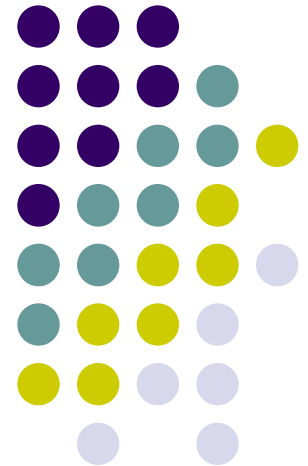


# Thyroid disorders

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**Prof. Assim A Alfadda**

MD,FACP,FRCPC,MSc

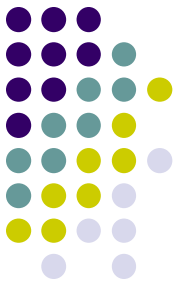




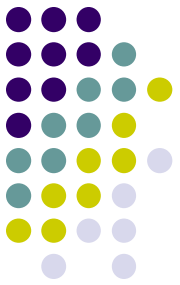
# Objectives

- \* How to evaluate a patient with thyroid disease?
- \* Hypothyroidism and Hyperthyroidism: causes, pathogenesis, diagnosis and treatment.
- \* Other thyroid disorders.

# Patients with thyroid disease

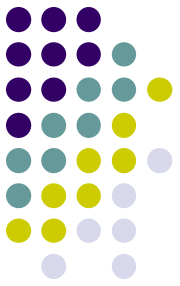


- Thyroid enlargement (goiter): diffuse or nodular
- Symptoms of hypothyroidism
- Symptoms of hyperthyroidism
- Complications of a specific form of hyperthyroidism- Graves' disease-which may present with:
  - Striking prominence of the eyes (exophthalmos)
  - Thickening of the skin over the lower leg (thyroid dermopathy)



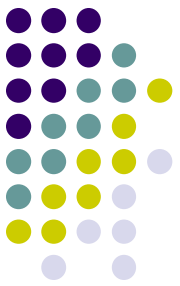
# History

- Exposure to ionizing radiation
- Iodide ingestion:
  - Kelp
  - Iodide-containing cough preparation
  - IV Iodide-containing contrast media
- Lithium carbonate
- Residence in an area of low dietary iodide



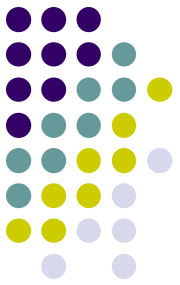
# History

- Family history
  - Thyroid disease
  - Immunologic disorders:
    - \* Diabetes
    - \* Rheumatoid disease
    - \* Pernicious anemia
    - \* Alopecia
    - \* Vitiligo
    - \* Myasthenia gravis
    - \* MEN 2A



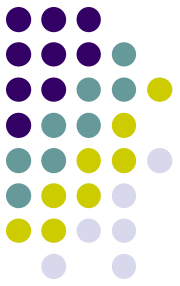
# Physical examination

- Observe the neck, especially as the patient swallows
- Examine from the front, rotating the gland slightly with one thumb while palpating the other lobe with the other thumb
- Examine from behind, using three fingers and the same technique
- Determine the size of the thyroid lobes, consistency, presence of nodules



# **HYPOTHYROIDISM**

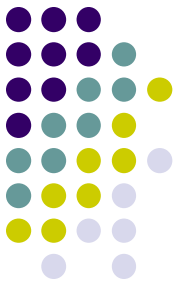
# Causes



## ● Primary:

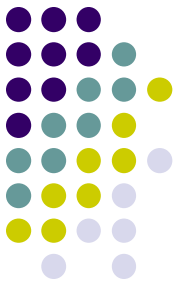
1. Hashimoto's thyroiditis:
  - With goiter
  - "Idiopathic" thyroid atrophy, presumably end-stage autoimmune thyroid disease, following either Hashimoto's thyroiditis or Graves' disease
  - Neonatal hypothyroidism due to placental transmission of TSH-R blocking antibodies
2. Radioactive iodine therapy for Graves' disease
3. Subtotal thyroidectomy for Graves' disease or nodular goiter
4. Excessive iodine intake (kelp, radiocontrast dyes)
5. Subacute thyroiditis
6. Iodide deficiency
7. Other goitrogens such as lithium, amiodarone, antithyroid drug therapy
8. Inborn errors of thyroid hormone synthesis





# Causes

- **Secondary**
  - Hypopituitarism due to:
    - a- Pituitary adenoma
    - b- pituitary ablative therapy
    - c- pituitary destruction
- **Tertiary**
  - Hypothalamic dysfunction (rare)
- **Peripheral resistance of the action of thyroid hormone**

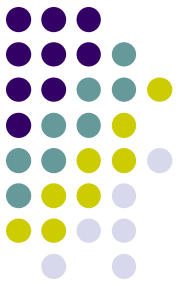


# Pathogenesis

- Thyroid hormone deficiency affects every tissue in the body, so that the symptoms are multiple
- Accumulation of glycosaminoglycans-mostly hyaluronic acid- in interstitial tissues
- Increase capillary permeability to albumin
- Interstitial edema (skin, heart muscle, striated muscle)



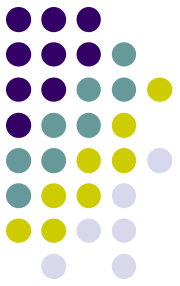
# Clinical presentations and findings



## ● Adults

- Common feature: easy fatigability, coldness, weight gain, constipation, menstrual irregularities, and muscle cramps.
- Physical findings: cool rough dry skin, puffy face and hands, hoarse husky voice, and slow reflexes, yellowish skin discoloration.
- Cardiovascular:
  - Bradycardia
  - Decreased cardiac output
  - Low voltage ECG
  - Cardiomegaly
  - Pericardial effusion
- Pulmonary function
  - Shallow and slow respiration
  - Respiratory failure

# Clinical presentations and findings



- Adults (cont')

- GI:

- Chronic constipation
- Ileus

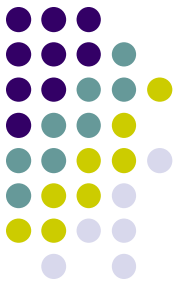
- Renal function:

- Impaired GFR
- Water intoxication

- Anemia:

- Impaired hemoglobin synthesis
- Iron deficiency
- Folate deficiency
- Pernicious anemia, with B12 deficient megaloblastic anemia

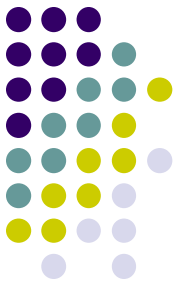
# Clinical presentations and findings

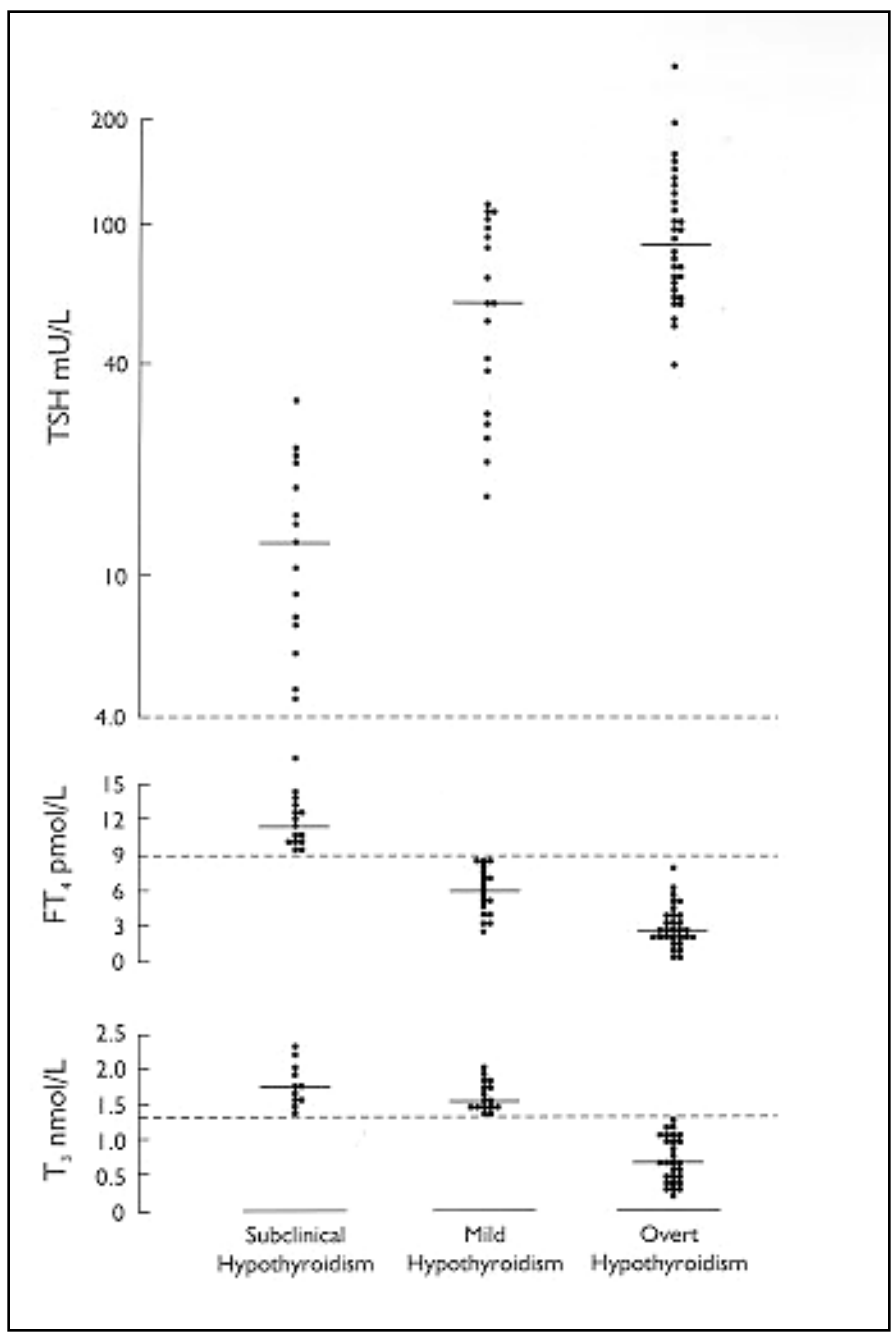


- Adults (cont')
  - Neuromuscular system:
    - Severe muscle cramps
    - Paresthesias
    - Muscle weakness
    - Carpal tunnel syndrome
  - CNS:
    - Chronic fatigue
    - Lethargy
    - Decreased concentration
    - Anovulatory cycles and infertility
    - Menorrhagia
    - Depression
    - Agitation

# Diagnosis

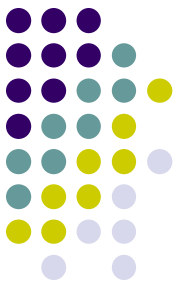
- Low serum FT4
- Elevated serum TSH
- Thyroid antibodies
- TRH stimulation test





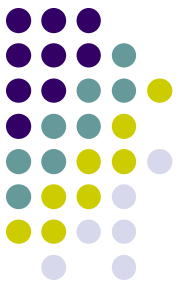
Individual and median values of thyroid function tests in patients with various grades of hypothyroidism. Discontinuous horizontal lines represent upper limit (TSH) and lower limit (FT<sub>4</sub>, T<sub>3</sub>) of the normal reference ranges. Reproduced with permission from Ord WM: On myxedema, a term proposed to be applied to an essential condition in the "cretinoid" affection occasionally observed in middle-aged women. *Medico-Chir Trans* 1878; 61: 57.





# Complications

- 1- Myxedema coma
  - The end stage of untreated hypothyroidism
  - Progressive weakness, stupor, hypothermia, hypoventilation, hypoglycemia, hyponatremia, water intoxication, shock, and death.
  - Associate illnesses and precipitating factors: pneumonia, MI, cerebral thrombosis, GI bleeding, ileus, excessive fluid administration, and administration of sedatives and narcotics.
  - Three main issues: CO<sub>2</sub> retention and hypoxia, fluid and electrolyte imbalance, and hypothermia.
- 2- Myxedema and heart disease
- 3- Hypothyroidism and neuropsychiatric disease

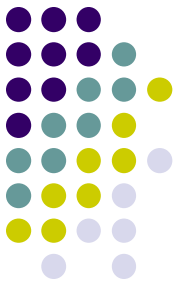


# Treatment

## ● A- Hypothyroidism

- Levothyroxine (T4).
- Follow serum Free T4 and TSH
- Take dose in AM
- Do blood test fasting before taking the daily dose
- Adults: 1.7 ug/kg/d, but lower in elderly (1.6 ug/kg/d)
- For TSH suppression (nodular goiters or cancer): 2.2 ug/kg/d
- Increase dose of T4 in malabsorptive states or concurrent administration of aluminum preparations, cholestyramine, calcium, or iron compounds
- Increase dose of T4 in pregnancy and lactation
- The  $t_{1/2}$  of levothyroxine is 7 days

# Treatment



- B- Myxedema coma

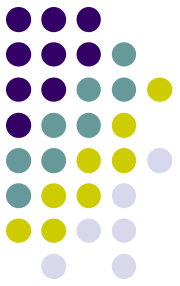
- Acute medical emergency
- Monitor blood gases
- Patient may need intubation and mechanical ventilation
- Treat associated medical problems
- Avoid excessive hydration
- Assess adrenal function and treat if needed
- In pituitary myxedema, glucocorticoid replacement is essential
- IV levothyroxine: loading 300-400 ug, daily maintenance 50 ug
- Be cautious in patients with coronary artery disease
- Active rewarming of the body is contraindicated

# Recommendations for the treatment of myxedema coma



• hypothyroidism	large initial intravenous dose of 300-500 $\mu$ g T <sub>4</sub> ; if no response within 48 hours, add T <sub>3</sub>
• hypocortisolemia	intravenous hydrocortisone 200-400 mg daily
• hypoventilation	don't delay intubation and mechanical ventilation too long
• hypothermia	blankets, no active rewarming
• hyponatremia	mild fluid restriction
• hypotension	cautious volume expansion with crystalloid or whole blood
• hypoglycemia	glucose administration
• precipitating event	identification and elimination by specific treatment (liberal use of antibiotics)

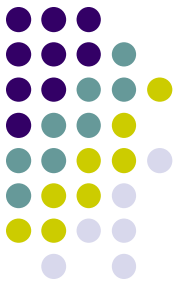
# Treatment



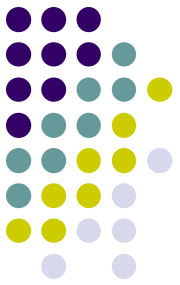
- C- Myxedema with heart disease

- Start treatment slowly in long standing hypothyroidism and in elderly patients particularly those with known cardiovascular disease
- 25 ug/d x 2 weeks, increase by 25 ug every 2 weeks until a daily dose of 100-125 ug is reached

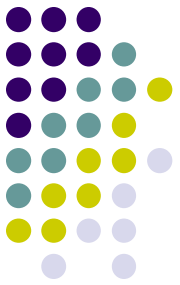
# Treatment



- Toxic effects of levothyroxine therapy
  - No allergy has been reported to pure levothyroxine
  - If FT4 and TSH are followed and T4 dose is adjusted, no side effects are reported
  - If FT4 is higher than normal: hyperthyroidism symptoms may occur:
    - Cardiac symptoms
    - Osteopenia and osteoporosis



# **HYPERTHYROIDISM & THYROTOXICOSIS**



# Definitions

- Thyrotoxicosis: is the clinical syndrome that results when tissues are exposed to high levels of circulating thyroid hormone
- Hyperthyroidism: is the hyperactivity of the thyroid gland

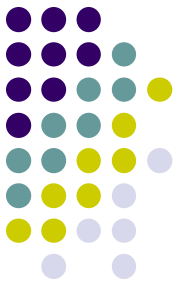


# Conditions associated with thyrotoxicosis



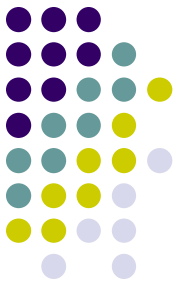
- Diffuse toxic goiter (Graves' disease)
- Toxic adenoma (Plummer's disease)
- Toxic multinodular goiter
- Subacute thyroiditis
- Hyperthyroid phase of Hashimoto's thyroiditis
- Thyrotoxicosis factitia
- Rare: ovarian struma, metastatic thyroid carcinoma (follicular), hydatiform mole, TSH secreting pituitary tumor, pituitary resistance to T3 and T4

# Diffuse Toxic Goiter (Graves' disease)



- Most common form of thyrotoxicosis
- Females > Males
- Features:
  - Thyrotoxicosis
  - Goiter
  - Orbitopathy (exophthalmos)
  - Dermopathy (pretibial myxedema)

# Etiology



- Autoimmune disease of unknown cause
- There is a strong familial predisposition
- Peak incidence in the 20- to 40- year age group

# Pathogenesis

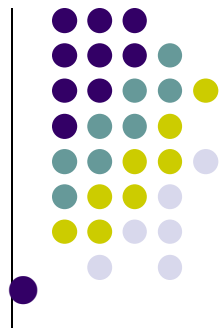
Local viral infection → inflammatory reaction  
leading to the production of IFN-g and other  
cytokines by non-thyroid-specific infiltrating immune  
cells

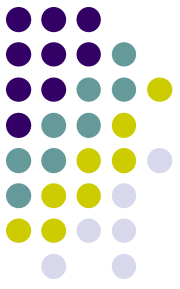


will induce the expression of HLA class II molecules on  
the surface of thyroid follicular cells.



Subsequently, thyroid specific T-cells will recognize  
the antigen presented on the HLA class II molecules  
and will be activated





# Pathogenesis

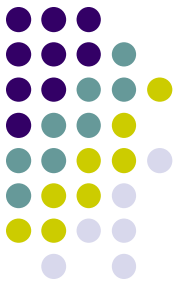
The activated thyroid-specific T-cells stimulate  
B cells to produce



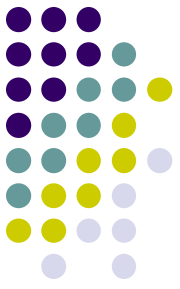
TSH receptor-stimulating antibodies



hyperthyroidism







# Diagnosis

Elevated FT4 ●

Suppressed TSH ●

Eye signs

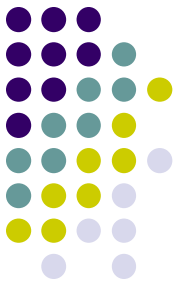
+

No further  
test

-

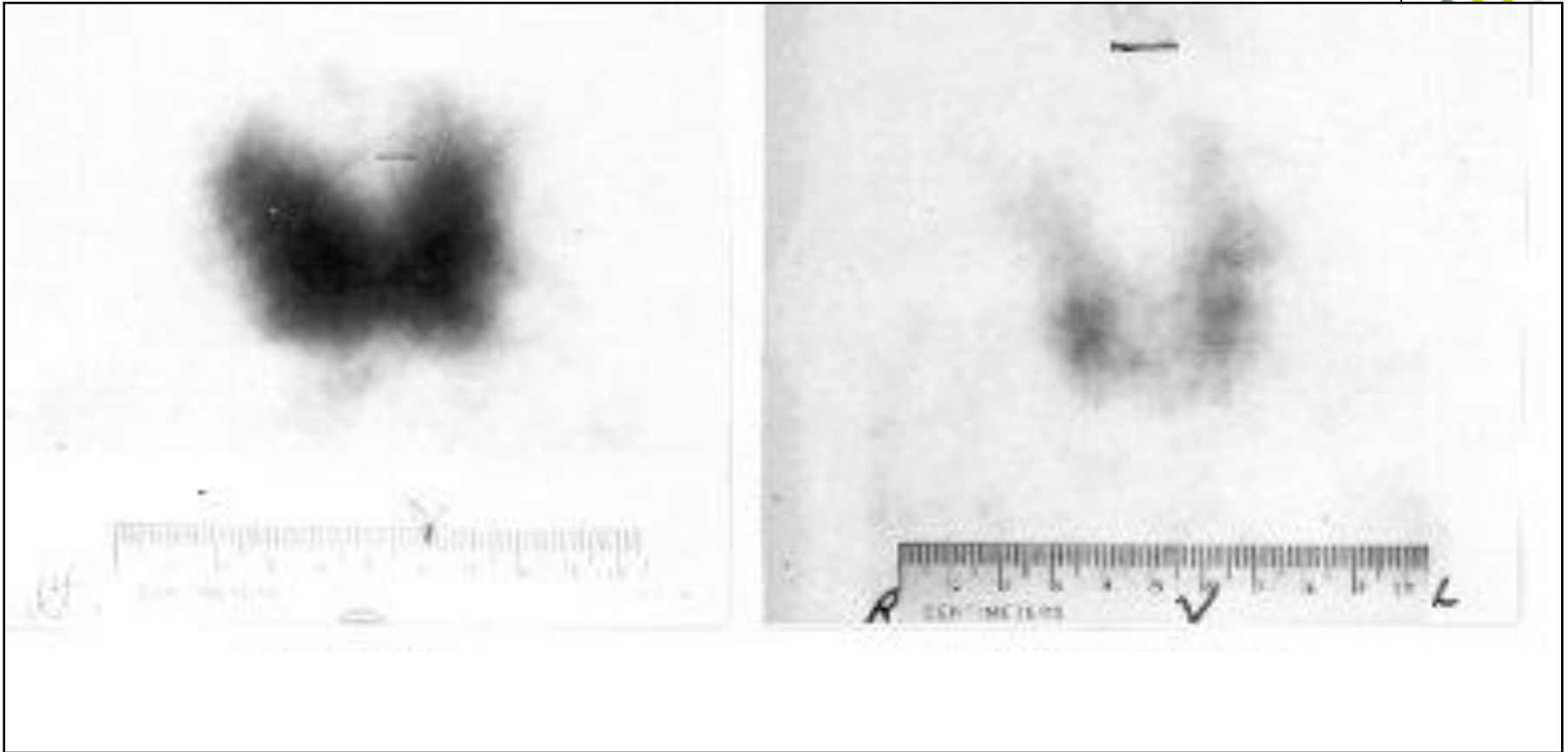
Thyroid scan

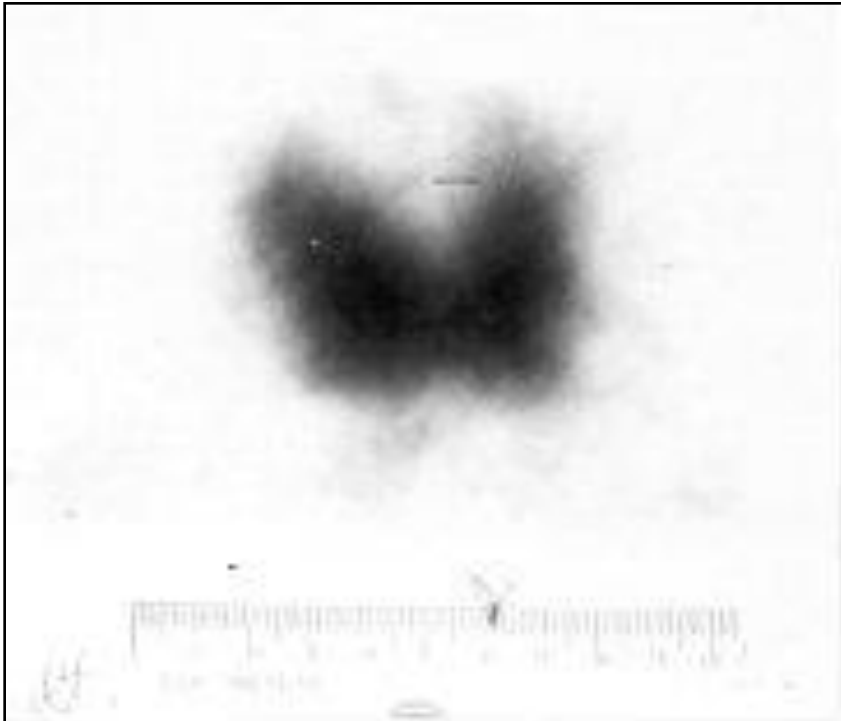




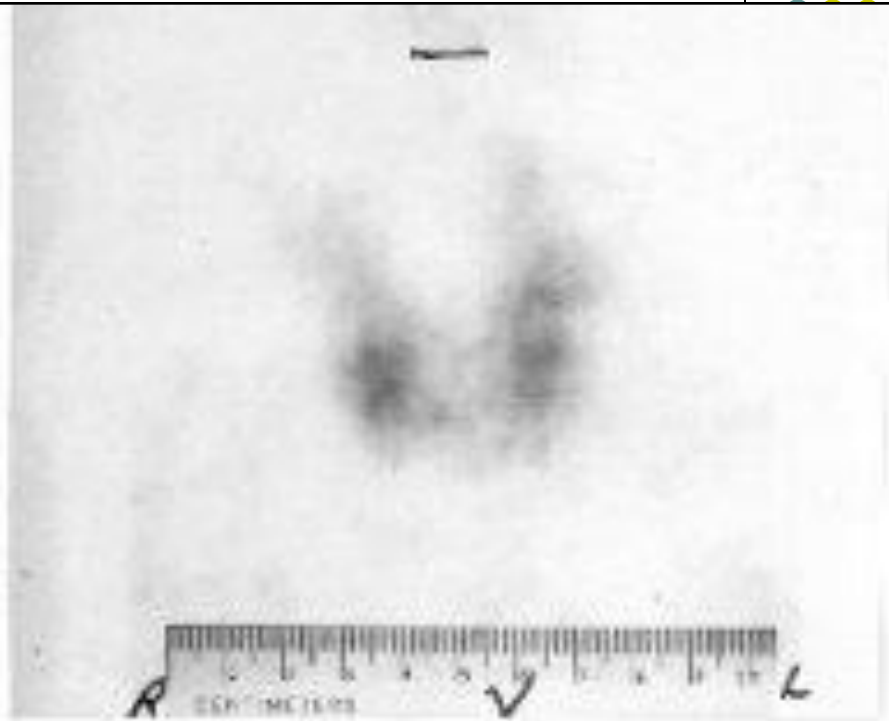
# Radioiodine uptake scan

- Elevated uptake:
  - Graves' disease
  - TMN
- Low uptake:
  - Spontaneous resolving hyperthyroidism
  - Subacute thyroiditis
  - Thyrotoxic phase of Hashimoto's thyroiditis
  - Iodine loaded patients
  - Patients on LT4 therapy
  - Struma ovarii

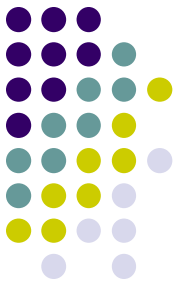
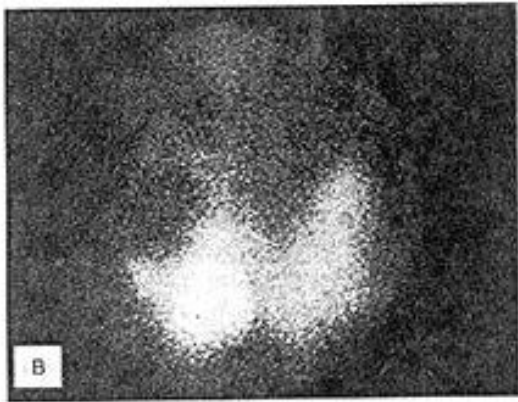
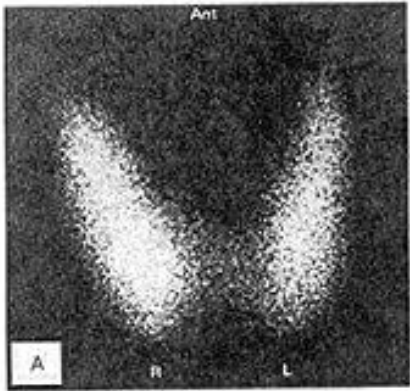


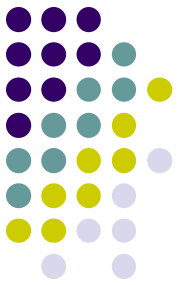


**NORMAL**

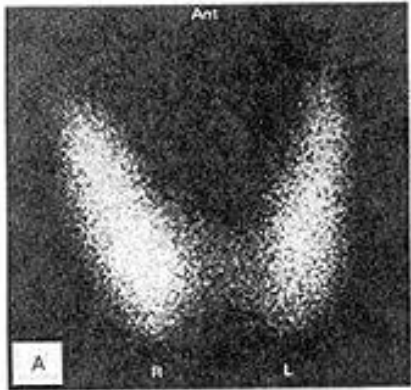


**THYROIDITIS**

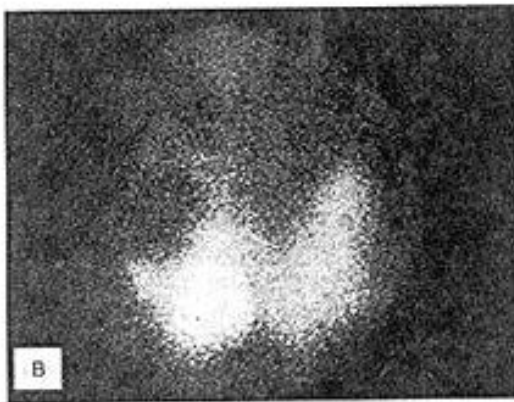




**Figure 6-6. Thyroid Scans.**



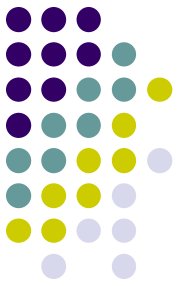
a. Normal thyroid imaged with  $^{123}\text{I}$ .



b. Cold nodule in the right lobe imaged by  $^{99\text{m}}\text{Tc}$ .

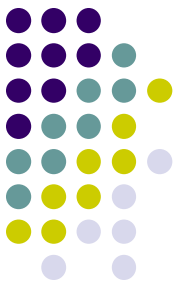


c. Elderly woman with obvious multinodular goiter and the corresponding radioiodide scan on the right.



# Diagnosis

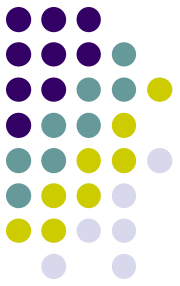
- TSH-R Ab [stim]
- Free T3
- Atypical presentations:
  - Thyrotoxic periodic paralysis
  - Thyrocardiac disease
  - Apathetic hyperthyroidism
  - Familial dysalbuminemic hyperthyroxinemia



# Complications

- Thyrotoxic crisis (thyroid storm)
  - Predisposing conditions
  - Clinical features:
    - \* Fever / Agitation
    - \* Altered mental status
    - \* Atrial fibrillation / Heart failure

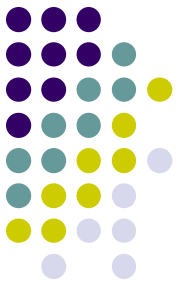
# Treatment of Graves' disease



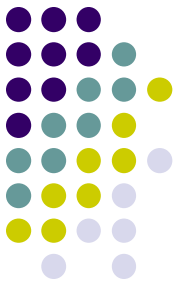
- Antithyroid drug therapy
  - Propylthiouracil or methimazole
  - Spontaneous remission 20-40%
  - Relapse 50-60%
  - Duration of treatment 6 months – years
  - Reactions to antithyroid drugs



# Treatment of Graves' disease



- Surgical treatment
  - Subtotal thyroidectomy
  - Preparation for surgery
  - Complications:
    - \* hypothyroidism/ hypoparathyroidism
    - \* Recurrent laryngeal nerve injury

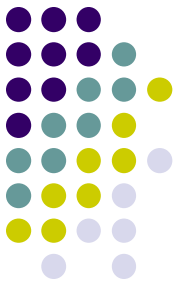


# Treatment of Graves' disease

- Radioactive iodine therapy
  - $^{131}\text{I}$  is most commonly used
  - Dose:

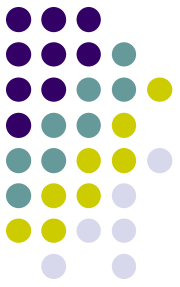
$$^{131}\text{I}_{(\text{uci/g})} \times \frac{\text{thyroid weight} \times 100}{24\text{-hr RAI uptake}}$$

# Treatment of Graves' disease



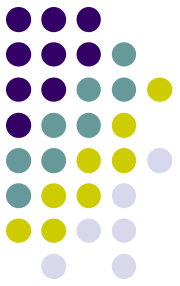
- $\beta$ -blockers
- SSKI

# Treatment of Graves' disease complications

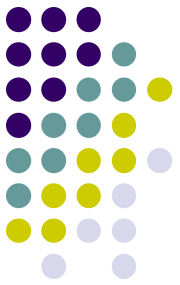


- Thyrotoxic crisis
- Orbitopathy
- Thyrotoxicosis and pregnancy

# Treatment of other forms of thyrotoxicosis

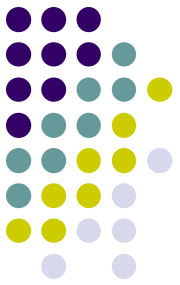


- Toxic adenoma
- TMN
- Amiodarone
- Subacute thyroiditis
- Thyrotoxicosis factitia
- Struma ovarii



# Other thyroid disorders

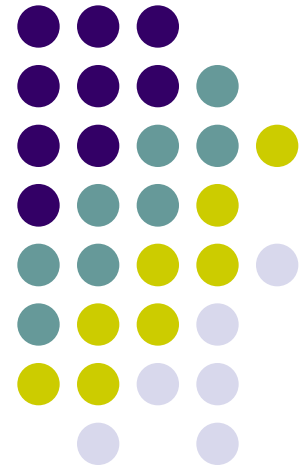
- Nontoxic goiter
- Subacute thyroiditis (De Quervain's)
- Chronic thyroiditis
- Acute thyroiditis
- Thyroid nodules
- Thyroid cancer



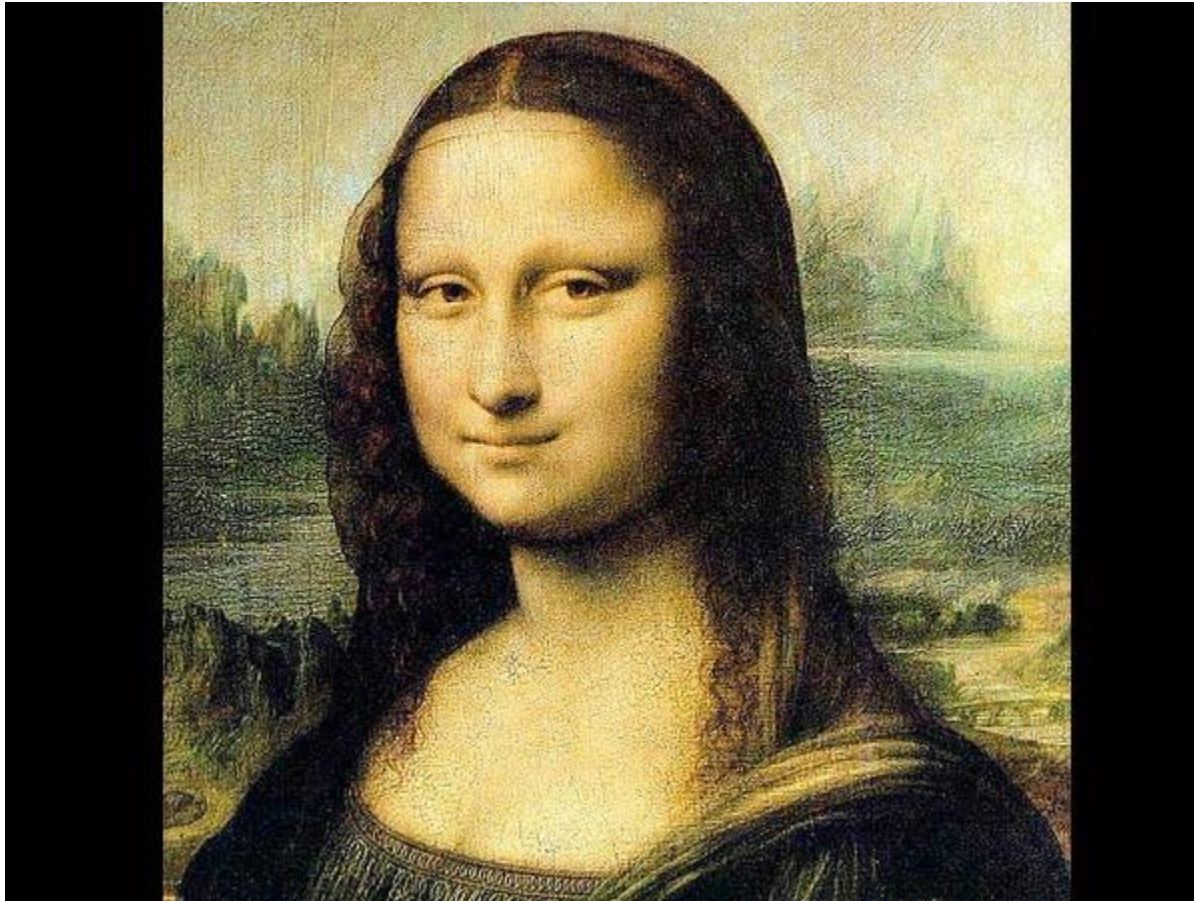
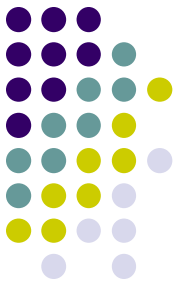
■ **Thank you**

# Goiter and thyroid nodules

Anwar Ali Jammah,

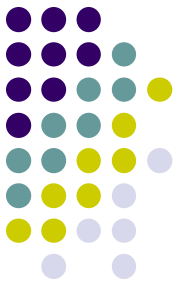






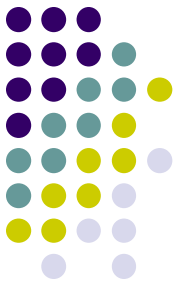
Thyroid enlargement  
Roman physicians: sign of puberty  
Egyptian: sign of beauty

# History



- Goiter
  - First described in China in 2700 BC
  
- Thyroid Function
  - Da Vinci – thyroid is designed to **fill empty spaces in the neck**
  - Parry – thyroid works as **a buffer to protect the brain from surges in blood flow**

# Surgical advances



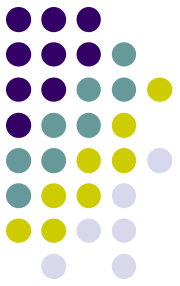
- 500 AD
  - **First goiter excision in Baghdad.**
  - **Procedure: unknown**
- 1200' s AD
  - **Advancements in goiter procedures included applying hot irons through the skin and slowly withdrawing them at right angles.**
  - **Most died from hemorrhage or sepsis.**
- 1646 AD
  - **Wilhelm Fabricus performed a thyroidectomy with standard surgical scalpels.**
  - **The 10 y/o girl died, and he was imprisoned**
- 1808 AD
  - **Guillaume Dupuytren performed a total thyroidectomy.**
  - **The patient died postoperatively of “shock”**

# Surgical advances



- 1866
  - “If a surgeon should be so foolhardy as to undertake it [thyroidectomy] ... every step of the way will be environed with difficulty, every stroke of his knife will be followed by a torrent of blood, and lucky will it be for him if his victim lives long enough to enable him to finish his horrid butchery.”
    - Samuel David Gross

# Surgical advances



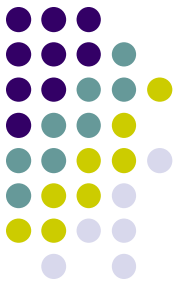
- 1883

Kocher's performs a retrospective review

- 5000 career thyroidectomies
- Mortality rates decreased
  - 40% in 1850 (pre-Kocher & Bilioth)
  - 12.6% in 1870's (Kocher begins practice)
  - 0.2% in 1898 (end of Kocher's career)
- Many patients developed cretinism or myxedema

His conclusions ....

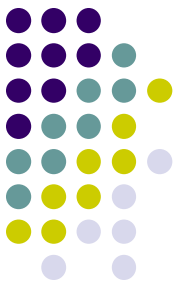
# Surgical advances



In presentation to the German Surgical Congress ...

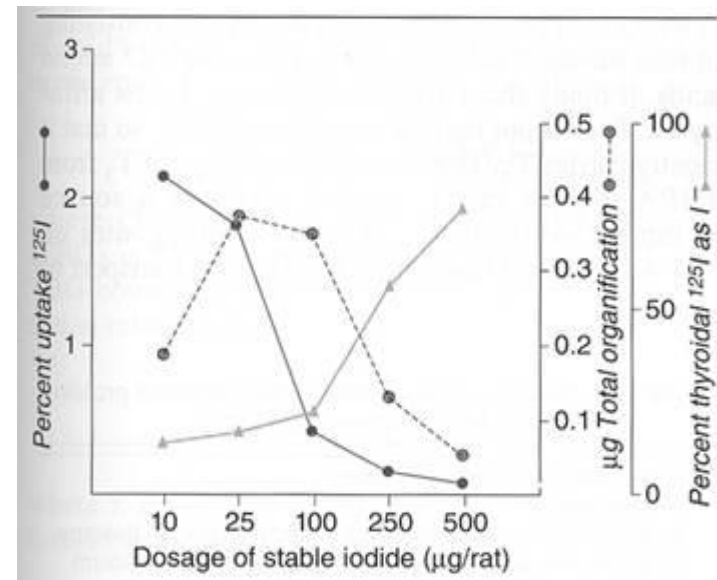
“ ...the thyroid gland in fact had a function....”

- Theodor Kocher, 1883

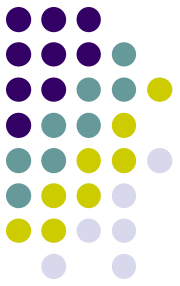


# Wolff-Chaikoff Effect

- Increasing doses of I<sup>-</sup> increase hormone synthesis initially
- Higher doses cause cessation of hormone formation.
- This effect is countered by the iodide leak from normal thyroid tissue.
- Patients with autoimmune thyroiditis may fail to adapt and become hypothyroid.



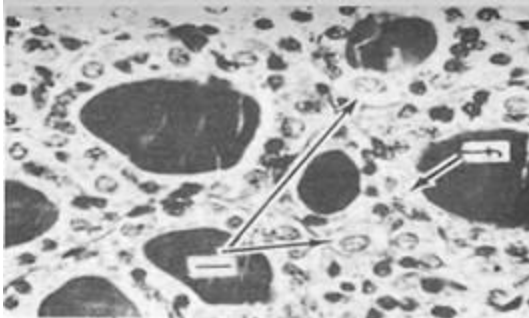
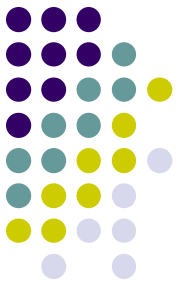
# Jod-Basedow Effect



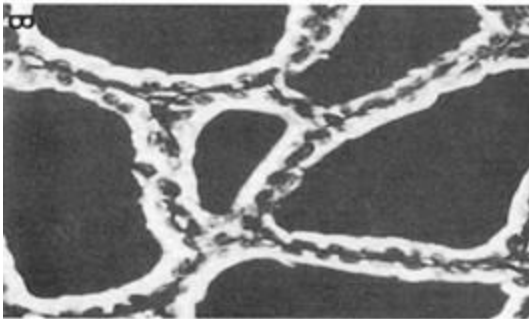
- Opposite of the Wolff-Chaikoff effect
- Excessive iodine loads induce hyperthyroidism
- Observed in hyperthyroid disease processes
  - Graves' disease
  - Toxic multinodular goiter
  - Toxic adenoma
- This effect may lead to symptomatic thyrotoxicosis in patients who receive large iodine doses from
  - Dietary changes
  - Contrast administration
  - Iodine containing medication (Amiodarone)



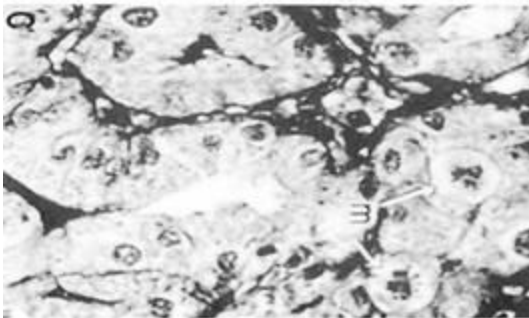
# Iodine states



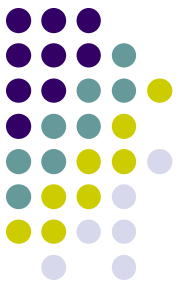
- Normal Thyroid



- Inactive Thyroid



- Hyperactive Thyroid



<u>Cause</u>	<u>Pathophysiology</u>	<u>thyroid activity</u>	<u>Growth pattern</u>	<u>Incidence and prevalence</u>
<b>Iodine deficiency</b>	Hyperplasia to compensate	Can cause hypothyroidism	Diffuse	90% cases of goiter worldwide
<b>Congenital hypothyroidism</b>	Inborn errors of hormone synthesis	Hypothyroidism	Diffuse	
<b>Hashimoto thyroiditis</b>	Autoimmune disease (Anti-TPO)	Hypothyroidism	Diffuse and lobulated	Prevalence: 1 to 1.5 in a 1000
<b>Thyroiditis</b>	inflammation	Hyper initially then hypo	Nodular	
<b>Pituitary TSHoma</b>	Hyposecretion of TSH		Diffuse	Very rare
<b>Thy.Hormon insensitivity</b>		hypothyroidism	Diffused	Very rare
<b>Graves' disease</b>	Autoantibodies (TSHR-Ab)	Hyperthyroid	Diffuse	1 to 2 cases per 1,000/y
<b>Benign neoplasms</b>	Adenoma	Euo,hypo,hyper if toxic	Nodular	7 % palpation
<b>Thyroid cancer</b>	Radiation, genetic	Euo/hypo rarely hyper	slow rapid in aggressiv Ca	