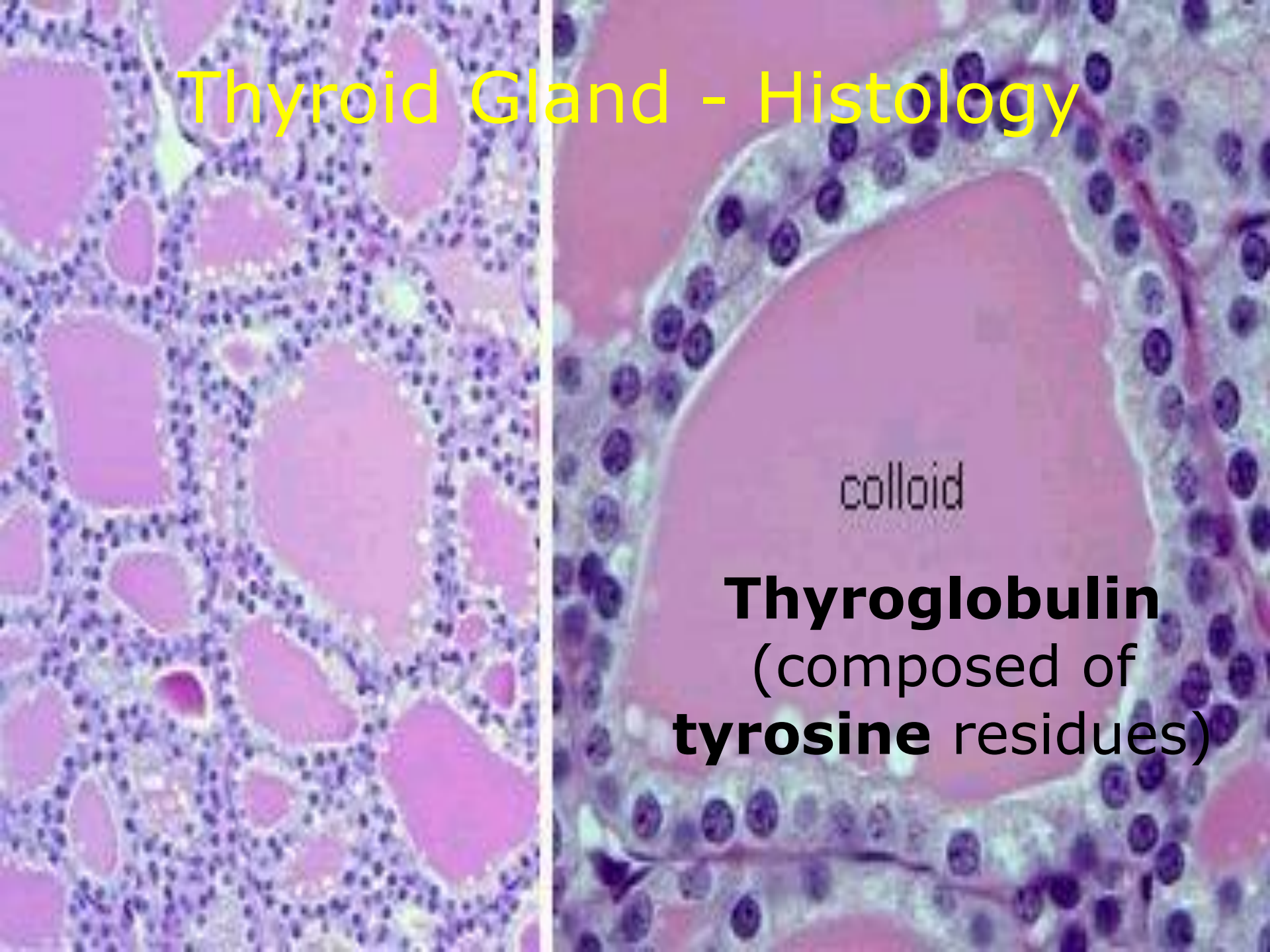


FIGURE 76–1

Microscopic appearance of the thyroid gland, showing secretion of thyroglobulin into the follicles.

Thyroid Gland - Histology



Thyroglobulin (composed of **tyrosine** residues)

Thyroid Hormones

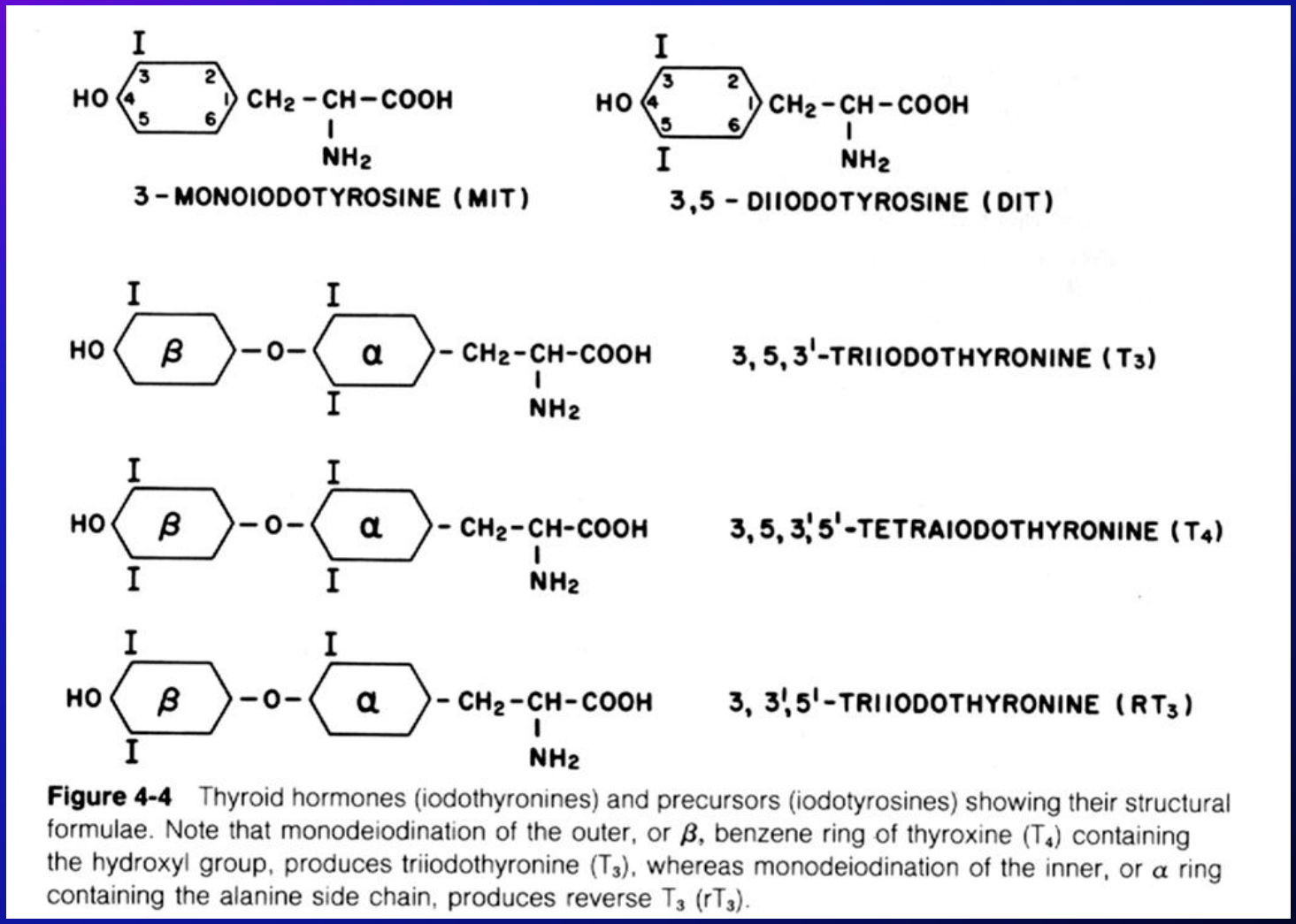


Figure 4-4 Thyroid hormones (iodothyronines) and precursors (iodotyrosines) showing their structural formulae. Note that monodeiodination of the outer, or β, benzene ring of thyroxine (T_4) containing the hydroxyl group, produces triiodothyronine (T_3), whereas monodeiodination of the inner, or α ring containing the alanine side chain, produces reverse T_3 (rT_3).

and Calcitonin

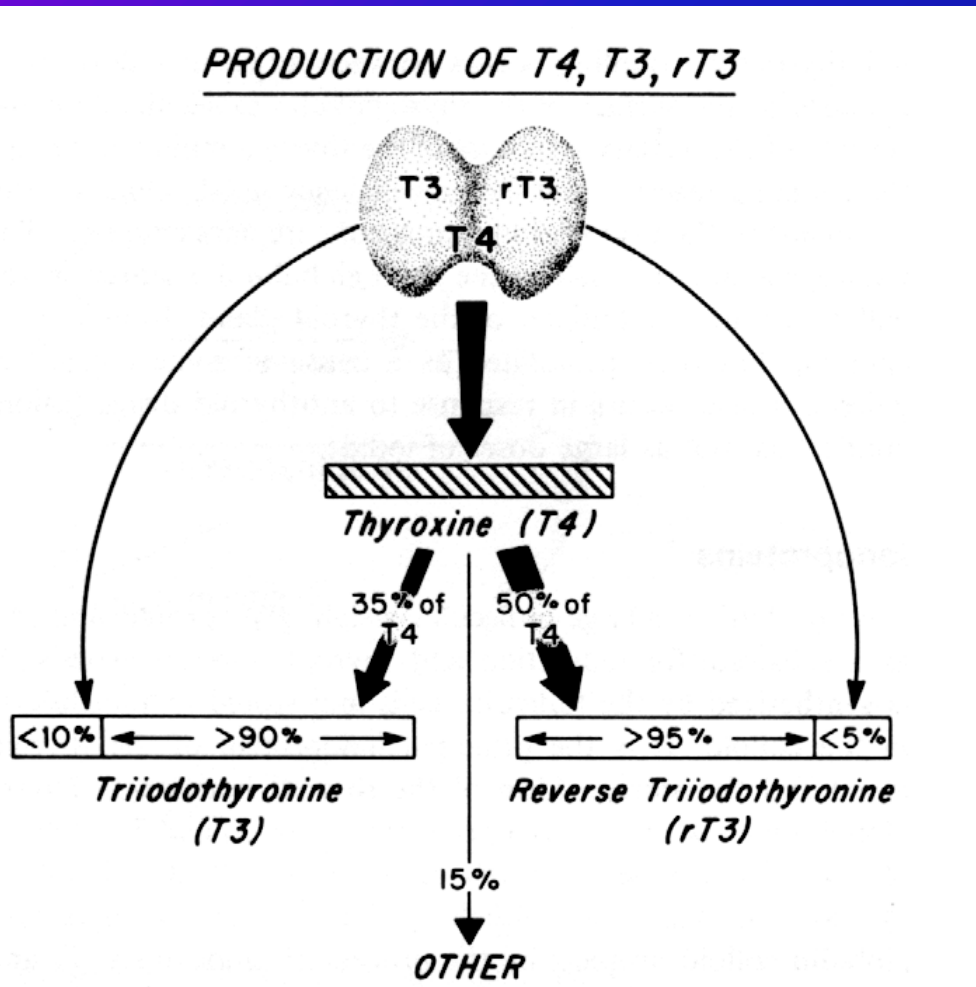
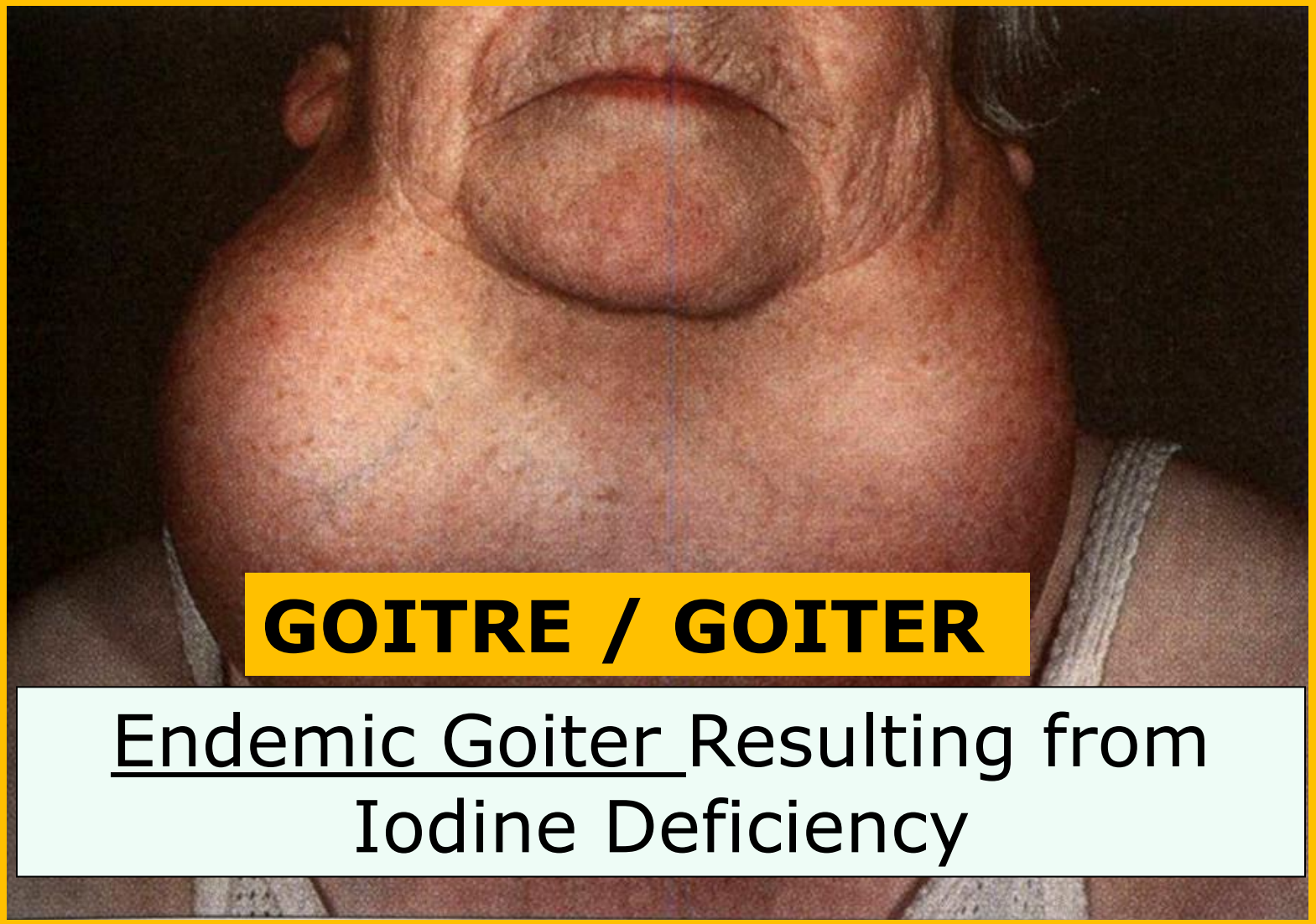


Figure 4-3 Production of T_4, T_3, and rT_3. The principal thyroid gland secretion is T_4, 85% of which is monodeiodinated by peripheral tissues to T_3 and rT_3. Under normal conditions only small amounts of T_3 and rT_3 are derived from thyroidal secretion, a discovery that has led to the concept of T_4 as a prohormone. In nonthyroidal illness peripheral conversion of T_4 to rT_3 is enhanced leading to a reduction in serum T_3 concentration ("sick euthyroid"). The physiological significance of this shift in T_4 metabolism is not well understood.

Exophthalmos

Hyperthyroidism
(Graves` Disease)

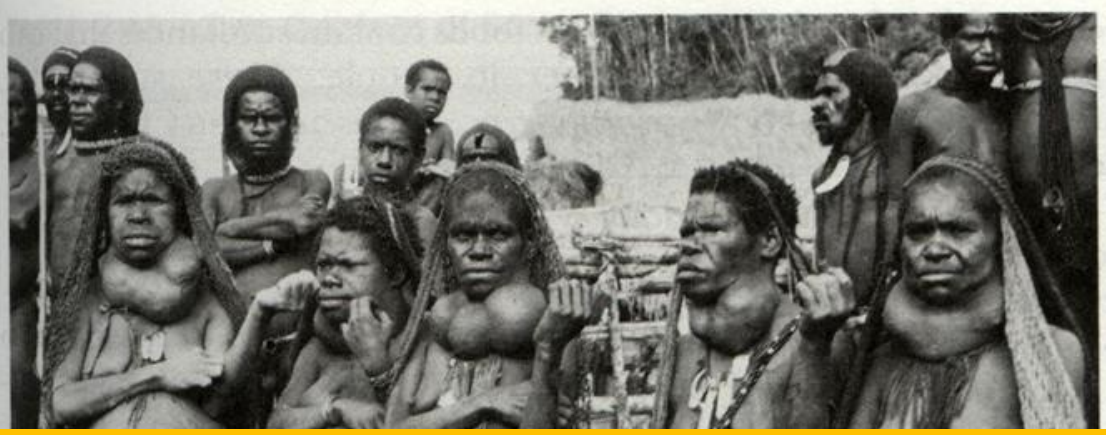
Hyperthyroidism

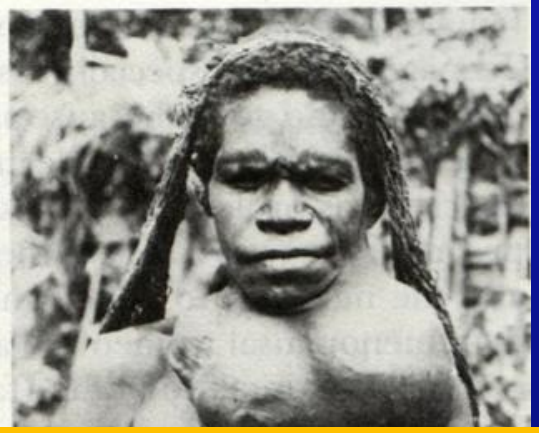


GOITRE / GOITER

Endemic Goiter Resulting from Iodine Deficiency

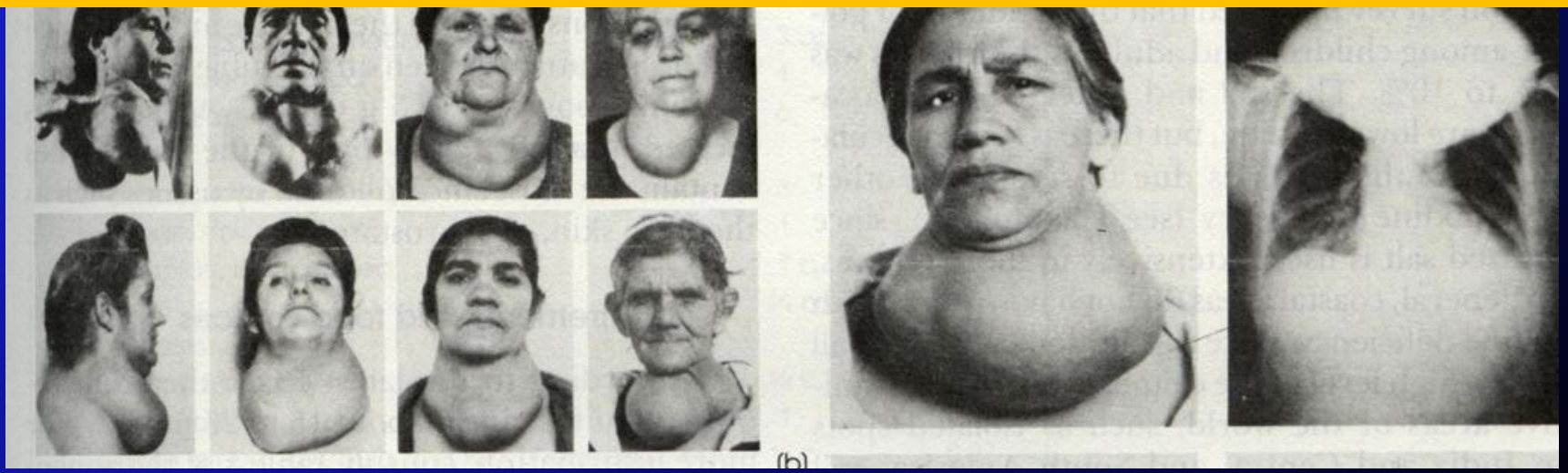
Hypothyroidism





ENDEMIC GOITRES:

- were common in Central Europe, the area around the Great Lakes in the USA,
- China, the Peruvian Andes,



Iodine:

- Sources: Iodized salt, dairy products, fish
- Adult RDA: 150 μg
- The average dietary intake - 500 μg /day
- Dietary intake below 50 μg /day →

  synthesis of thyroid hormones inadequate

Iodide:

- A circulating (extrathyroidal) pool - 250 - 750 μg
- The total iodide content of the thyroid - 7 500 μg

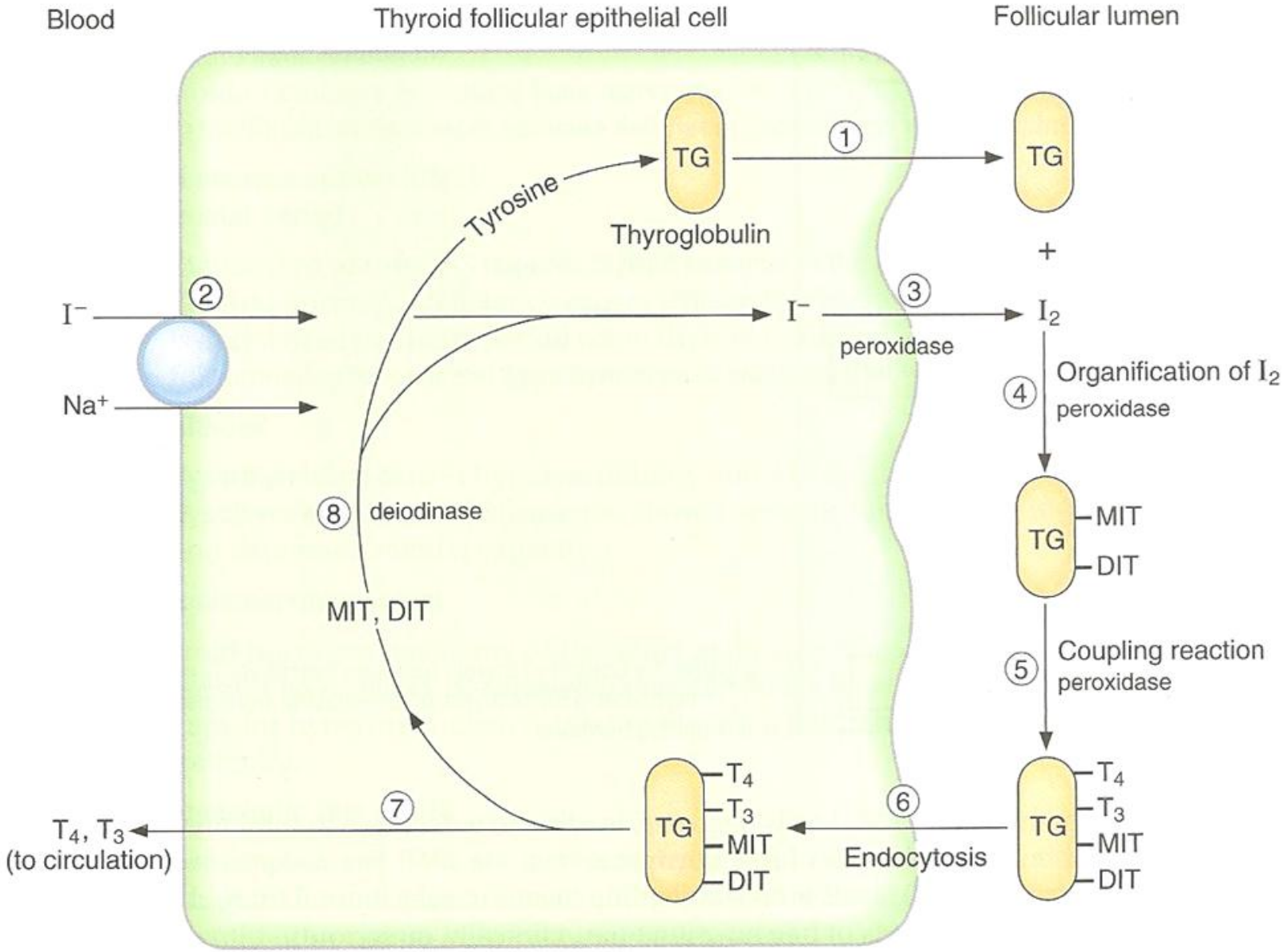


FIGURE 7-8 Steps in the synthesis of thyroid hormones. Each step is stimulated by thyroid-stimulating hormone. DIT = diiodotyrosine; I^- = iodide; MIT = monoiodotyrosine; T_3 = triiodothyronine; T_4 = thyroxine; TG = thyroglobulin.

Synthesis

- Iodide (I^-) pump ("trap") (inhibited by high blood I^- level)
- Conversion of I^- to I_2 /THYROID PEROXIDASE/
- Binding of iodine with thyroglobulin /THYROID PEROXIDASE/

→ monoiodotyrosine (MIT), diiodotyrosine (DIT)

- Coupling of DIT (MIT) and DIT - oxidative condensation

/THYROID PEROXIDASE ?/

- Storage of the thyroid hormones in the follicular colloid

Secretion

- Formation of pinocytic vesicles
- Fusion with lysosomes → digestive vesicles
- Digestion of thyroglobulin, liberation of the thyroid hormones
- Deiodination of iodinated tyrosine residues (MIT, DIT) which had not been coupled (deiodinase)

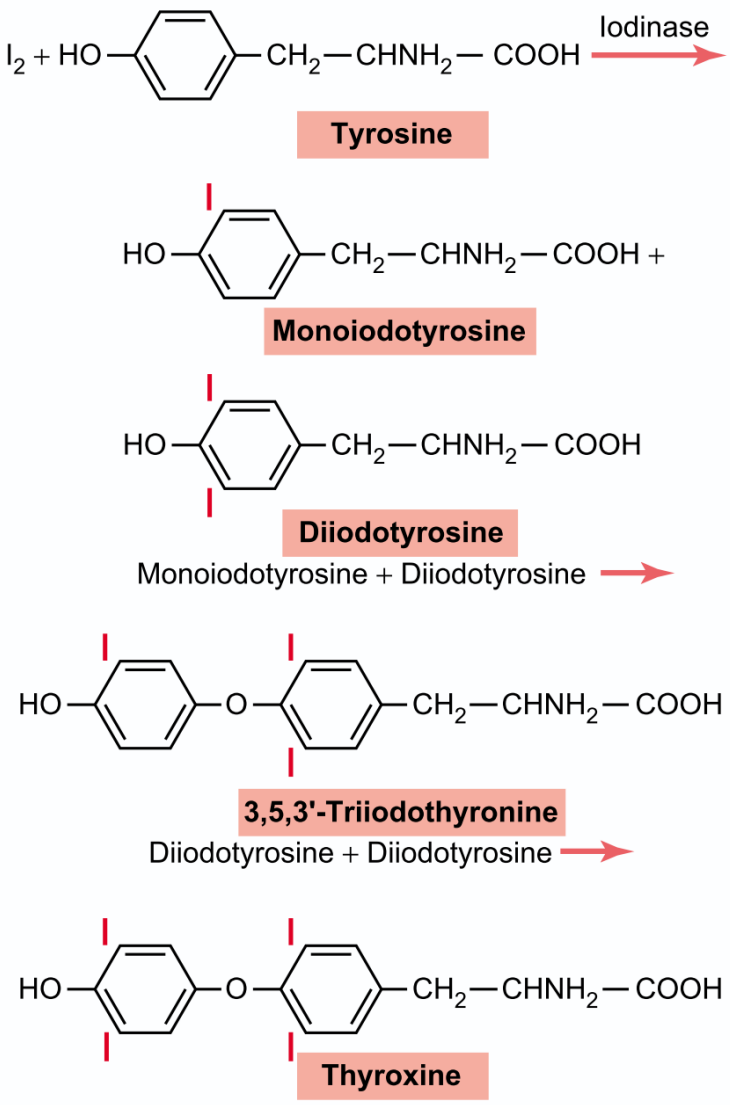
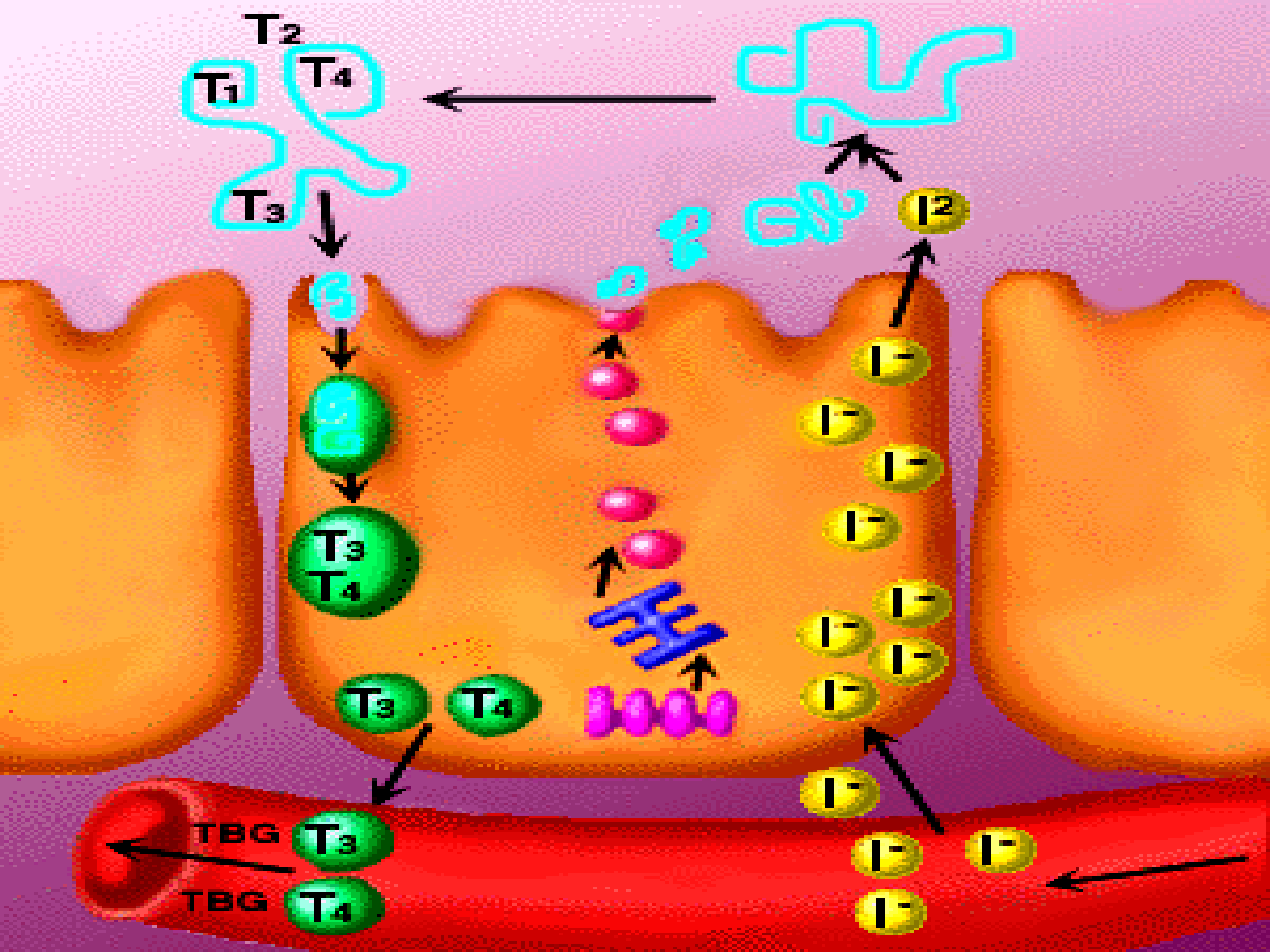


Figure 76–3

Chemistry of thyroxine and triiodothyronine formation.


T2
T1
T4
T3
I2
I-
I-
I-
I-
I-
I-
I-
I-
I-
I-
I-
I-
T3
T4
T3
T4
TBG
T3
TBG
T4

Transport of Thyroid Hormones in the Blood

	T_4	T_3
Bound	**99,98%**	**99,8%**
Thyroxine- binding globulin (TBG):	67%	46%
Thyroxine - binding prealbumin (TBPA): (Transthyretin)	20%	1%
Albumin:	13%	53%
Free	**0,02%**	**0,2%**

Plasma levels

Total	8 μg/dl	0,15 μg/dl
Free	2 ng/dl	0,3 ng/dl

Thyroxine **Triiodothyronine**

- **Binding affinity of TBG and other plasma proteins**

6 times greater

- **Release to the tissues**

Slower

- **Biologic half-life**

Longer (6-7 days) ***1 day***

- **Binding with intracellular proteins**

Stronger

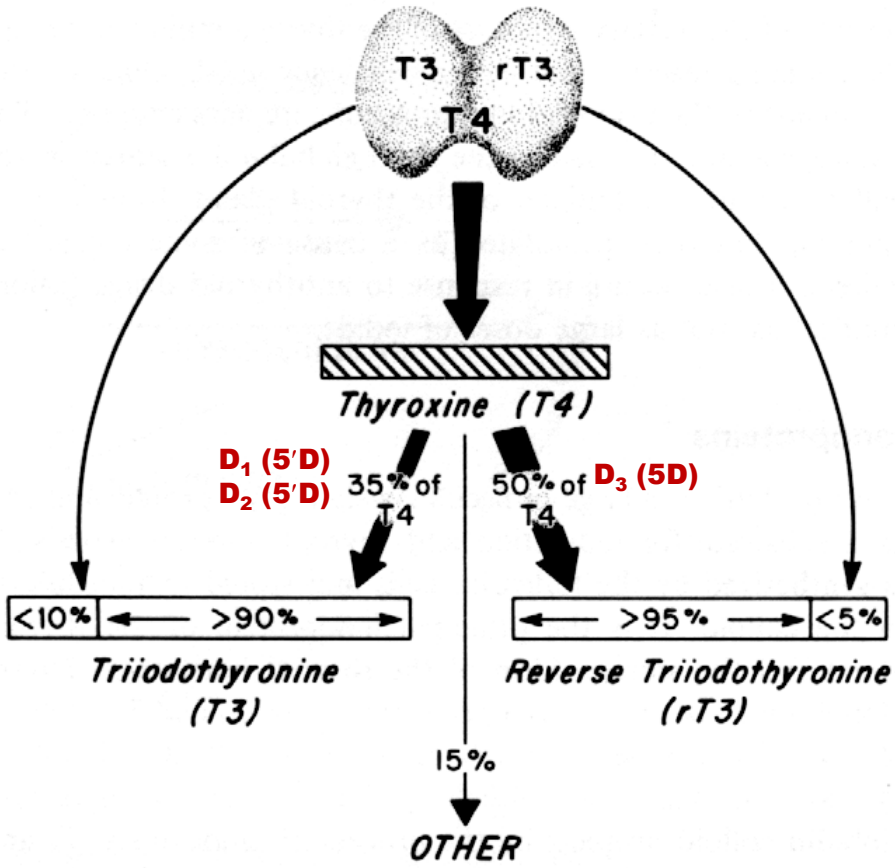
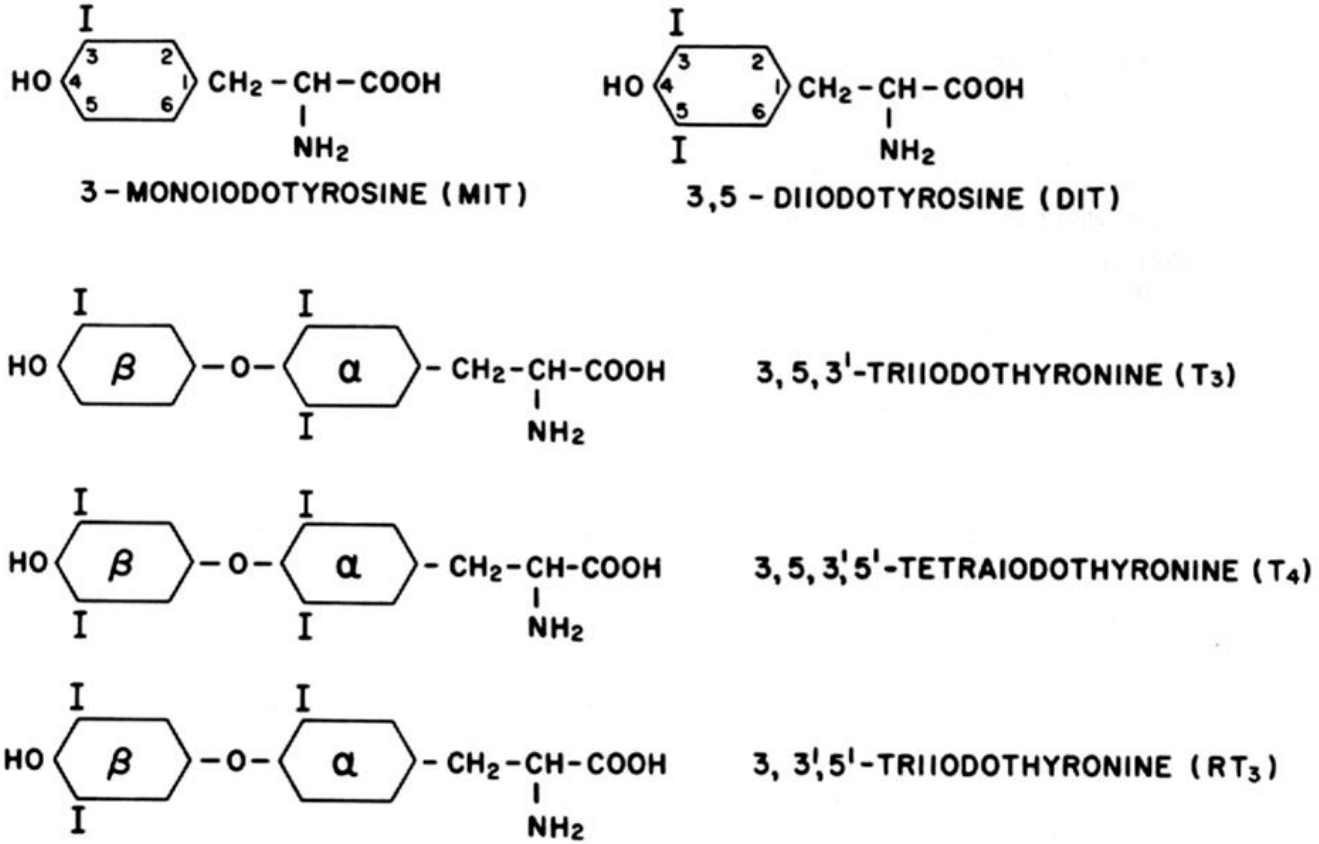


Figure 4-3 Production of T_4, T_3, and rT_3. The principal thyroid gland secretion is T_4, 85% of which is monodeiodinated by peripheral tissues to T_3 and rT_3. Under normal conditions only small amounts of T_3 and rT_3 are derived from thyroidal secretion, a discovery that has led to the concept of T_4 as a prohormone. In nonthyroidal illness peripheral conversion of T_4 to rT_3 is enhanced leading to a reduction in serum T_3 concentration (''sick euthyroid''). The physiological significance of this shift in T_4 metabolism is not well understood.

Thyroid Hormones



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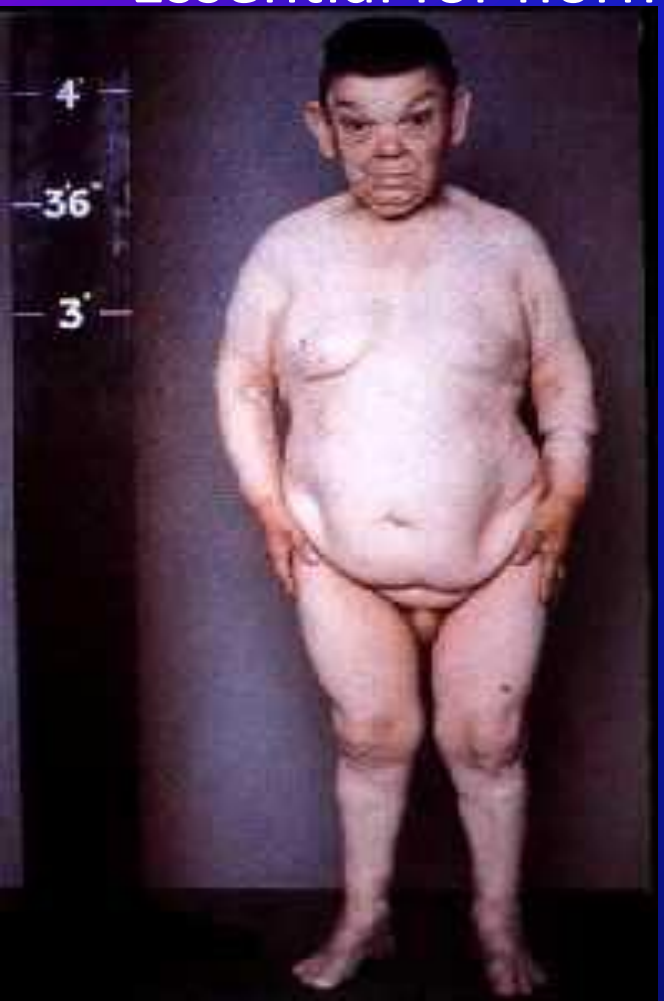
Thyroid Hormones - Effects

Nervous System

(fetal life, childhood)

Essential for normal growth and development of brain;

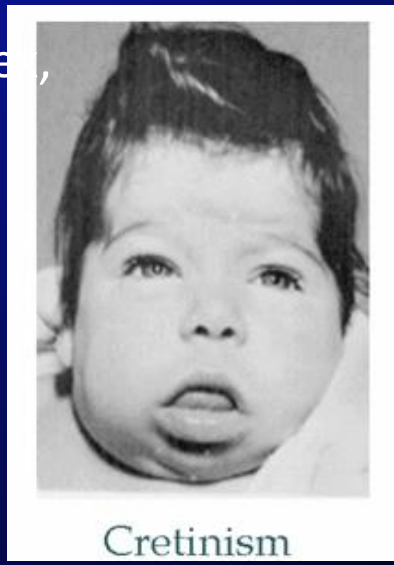


Proliferation of axons, branching of dendrites,

Synaptogenesis,

Cell migration, growth of cerebral cortex,

Myelin formation

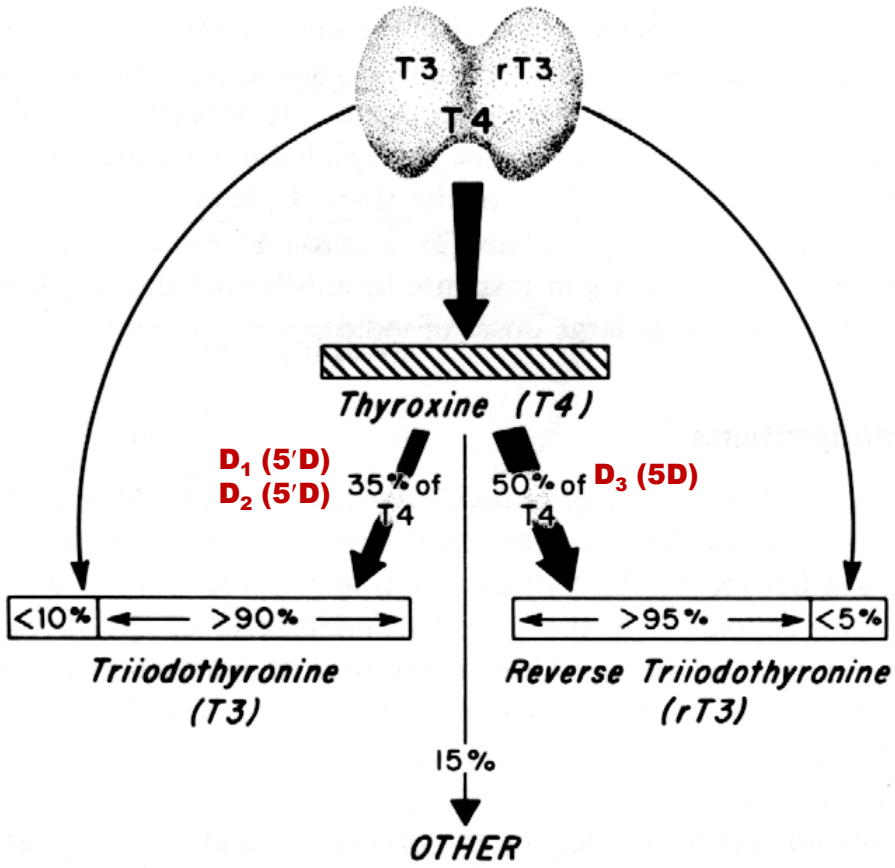


Cretinism

Congenital Hypothyroidism

Cretinism (mental retardation)

Failure of growth, thickened facial features



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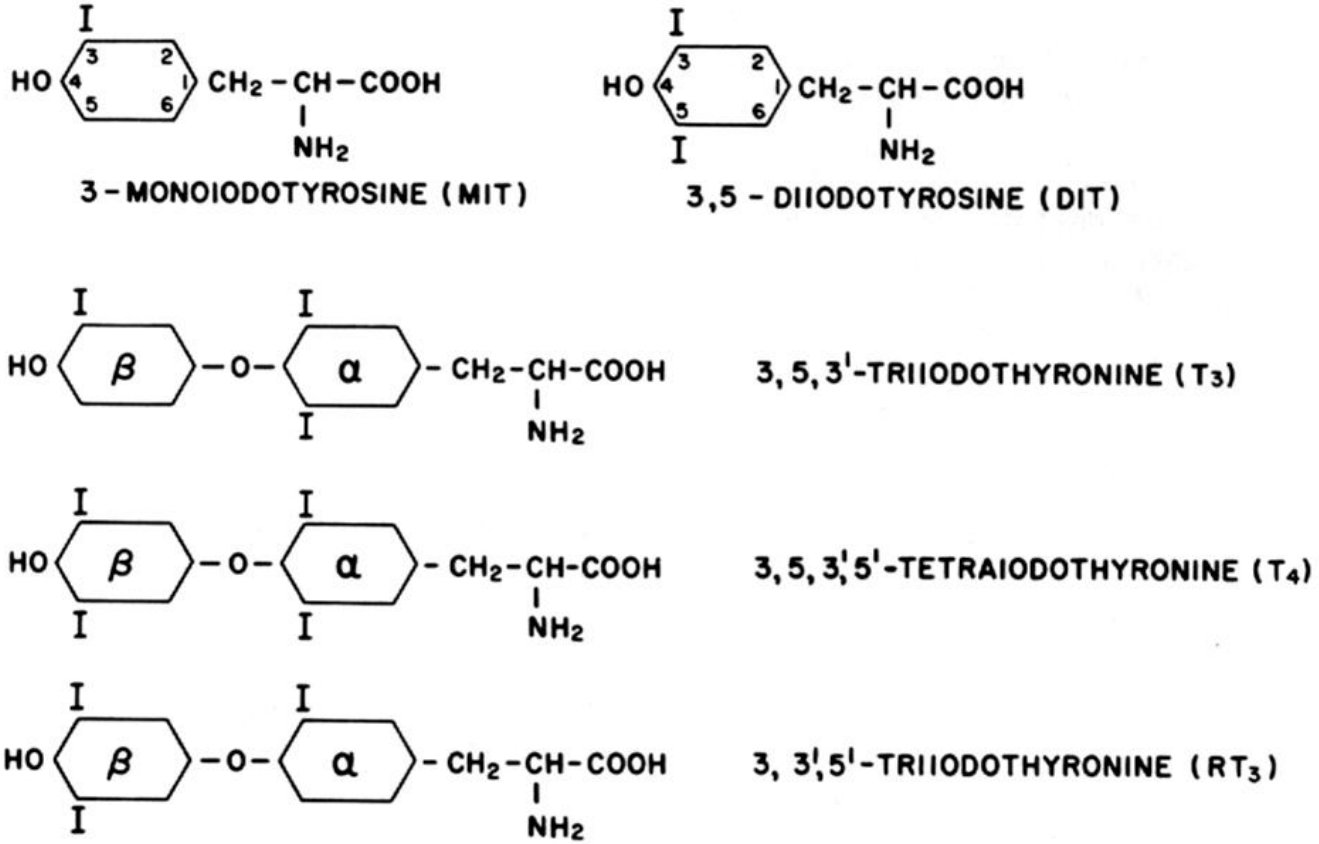
Thyroid Hormones



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Case 1

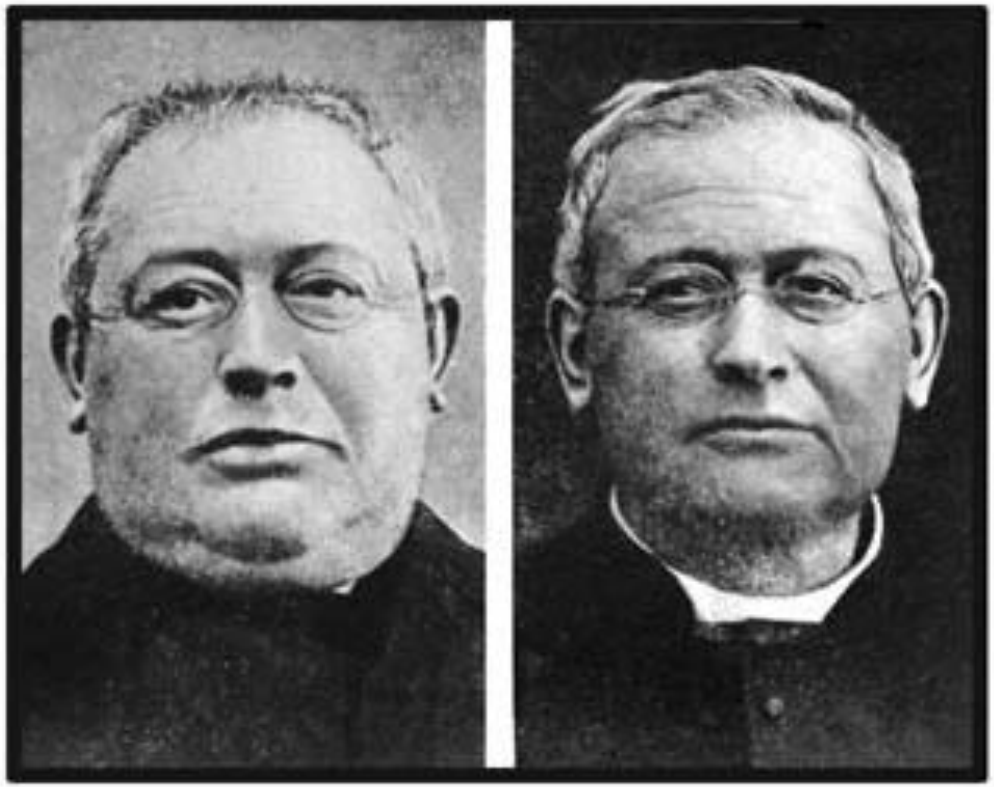
My old good friend Shirley called me last Monday to invite me to dinner. Shirley is a 43-year-old university teacher. I have known her for over 20 years, since we studied at the University. However we have not met within the last year. I was very surprised that I did not recognize her voice on the phone. It was hoarse and deep as that of a man, especially smoking. Besides Shirley spoke slower than usual and mainly about her complains. She told me that in spite of eating less her weight had increased by 16 lb in the last year, but she has attributed her weight gain to "getting older". Later Shirley complained that she has very little energy, always feels weak, tired, and cold. She also suffers from muscle cramps and stiffness.

When I saw her in the evening, I noticed that Shirley's neck was very full. Her face was slightly edematous and her skin was dry and cold. She added that she was constipated and had too frequent menses.

I suspected that Shirley had _ _ _ _ _ _ _ _ .

- ***Hoarseness, deep voice***
- ***Slow speech***
- ***↓appetite, weight gain***
- ***↓energy level***
- ***Cold intolerance***
- ***Muscle weakness, cramps, stiffness***
- ***Thyroid enlargement***
- ***Myxedema***
- ***Dry, cold skin***
- ***Constipation***

Hypothyroidism



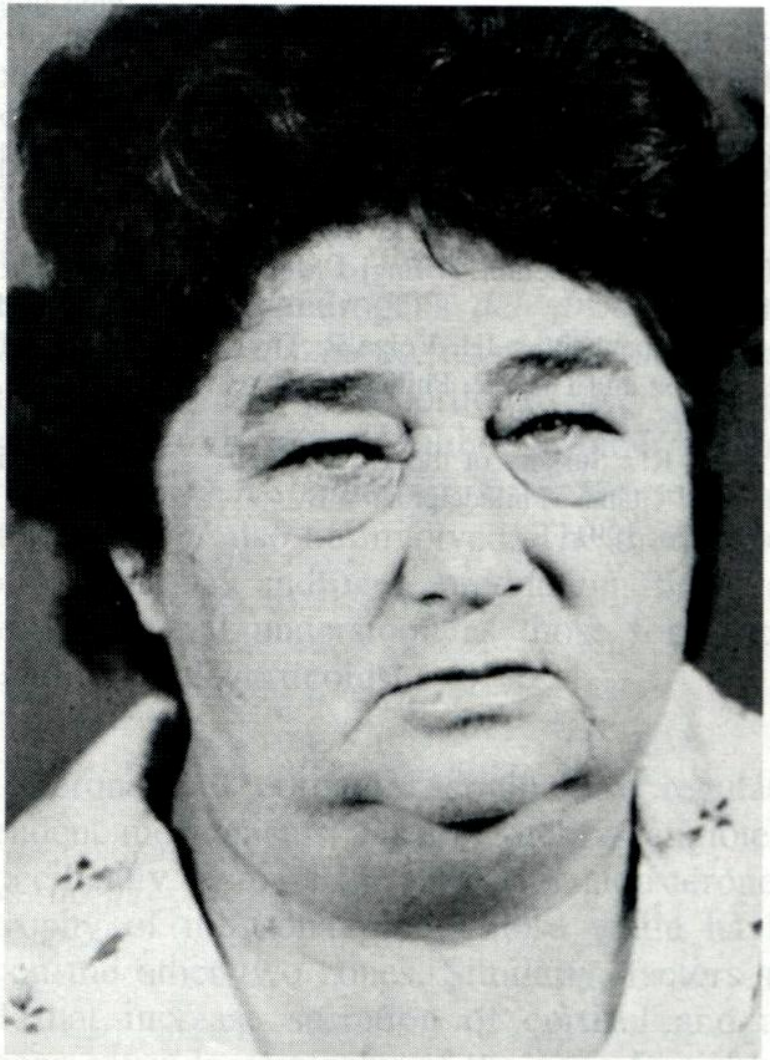
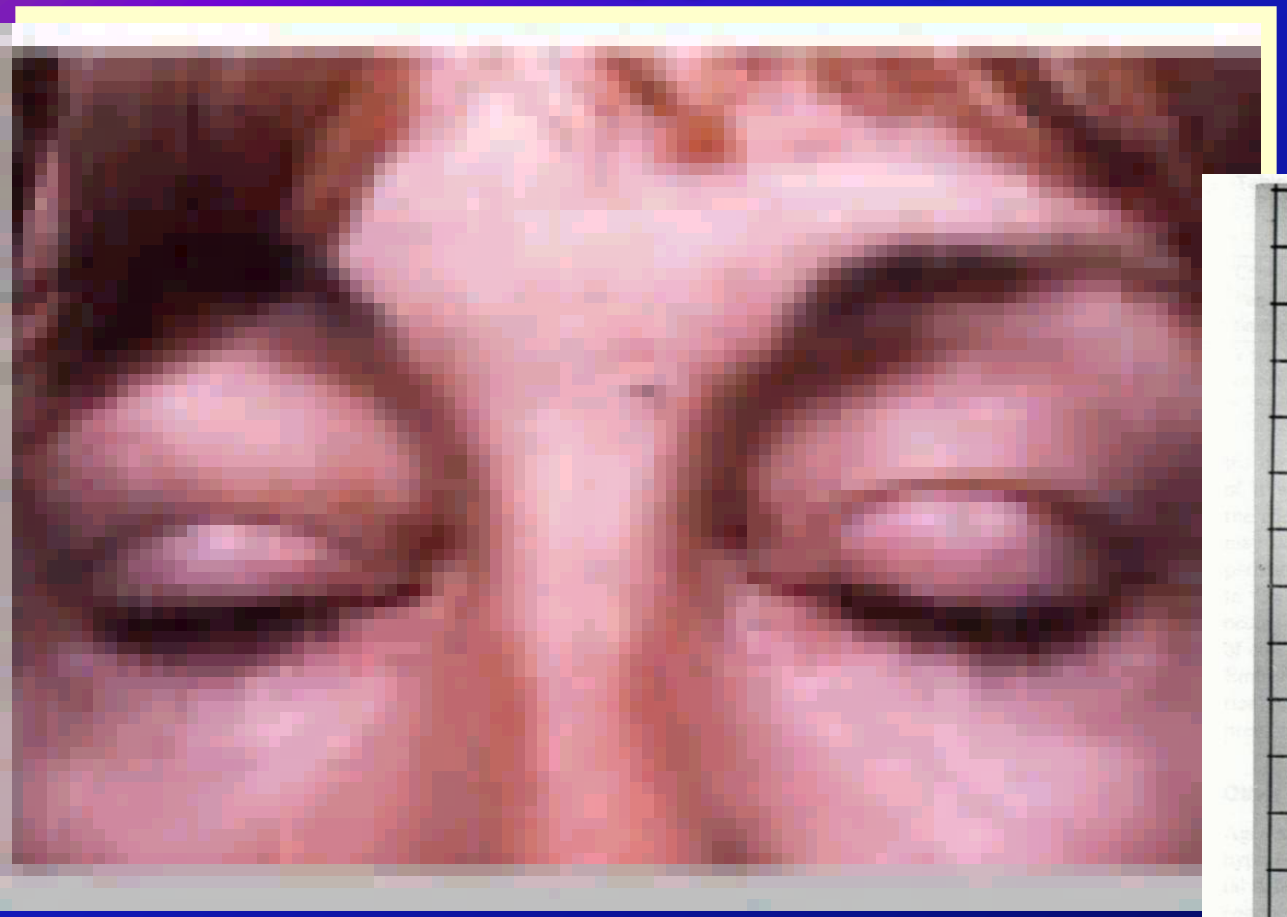


FIGURE 76–8

Patient with myxedema. (Courtesy Dr. Herbert Langford.)

Hypothyroidism



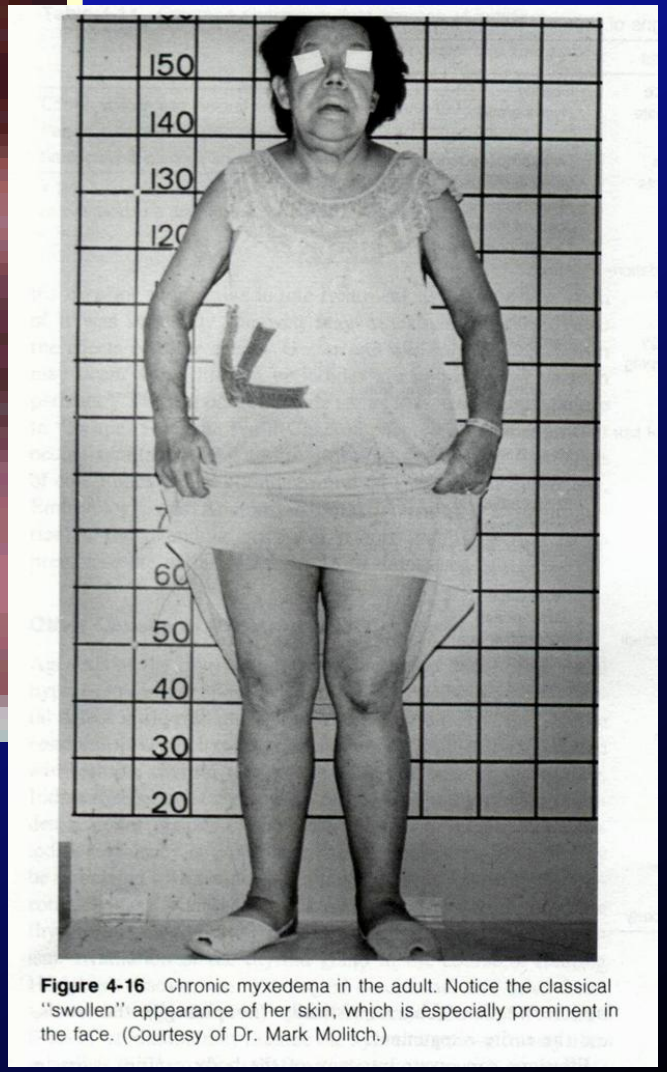


Figure 4-16 Chronic myxedema in the adult. Notice the classical "swollen" appearance of her skin, which is especially prominent in the face. (Courtesy of Dr. Mark Molitch.)

Case2

Natasha is a 23-year old woman who has always dieted to keep her weight on an "acceptable" level. However, within the last three months she has lost 20 lb in spite of a big appetite. She also notes that she always wants the thermostat set lower than her apartment mates. She complains of heart palpitations, increased frequency and softening of bowel movements, difficulty sleeping, irritability, and irregular menstrual periods. Besides she easily gets tired. During interview she was restless and she spoke very quickly.

On physical examination Natasha weighted only 110 lb. Her skin was smooth and warm. Her heart rate was 110 beats/min and her arterial pressure was 160/70. She had a tremor in her fingers and hands. Natasha had a wide-eye stare, and her lower neck appeared full; these characteristics were not present in photographs taken 1 year earlier.

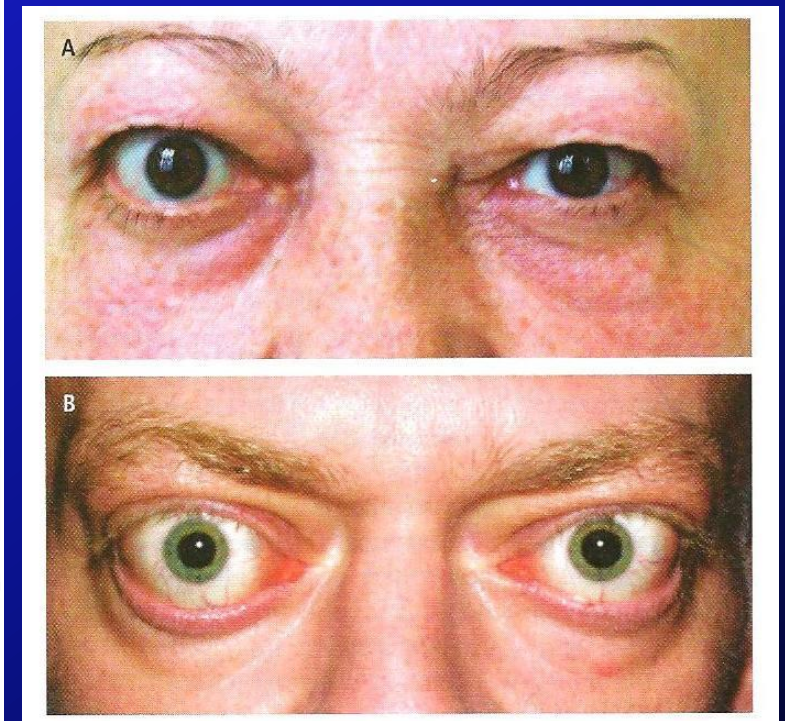
Based on her symptoms, I suspected that Natasha had _ _ _ _ _ _ .

- ***Weight loss***
- ***↑appetite***
- ***Heat intolerance***
- ***Palpitations***
- ***↑frequency, softening of bowel movements***
- ***Irregular menstrual periods***
- ***Difficulty sleeping***
- ***Irritability, fatigue***
- ***Rapid mentation***
- ***Smooth, warm skin***
- ***Tachycardia***
- ***Systolic hypertension***
- ***Tremor in hands***
- ***Ophthalmopathy***
- ***Thyroid gland enlargement - goiter***

Hyperthyroidism

Figure 76–8

Patient with exophthalmic hyperthyroidism. Note protrusion of the eyes and retraction of the superior eyelids. The basal metabolic rate was +40. (Courtesy Dr. Leonard Posey.)



Ryc. IV.B.3-7. Orbitopatia tarczycowa: **A** – łagodna (retrakcja powieki, niewielkie wysunięcie prawej gałki ocznej bez innych objawów ze strony tkanek miękkich), **B** – jawna (ryc. B. udostępniła prof. dr hab. med. Ewa Bar-Andziak)

Thyroid Hormones

- **nuclear transcription of large numbers of genes**
- **↑ formation of RNA, proteins (enzymatic, structural, others)**
- **↑ functional activity throughout the body**

↑ BMR;

↑oxygen consumption, ↑ energy production (ATP and heat)

HYPERTHYROIDISM

Symptoms	*Signs*
↑ appetite	**Sweating**
Weight loss	
Heat sensitivity	
Relative vitamin deficiency	

HYPOTHYROIDISM

Symptoms	*Signs*
↓ appetite	**Obesity**
Weight gain	
Cold sensitivity	

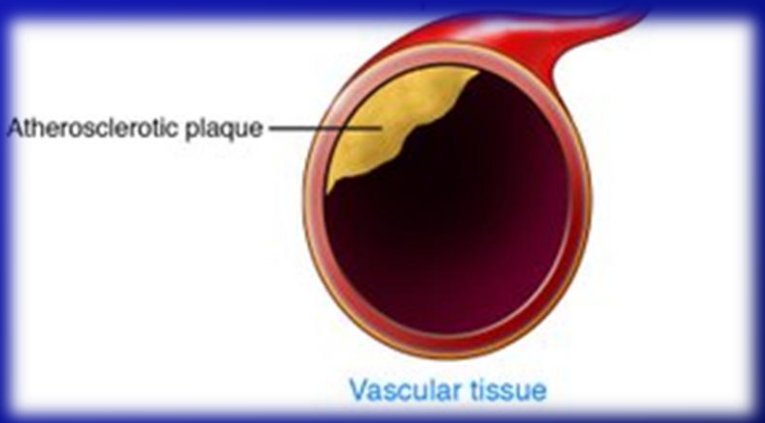
Thyroid Hormones - Effects

Carbohydrate Metabolism

- ↑ rate of absorption from GI tract
- ↑ all aspects of metabolism

Lipid Metabolism

- ↑ lipolysis, ↑ blood FFA level
- ↓ blood cholesterol level



HYPOTHYROIDISM

↑ blood cholesterol level (LDL)

↓

severe atherosclerosis

Thyroid Hormones - Effects

Protein Metabolism

- ↑ synthesis ,↑ breakdown
- Action synergetic with GH and IGFs
  (promotion of protein synthesis, bone formation)

HYPERTHYROIDISM

↑ catabolism

Muscle weakness

(thyrotoxic myopathy)

HYPOTHYROIDISM

Muscle weakness

Muscle stiffness

- ↑ muscle mass
- ↑ mucopolisaccharides

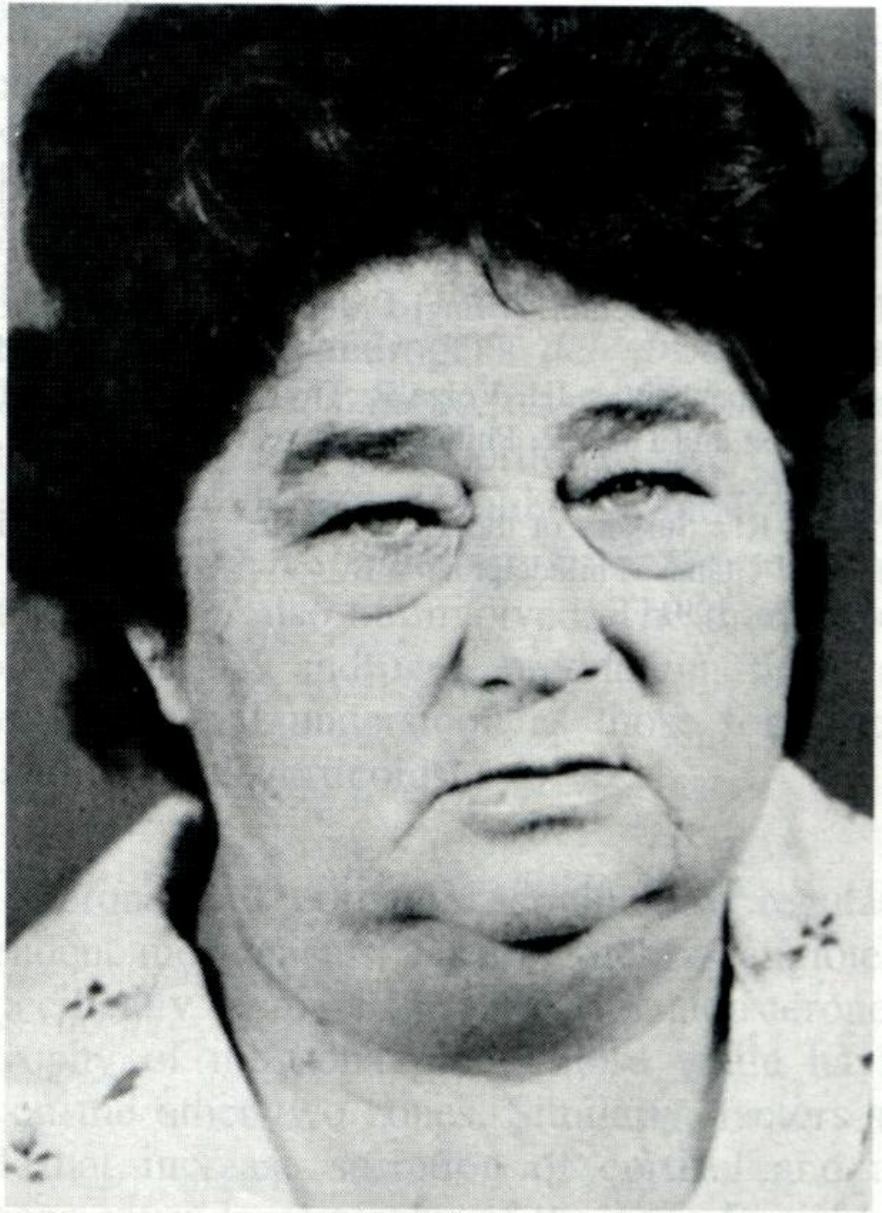


FIGURE 76–8

Patient with myxedema. (Courtesy Dr. Herbert Langford.)

Thyroid Hormones - Effects

Skin, Connective tissue

- integrity of collagen
- ↓ synthesis, ↑ degradation of mucopolisaccharides

HYPERTHYROIDISM

Smooth, warm skin

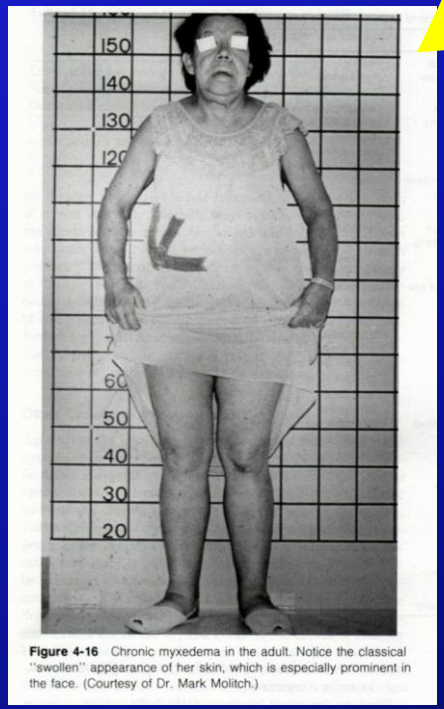


Figure 4-16 Chronic myxedema in the adult. Notice the classical "swollen" appearance of her skin, which is especially prominent in the face. (Courtesy of Dr. Mark Molitch.)

HYPOTHYROIDISM

Cool, dry skin

Myxedema (nonpitting edema)

Accumulation of mucopolisaccharides ("-" charge)

↓

Retention of osmotically active cations (Na^+)

↓

Retention of water

↓

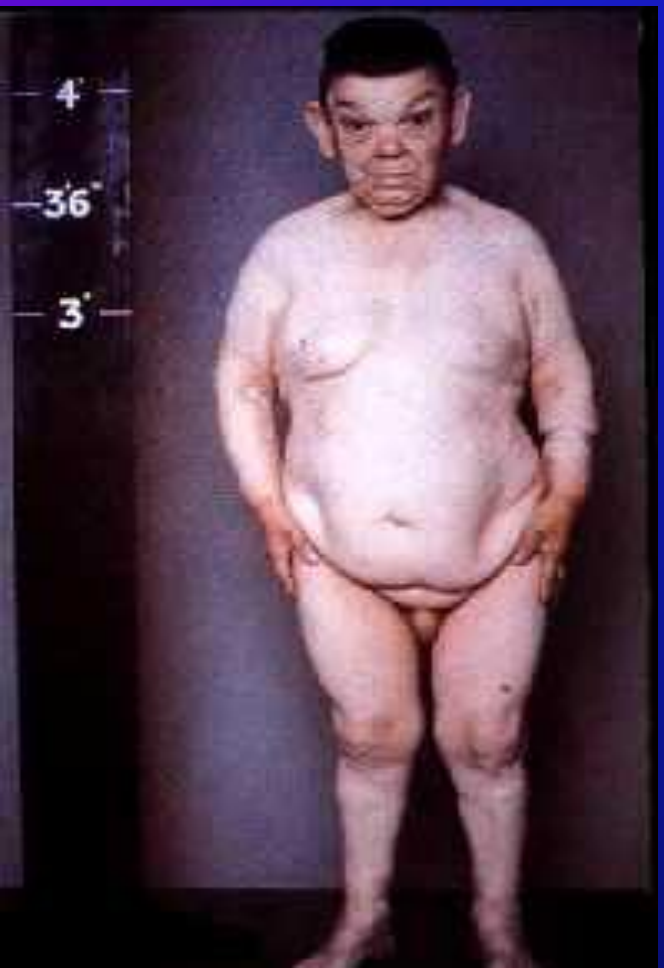
Puffiness of skin

Thyroid Hormones - Effects

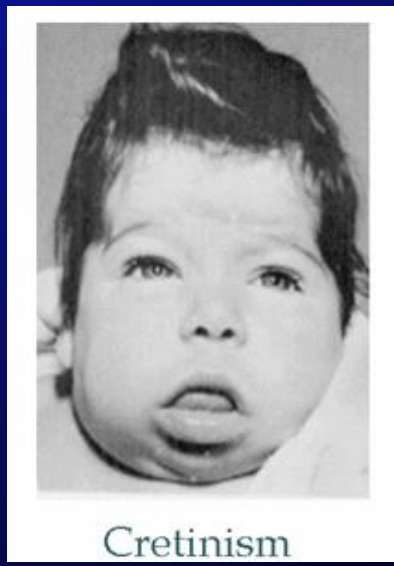
Nervous System

(fetal life, childhood)

Essential for normal growth and development of brain;



Proliferation of axons, branching of dendrites,
Cell migration, growth of cerebral cortex,
Myelin formation


Cretinism

Congenital Hypothyroidism

Cretinism (mental retardation)

Failure of growth, thickened facial features

Thyroid Hormones - Effects

Nervous System

- ↑ rapidity of cerebration

HYPERTHYROIDISM		***HYPOTHYROIDISM***	
Symptoms	*Signs*	*Symptoms*	*Signs*
Rapid mentation	Emotional liability	Slow mentation	Dementia
Irritability			
Difficulty sleeping		Somnolence	
Fatigue	Tremor		

Thyroid Hormones - Effects

Bone, Growth

- Essential for normal growth and skeletal maturation;
  - Growth of bone
  - Ossification of cartilage
  - Maturation of epiphyseal growth centres
  - Closure of epiphyses

HYPERTHYROIDISM	***HYPOTHYROIDISM***
Excessive skeletal growth	Retarded growth rate
Earlier closure of epiphyses	Delayed closure of epiphyses
Bone resorption	

Thyroid Hormones - Effects

Cardiovascular System

↑ blood flow, ↑ cardiac output (↑ stroke volume, ↑ heart rate)

- ↑ myocardial calcium uptake, ↑ Na^+,K^+-ATPase activity, ↑ α-MHC (myosin heavy chain)
- ↑ number, ↑ affinity of β-adrenergic receptors (heart)

↓

↑ sensitivity to catecholamines - adrenergic stimulation of the heart

↑

Vasodilatation

↑

↑ heat, CO_2 production

HYPERTHYROIDISM

Symptoms	***Signs***
	Tachycardia
	Arrhythmia
	Systolic hypertension

HYPOTHYROIDISM

Symptoms	***Signs***
CHD	**Bradycardia**

Thyroid Hormones - Effects

Respiratory System

↑ rate of breathing, ↑ depth of breathing,

Gastrointestinal System

↑ motility of GI tract, ↑ secretion

HYPERTHYROIDISM

↑ frequency and softening of bowel movements

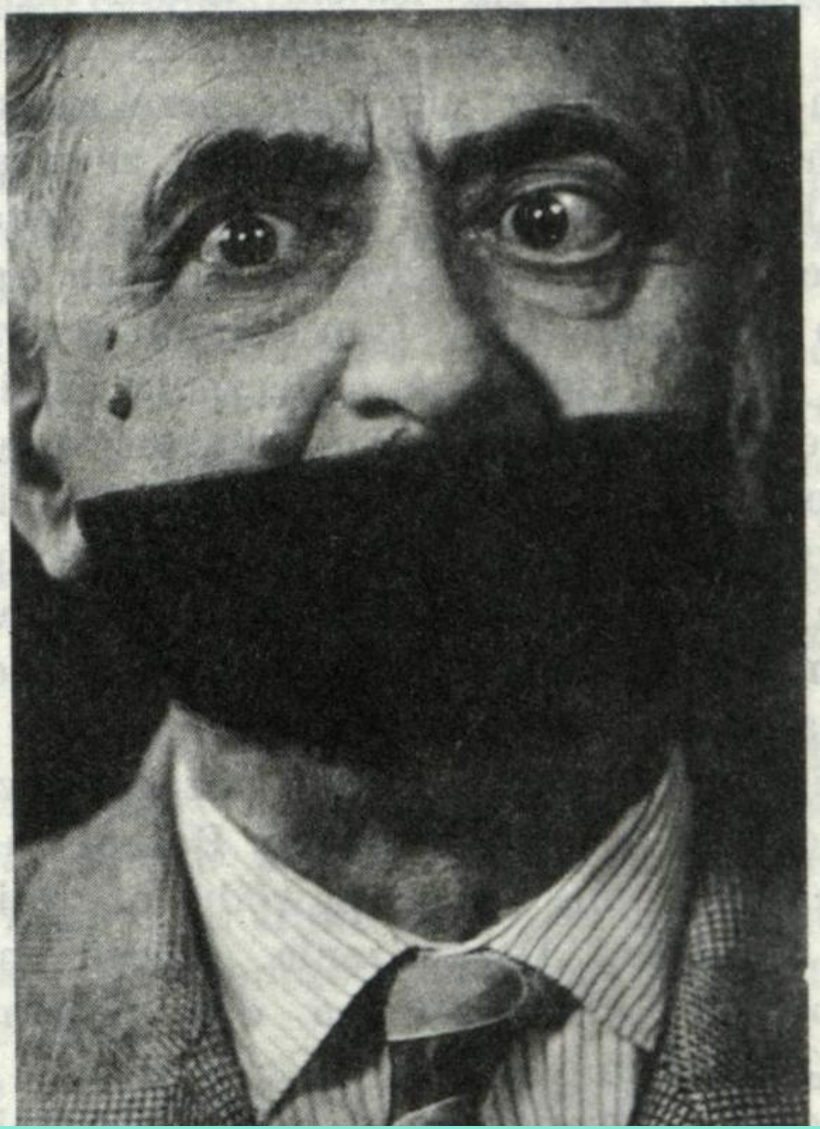
Diarrhea

HYPOTHYROIDISM

Constipation

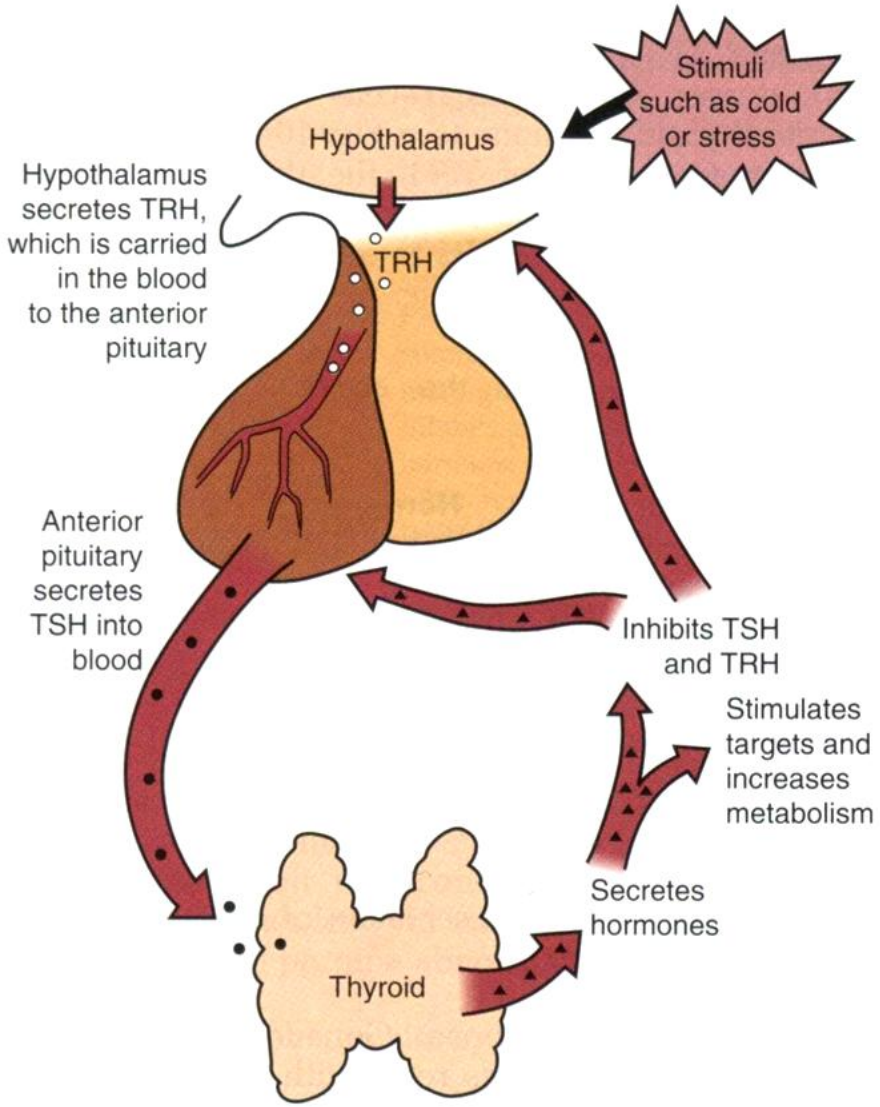
Figure 76–8

Patient with exophthalmic hyperthyroidism. Note protrusion of the eyes and retraction of the superior eyelids. The basal metabolic rate was +40. (Courtesy Dr. Leonard Posey.)



Infiltrative ophthalmopathy-

Exophthalmos



TRH = Thyrotropin-releasing hormone
TSH = Thyroid-stimulating hormone

Figure 10–6 Interaction of hypothalamus, anterior pituitary, and thyroid.

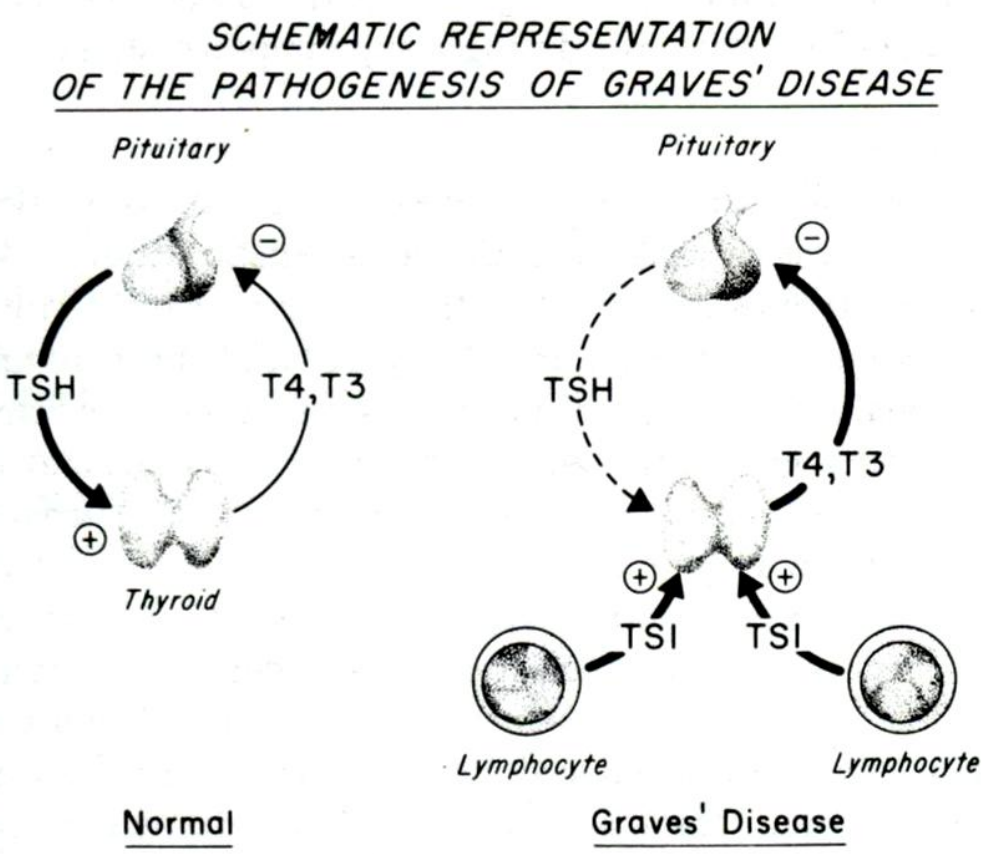
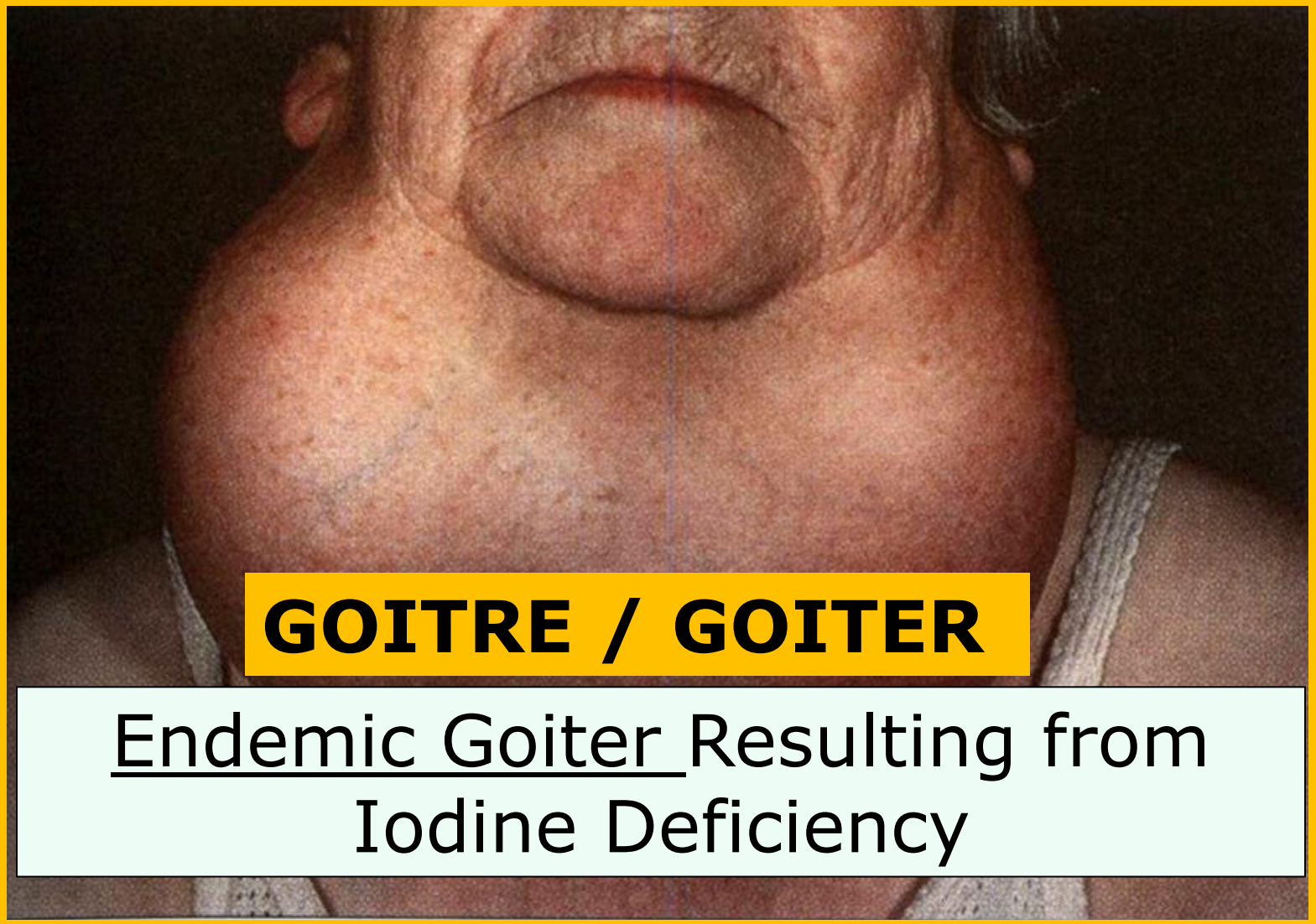


Figure 4-8 Schematic representation of the pathogenesis of Graves' disease. TSI, synthesized by B lymphocytes, stimulates thyroid gland activity in a manner similar to TSH. Negative feedback by thyroid hormones results in TSH suppression. Unlike TSH, TSI is not under negative feedback control and hyperthyroidism may ensue.



GOITRE / GOITER

Endemic Goiter Resulting from Iodine Deficiency

Hypothyroidism


Thank you