

SEMINAR ON TROPICAL AND TRAVEL MEDICINE

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**"Iodine deficiency and  
goiter"**

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# TOPICS OF PRESENTATION

- Introduction to thyroid gland's physiology
- Contribution of iodine to thyroid function
- Iodine deficiency disorders in different parts of the world
- Prophylaxis from iodine deficiency and proper monitoring

# Thyroid gland physiology-1

- Thyroid function is controlled by the thyroid stimulating hormone (TSH) whose principal role is the regulation of thyroid hormone biosynthesis.
- Thyroid hormones play an important role on growth and maturation of a variety of tissues as well as on their metabolism.

## Thyroid gland physiology-2

- TSH binds to its receptor located on the basolateral membrane of thyroid follicular cells and activates proper intracellular signal pathways that regulate their function and growth.

## Iodine transportation and action -1

- Iodine is actively transported together with two sodium atoms into the cell via an intrinsic plasma membrane protein called the Na<sup>+</sup>/I<sup>-</sup> symporter (NIS).

Energy for this process is provided by oxidative metabolism in the gland.

## Iodine transportation and action -2

- Following entrance in to the cell, iodine is translocated across the apical membrane of the cell where, after oxidation by the enzyme thyroid peroxidase (TPO), it becomes capable of binding to tyrosyl residues in the thyroglobulin (Tg).

## Iodine transportation and action -3

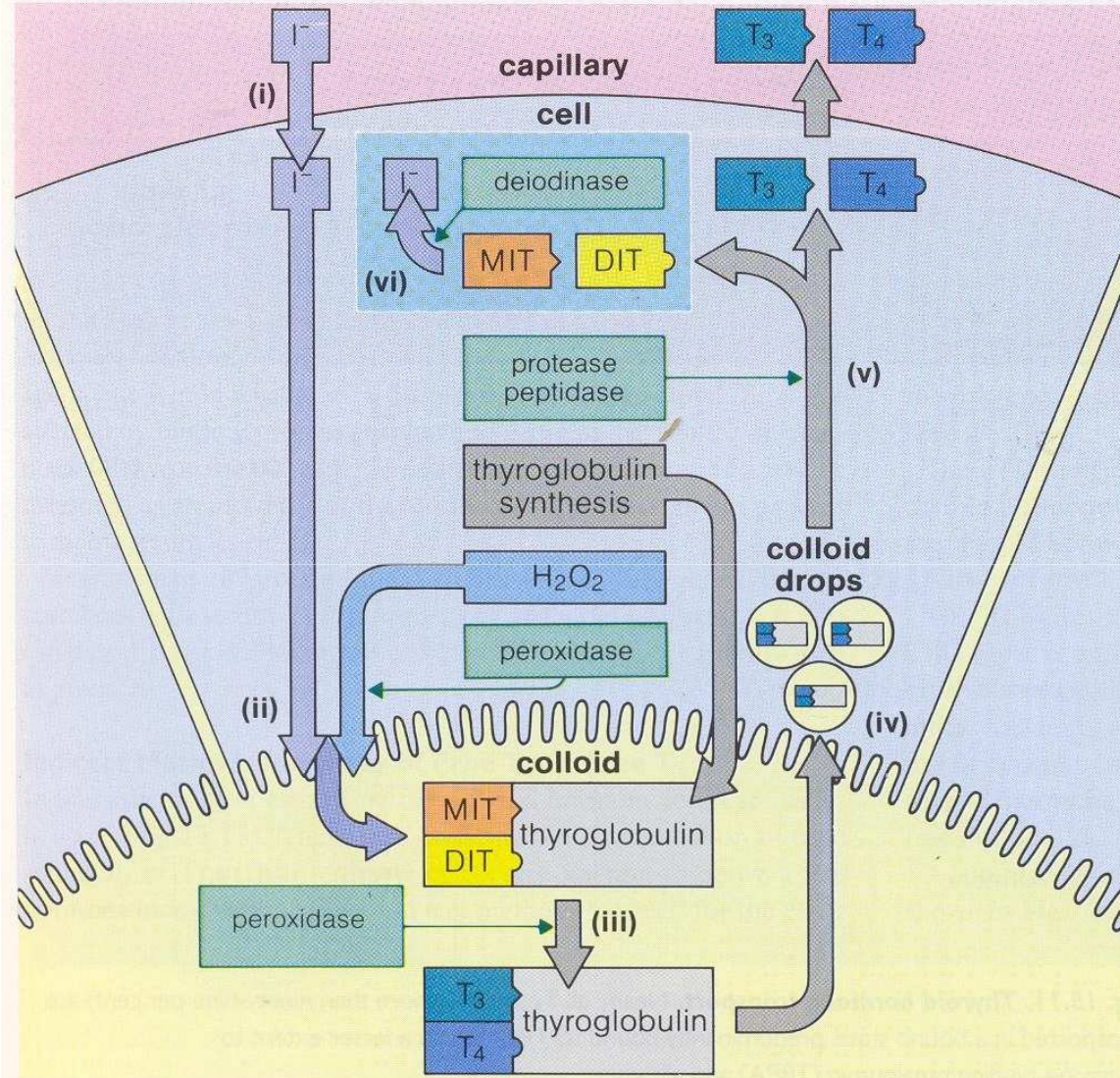
- After formation of the Tg-bound mono-iodotyrosine (MIT) and di-iodotyrosine (DIT) a coupling reaction takes place within the Tg molecule and leads to triiodothyronene ( $T_3$ ) and thyroxine ( $T_4$ ) formation.

## Iodine transportation and action -4

- The thyroid hormone-Tg complex is stored in the colloid matter of the epithelial cell, then is taken up by the thyrocytes, is hydrolyzed by proteases and eventually the free thyroid hormones are released in to the circulation.

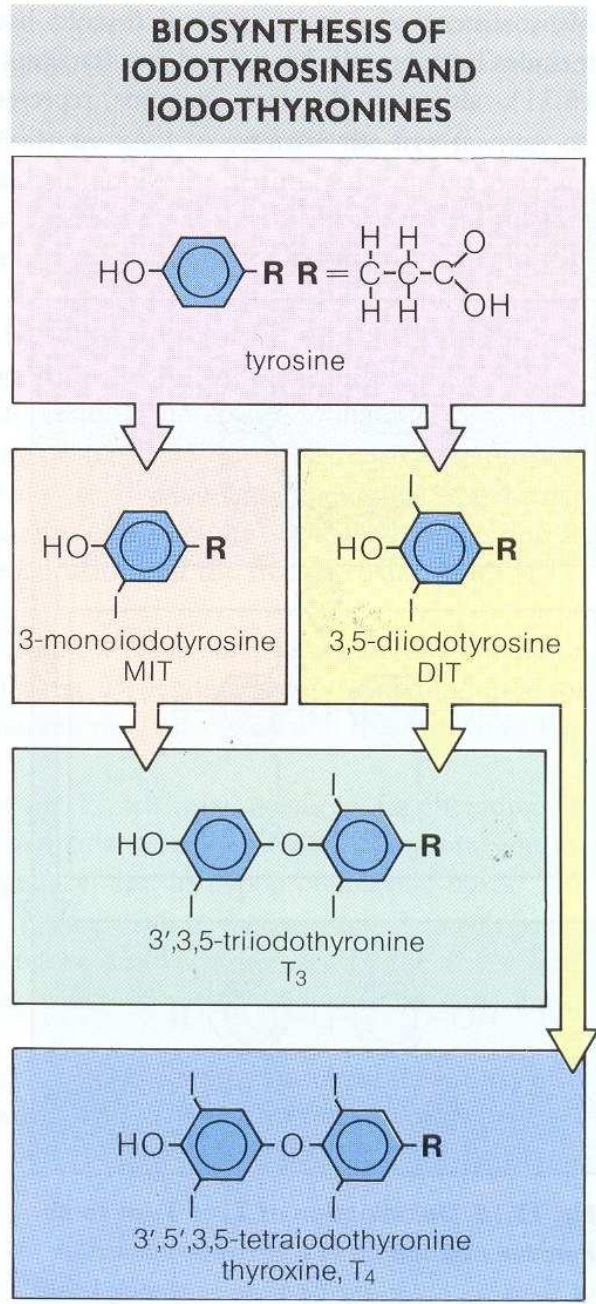


## THYROID HORMONE SYNTHESIS AND RELEASE



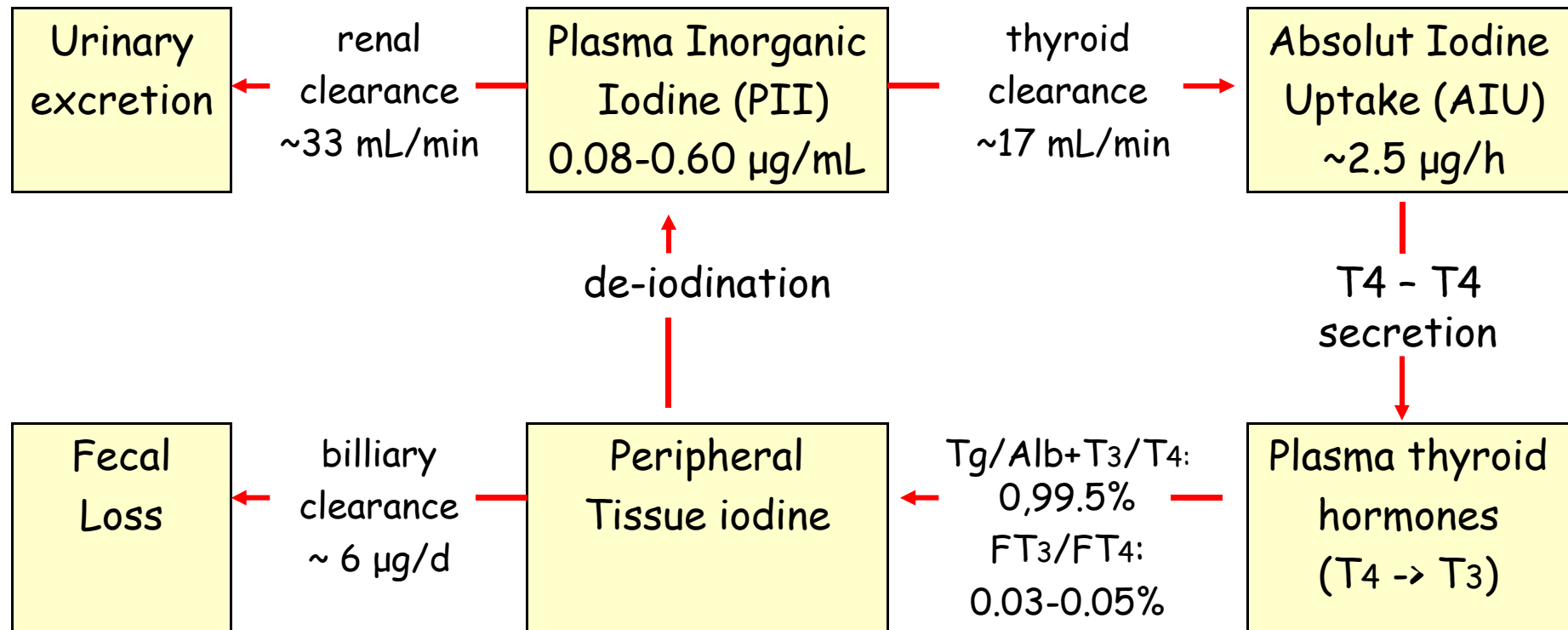
**Fig. 15.8 Schematic representation of thyroid hormone synthesis and release in a single cell of a thyroid follicle.** The six major stages in the biosynthesis and release of thyroid hormones, namely (i) iodine transport, (ii) oxidation, (iii) coupling, (iv) colloid resorption, (v) proteolysis, and (vi) deiodination, are shown.





**Fig. 15.9 Biosynthesis of iodotyrosines and iodothyronines from tyrosine.**

# IODINE METABOLIC CYCLE



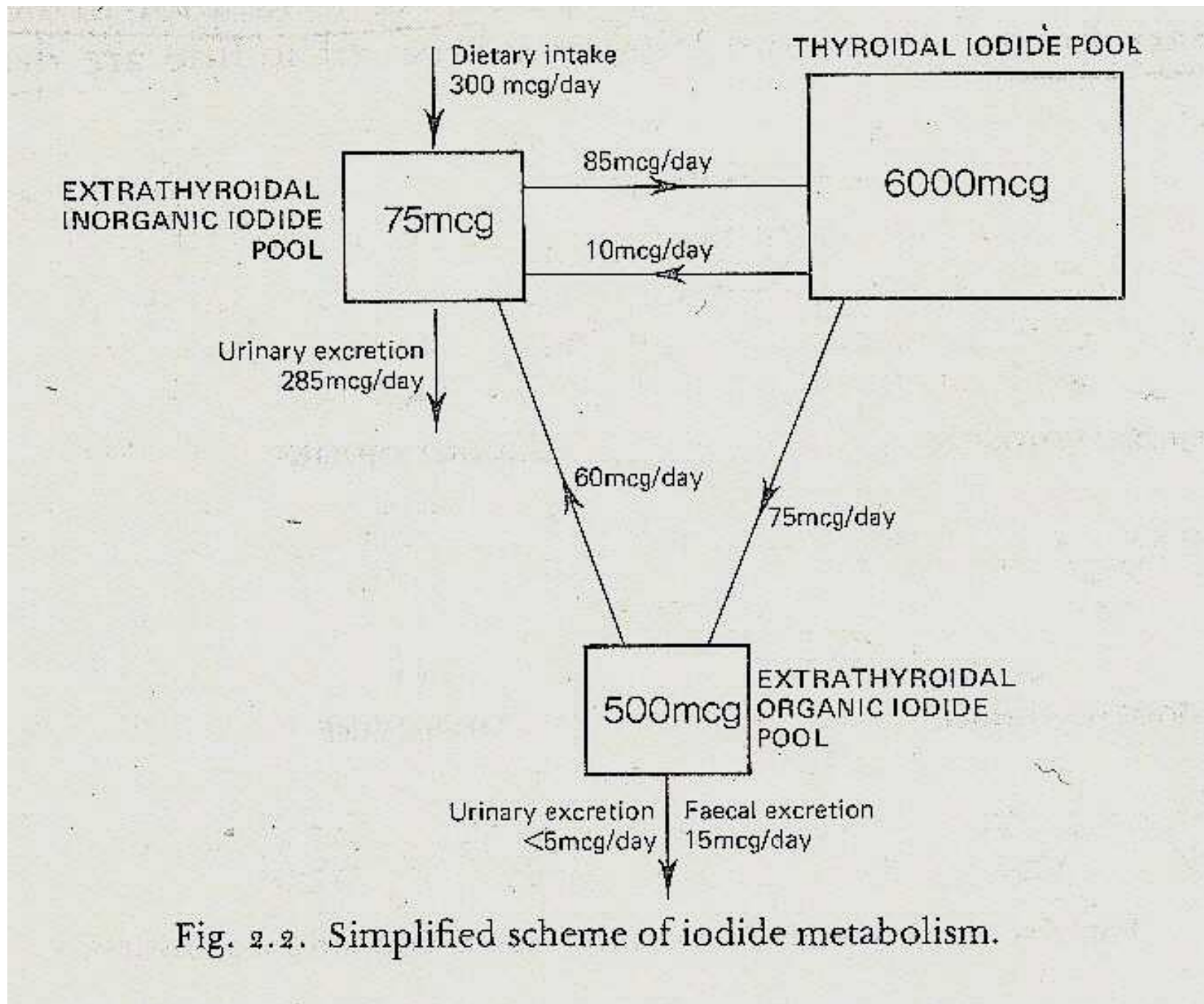


Fig. 2.2. Simplified scheme of iodide metabolism.

# Iodine and health -1

- ❖ Iodine is an essential micronutrient and an integral component of thyroid hormones. It is obtained only through the diet and it is mainly absorbed by the gastrointestinal track as the inorganic anion **iodide**.
- ❖ Deficiency of iodine intake is a global health problem and approximately 2 billion people are at risk of developing an iodine deficiency disorder (IDD) worldwide (W.H.O, 2002)

## Iodine and health -2

- ❖ the consequences of IDD include:
  - goiter
  - hypothyroxinemia
  - neurodevelopmental anomalies
  - cretinism
  - still-births
  - raised perinatal mortality
- ❖ worldwide, at least some 50 million people are affected by some degree of IDD-related brain damage (W.H.O., 2002).

## Iodine and health -3

- ❖ In pregnancy demands for iodine are higher for a number of reasons (increased glomerular filtration rate, fetal needs, etc).
- ❖ Daily iodine intake is estimated by measuring:
  - a. daily iodine excretion in 24 hour urine collection
  - b. random spot urine sample in relation to creatinine

## Iodine requirements and thyroid function -1

- Entry of adequate quantities of iodine into the thyroid is a prerequisite for thyroid hormone biosynthesis.
- Iodine enters the thyroid in its organic form as iodide derived either from food, water and drugs or from deiodination of thyroid hormones



## Iodine requirements and thyroid function -2

- An average intake of 150-200  $\mu\text{g}$  per day is considered sufficient to sustain a plasma iodide concentration of 0.5  $\mu\text{g}/\text{dL}$  and a urinary excretion greater than 100  $\mu\text{g}/\text{g}$  creatinine.

## Iodine containing foods

- table salt
- seaweed
- I-enriched vitamins
- dietary supplements
- cow's milk
- yogurt - ice cream
- cheese
- soy sauce
- eggs
- bread-baggets
- saltwater fish
- shell fish

## Iodine containing pharmaceutical products-cosmetics

- thyroid hormones
- I-containing substances
- I.V. contrast media
- anti-septic skin cleaners
- vaginal rings
- amiodarone
- cosmetics
- sun protectors

# Evolution of iodine availability in Greece

Studies in mountainous and remote areas (Epirus, Thessaly & Crete) showed that:

plasma inorganic iodine	}	very low in 1960's
urinary iodine excretion		
prevalence of goiter in schoolchildren	}	high (40-60%)

Re-evaluation after "silent iodine prophylaxis" in the 1980's and 1990's showed that:

plasma inorganic iodine	}	normal values
urinary iodine excretion		
prevalence of goiter in school children	}	1.7 - 12.5%

# Iodine deficiency in the world-1

## Europe:

- Prevalence of ID is still very common in Europe. In the late 1990's, 32 European countries were still affected by mild to severe ID (mostly from Eastern Europe)
- Access to iodized salt in ID affected countries was 5-10% in 1990 and 28% in 1999 (worldwide: 68%)

## Iodine deficiency in the world-2

**Africa:** Mild to severe ID but with recent improvements in Ivory Coast, Ethiopia, Kenya, Nigeria, South Africa, Uganda (Tanzania?)

**Asia:** Mild to severe ID with improvements in most Asian countries with few exceptions (Japan).

**Americas:** Selected areas with mild to moderate ID in North and South sub-continent, and severe form in Central America.

# Iodine deficiency in the world-3

## Ethiopia -1

- data from 2005
- median urine excretion: 2.45  $\mu\text{g}/\text{dL}$
- 4.2% of households use iodized salt
- 39.9% the prevalence of goiter in 6-12 year olds

# Iodine deficiency in the world-4

## Ethiopia-2

- data from 2005: ID and reproductive performance
- in women of childbearing age (15-49 years) the goiter prevalence was 35.8%
- a history of pregnancy failure was found in 16.7% of women with goiter and in 13.7% of women with normal gland.
- reproductive failure in severe ID and goiter endemic areas was 16.0% and in mild areas only 7.8%.



# Optimal iodine supplementation - 1

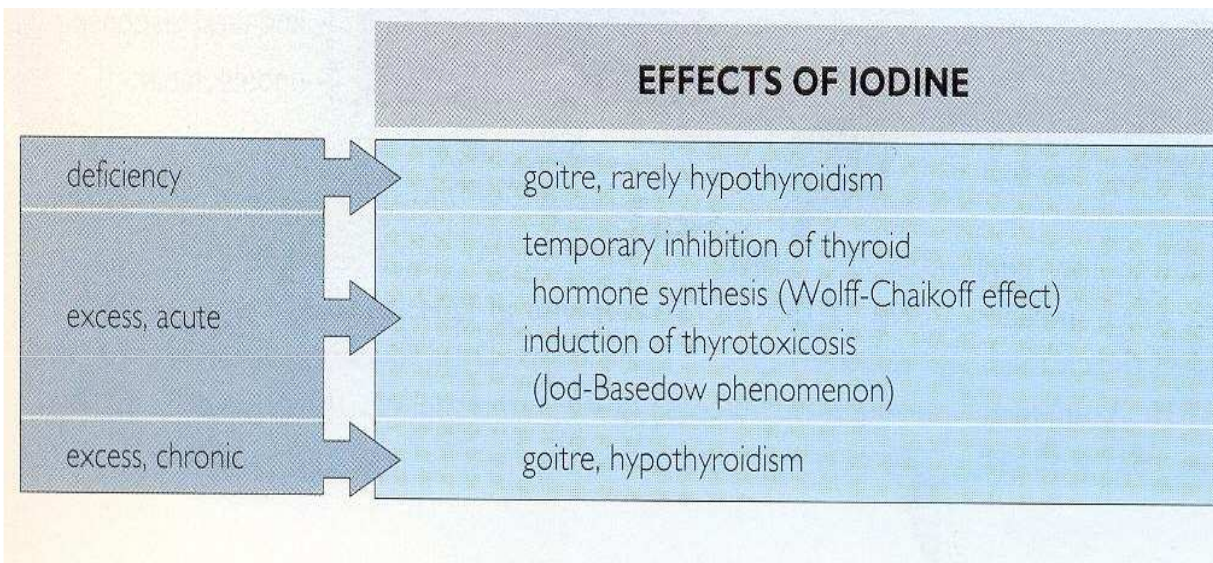
- factors involved:
  - level of iodine intake
  - genetic background
  - tobacco smoking
- aims of prophylaxis
  - provision of adequate iodine
  - avoid the risks of excess

## Optimal iodine supplementation - 2

- mapping of dietary habits of a population
- data on iodine content of the food items available locally
- intervention during pregnancy-lactation
- centrally regulated programme of I availability

## Optimal iodine supplementation - 3

- pregnancy and lactation: ID remains the most frequent cause of preventable mental retardation in children. Even a mild ID increases the relative risk.
- the ATA recommends a daily supplement of 150  $\mu\text{g}$  with iodine during pregnancy and lactation in addition to the use of iodized salt.



**Fig. 15.20 Various effects of iodine on thyroid function.** Whereas iodine deficiency will lead to goitre formation and rarely hypothyroidism, iodine excess can temporarily inhibit thyroid hormone synthesis (Wolff-Chaikoff effect) or induce thyrotoxicosis (Jod-Basedow phenomenon). Chronic iodine excess can also cause goitre formation and hypothyroidism.

# Iodine prophylaxis and thyroid autoimmunity - 1

- contradicting observations have been reported regarding a possible causal relationship between iodine prophylaxis and thyroid autoimmunity:
  - those advocating to a positive relationship, suggest an early phase development of anti-Tg and a late phase appearance of anti-TPO antibodies.
  - a few studies failed to demonstrate any permanent and marked interrelationship between the two variables.

## Iodine prophylaxis and thyroid autoimmunity - 2

- despite the diversity of observations, the prevailing view is that iodine administration is causatively related with autoimmunity
- this is more relevant in contemporary societies in which iodine is amply available in the form of dietary products, food additives and widely used pharmaceutical agents.

# Iodine deficiency disorders-goiter/1

- Insufficient iodine intake for a prolonged period of time is associated with a spectrum of iodine deficiency disorders (IDD).
- This is the consequence of the gland's dependence on dietary iodine intake to maintain plasma inorganic iodide within normal limits (no renal homeostasis mechanisms are available)
- Prevalence of goiter in more than 5-10% of a population defines the so-called "endemic goiter"



# Iodine deficiency disorders-goiter/2

- Goiter is the term used to describe a non-neoplastic enlargement of the thyroid gland, sometimes visible on inspection or palpated as an enlargement of the gland exceeding the size of the distal thumb phalange.
- Grading of goiter on clinical examination (W.H.O., 2001):
  - grade 0: not palpable or visible
  - 1: palpable - not visible
  - 2: visible and palpable



## Iodine deficiency disorders-goiter/3

- The size of thyroid gland depends on sex, age and body surface (BSA) until adolescence is completed. Moreover, it is related to nutritional habits and racial characteristics. Thyroid volume greater than 18 mL in males and 14mL in females is considered abnormal.

# Classification of goiter

- **Based on prevalence**
  - sporadic <4%
  - endemic >5-10%
- **Based on morphology**
  - diffuse - homogenous hyperplasia-hypertrophy
  - nodular - nodule(s) structurally/functionally heterogenous
- **Based on functional state**

hyperfunctioning	}	in association with autoantibodies
hypofunctioning		

# Benign nodular thyroid disease

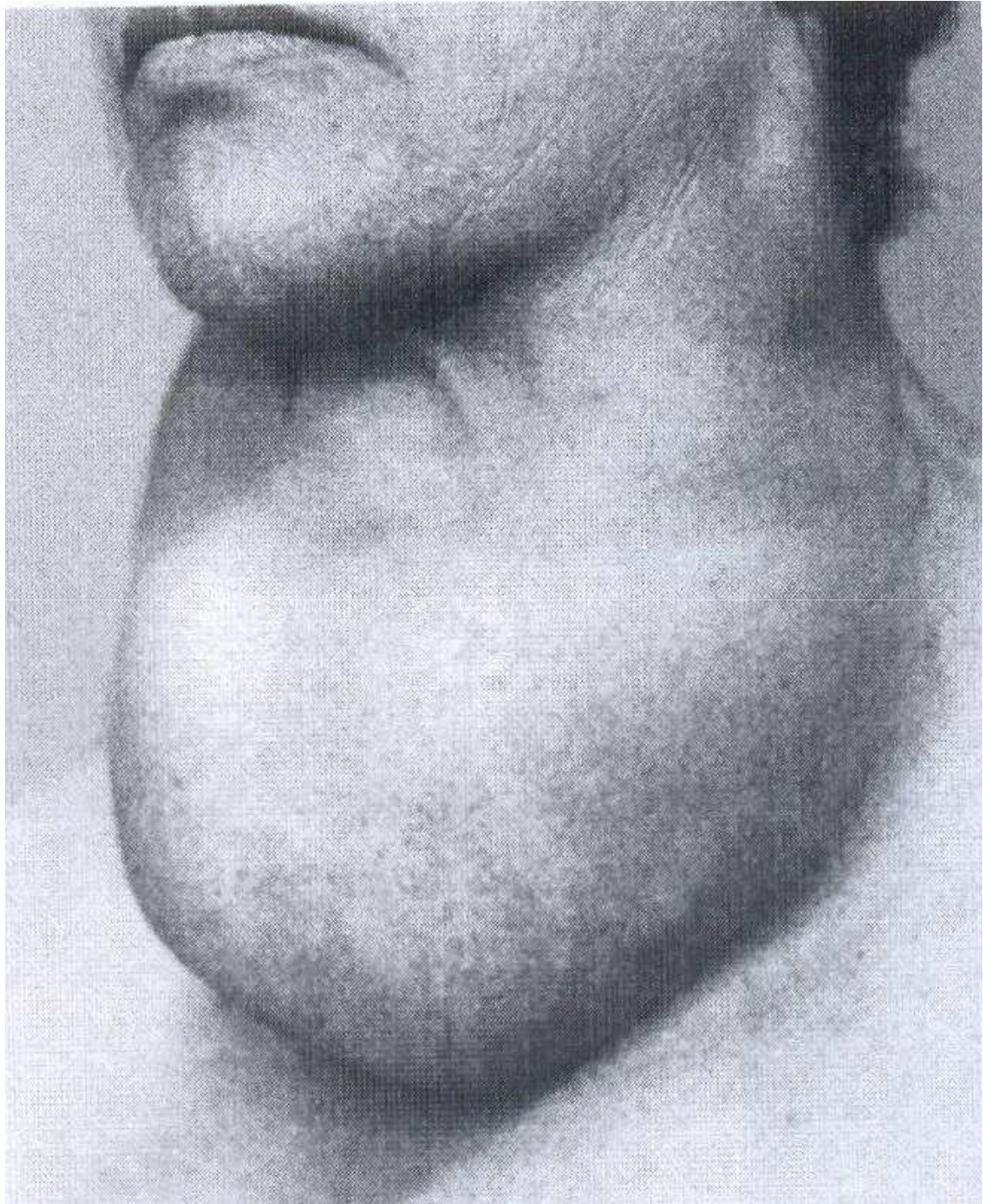
(a heterogenous disorder highly prevalent in iodine deficient areas)

## Classification:

1. Solitary nodules-encapsulated or not (histologically).

Solitary nodules cold (85%), normal (15%) or hot (5%) (functionally).

2. Multinodular goiter - a mixed group of nodules (hyper-, hypo- or normo-functional)



# Frequency of nodular thyroid disease

Promoting factors:

genetic sex

raised BMI

radiation

smoking

Prevalence in iodine deficient areas (US diagnosis)

adult women 30-40%

adult men 20-30%

Peak frequency occurs around the age of 40's with a plateau or a decline thereafter

## Aetiology of goiter

- environmental factors: iodine deficiency is the main cause world-wide
- enzymatic defects: impairment of thyroid synthesis leading to sporadic goiter
- genetic causes (familial aggregation): activating TSHR and G<sub>S</sub>α gene mutations.



## Environmental factors -1

The thyroid gland is very vulnerable to exogenous agents and a number of natural or synthetic compounds (disruptors) which may interfere with normal thyroid function leading to goiter formation. These include:

## Environmental factors -2

**Iodine deficiency:** is the main pathogenetic factor contributing to endemic goiter:

- i. direct action through local feedback mechanisms or
- ii. indirectly through a TSH rise in response to low T3/T4 production

**severity:** the incidence of goiter increases in line with distance of an area from the sea and inversely with soil's iodine content

**localities:** remote mountainous areas, newly formed soils and poor transportation facilities.



## Environmental factors -3

**Plant products:** cabbage, brussel sprout, broccoli, sorghum cassava leaves, millet, etc. Their goitrogenic action is mostly exerted by glucosinolates which are converted to thiocyanide, goitrin and allyl isothionate

**Chemical compounds:** polychlorinated biphenyls, organophosphate, organocholine pesticides, dioxin by-products of organochlorine and cyanates

# CONCLUSIONS

- ✓ Iodine deficiency disorders are very common in both developing and developed societies.
- ✓ The consequences of this problem are very severe mostly in terms of neurocelebral development and thyroid dysfunction.
- ✓ Adequate iodine supplementation and monitoring of its observance are cheap and effective means of combating the problem.