Differential diagnosis and investigation for endocrinology

Dr Mousa Tuwati Alfakhri

1/12/2020

Objectives

- Pitutary gland disorders clinical features ,and investigation
- Adrenal glands disorders clinical features ,and investigation
- Thyroid diseases clinical features ,and investigation (hyper and hyperthyroidism)
- Diabetes mellitus clinical features ,and investigation

Pituitary gland diseases
Clinical features and investigation

- Hypopituitarism(hypocortisoliemia,growth hormone deficiency ,hypogonadism ,and diabetes insipidus)
- Pitutary gland tumour(acromegaly and prolactinoma)

Hypopituitarism

- Deficiency of one or more hormones of pituitary gland ,due to pituitary disease or hypothalamic pathology
- Deficiency of one or multiple hormones of the anterior pituitary –**hypopituitarism**
- Deficiency of the posterior lobe -**central diabetes insipidus**
- Deficiency of all pituitary hormones **panhypopituitarism**

Diagnosis

- **Biochemical diagnosis of pituitary insufficiency**

  Demonstrating low levels of trophic hormones (LH ,FSH,ACTH,GH,TSH)-in the setting of low target hormone levels (testosteron,estrogen,cortisol ,IGF1,thyroxin)

- **Provocative tests may be required to assess pituitary reserve**

➢ **Short ACTH stimulation test(synacthin test)**

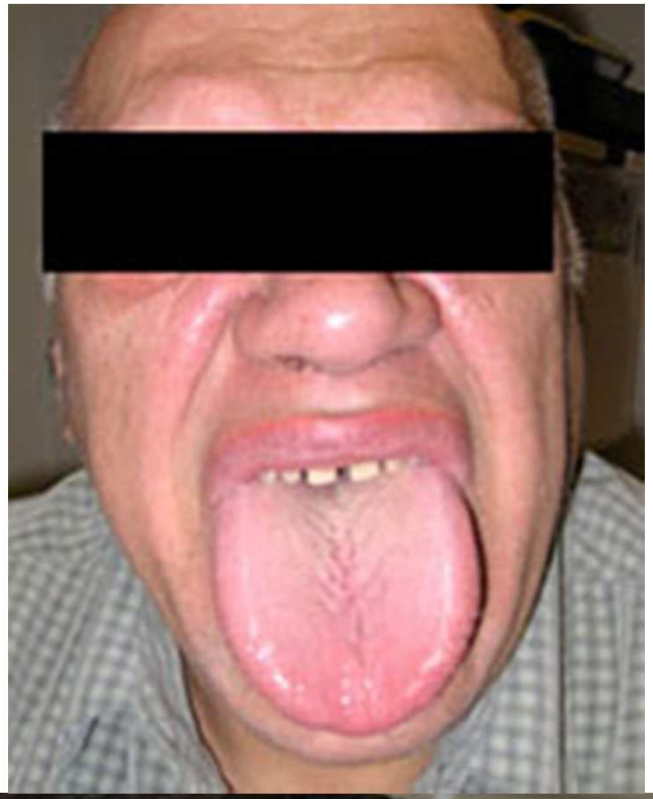
➢ **Insulin tolerance test**

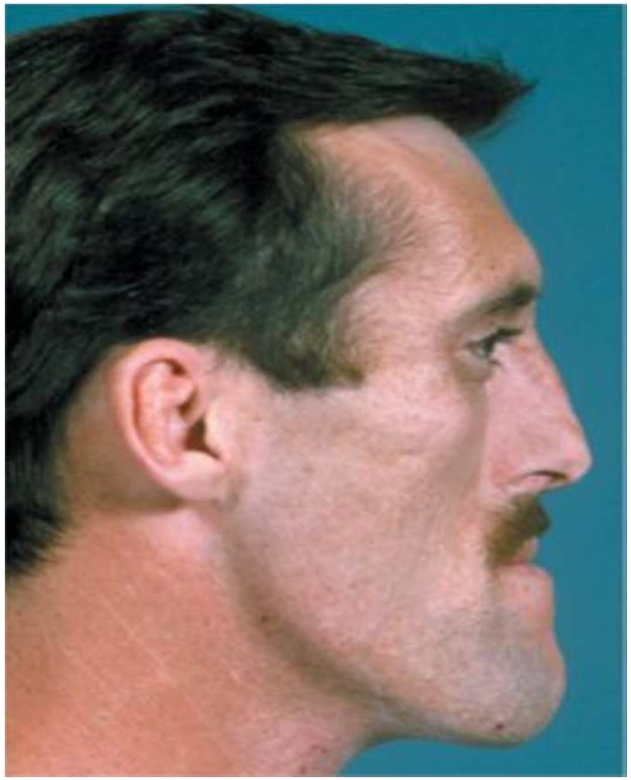
- **Imaging to assess of pituitary gland for any pathological lesion -MRI**

Acromegaly

Clinical features

- Prominent supraorbital ridge
- Prognathism
- Interdental separation
- Large tongue
- Thick greasy skin
- Spade-like hands and feet
- Tight rings
- Carpal tunnel syndrome
- Visual field defects
- Hypertension
- Heart failure
- Arthropathy
- Proximal myopathy






Normal peripheral vision
Loss of peripheral vision with optic chiasm compression

Investigation

- GH level -not diagnostic –may be normal
- IGF1
- Glucose tolerance test
- MRI pituitary

Prolactinoma

- It is prolactin secreting pituitary adenoma ,most common hormone-secreting pituitary adenoma

Clinical features

- Galactorrhoea
- Oligomenorrhoea or amenorrhoea
- Decreased libido in both sexes
- Decreased potency in men
- Subfertility
- headaches and visual field defects more common in men.

Investigation

- S. prolactin level-repeated more than once-level depend on size of prolactinoma –think of deferrential diagnosis if not very high (drugs,CRF,PCOS,hypothyroidism)

- MRI Pituitary

Adrenal glands disorders

- Clinical features ,and investigation

(cushing syndrome,adrenal insufficiency ,hyperaldoseronism, pheochomocytoma)

Cushing's Syndrome

Clinical features

General:

- Dorsocervical fat pad (buffalo hump)
- Facial Plethora (Moon Facies)
- Central obesity
- Proximal muscle weakness
- Hypertension

Skin:

- Wide(>1cm), purple striae
- Spontaneous echymoses
- Hyperpigmentation
- Acne- Hirsutism
- Fungal skin infections

Facial Plethora i.e. “Moon Facies”

Striae in Cushing's disease

Axillary and lower abdominal striae in a 21-year-old man with Cushing's disease. Abdominal obesity is also present.
Courtesy of David N Orth, MD.

UpToDate®

Dorsocervical fat pad i.e. “buffalo hump”

Cushing's Syndrome/Diagnostic approach

1. Establishing the diagnosis of C S

- 24hr urine for free cortisol
- Overnight dexamethason supresion test
- Late night Salivary cortisol level

↓

2. Establishing the cause of CS

a. ACTH-dependent vs independent

- Serum ACTH

b. Identifying the source in ACTH-dependent

- High dexamethason suppresion test
- CRH stimulation test

↓

3. Imaging

Hyperaldosteronism

- ✓ Individuals with primary hyperaldosteronism are usually asymptomatic
- ✓ features of sodium retention (oedema)
- ✓ potassium loss(muscle weakness , or even paralysis)
- ✓ Polyuria (nephrogenic diabetes insipidus)
- ✓ tetany (metabolic alkalosis and low ionised calcium).
- ✓ Systemic hypertension

Investigation :

Aldosteron level

Renin level

Aldosteron to renin ratio

Phaeochromocytomas

Classically, pheochromocytoma manifests as spells with the following 4 characteristics

- Headaches
- Palpitations
- Diaphoresis
- Severe hypertension

Excessive secretion of catecholamines can be confirmed by measuring metabolites in plasma and/or urine (metanephrine and normetanephrine).

.

Adrenal Insufficiency

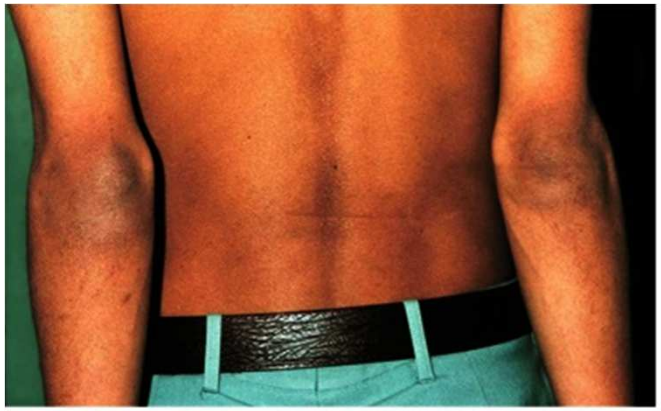
Clinical features

- Weight loss
- Postural hypotension

Pigmentation of:

- Sun-exposed areas
- Pressure areas (e.g. elbows, knees)
- Palmar creases,knuckles
- Mucous membranes
- Recent scars

- Hypoglycaemia
- Hyponatraemia
- Hyperkalaemia



Investigation

- Blood glucose (hypoglycemia)
- Na and k (hyponatremia ,hyperkalemia)
- S.cortisol –low ,may be normal
- Synacthin test –diagnostic

Thyroid diseases

Clinical features ,and investigation

(hyper and hypothyroidism)

Investigation for thyroid diseases

1. Thyroid function test
2. Anti-Thyroid Antibodies
3. Thyroid ultrasound scan
4. Nuclear Scintigraphy

Thyroid fuction test

Normal thyroid function

- TSH (thyrotropin)= 0.2-4.9 mU/L
- Total T4 Normal range: 65 –150nmol/L
- Free T4=9-22 pmol/l
- Total T3 Normal range: 1.8 – 3nmol/L
- Free T3=3.5-7.8 pmol/l

Why free T4 is preferred over total T4?

Total T4 levels are affected by medications and medical conditions that change thyroid hormone binding proteins:

- Estrogen, oral contraceptive pills, pregnancy, and liver disease : increased thyroid hormone binding proteins and will result in a high Total T4.
- Testosterone or androgens and anabolic steroids: decrease thyroid hormone binding proteins and will result in a low Total T4

Antithyroid Antibody

- used to evaluate for autoimmune thyroid problems.
- Antibodies directed against 3 major thyroid antigens are as follows:

➢ Thyroglobulin: Antithyroglobulin antibody (TgAb)

➢ Thyroid peroxidase (microsomal antigen): Antithyroid peroxidase antibody (TPOAb)

➢ TSH receptor: Anti-TSH receptor antibody (TRAb)

Antithyroid Antibody

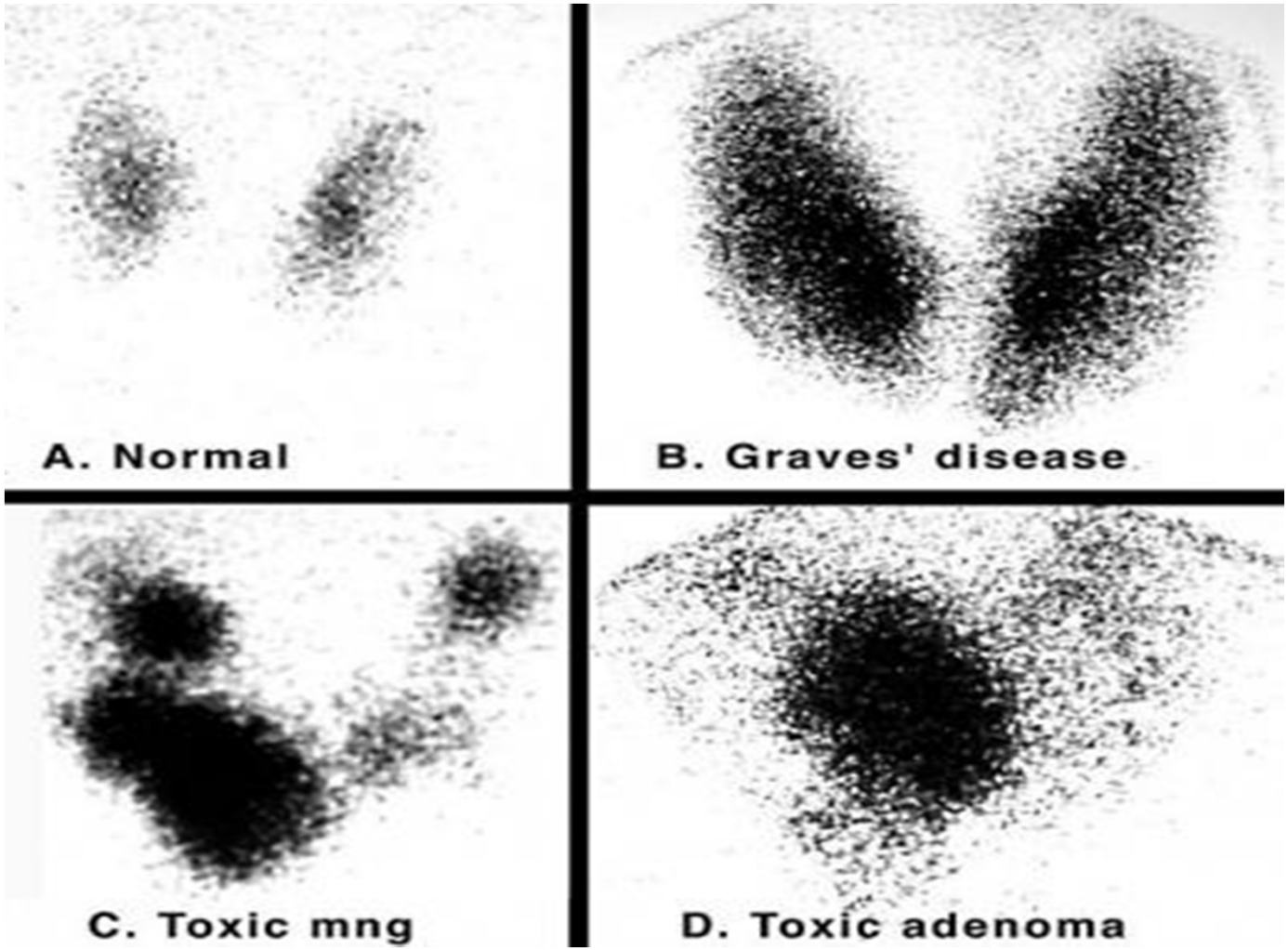
- **Elevated serum TPOAb and TgAb**
- Hashimoto disease (90%-100%)
- Graves disease (50%-80%)
- **Elevated serum Anti-TSH receptor antibody (TRAb)**
- Graves disease (80%-90%)
- Hashimoto disease (15%)

Radioactive iodine uptake (RAIU)

- Nuclear medicine study evaluating thyroid function. Measures ability of thyroid gland to concentrate and retain iodide .
- useful in the diagnosis of hyperthyroidism.
- small dose of radioactive iodine is administered orally, and images are taken at intervals. The uptake of radionuclide in thyroid gland is measured as the percentage

Iodine Uptake	Percentage of Radionuclide
2-hr absorption	1%–13%
6-hr absorption	2%–25%
24-hr absorption	15%–45%

Abnormal results of radioiodine uptake scan	
High • *G*raves disease • Toxic multinodular goiter • Toxic adenoma • HCG-induced hyperthyroidism • TSH-producing pituitary tumor	**Low** • Silent thyroiditis • Postpartum thyroiditis • Subacute (granulomatous) thyroiditis • Iodine-induced hyperthyroidism • Amiodarone-induced hyperthyroidism • Iatrogenic hyperthyroidism • Struma ovarii


A. Normal
B. Graves' disease
C. Toxic mng
D. Toxic adenoma

Clinical signs of Thyrotoxicosis

Common Signs

- Weight loss
- Tremor
- Palmar erythema
- Sinus tachycardia
- Lid retraction, lid lag

Rare signs

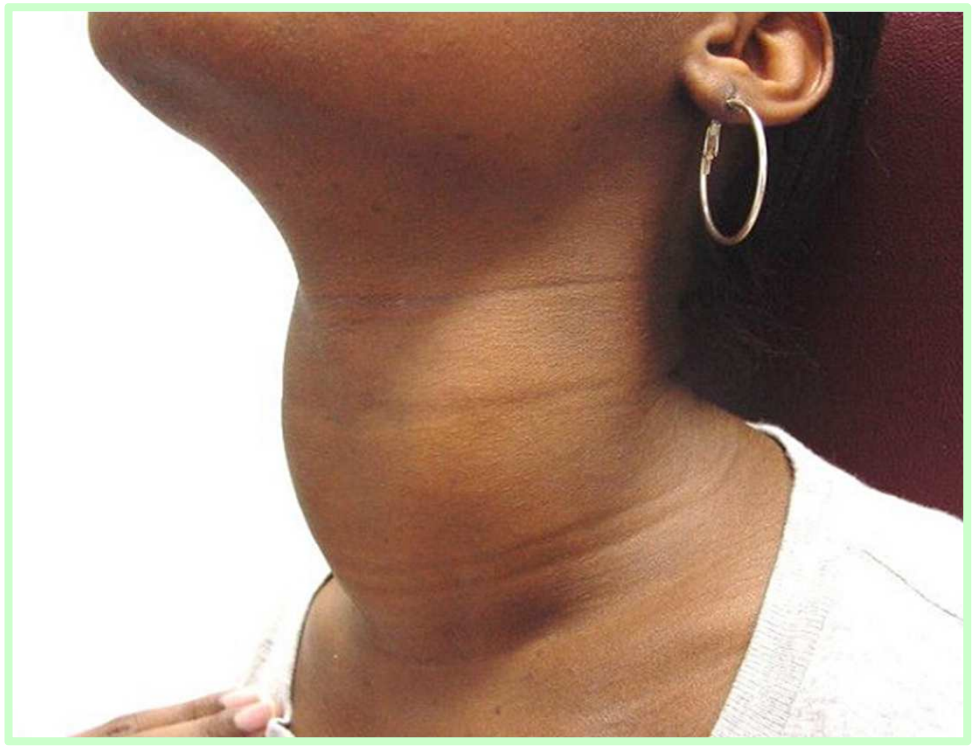
- Gynaecomastia
- Spider naevi
- Onycholysis

Less common signs

- Goitre with bruit(graves disease)
- Atrial fibrillation
- Systolic hypertension
- increased pulse pressure
- Cardiac failure
- Hyper-reflexia
- Proximal myopathy

Components of Graves' disease

Feature	Prevalence
Hyperthyroidism and goiter	95%
Thyroid eye disease	50%
Pretibial myxoedema	5%
acropathy	1%
Thyroid eye disease without hyperthyroidism ['Euthyroid Graves' disease']	5%



Goiter

Symmetrically enlarged with bruit

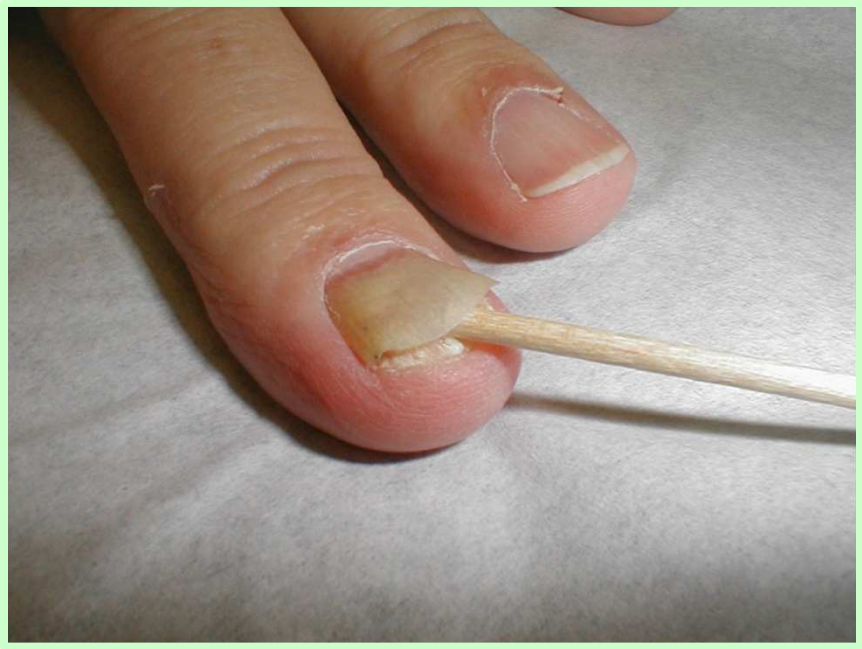
Thyroid Dermopathy

Pretibial region Raised, yellow-reddish lesion with orange peel apperance .Sometimes pruritus

Thyroid Acropathy

Clubbing

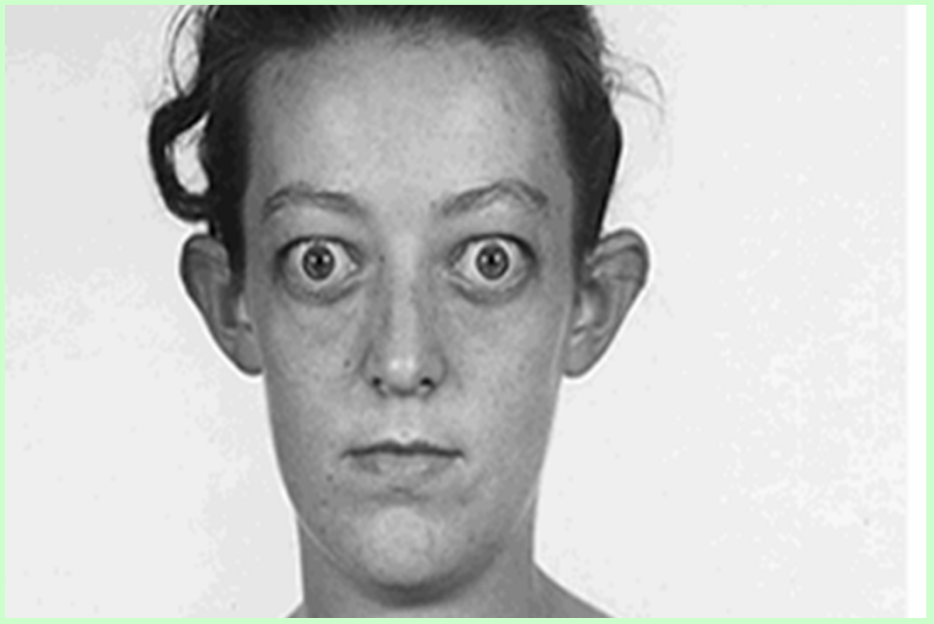
Onycholysis



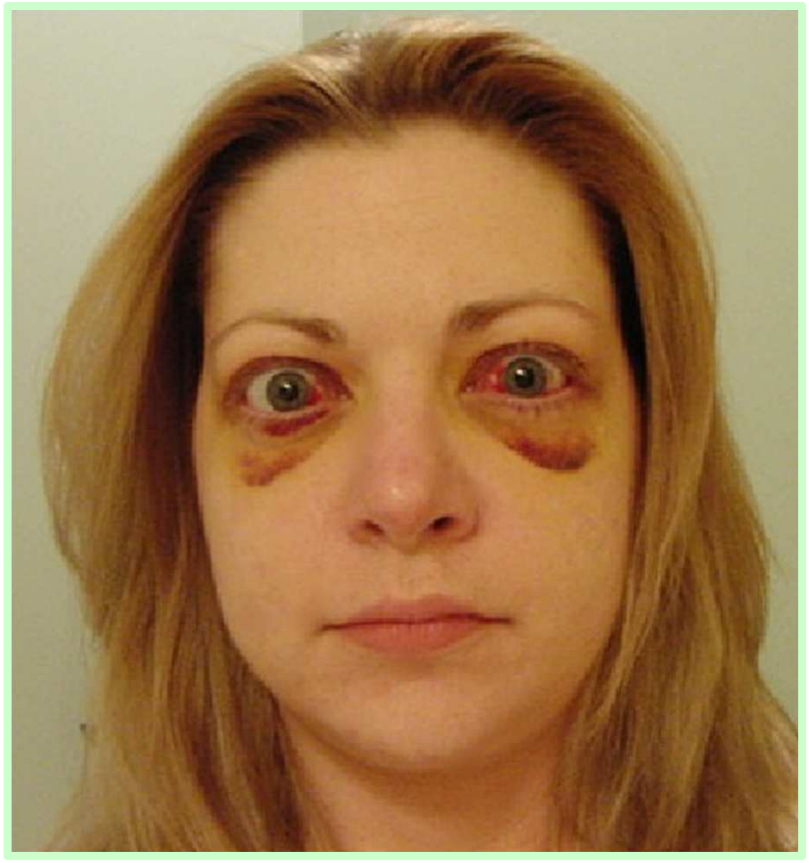
Thyroid Ophthalmopathy

Proptosis

Lid lag



Ophthalmopathy in Graves



Periorbital edema and chemosis

Diagnosis of thyrotoxicosis

- **In thyrotoxicosis (Primary)**

  TSH will be low and T4 and T3 is high

- **In TSH dependent causes(secondary thyrotoxicosis) of thyrtoxicosis** such asTSH-secreting pituitary adenoma.

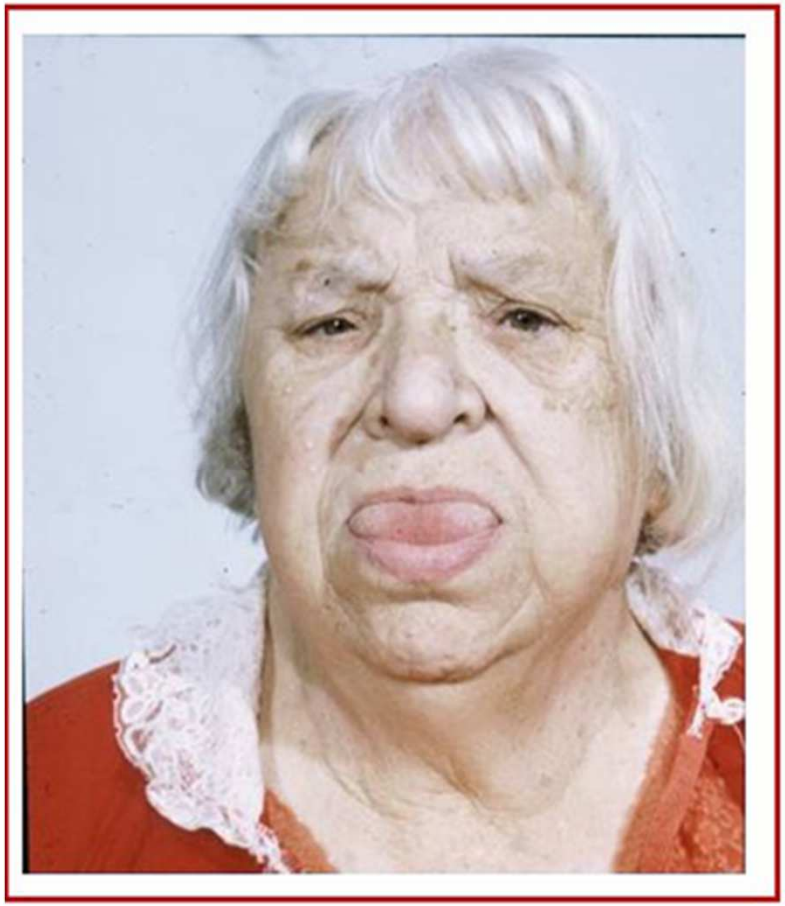
  TSH is high and T3 and T4 are high

Clinical features Hypothyroidism

- Mental slowness
- Psychosis/dementia
- Periorbital oedema
- Ataxia
- Hoarseness of voice
- Goitre
- Deafness
- Dry skin
- Mild obesity
- Dry thin hair
- Loss of eyebrows

- Hypertension
- Hypothermia
- Heart failure
- Proximal myopathy
- Bradycardia, pericardial effusion ,pleural effusion
- Slow-relaxing reflexes
- Anaemia
- Carpal tunnel syndrome
- Non-pitting oedema (myxoedema)

Clinical features of hypothyroidism




A
B


C


D

Diagnosis of hypothyroidism

- Primary hypothyroidism is characterized by high serum TSH concentration and low T4 and T3 concentration.
- Patients with a high serum TSH concentration and a normal serum free T4 and T3concentration may have subclinical hypothyroidism.
- Secondary or Central hypothyroidism is characterized by low serum T4 and T3 concentration and serum TSH noramal or low.

Diabetes Mellitus

Diabetes mellitus clinical features and investigation

Diabetes Mellitus

is clinical syndrome characterised by increase in plasma blood glucose (hyperglycaemia).It is result of absolute decreased production of insulin (Type 1) or resistance of cells to circulating insulin (Type 2).

- Three cardinal signs of DM
  - Polyuria
  - Polydipsia
  - Polyphagia

Blood testing for glucose

- Fasting blood glucose(FBG) is defined as no caloric intake for at least 8 h.
  - Normal FBG is less than 100 mg /dl
  - FBG ≥126 mg/dL is diagnostic for DM
  - FBG 100-125mg/dl is impaired fasting (prediabetic)

- Randome blood glucose ≥ 200 mg/dL in presence of symptomes of hyperglycemia is diagnostic for DM

Glycated haemoglobin(HbA1c)

- It results from non-enzymatic covalent attachment of glucose to haemoglobin
- Various methods used to measure HbA1c, most laboratories reporting HbA1c values as %
- formation of HbA1c is directly proportional to blood glucose conc(rise of 1% in HbA1c corresponds to increase of 36 mg/dLin blood glucose).
- HbA1c provides accurate objective measure of glycaemic control over period of weeks to months.
- HbA1c estimates may diminished in anaemia or during pregnancy, and difficult to interpret with in uraemia or haemoglobinopathy

- Normal HbA1C <5.7%
- HbA1C ≥ 6.4% -diabetic
- HbA1C 5.7–6.4% - prediabetes

ADA Criteria for diagnosis of diabetes mellitus

1- FPG ≥126 mg/dL.

Fasting is defined as no caloric intake for at least 8 h.

OR

2- 2-h PG ≥ 200 mg/dL during an 75 g OGTT.

OR

3- HbA1C ≥ 6.4%

OR

4- In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥ 200 mg/dL

Gestational diabetes

- Defined as any degree of glucose intolerance that was first recognized during pregnancy
- **Screening for and diagnosis of GDM**

Perform a 75-g OGTT, with plasma glucose measurement when patient is fasting and at 1 and 2 h, at 24–28 weeks of gestation in women not previously diagnosed with diabetes.

- **The diagnosis of GDM is made when any of the following**
- **Fasting ≥ 92 mg/dL**
- **1 h PG ≥ 180 mg/dL**
- **2 h PG ≥153 mg/dL**

Pre-diabetes

- characterized by elevated blood sugar levels that fall below the threshold to diagnose diabetes mellitus.
- can be diagnosed by measuring hemoglobin A1c, fasting glucose, or glucose tolerance test

Prediabetes

FPG 100-125 mg/dL (IFG)

OR

2-h PG in the 75-g OGTT 140- 199 mg/dL (IGT)

OR

Hb A1C 5.7–6.4%

Oral glucose tolerance test (OGTT)

Which patients to test

- Fasting plasma glucose (100–125 mg/dL)
- Uncertainty about diagnosis of diabetes
- Diagnosis of gestation diabetes

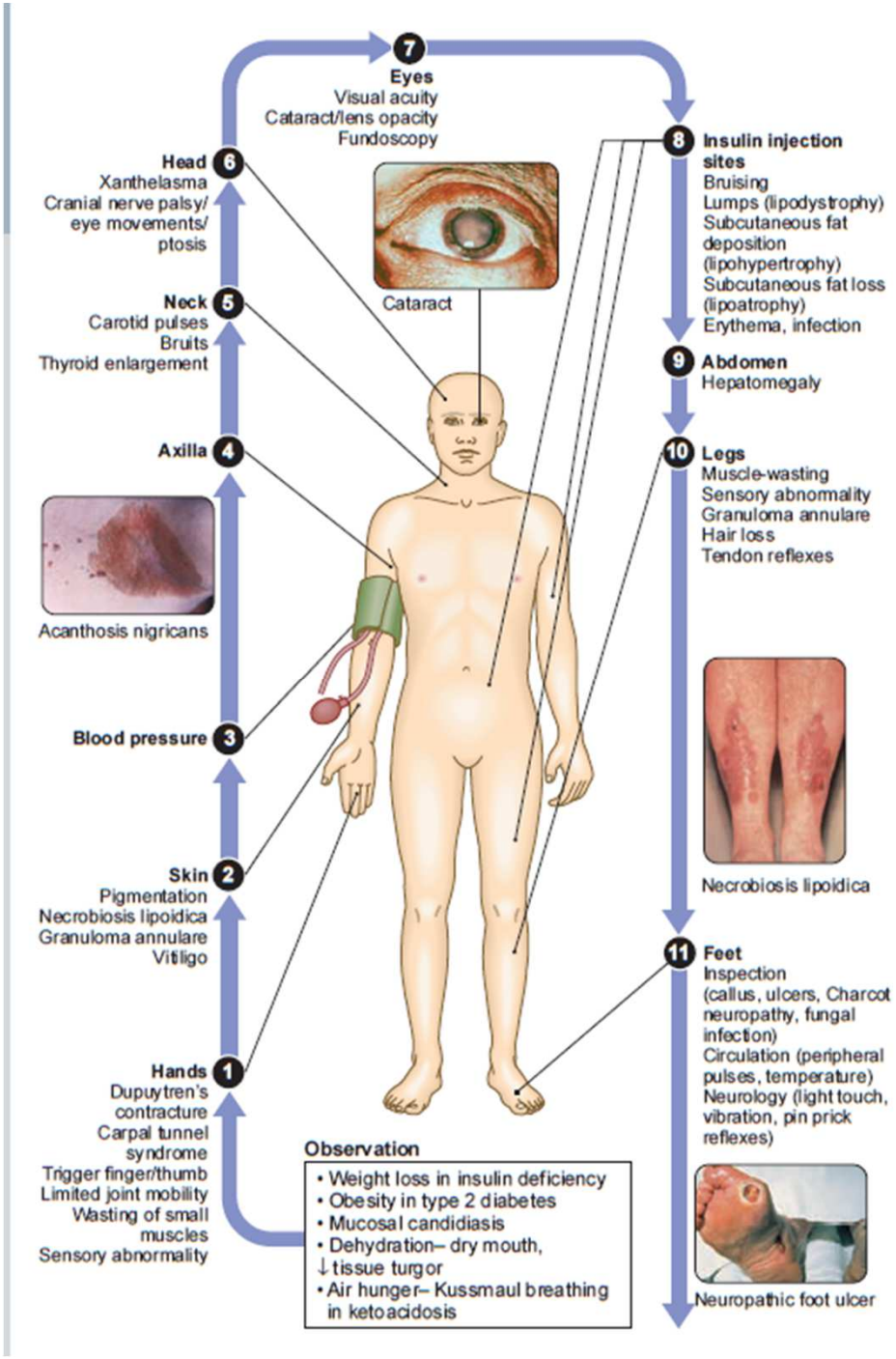
Sampling

- Measure plasma glucose before and 2 hrs after a 75 g oralglucose drink

- **Interpretation (venous plasma glucose)**

	Fasting	2 hrs after glucose load
Impaired fasting glucose	**100–125 mg/dL**	**< 140 mg/dL**
Impaired glucose tolerance	**< 126 mg/dL**	**140–199 mg/dL**
Diabetes	**≥ 126 mg/dL**	**≥200 mg/dL**

Clinical examination of the patient with diabetes

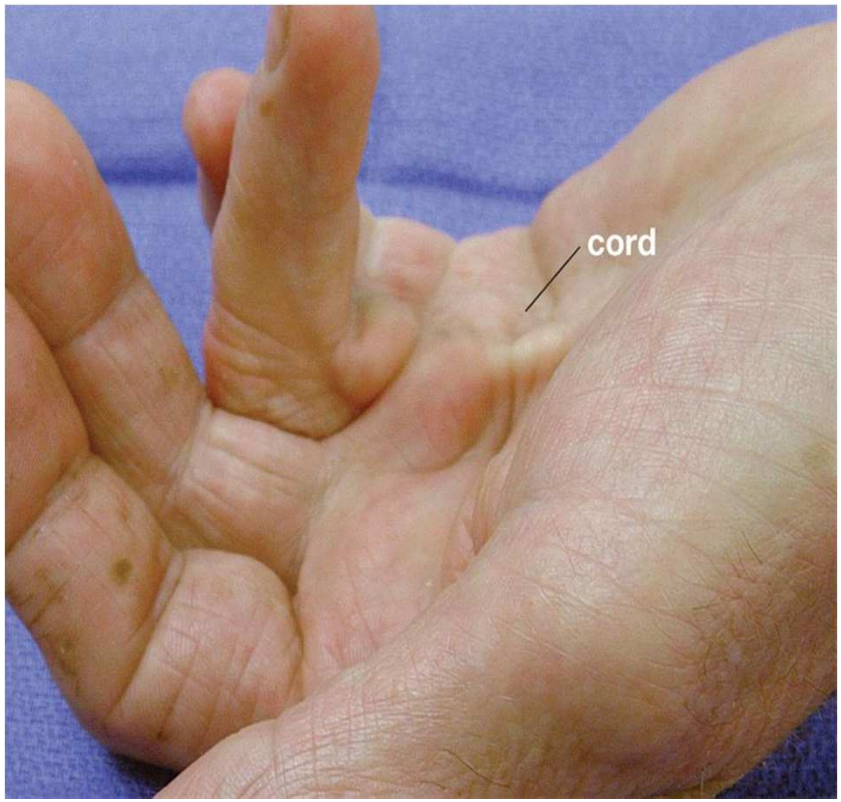


Examination of the hands

Diabetic **cheiroarthropathy**

- characterized by thickened skin and limited joint mobility of the hands and fingers, leading to flexion contractures

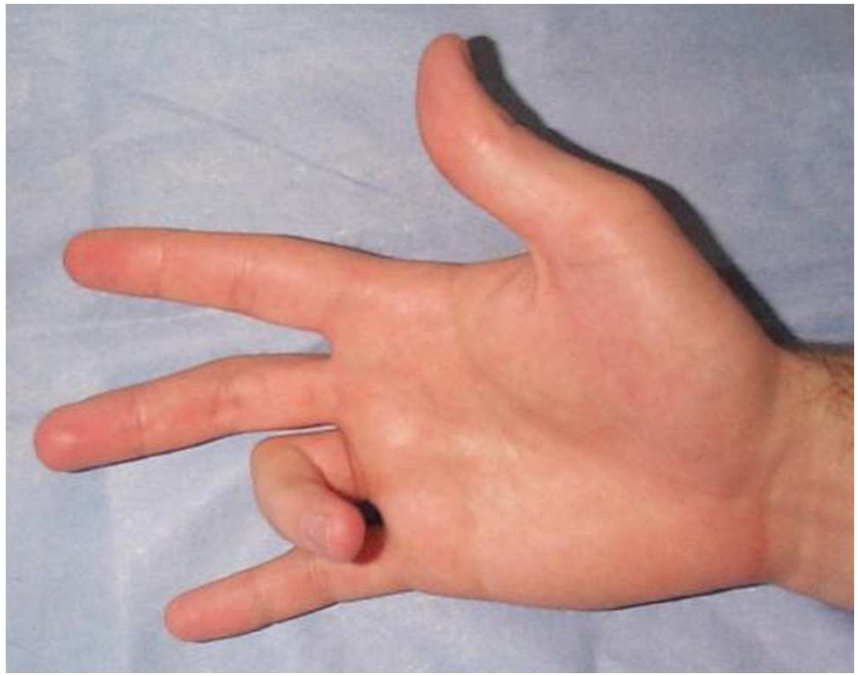
Dupuytren’s contracture



Dupuytren's contracture

one or more fingers become permanently bent in flexed position. It usually begins as small hard nodules just under skin of palm. It then worsens over time until fingers can no longer be straightened.

Trigger finger



Trigger finger

pain,stiffness, and sensation of locking or catching when you bend and straighten the finger.The ring finger and thumb are most often affected

Examination of the feet

Inspection

- Look for evidence of callus formation on weight-bearing areas, clawing of the toes (in neuropathy), loss of the plantar arch, discoloration of the skin (schaemia), localised infection and ulcers Deformity may be present, especially in Charcot neuroarthropathy
- Fungal infection may affect skin between toes, and nails
- Pitting Pedal oedema(diabetic nephropathy)

Circulation

- Peripheral pulses, skin temperature

Sensation

- Testing light touch with monofilaments is sufficient for risk assessment; test other sensation modalities (vibration, pain , proprioception

Charcot arthropathy

- Ch. by Swelling readness,hot ,and mild pain
- Due to joint dislocations, pathologic fractures, and deformities of weight - - bearing joints; in severe form, it may cause significant disruption of the bony architecture

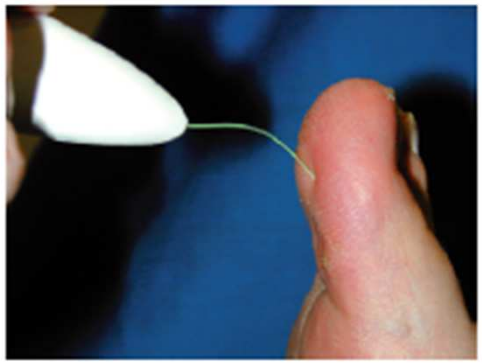
Clawing of toes

Clawed toes;extension of the metatarsophalangeal joint and flexion of the proximal and distal interphalangeal joints

Peripheral pulses

Sensation

Testing light touch



Monofilaments. The monofilament is applied gently until slightly deformed at 5 points on each foot. Callus should be avoided as sensation is reduced. If the patient feels fewer than 8 out of 10 touches, the risk of foot ulceration is increased 5–10-fold.

proprioception

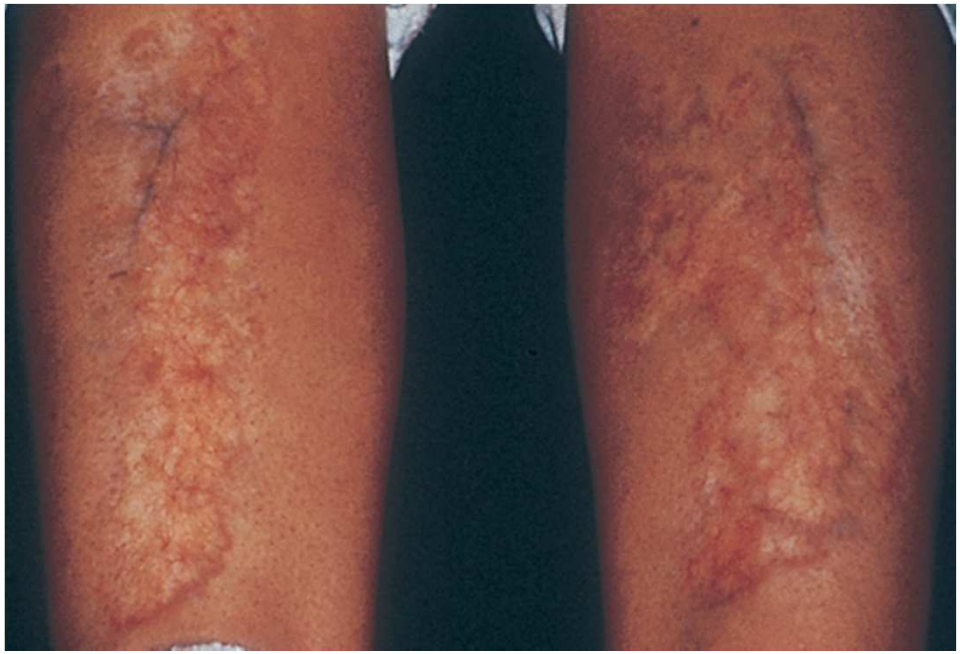
Vibratory Sense

- 128 or 256 Hz Tuning fork
- If impaired, proceed proximally

Skin lesion in diabetes mellitus

Acanthosis Nigricans

Necrobiosis lipoidica



THANKS