
In the name of God

اقایی 47 ساله چاق با بی ام ای 28 مراجعه کرده است درشکل ظاهری بیمار بنظر رنگ پریده وزرد است سونوی بیمار گرید دو فتی لیوردر ازمایشات انجام شده تی اس اچ 10 و انزیم کبدی بیش از دو برابر طبیعی

کلسیم پایین و فسفرنسبتا نرمال ولی ویتامین دی بسیار پایین ولی با کمال تعجب پی تی اچ نزدیک به طبیعی است

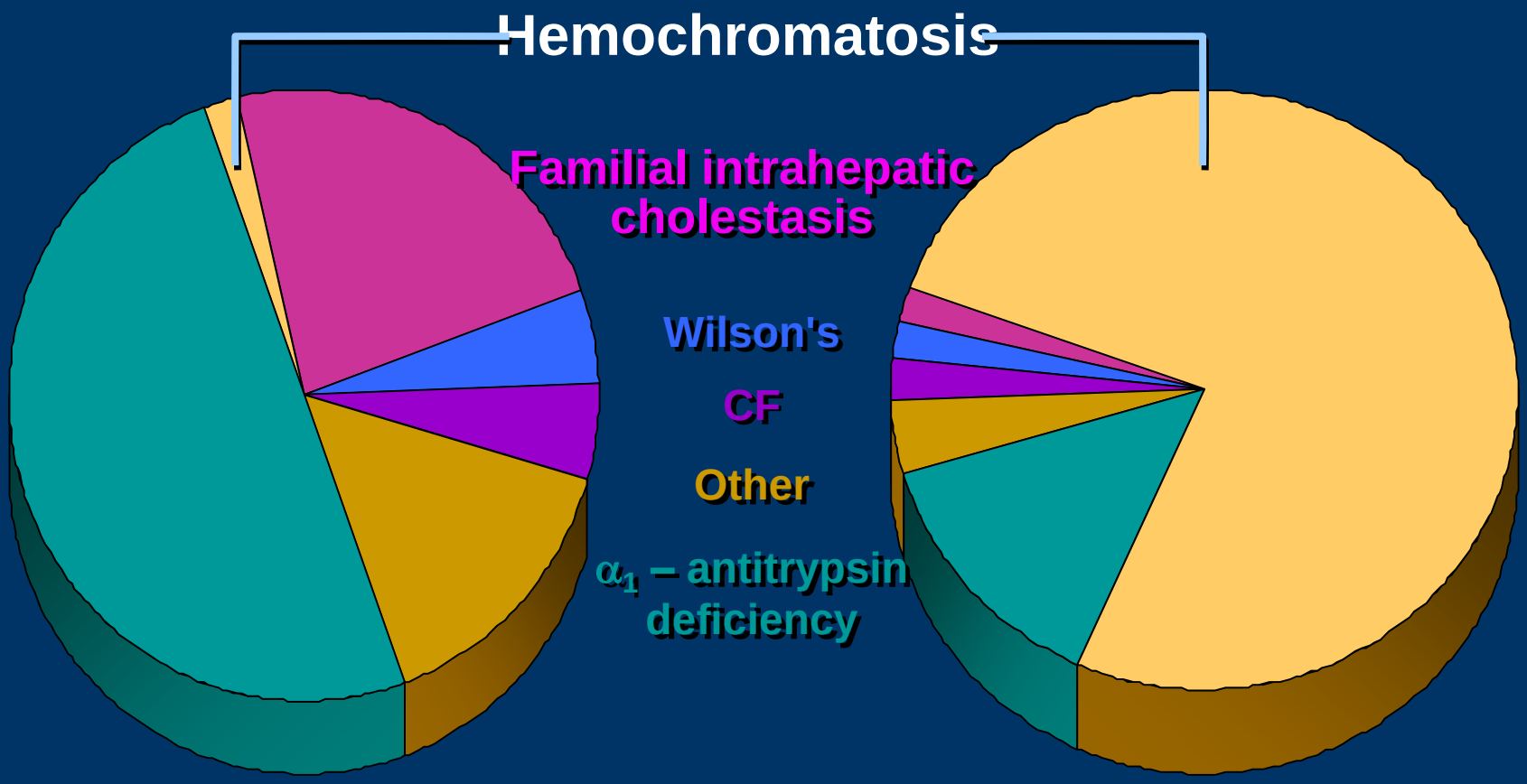
انتی تی پی او منفی کلسترول 250 و ال دی ال بالا وقند خون
ناشتا دوبار بالاتر از170

چی تشخیصی مطرح است
ازام پو تنس شکایت دارد ولی با کمال تعجب اف اس اچ وال اچ و پرولاکتین نرمال است چی تشخیصی مطرح است
علیرغم زردی جنرالیزه سی بی سی نرمال است و فقط ام سی وی بالاتر از 100 است وبیلی ها نرمال است چی تشخیصی مطرح است

پس ازسه ماه درمان با لوتیروکسین تی اس
اچ نرمال و رنگ پریدگی برطرف گردید
ولی متاسفانه انزیم های کبدی تغییرات
چندانی نکردندهرچند که لپیدها نرمال و وزن
بیماروقند خون به حالت
طبیعی گردید
چی تشخیصی مطرح است

Inherited Causes of Cirrhosis

Inherited Causes of Cirrhosis



Target populations for screening for HH

Target Populations for Hemochromatosis Evaluation
Symptomatic patients
Unexplained manifestations of liver disease or a presumably known cause of liver disease with abnormality of one or more indirect serum iron markers.
Type 2 diabetes mellitus, particularly with hepatomegaly, elevated liver enzymes, atypical cardiac disease or early-onset sexual dysfunction.
Early-onset atypical arthropathy, cardiac disease, and male sexual dysfunction.

Hemochromatosis

	Serum Iron (µg /dl)	TIBC (µg /dl)	Transferrin Saturation (%)	Ferritin (µg /L)	Quantitative Hepatic Iron (µg /g dry weight)
Normal	50-150	230-370	20-50	30-270	150-1850
Hemochromatosis	>175	<300	>50	>300	>5600

Criteria for initiating therapeutic phlebotomy

Patient	Serum ferritin, ng/mL
Persons <18 years of age	≥200
Women	
Reproductive years, not pregnant	≥ 200
Reproductive years, pregnant	≥ 500
Postreproductive years	≥ 200
Men	≥ 300

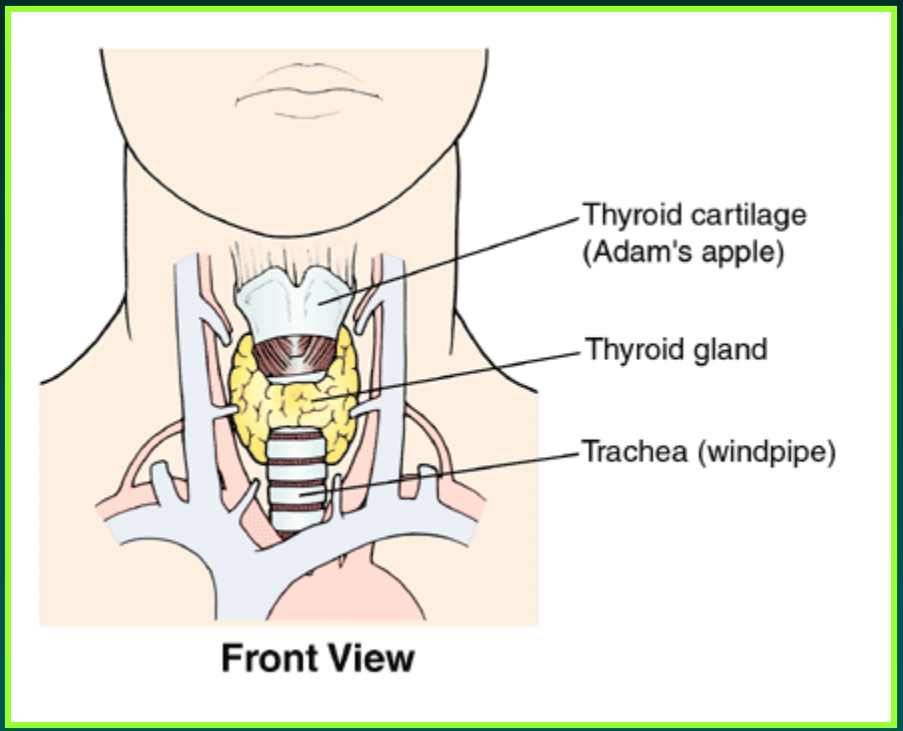
Results of therapeutic phlebotomy in patients with hemochromatosis

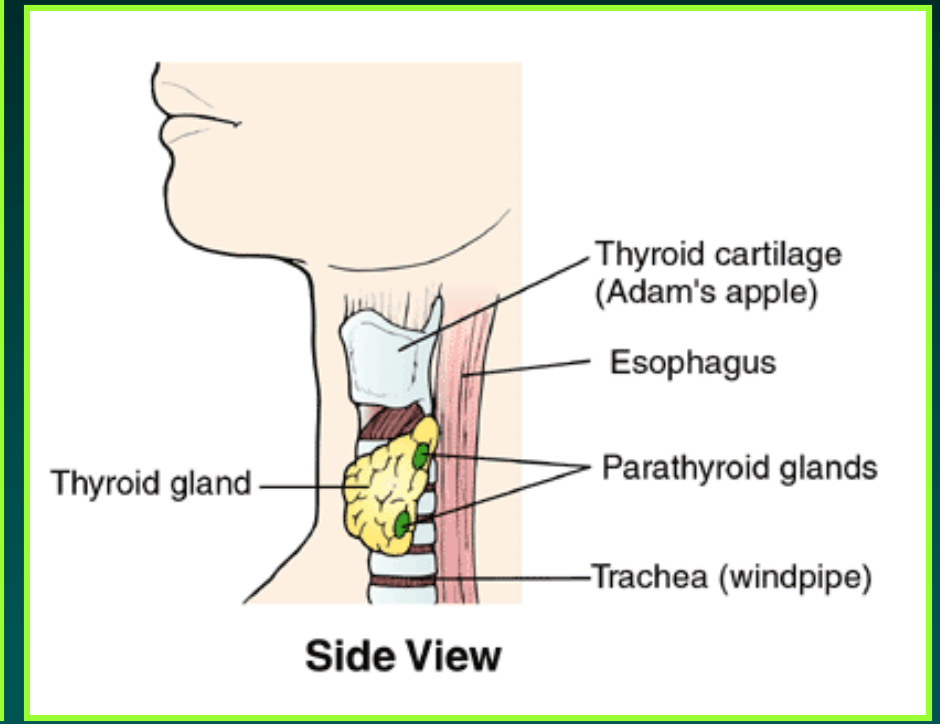
Complications of Iron Overload	Expected Treatment Outcome
Hypogonadotrophic hypogonadism	Resolution is rare
Diabetes mellitus	Occasional improvement, often temporary
Hypothyroidism, hypogonadism	Resolution is rare
Cardiomyopathy	Resolution sometimes occurs
Hyperpigmentation	Resolution usually occurs
Hyperferritinemia	Resolution
Excess absorption and storage of nonferrous metals	
Infection with Vibrio vulnificus or other bacteria	Little or no change

Clinical Exam. of Thyroid

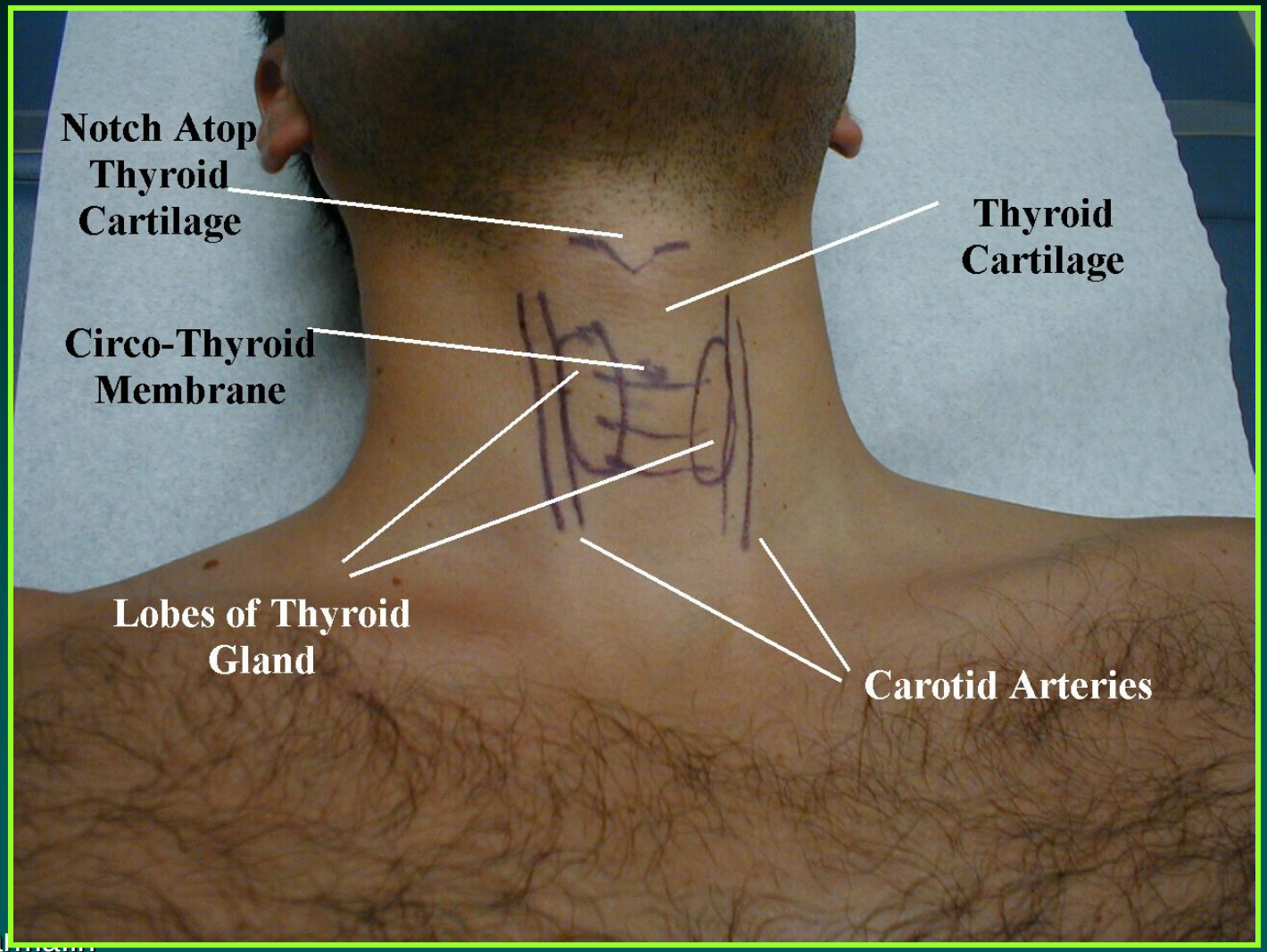
- Have patient seated on a stool / chair
- Inspect neck before & after swallowing
- Examine with neck in relaxed position
- Palpate from behind the patient
- Remember the rule of finger tips
- Use the tips of fingers for palpation
- Palpate firmly down to trachea
- Pemberton's sign for RSG

Where to look for Thyroid ?





Clinical Anatomy of Thyroid

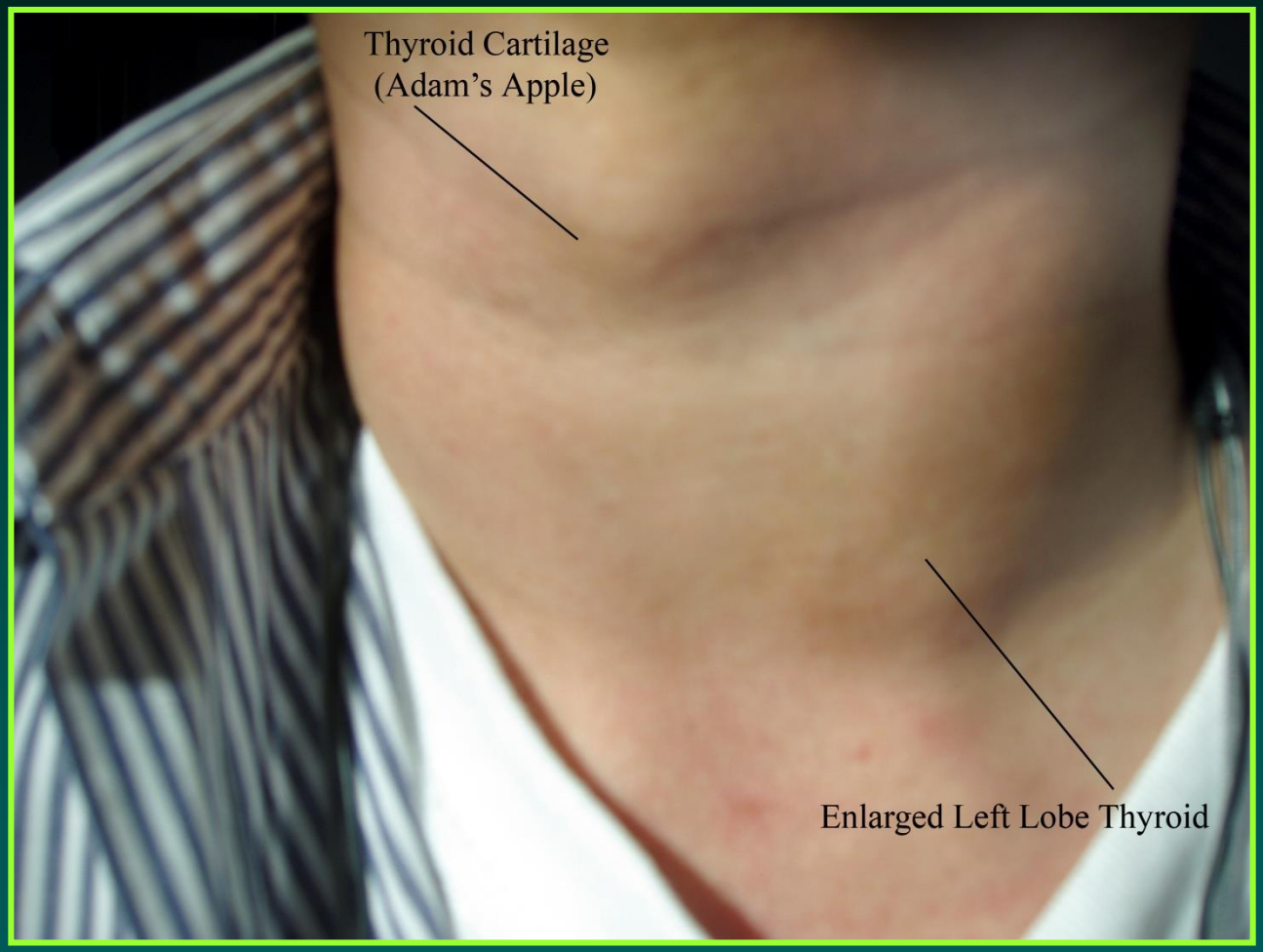


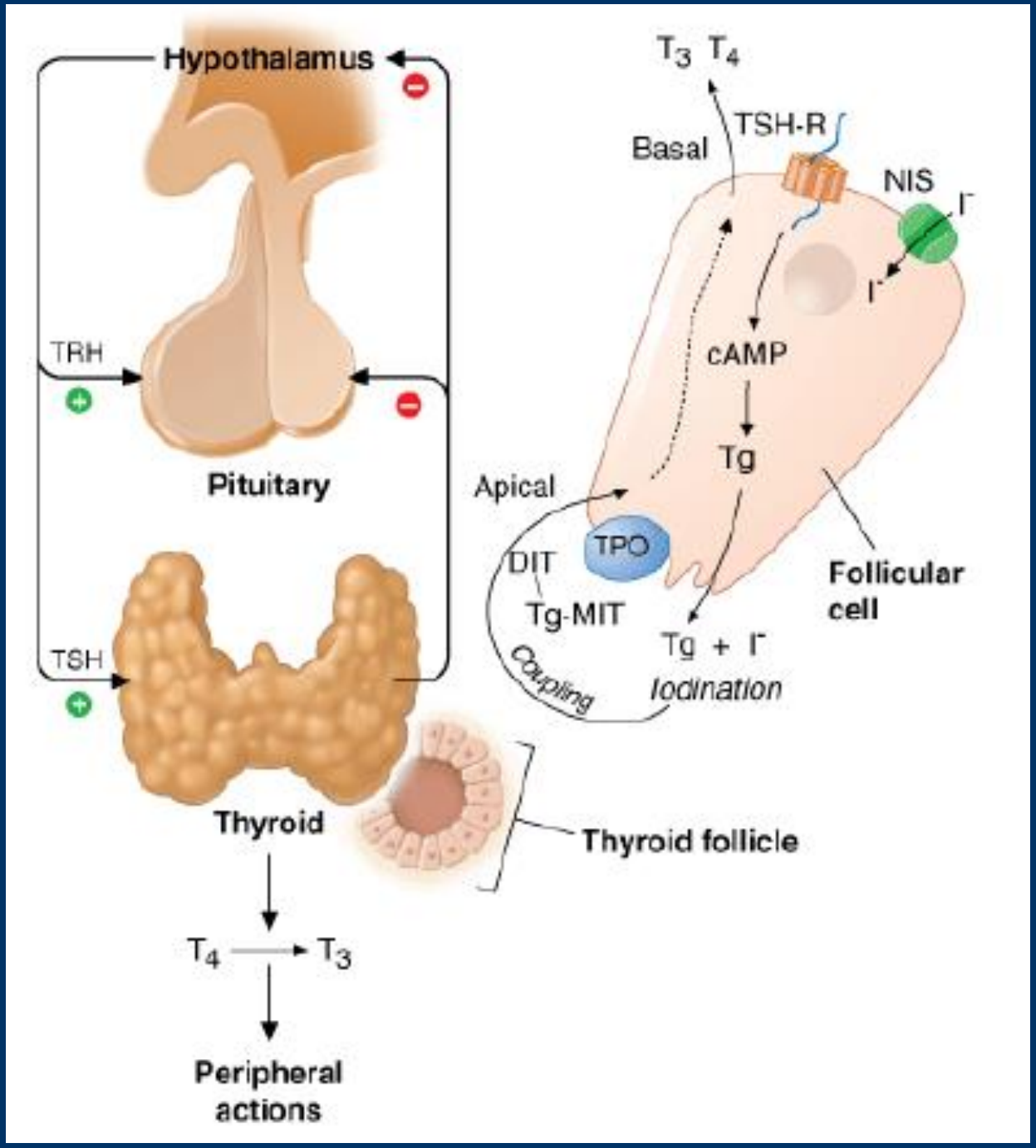
Clinical Exam of Thyroid

Clinical Exam of Thyroid

Clinical Exam of Thyroid

Thyromegaly




Hypothalamus
TRH
Pituitary
TSH
Thyroid
T_4 → T_3
Peripheral actions
T_3 T_4
Basal
TSH-R
NIS
I^-
I^-
cAMP
Tg
Apical
TPO
DIT
Tg-MIT
Coupling
Tg + I^-
Iodination
Follicular cell
Thyroid follicle

Effects of Thyroid Hormone

- Fetal brain and skeletal maturation
- Increase in basal metabolic rate
- Inotropic and chronotropic effects on heart
- Increases sensitivity to catecholamines
- Stimulates gut motility
- Increase bone turnover
- Increase serum glucose, decrease serum cholesterol

Clinical / Subclinical Hypothyroidism

- Serum TSH level > 5.0 mIU/l
- Subclinical hypothyroidism → elevated TSH with normal FT4, FT3.

TSH	High (>10)	High (>5 - <10)
Free T4	Low	Normal
Free T3	Normal or low	Normal

Introduction

Many structural or functional abnormalities can impair thyroid hormones production.

Classified as :

1- Primary (95%)

2-Central (5%)

Prevalence

Neonatal screen:

Congenital hypothyroidism **1/4000 newborn**

1/1000 (Iran)

Acquired hypothyroidism:

Adult women 2%

Adult men 0/2%

Old age hypothyroidism: *

Female %9.3

Male %1.3

*2779 people in UK with a medium age of 58 years

Etiology

Primary 95%

- Hashimoto disease or chronic autoimmune thyroiditis (goitrous & atrophic forms)
- Radiation
- Surgery
- Infiltrative(amyloidosis,sclerodermia)
- Iodine deficiency
- Biosynthetic defect
- Drugs (lithium,iodine,contrast agents)
- Agenesis – dysgenesis
- Antithyroid agents.
- Inherited defect of hormonogenesis
- Riedel struma

Secondary 5%

- Pituitary disease
- Hypothalamic disease

Transient

- Following of:

  Subacute thyroiditis

  Postpartum thyroiditis

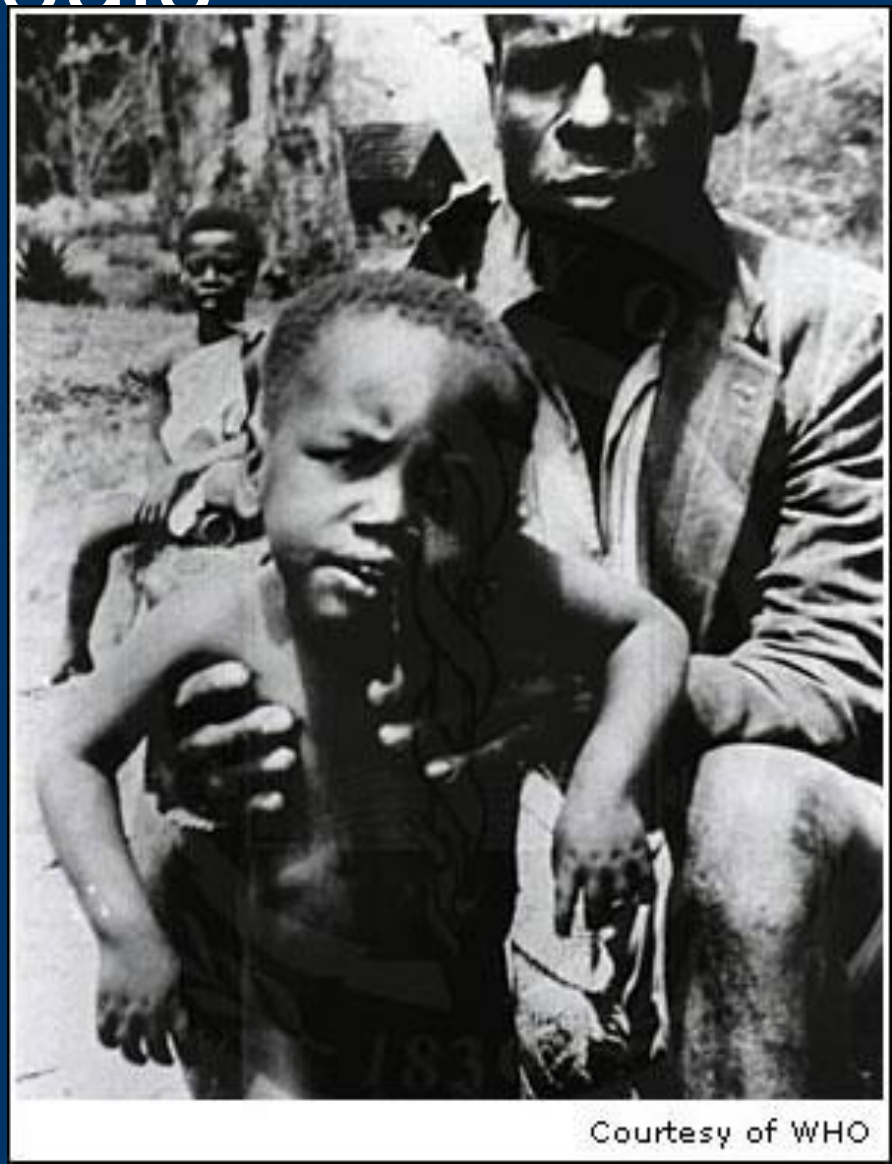
  Iodine therapy for Graves dis.
- Withdrawal of thyroid hormone treatment

Congenital Hypothyroidism

- Rare
- Absent thyroid tissue or hereditary defects in TH synthesis
- Mental retardation due to lack of T_4
- Symptoms
  - difficulty eating, hoarse cry, abdominal protrusion, excessive sleeping, slow pulse, cold skin
  - impaired growth, cretinism

Two Forms of Cretinism: Neurologic

- Neurologic form - neuromotor defects, deaf-mutism, problems with gait and coordination

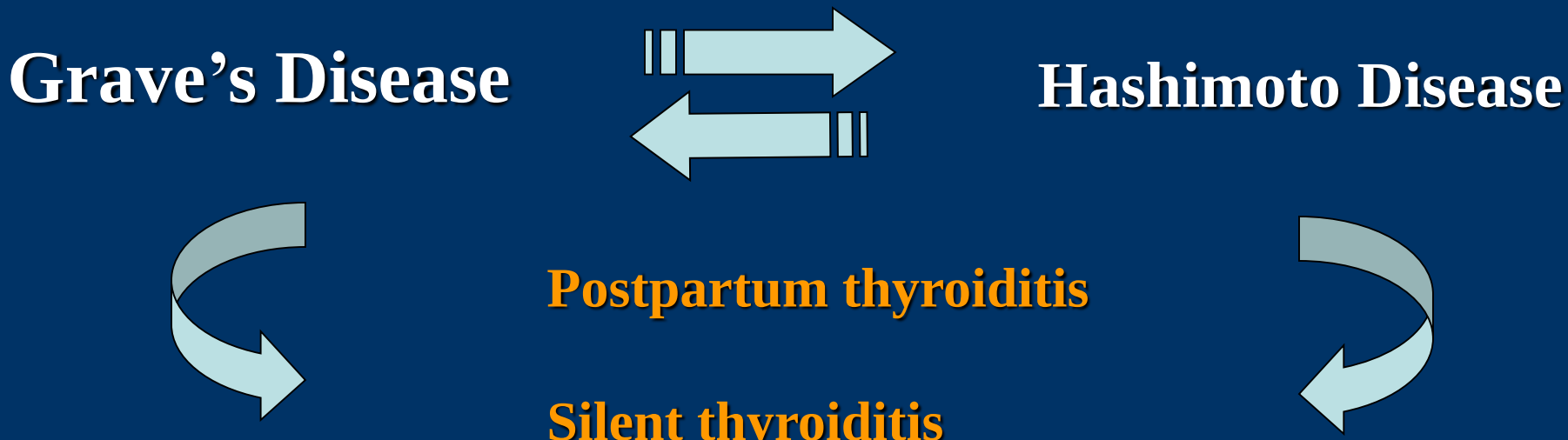


Courtesy of WHO

Chronic Autoimmune Thyroiditis
Hashimoto disease

Hashimoto's thyroiditis (chronic autoimmune thyroiditis) is the most common cause of hypothyroidism in iodine-sufficient areas of the world. It is characterized clinically by gradual thyroid failure, goiter, or both, due to autoimmune-mediated destruction of the thyroid gland. Nearly all patients have high serum concentrations of antibodies against one or more thyroid antigens, lymphocytic infiltration of the thyroid, which includes thyroid-specific B and T cells, and apoptosis of thyroid follicular cells.

Spectrum of thyroid autoimmunity



•The disease clusters in families, sometimes alone and sometimes in combination with Graves' disease

• It is more common in women.

• The concordance rate in monozygotic twins is 30 to 60 percent

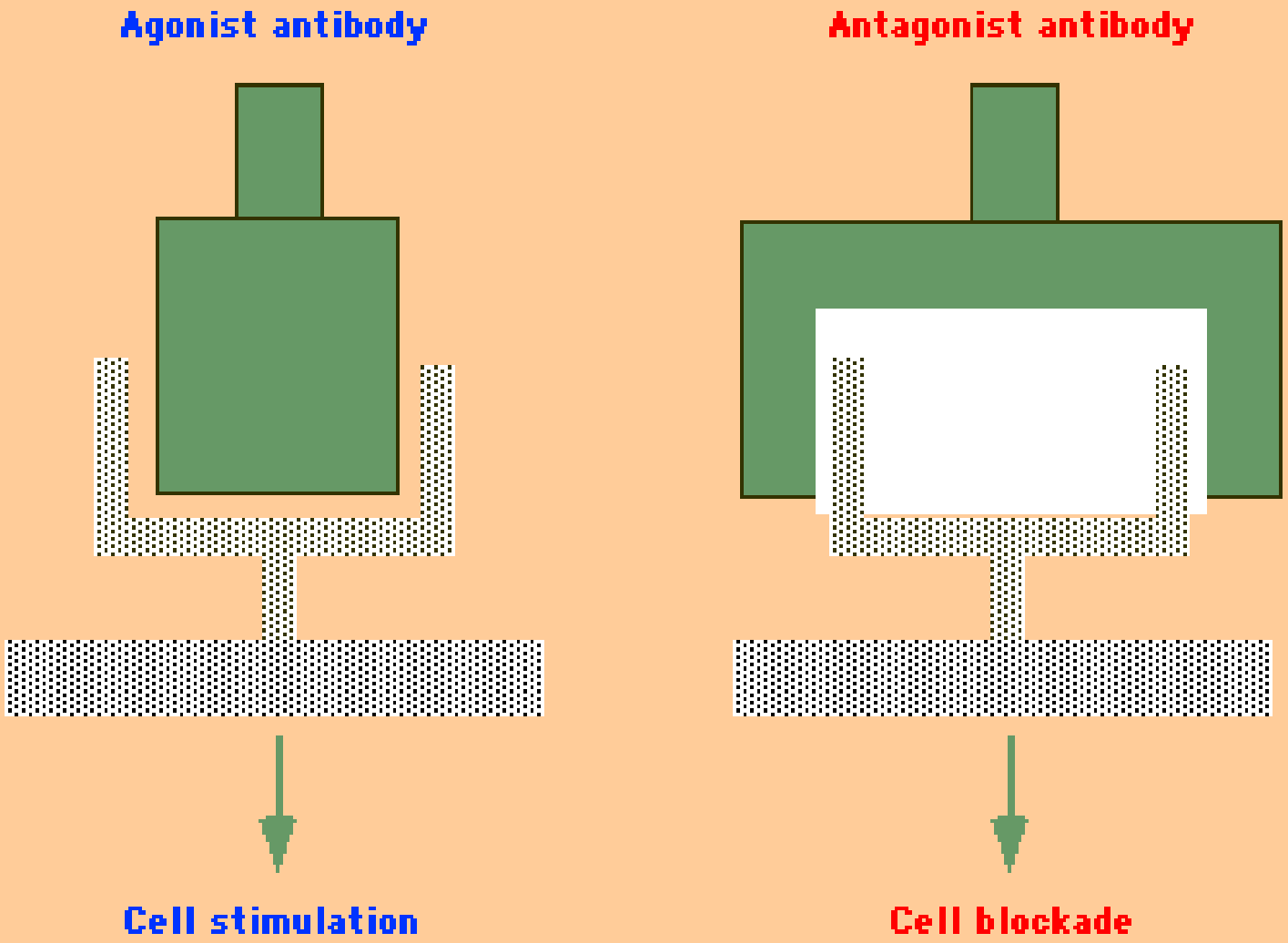
• It occurs with increased frequency in patients with Down's syndrome and Turner's syndrome.

• There is an association, albeit relatively weak, with certain HLA alleles.

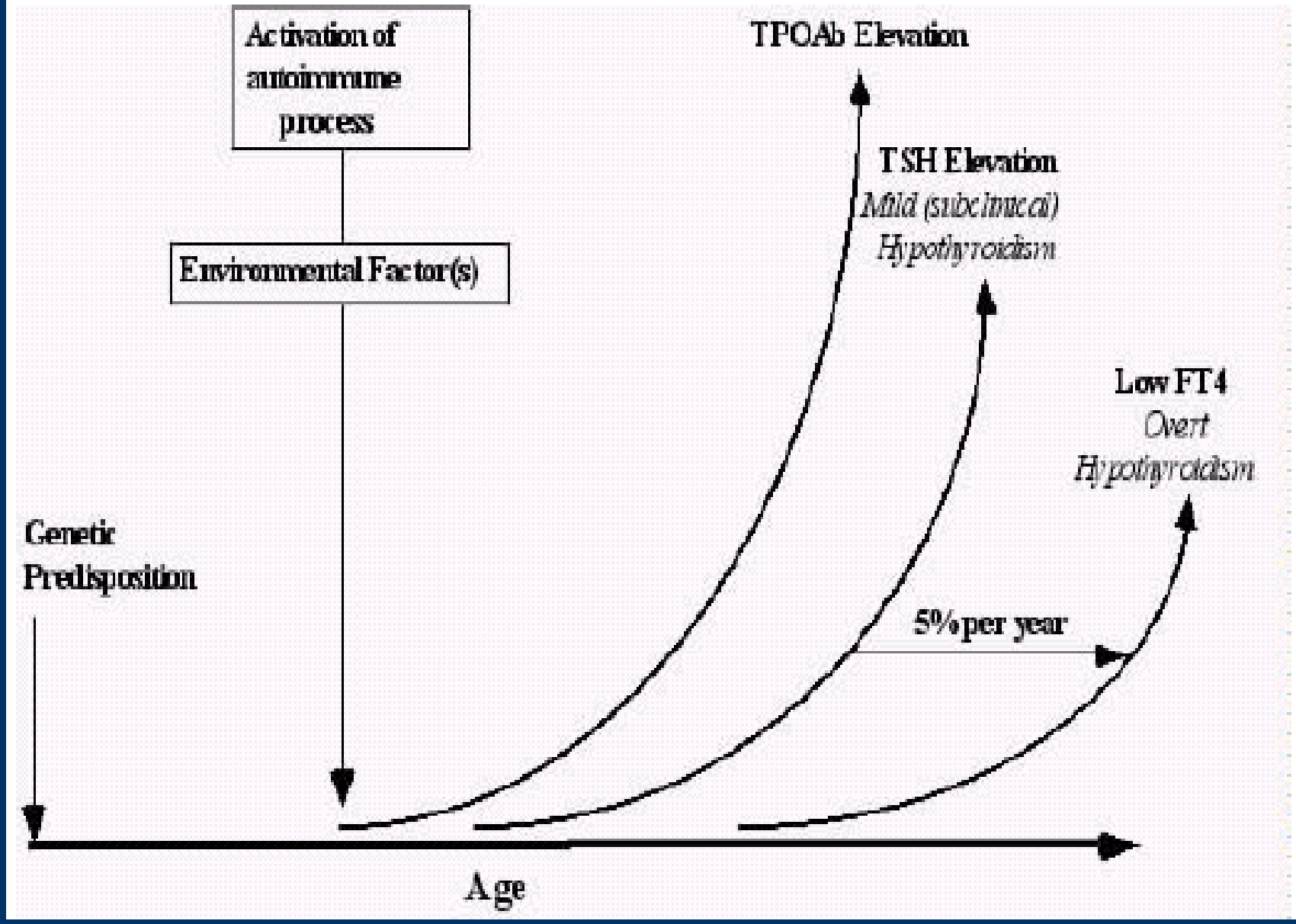
Estimated Prevalence of Antithyroid Antibodies (in percent)

Group	Anti-TSHR Ab	Anti-Tg Ab	Anti-TPO Ab
General population	0	5-20	8-27
Graves' disease	80-95	50-70	50-80
Autoimmune thyroiditis	10-20	80-90	90-100
Relatives of patients with autoimmune thyroiditis	0	30-50	30-50
Type 1 diabetes	0	30-40	30-40
Pregnant women	0	about 14	about 14

Anti-TSHR Ab = Antithyrotropin receptor antibodies
Anti-Tg Ab = Antithyroglobulin antibodies
Anti-TPO Ab = Antithyroid peroxidase antibodies



TSH receptor antibodies Antibodies to the TSH receptor may be stimulatory (eg, in patients with Graves' disease) and cause hyperthyroidism, or inhibitory (eg, in chronic autoimmune thyroiditis) and cause hypothyroidism.


Activation of autoimmune process
Environmental Factor(s)
TPOAb Elevation
TSH Elevation
Mild (subclinical) Hypothyroidism
Low FT4
Overt Hypothyroidism
Genetic Predisposition
5% per year
Age

Organ-Specific Autoimmune Diseases	
chronic hepatitis	hypoparathyroidism (some forms)
Hashimoto's disease	
myxoedema	diabetes mellitus (some forms)
lymphocytic thyroiditis	vitiligo
Graves' disease	
pernicious anaemia	premature ovarian failure
Addison's disease	allergic alveolitis

Fig. 15.5 Table of the organ-specific autoimmune diseases. All of these disorders are characterised by the presence of circulating antibodies and lymphocytic infiltration of the gland or tissue.

Clinical presentation

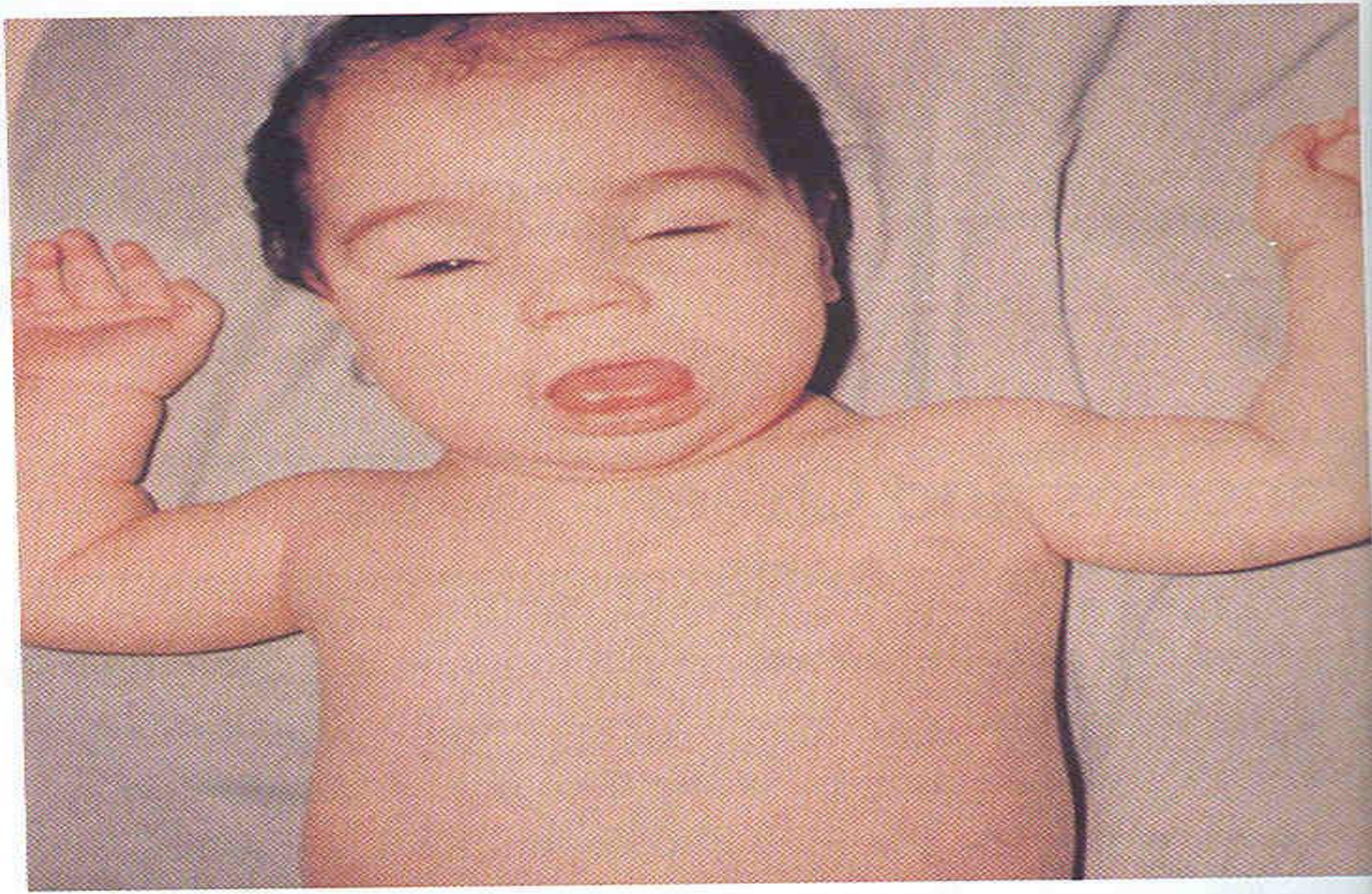
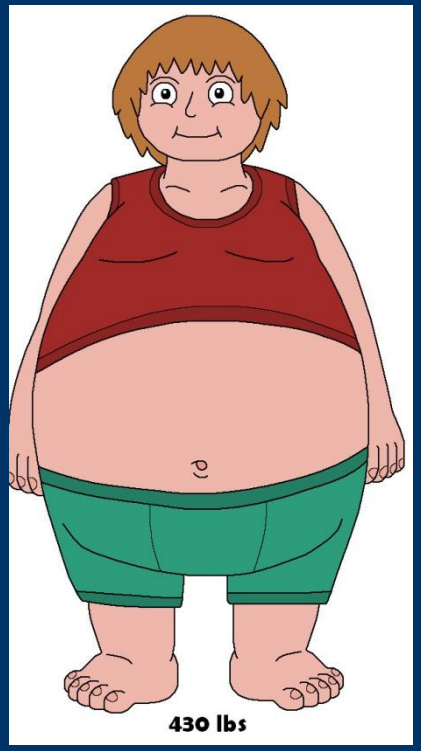
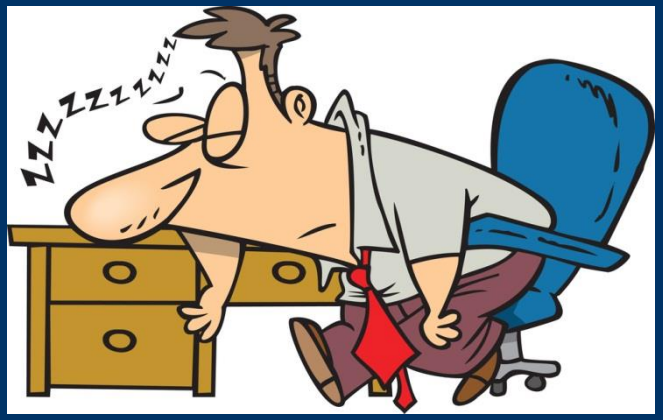


Figure 11.27 **Cretinism.** Cretinism is a disease of infancy caused by an underactive thyroid gland.

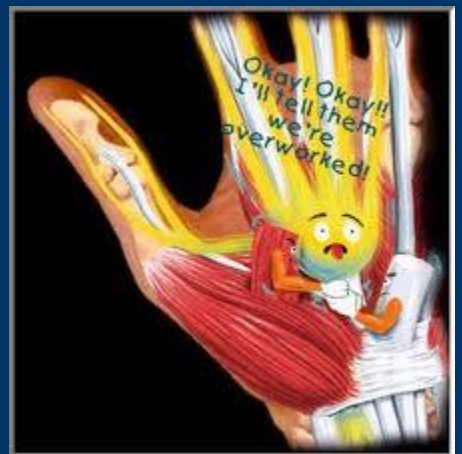
Cretinism Cont…

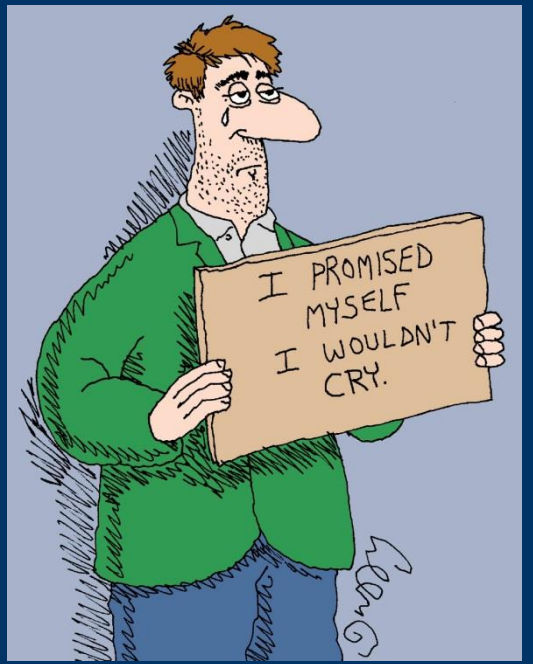
www.emedicine.com/ped/topic501.htm


430 lbs


zzzzzzzzzz


Argh, stomach pain, but I cannot poop... Help! Help!


Okay! Okay!! I'll tell them we're overworked!

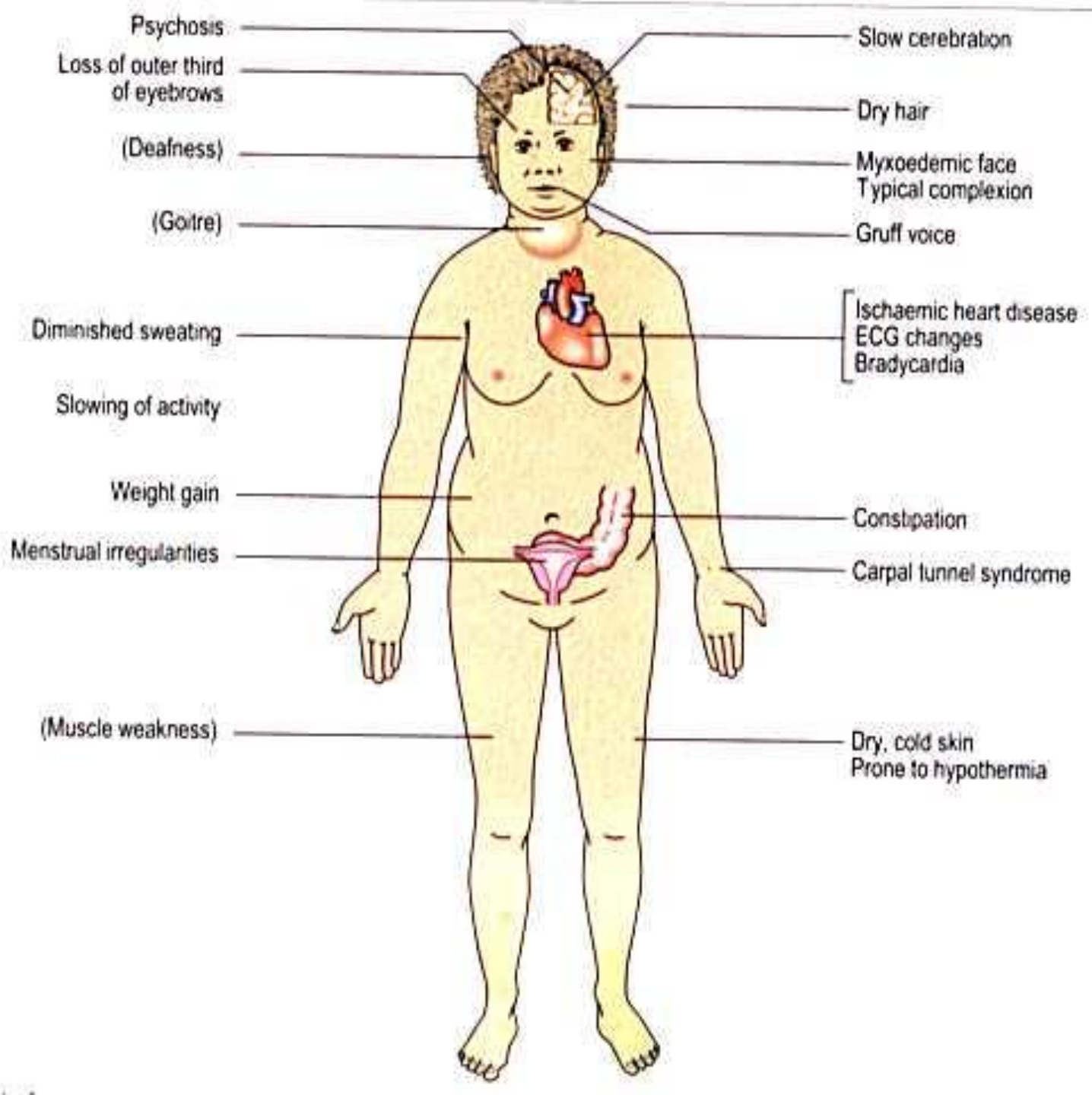

I PROMISED MYSELF I WOULDN'T CRY.

Adult male with 3 women of same age (17-20 years) from Congo with myxedamatous form

Hypo-thyroidism

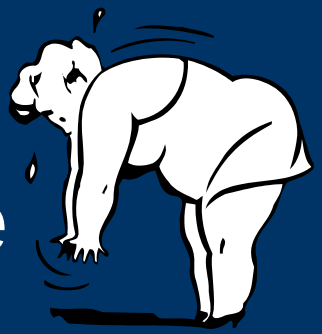
Myxedema

Features:



Hypothyroidism & Signs & Symptoms:

- Shrunken fibrotic thyroid gland by palpation
- Cool peripheries
- Dull facial expression
- Hoarse voice with slow speech
- Intolerance to cold
- Hair and skin is coarse and dry
- Bradycardia
- Weight gain
- Carpal tunnel syndrome
- Drooping eyelids



Hypothyroid Face

Notice apathetic facies, bilateral ptosis, & absent eyebrows

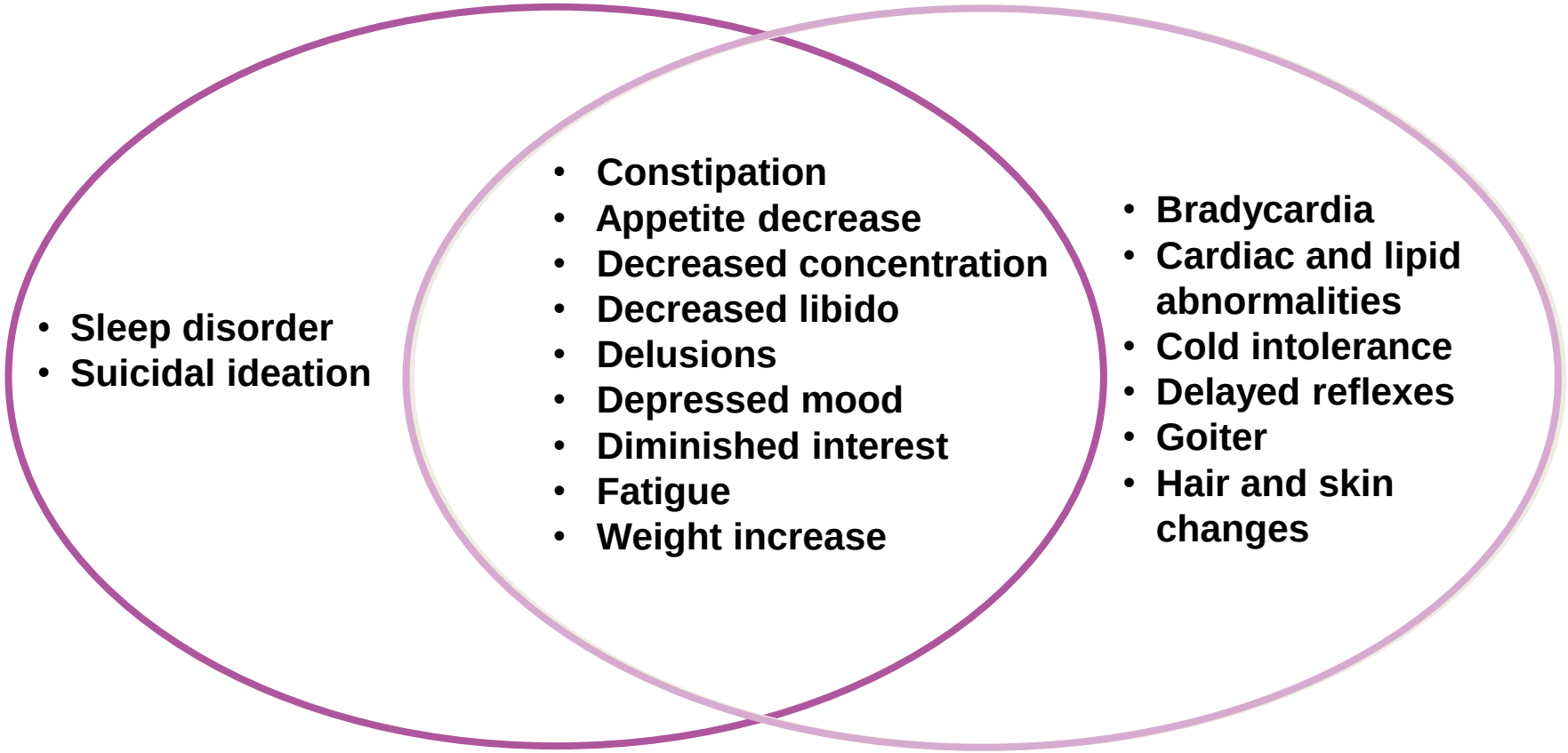
Faces of Clinical Hypothyroidism

Hypothyroidism & Signs & Symptoms:

- Lethargy
- Puffy face
- Muscle fatigue
- Loss of eyebrows in outer third
- Depression

- Headaches
- Menstrual disturbance
- Growth retardation in children, delayed teething and slow mental development

Hypothyroidism and Depression – Many Common Features



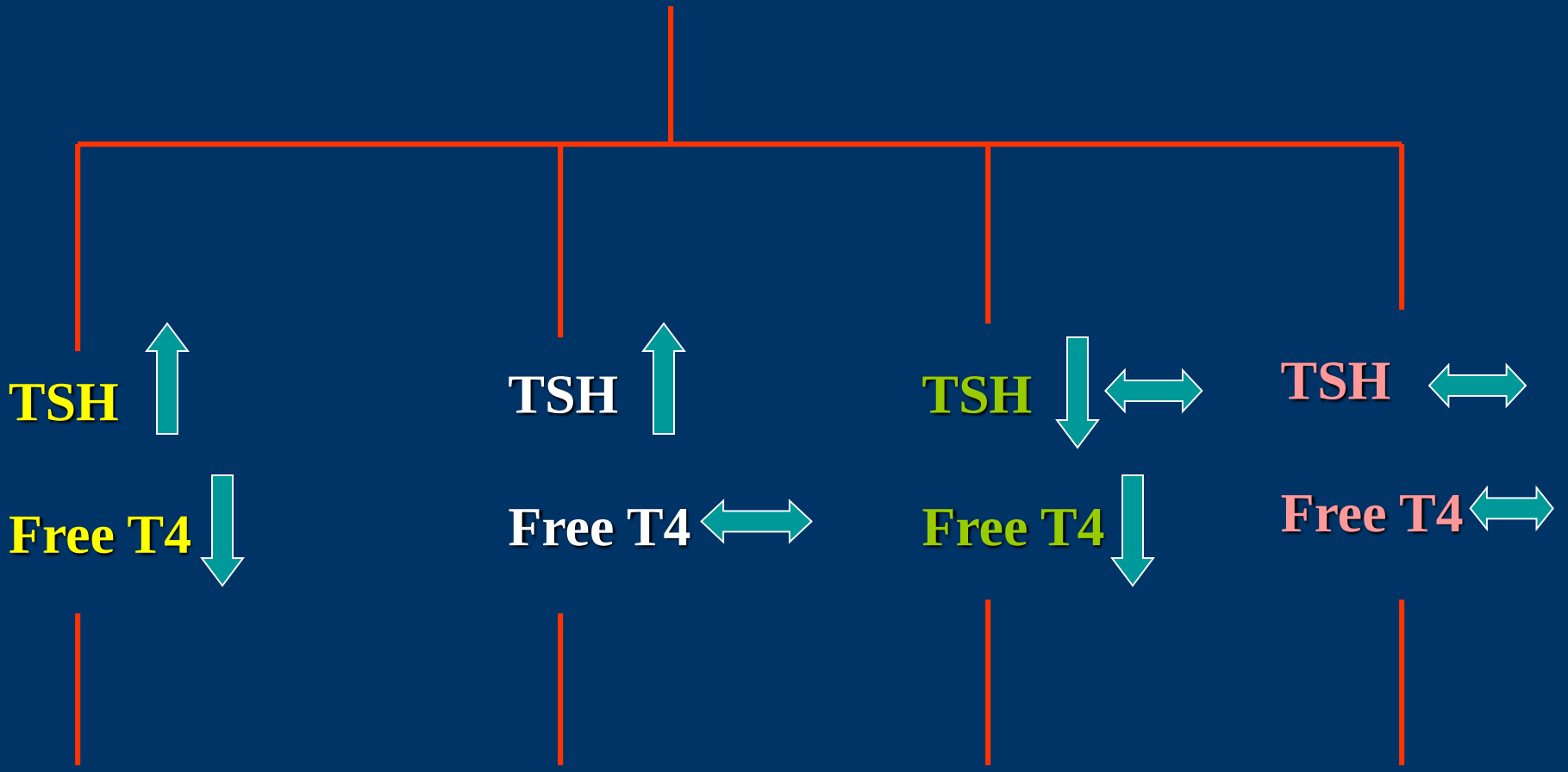
Nemeroff CB. *J Clin Psychiatry* 1989; 50(Suppl):13–20; discussion 21–22


A
B
Before treatment
After treatment

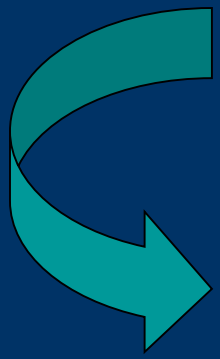
In this patient with advanced pretibial myxedema, these striking skin changes are due to accumulations of mucopolysaccharides ("myxedema"). These changes are reversible with thyroid hormone.

Diagnosis

TSH and Free T4



Central Hypothyroidism



- **Imaging (R/O SOL)**
- **Functional status of the other axis**

Treatment

Thyroid hormone preparations

- **Synthetic L-T4**
- **Synthetic L-T3**
- **Combined T4 & T3**

Pharmacokinetics of oral thyroid hormones

	T4	T3
Absorption	~ 80%	~90%
Time to peak level	2-4 h	1-2h
Half-life	6-7days	~1days

Average Replacement Dose of T4

- I.6 to 1.8µ/kg ideal body Wight/day
- 75-125µg/day in women and 125-200µg/day in men
- Older patients(>60years) require 20% to 30% less T4 per kg ideal body weight than do younger patients

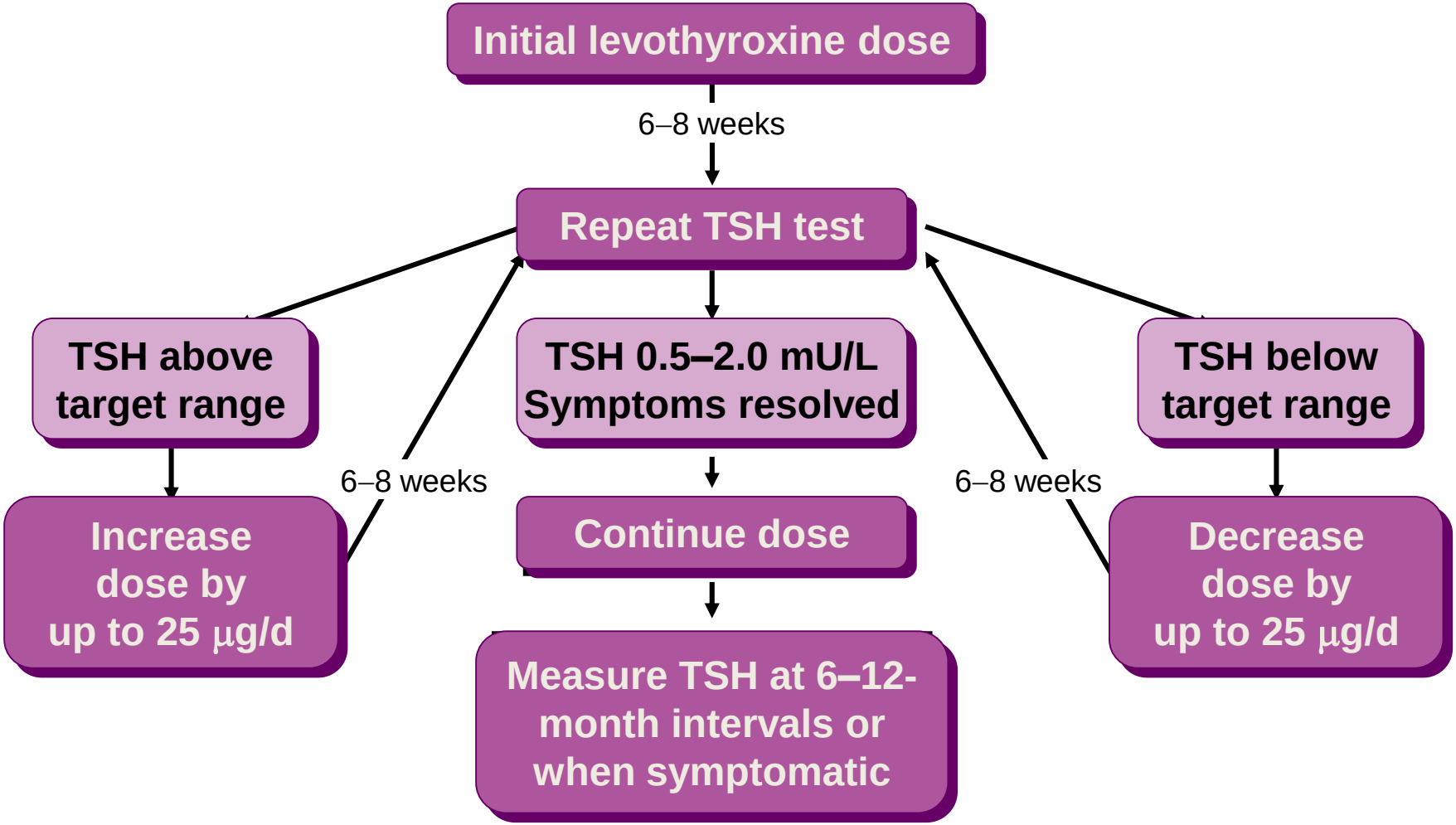
Initial Dosing of Levothyroxine in Primary Hypothyroidism

- Newborns
  - 10–15 µg/kg/day, ie, 50 µg/day
- Children
  - 4-5 µg/kg/day, ie, 12.5–50 µg/day
- Adults:
  - Approximately 1.6 µg/kg/day (eg, 100–125 µg/day for a 70 kg adult)
  - Patients with known (severe) coronary disease: up to 25–50 µg/day
- Older patients
  - Patients >60 years with long duration of hypothyroidism: 50 µg/day or less
  - Patients without clinically overt cardiac disease: 50 µg/day
    - Treatment may aggravate angina in ~20% of patients

Woeber KA. *The Thyroid*, 9th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:864-869;
Van Viet G. *The Thyroid*, 9th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005;1029-1047

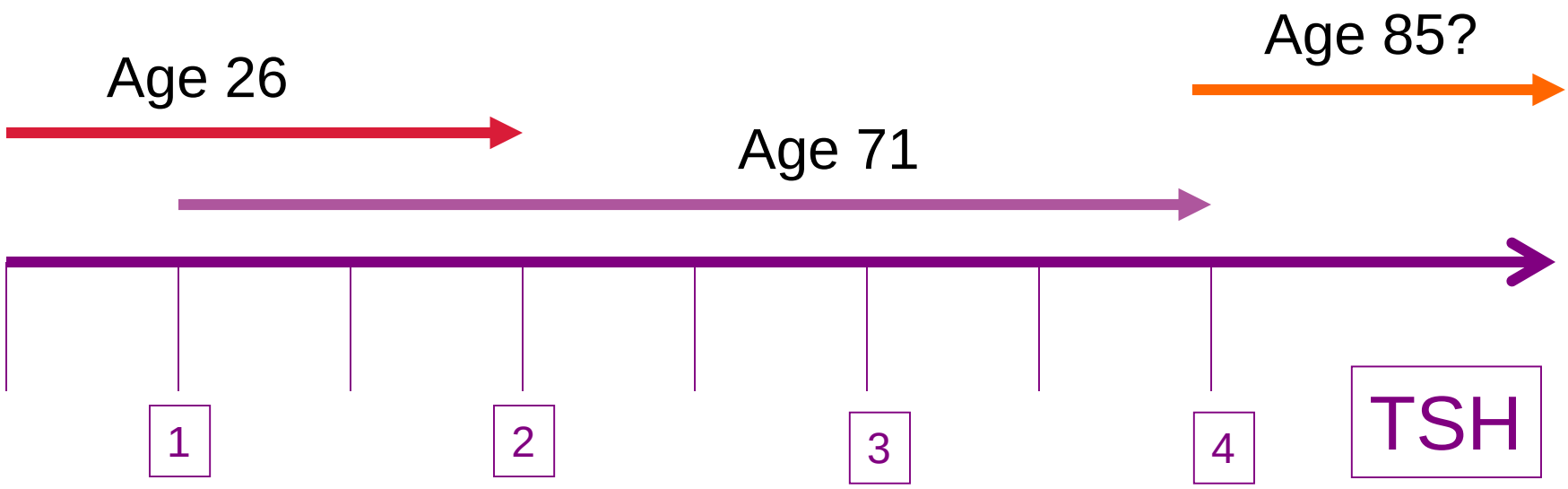
It is prudent to keep TSH values in the lower normal range(0.4-2.0 mU/l), and to avoid TSH levels of <0.1 mU/l

Treatment of Primary Hypothyroidism



Demers LM, et al. *Clin Endocrinol (Oxf)* 2003;58:138–140

Target TSH in Hypothyroidism



Current recommendation for levothyroxine replacement: TSH 0.5–2.0 mU/L

Special treatment situation

- Elderly patients
- Underlying CAD
- Pregnancy
- Concomitant drug administration
- Surgical patients

Risk of a suppressed TSH

- **Effects on Bone Mass**
- **Cardiac Effects**

Cardiac effects

- Increased heart rate
- Atrial fibrillation , 3-fold greater risk of Af over the next decade in thyrotoxic 60-year-olds
- Increase in myocardial contractility

Factors that Increase Levothyroxine Requirement

- Pregnancy, oestrogen, tamoxifen, raloxifene
- Small bowel disease
- Drugs or dietary supplements that reduce absorption
  - Large amounts of fiber, bran, soy protein
  - Aluminium- or iron-containing drugs, calcium carbonate
- Drugs that increase metabolism
  - Rifampin, carbamazepine, phenytoin, phenobarbital
- Drugs that reduce T_4 to T_3 conversion
  - Amiodarone, β-blockers, propylthiouracil, glucocorticoids and iodine containing contrast media
- Others (mechanism not known)
  - Sertraline, chloroquine/proguanil, lovastatin

Woeber KA. *The Thyroid*, 9th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:864-869

Euthyrox® package insert. Merck KGaA; 2005

Sub clinical hypothyroidism

Preclinical hypothyroidism

Introduction

High serum TSH + normal T4 & T3 and few or no signs and symptoms. Such patients are often identified through routine screening or in the course of an evaluation of common nonspecific symptoms or hypercholesterolemia.

Prevalence

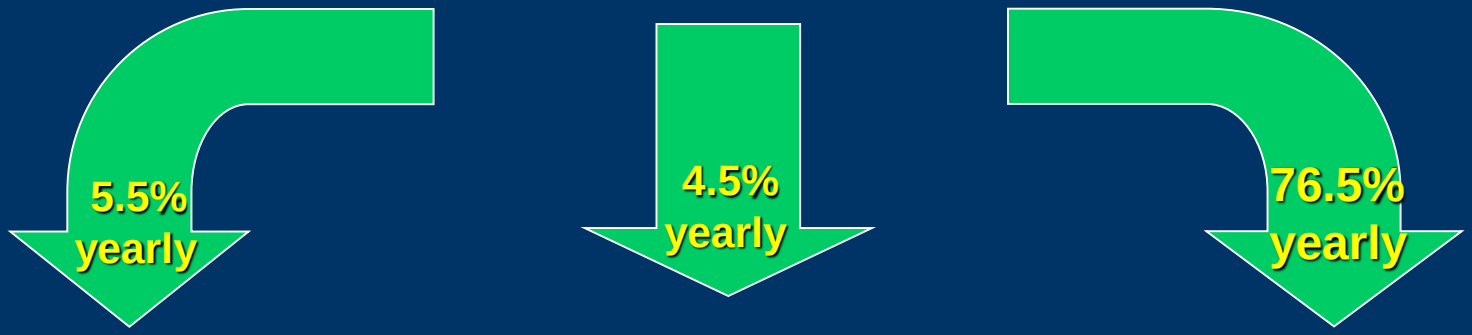
There is an age dependent increase in TSH level.

Women older than 65 >10%

Men older than 65 > 4%

Natural history

Subclinical hypothyroidism



Normal TSH

Overt hypothyroidism

S.C.H

Treatment

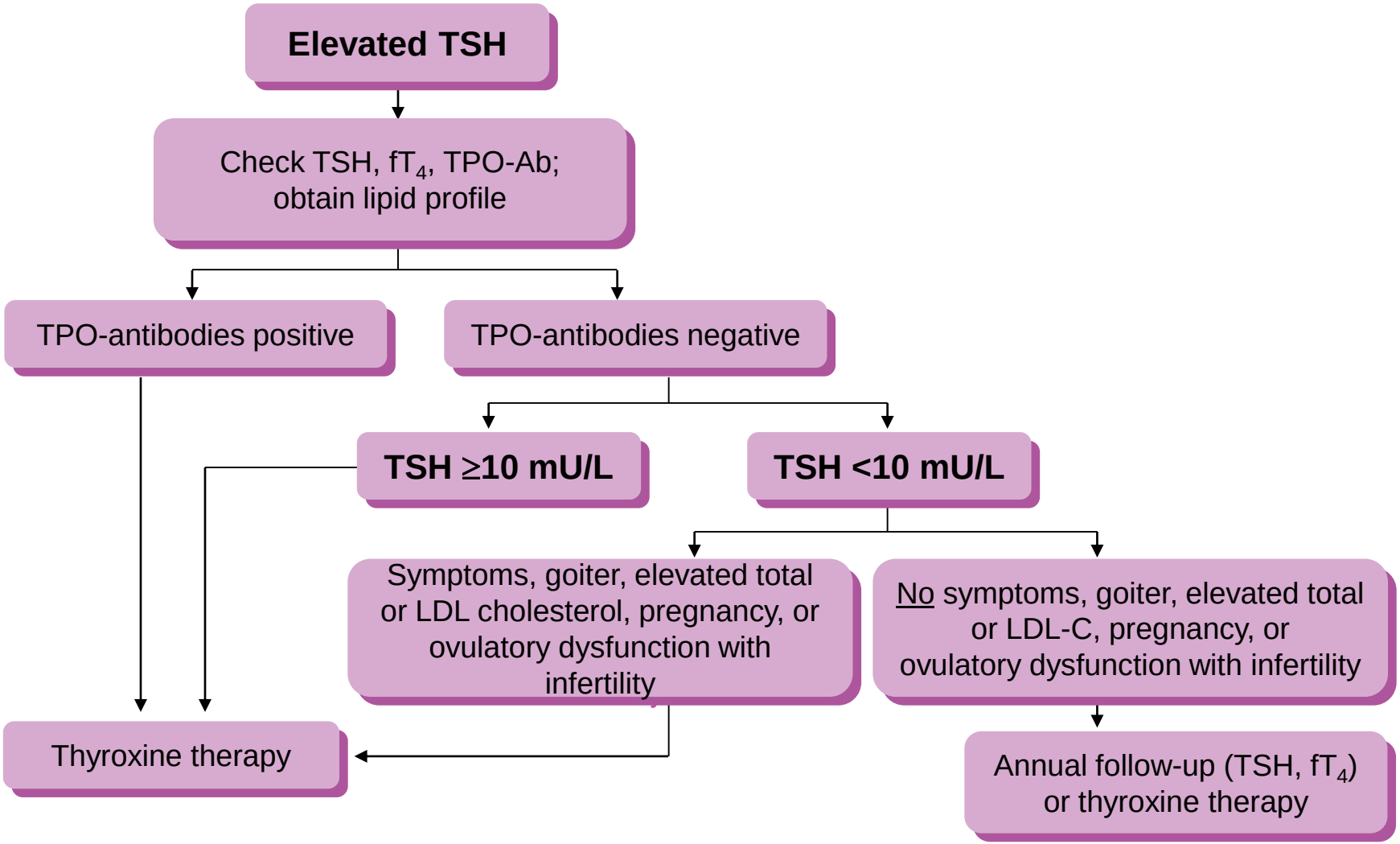
Subclinical hypothyroidism is common especially among older women.

Who must be treated?

- **TSH > 10**
- **Goiter**
- **Positive titer of anti- TPO**
- **Hyperlipidemia**
- **Menstrual disturbance , infertility.**
- **Pregnancy**

The others must be followed annually.

Subclinical Hypothyroidism – Recommendations for Therapy



Adapted from Cooper DS. *N Engl J Med* 2001;345(4):260–265

Question – *When should subclinical hypothyroidism not always be treated?*

1. Hyperlipidaemia
2. Elderly (>80 years)
3. Positive TPO-antibodies
4. TSH >10 mU/L
5. Symptomatic patients
6. Pregnant women

Question – *When should subclinical hypothyroidism not always be treated*?

1. Hyperlipidaemia
2. Elderly (>80 years)
3. Positive TPO-antibodies
4. TSH >10 mU/L
5. Symptomatic patients
6. Pregnant women

Correct answer: 2

In the elderly (>85 years) mortality is higher in low TSH


Thank you
Any question?