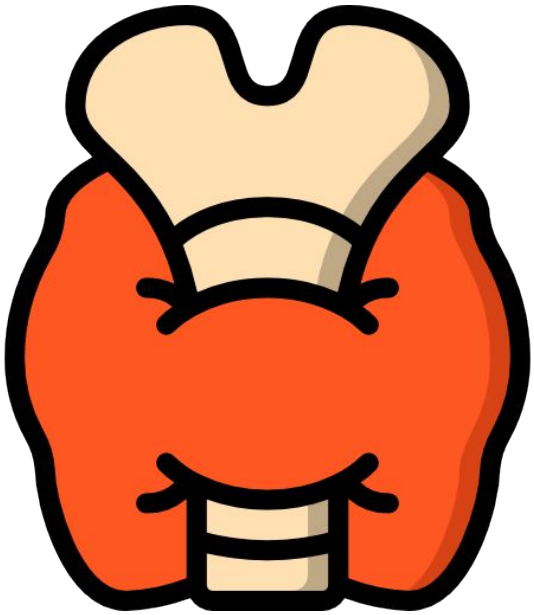


Endocrinology

This file was done by:

- Razan Alrabah
- Taif Alotaibi
- Lama Alzamil
- Sedra Elsirawani
- Amirah Alzahrani
- Ghalia Alnufaei
- Njoud Alali
- Shahad Selayem
- Ajeed Alrashoud
- Rahaf Alshabri
- Mohammed Alhumud
- Hashem Bassam

Team leaders:

- **Raghad AlKhashan**
- **Amirah Aldakhilallah**
- **Mashal AbaAlkhail**
- **Nawaf Albhijan**

L44- Pitutary disorders

	Functional adenoma	Non-functional adenoma (incidentaloma)
Epidemiology	10 % of all pituitary lesions • Genetically-related to MEN-1, Gs-alpha mutation, PTTG gene, FGF receptor-4) • Or idiopathic	1.5 -31% in autopsy (prevalence) 10% by MRI most of them < 1 cm
Clinical (History and Examination)	• Function (oversecretion or hyposecretion) • Mass (headache,visual symptoms)	• **Asymptomatic** • Incidentaloma by imaging. • Mass-effect (Bitemporal hemianopia) • Gonadal hypersecretion
Biochemical	Screen Test, Confirmatory Test	**GH, LH, FSH, TSH, ACTH:** not high. **PRL could be:** low, high or normal.
Anatomy	**MRI** of sella turcica (MRI is superior to CT)	
Treatment	• Surgical >Medical >Radiation or Medical >Surgical >Radiation (Depend on the type)	• Surgery if indicated • Observation • Adjunctive therapy

1- Prolactinomas	
General info	• **Prolactinomas are the most common of functional pituitary adenomas**
Causes of hyperprolactinemia	• Prolactin secreting pituitary **adenoma** (Most common) • **Renal failure** (returns to normal after transplant), **Liver failure**, **primary hypothyroidism** (high TRH levels stimulate prolactin). • **Drugs** which interfere with dopamine: (Phenothiazines, Domapine receptor antagonists metoclopramide, a-methyldopa, verapamil, H2 blocker, estrogen, opiates, reserpine). • **Pregnancy** is the most common **physiological** cause.
Clinical features	• **Galactorrhoea**, oligo or amenorrhoea, infertility, Decreased libido, subfertility, erectile dysfunction, gynecomastia • It may have mass effect ⟶ Bitemporal hemianopia
Diagnosis	• **Serum prolactin level:** At least 3 measurements should be taken, Very high level suggests prolactinoma (>5000mU/L). • **Thyroid function test:** TSH must be tested to rule out primary Hypothyroidism. • **IGF-1** must be tested to rule out acromegaly co-secretion. • **Pregnancy test:** Always exclude pregnancy first
Treatment	***1st line:*** • **Medical:** Dopamine agonist drugs (e.g. Bromocriptine,Cabergoline (Drug of choice), Quinagolide) (Bromocriptine is preferred in pregnancy) **2nd line:** • Surgery and radiation

L44- Pituitary disorders *(cont.)*

2- GH excess (Acromegaly/Gigantism)	
General info	• **98% of cases are due to GH pituitary adenoma**

Clinical features	• **The most common complaints are headache and sweating.**
	• **Acral enlargement:** large thick hands & feet with osteoarthritis
	• **Gross features of acromegaly:** Face gross features, enlarged tongue, and jaw
	• **Galactorrhea** (Due to co-secretion of prolactin from the tumor)
	• Gingiva enlargement, constipation and **deep voice**
	• May have mass effect → Bitemporal hemianopia
	• Carpal tunnel syndrome (Median nerve compression)
	• **irreversible cardiovascular effect: (major cause of death)**
	  ○ **Cardiomegaly and CHF with Diastolic dysfunction being an early sign of cardiomyopathy.**
	  ○ **HTN** in 40%, LVH in 50% and they present with **Obstructive sleep apnea** (due to Neck enlargement)

Diagnosis	• **Initial test (screen): Measure IGF-1.** (Will be high in acromegaly) • **Confirmatory Test: 75g OGTT for GH suppression** • **MRI** or CT for the pituitary

Treatment	***1st line:***
	• **Surgery**
	2nd line:
	• **Medical:**
	  ○ **Somatostatin analogues (octreotide, lanreotide or pasireotide).**
	  ○ Dopamine agonist (**bromocriptine or cabergoline**) "especially **if associated with prolactin excess**"
	  ○ **Didn't work?** use GH receptor antagonist (Pegvisomant)
	3rd line:
	• **Radiotherapy**

3- Diabetes insipidus	
Types	• **Central DI:** Deficiency of vasopressin (ADH), caused by a hypothalamic disorder (adenoma of pituitary does not cause it because it is only stored there) • **Nephrogenic DI:** Renal resistance to ADH action • **Psychogenic DI:** is an excessive water intake seen in some patients with mental illnesses such as schizophrenia.
Symptoms	• Abrupt onset of **polyuria** (1st manifestation), **polydipsia** (2nd manifestation)
Investigations	• **Urine: ↑urine volume** (2 – 15 L/day), **↓urine osmolality,** ↓specific gravity . • **Serum Na+:** usually **high** • High or high-normal plasma osmolality **Water deprivation test** (To differentiate between CDI,NDI and PDI) • **Central DI:** urine osmolality will still low (Before giving vasopressin) and returns to normal after administer vasopressin. • **Nephrogenic DI:** exogenous vasopressin does not alter urine osmolality much. • **Psychogenic DI:** Urine will be become concentrated as they aren't really a problem with either the pituitary nor the kidney
Treatment	CDI → DDAVP. NDI→ Correct underlying cause, Hydrochlorothiazide.

When The Level of Glucose is high:

- **Hormone**: **Insulin**
- ↑ glycolysis
- ↑ ion uptake especially K and PO_4^{3-}
- ↓Ketogenesis
- Effect on **Liver**:
1. ↑ Glycogen synthesis

- Effect on **Liver**:
1. ↑ Glycogen synthesis
2. ↓ Gluconeogenesis
3. ↓ Glycogenolysis
4. ↑ lipogenesis (FA synthesis)
5. ↑ Lipoprotein synthesis

- Effect on **Muscles**:
1. ↑ protein synthesis
2. ↓ Proteolysis
- Effect on **Adipose tissue**:
1. Inhibition of intracellular lipase > No lipolysis
2. ↑ TGs deposition

	T1DM	T2DM
pathogenesis	- Interactions of genetic, environmental, and immunological factors that lead to the destruction of the pancreatic Beta cells and insulin deficiency. - Most, but not all, individuals have evidence of islet-directed autoimmunity. - There is a loss of both first and second phase of insulin secretion.	Two defects are necessary: - Abnormalities of insulin action:(resistance), characterized by ability of insulin to: - Inhibit hepatic glucose output - Suppress lipolysis in adipose tissue. - Stimulate glucose uptake into skeletal muscle - Abnormalities of insulin secretion: - The body responses to insulin resistance by increasing insulin secretion, early sign is loss of the first phase of the normal biphasic insulin secretion. - This level is still inadequate to restore glucose homeostasis. By the time of diagnosis, at least 50% of B-cell mass and function has been lost. - Glucotoxicity thought to cause further B-cell loss and further deterioration of glucose homeostasis. With time, insulin secretion declines. 'Starling curve' of the pancreas.
Age	Usually <30y/o	Usually >30y/o
Course	Rapid From DPT-I can be indolent	Indolent Virtually none found on screening
risk factors	1- Genetic: HLA- DR3-DQ2, HLA- DR4-DQ8 or both. By contrast, certain HLA alleles confer protective effects, for example DQB1*0602. Increased susceptibility to type 1 diabetes is inherited but **the disease is not genetically predetermined.** 2- Environmental: - maternal factors: such as gestational infection and older age. - viral infection: such as Coxsackie B4. - Childhood obesity and early introduction of cow's milk.	- Diet: dietary fat, red and processed meat, consumption of fried food. - Aging: B-cell function declines with age - Obesity: accounts for 80-85% of the overall risk - Fetal origins of diabetes: low weight at birth associated with glucose intolerance later in life - Physical inactivity. - Genetic susceptibility and inheritance: Identical twins have more than a 50% chance - TNF-alpha may induce insulin resistance in obesity - Others: urbanization, poverty, abnormal sleep patterns, environmental toxins and mental illness.

L45,46- T1&T2 DM

	T1DM	T2DM
Comorbid	**Thyroid, adrenal, vitiligo, celiac** and pernicious anaemia.	**Increase in polycystic ovary syndrome** **Acanthosis nigricans**
C- peptide	C-peptide can be preserved at DX , eventually it will disappear	Normal or increased (more useful in T2)

presentation	- acute: 2–6-week history of the classic triad
	  - polyuria -thirst and polydipsia -weight loss
	- subacute: several months or years, particularly in older people.
	  - triad + lack of energy, visual blurring, pruritus vulvae or balanitis due to Candida infection.	

complications	Staphylococcal skin infections, retinopathy, polyneuropathy, erectile dysfunction, and arterial disease.	
diagnosis	**Gold standard for the diagnosis of DM is HbA1C** *Criteria: One abnormal laboratory value is diagnostic in symptomatic individuals; two values are needed in asymptomatic people. - Impaired fasting glycaemia (IFG) and impaired glucose tolerance (IGT) associated with insulin resistance syndrome or syndrome X: - Insulin resistance, Hyperinsulinemia, Obesity, Dyslipidemia (High triglycerides and\or low HDL), Hypertension. - Glycosuria: cannot be used to diagnose DM - other investigation: measurement of C- peptide and islet autoantibodies can help determine the type of diabetes. - Routine investigations: urine testing for protein, a full blood count, urea and electrolytes, liver biochemistry and random lipids.	

management	Insulin is necessary for survival:
	- Basal/bolus insulin concept:
	  - Basal insulin: suppresses glucose production between meals and overnight. 50% of daily insulin needs
	  - Bolus insulin(prandial): limits hyperglycemia after meals, immediate and sharp peak at 1hr. 10-20% of daily insulin needs.
	- Therapeutic regimens:
	  - Conventional therapy: 1 or 2 injections/day
	  - **Multiple daily injections** (MDI): 3-6 injections/day, it is the preferred regimens.
		- Diet and lifestyle
		  - Medication should never be prescribed until lifestyle changes have been implemented.
		- For medications: three main options are metformin, a sulfonylurea or a thiazolidinedione.
		  - HgbA1c target: 7% for young without atherosclerosis, and 8% for late old
		- Insulin: If control is inadequate on oral therapy

Table 2 – American Diabetes Association diagnostic criteria for diabetes[18]

Test*	Threshold	Qualifier
Hemoglobin A_{1c} or	≥ 6.5%	Lab NGSP-certified, standardized DCCT assay
Fasting glucose or	≥ 126 mg/dL (7.0 mmol/L)	No caloric intake for at least 8 hours
2-hour glucose or	≥ 200 mg/dL (11.1 mmol/L)	After 75 g of anhydrous glucose
Random glucose	≥ 200 mg/dL (11.1 mmol/L)	Plus classic hyperglycemia symptoms or crisis

NGSP, National Glycohemoglobin Standardization Program; DCCT, Diabetes Control and Complications Trial.
* Results must be confirmed by repeated testing.

L45,46- T1&T2 DM *(cont.)*

Bolus (preprandial or mealtime) insulins	Basal insulin
Rapid-acting insulin analogues (clear) - Insulin aspart (NovoRapid®) - Insulin lispro (Humalog®) - Insulin glulisine (Apidra®) - Faster-acting insulin aspart (Fiasp®)	Intermediate-acting (cloudy) - Insulin neutral protamine Hagedorn (Humulin® -N, Novolin® ge NPH)
Short-acting insulins (clear) - Insulin regular [Humulin®-R, Novolin® ge Toronto] - Insulin regular (Entuzity®)	Long-acting insulin (clear) - Insulin detemir (Levemir®) -Insulin glargine U-100 (Lantus®) - Insulin glargine U-300 (Toujeo®) - Degludec U-100, U-200 (Tresiba®) - Insulin glargine biosimilar (Basaglar ®)
Premixed insulins	
Premixed regular insulin –NPH (cloudy) - Humulin 30/70 - Novolin® ge 30/70, 40/60, 50/50	Premixed insulin analogues (cloudy) - Biphasic insulin aspart (NovoMix® 30) - Insulin lispro/lispro protamine (Humalog® Mix25 and Mix50)
insulin complications	
- Hypoglycaemia (The most common) ,Weight gain, Insulin antibodies, insulin resistance, Peripheral oedema, Local allergy (rare), Lipohypertrophy or lipoatrophy at injection sites	

Biguanides: metformin

increases insulin sensitivity, peripheral glucose utilization and reduces gluconeogenesis
first-line pharmacological agent in all type diabetes guidelines.

GI: anorexia, nausea, abdominal discomfort and diarrhoea.

- Contraindicated in: renal impairment, cardiac failure and hepatic failure because of the risk of lactic acidosis.

Sulphonylureas

Gliclazide, Glimepiride, Glibenclamide, Glipizide, Tolbutamide

Act on the B cell to induce insulin secretion. no effect in people with type 1 diabetes.
can be used as an alternative first-line agent where metformin is contraindicated or not tolerated.

Adverse effects:Weight gain and hypoglycaemia.

- used with care in people with liver or renal disease.

Thiazolidinediones : pioglitazone

Reduce insulin resistance by interaction with peroxisome proliferator-activated receptor-gamma (PPAR-Y), a nuclear receptor that regulates large numbers of genes, including those involved in lipid metabolism and insulin action.

Pioglitazone may specifically benefit people with non-alcoholic fatty liver disease, a frequent co-morbidity of type 2 diabetes.

Adverse effects: weight gain, fluid retention.

Meglitinides or post-prandial insulin releasers

Repaglinide, Nateglinide

Mode of action Like sulphonylureas, meglitinides act by closing the K*-ATP channel in the ß cells have a short duration of action of less than 3 hours.
used to treat people with post-prandial hyperglycaemia with normal fasting glucose levels.
Hypoglycaemia and weight gain but these are generally less severe than with sulphonylureas.

Dipeptidyl peptidase-4 inhibitors or 'gliptins

Sitagliptin, Linagliptin, Vlidagliptin, Alogliptin, Saxagliptin

These drugs inhibit the enzyme DPP4, which prevents the rapid inactivation of glucagon-like peptide-1 (GLP-1), which increases insulin secretion and reduces glucagon secretion.
most effective in the early stages of type 2 diabetes, when insulin secretion is relatively preserved, and are currently recommended for second-line use in combination with metformin or a sulphonylurea.
Occasional reports of acute pancreatitis., Saxagliptin may increase the risk of heart failure.

GLP-1 receptor agonist

Exenatide, Liraglutide, Lixisenatide, Dulaglutide, Semaglutide, Albiglutid

more potent that DPP-4 inhibitors. they also act on the hypothalamus to reduce appetite and food intake leading to weight loss. The size of effect has led to the licensing of liraglutide as an anti-obesity treatment.
now used in combination with other antidiabetic agents, as second- or third-line therapies. They should not be combined with DPP-4 inhibitors
Adverse effects: gastrointestinal and include nausea and vomiting, bloating and diarrhoea.

Sodium-glucose transporter 2 inhibitors ('flozins')

Dapaglilozin ,Empaglilozin, Canaglilozin

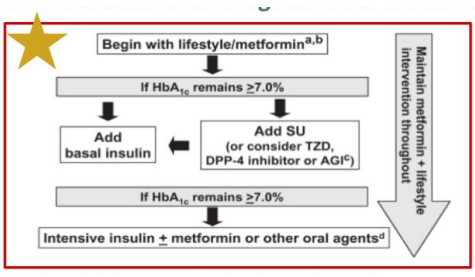
In addition to their effects on blood glucose, they lower body weight, improve renal dysfunction and reduce the risk of atherosclerotic cardiovascular events and heart failure

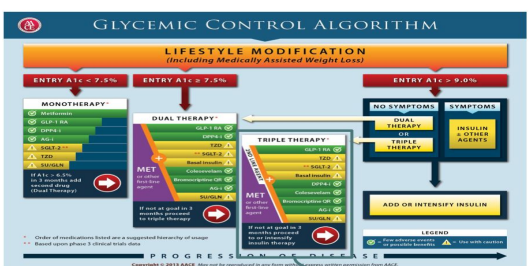
- Lower the renal threshold for glucose, increasing urinary glucose excretion.
- can be used as monotherapy but are used more typically in combination with all other antidiabetes drugs.
- This class has become rapidly established in clinical practice and in type 2 diabetes guidelines because of their cardiovascular benefits, weight loss and low risk of hypoglycaemia. SGLT2 inhibitors are licensed as adjunctive therapy to insulin in type 1 diabetes.
- Adverse effects : genital candidiasis and dehydration.
- Rarer side effects include diabetic ketoacidosis, Fournier's gangrene and lower limb amputation.

Alpha-glucosidase inhibitors

Acarbose ,Miglitol ,Voglibose

Can be used as monotherapy or in combination with all other antidiabetes drugs, they are not widely used because of their limited efficacy and gastrointestinal side-effects.
The major side-effects are gastrointestinal and include flatulence, abdominal distension and diarrhoea, as unabsorbed carbohydrate is fermented in the bowel.





L47-Diabetic Complications

◄ How to Reduce the Risk of Diabetes Complications?

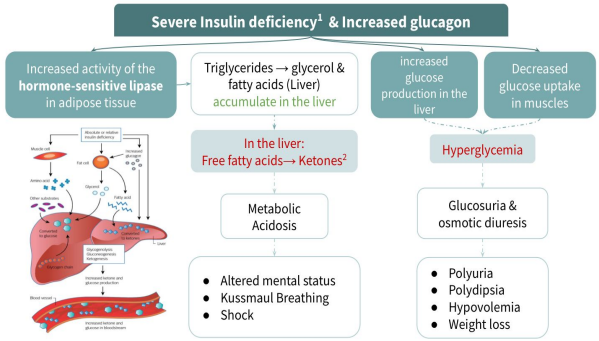
- Maintain a good glucose control (A1C around 7%)

◄ Diabetic Ketoacidosis (DKA)

- Status of metabolic acidosis due to absolute (or relative) insulin deficiency in association with increased levels of glucagon and other counter-regulatory hormones resulting in increased ketone production.

- **Precipitating Causes of DKA**
  - Non compliance with insulin therapy
  - Drugs: SGLT-2 inhibitors
- **Clinical Features of DKA**

◄ Pathophysiology of DKA



*The most important biochemical abnormality in is the uncontrolled lipolysis due to increased activity of hormone-sensitive lipase in adipose tissue and uncontrolled ketogenesis in the liver.

-Polyuria, Polydipsia, Weight loss, abdominal pain,Hypothermia, change in mental status, Nausea and Vomiting, Deep labored breathing (Kussmaul respiration), Dehydration (as a consequence of two parallel processes):

- Hyperglycemia
- Renal hypoperfusion

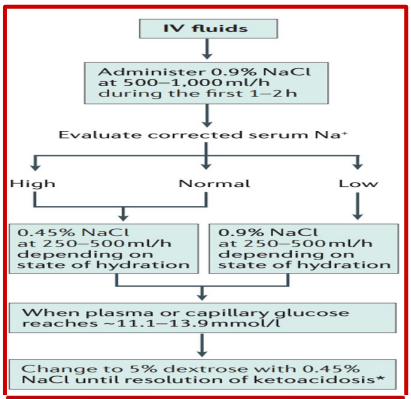
- **Laboratory Findings in DKA**
  - Hyperglycemia >250 mg/dL + Hyperketonemia (or heavy ketonuria) +High anion gap (> 12 mmol\l) metabolic acidosis <18 mEq/L
  - Blood electrolytes should be assessed as potassium abnormalities occur frequently
- **Management of DKA**
  - Aggressive rehydration + Lowering glucose + Cessation of ketogenesis + Correcting electrolyte imbalance

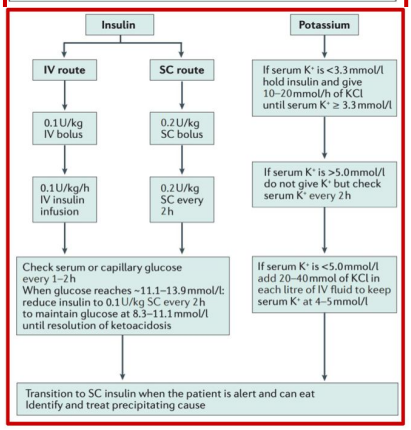
1) Rehydration

- IVF is the most critical step.
- Once the plasma glucose is ~250 mg/dl, switch IVF to D5% IVF.

2) Insulin

- Insulin is the next step after IVF
- Reduces serum glucose, suppresses ketogenesis, and correct the electrolyte disturbance.
- Most of the time: we use IV insulin infusion
-





3) Electrolytes

- DKA is associated with total-body K+ deficit
- Serum K+ is often normal or high (do not get fooled!) .
- K+ Shift from intracellular to extracellular compartment with acidosis (serum K+ looks falsely normal). Metabolic acidosis causes hyperkalemia as potassium is exchanged for hydrogen ions moving into the cell. As insulin promotes the co-transport of potassium along with glucose into cells. Although serum potassium may be elevated, there is a severe whole-body potassium deficiency as significant quantities of potassium are lost in vomit and urine.
- Insulin therapy moves K+ back into the cells (watch for a drop in K+).

4) Restoration of the acid-base balance

- Consider bicarbonate infusion if pH <7

◄ Hyperglycemic Hyperosmolar State (HHS)

- Status of severe hyperglycemia due to **insulin resistance** (not absolute insulin deficiency) & relative insulin deficiency resulting in increased serum osmolality.
- What is the characteristic metabolic emergency of uncontrolled type 2 diabetes?
- Severe hyperglycemia development without significant ketosis
- **Lab findings**
  - Severe hyperglycemia (> 30 mmol/L (600 mg/dL)
  - Hyperosmolality (serum osmolality >320 mOsmol/kg)
  - Without significant ketonaemia (<3 mmol/L) or acidosis (pH >7.3 (H+ <50 nmol/L), bicarbonate >15 mmol/L)

Management of HHS

- Management of HHS is similar to that of DKA
- The most important aspect of management is fluid replacement; 0.9% sodium chloride is the treatment of choice

but 0.45% sodium chloride may be considered if the osmolality is not declining despite adequate fluid balance.

◄ Hyperglycemic Hyperosmolar State (HHS)

- Plasma glucose <3.9 mmol/L (<70 mg/dl)
- Severe hypoglycemia: need for assistance from another person to correct glucose
- What is the most frequent & serious adverse effect of glucose-lowering therapies such as insulin? Hypoglycemia
- **Clinical features:**
  - related to acute activation of the autonomic nervous system
  - secondary to glucose deprivation of the brain (neuroglycopenia)
- **Management of Hypoglycemia:**
  - Give 15 grams of carbohydrates
  - Wait 15 minutes and re-check glucose
  - Repeat the same if glucose is still less than 70 mg/dl
  - If glucose is above 70 mg/dl, have the patient eat a regular meal or a snack that contains protein

◄ Diabetic retinopathy

- **Most commonly diagnosed diabetes-related complication**

1) **Non-proliferative (earliest change):** Usually appears in the 1st decade of the disease or early 2nd decade, Characterized by retinal vascular microaneurysms, blot hemorrhage, and cotton-wool spots
2) **proliferative:** Hypoxemia & neovascularization leading to virtuous hemorrhage, fibrosis, and retinal detachment
3) **Macular edema**
   can occur in non proliferative or proliferative stage

- **Treatment :**
  - Prevention (most effective treatment) ⟶ easier than treating

◄ Diabetic Nephropathy

- If your patient with diabetes has nephropathy but no retinopathy; it is very likely that the nephropathy is NOT due to diabetes
- Screen with Urinary Albumin: Creatinine & eGFR
- Albuminuria (Albumin: Cr >30 mg/g)
- Prevention (most effective treatment)
  - ACEI (or ARBs) are recommended to treat nephropathy.
  - SGLT-2 inhibitors can be used, decrease the risk and progression of diabetic nephropathy.

◄ Diabetic Neuropahty

- Treat with preventive foot care
- What is the most common form? distal symmetric polyneuropathy

L48- Adrenal Disorders

Primary adrenocortical insufficiency (Addison's disease)

Causes

Major:

- **Autoimmune** (The most common cause)
  - **Type I** (APECED) : affects children: Adrenal insufficiency, hypoparathyroidism, pernicious anaemia, chronic candidiasis, chronic active hepatitis, and hair loss)
  - **Type II** (Schmidt's syndrome) usually affects young adults : hypothyroidism, adrenal insufficiency and diabetes mellitus, vitiligo
- **Tuberculosis**

other:

- Infection, Infiltration, Iatrogenic, Medications, Hereditary, Miscellaneous.

Evaluation

Clinical	Biochemical	Anatomical
Hyperpigmentation, weakness and fatigue, weight loss, anorexia, and GI disturbances, hypoglycemia, salt craving, amenorrhea, hypotension (Think about Adrenal insufficiency if not respond to IVF and initial management)	- Hyponatremia, hyperkalemia. mild to moderate hypercalcemia - **Measure a.m. cortisol:** • If high: rule out • If very low : diagnosis • If borderline result : proceed for confirmatory test (ACTH stimulation test) - **Measure ACTH Plasma levels:** it differentiates between primary and secondary	Adrenal insufficiency is clinical and biochemical diagnosis , no indications to do imaging unless clinically indicated such as: • Patient on anticoagulation • Malignancy with metastasis • Other infiltrative disease

Treatment

- IVF: dextrose and salt
- Electrolytes replacement

Steroid replacement for **primary** adrenocortical insufficiency:

- hydrocortisone
- Fludrocortisone

Steroid replacement for **secondary** adrenocortical insufficiency:

- hydrocortisone only

Secondary/ Tertiary adrenal insufficiency

Causes

- The commonest cause of ACTH deficiency is exogenous glucocorticoid administration.
- Pituitary/hypothalamic tumors are the most common causes of naturally ACTH hyposecretion.

Clinical Features

- The clinical features may be non-specific, **Hypoglycemia** is occasionally the presenting feature.
- hyperpigmentation and Electrolytes abnormalities are absent.

Congenital Adrenal Hyperplasia

Clinical Features

- 90–95% of CAH cases are caused by deficiency of 21-hydroxylase enzyme.
- Ambiguous genitalia (Female)
- Failure to thrive
- Dehydration & Shock (usually male)

- Salt-loss presentations with electrolytes imbalance:
  - Hyponatremia
  - Hyperkalemia
  - Hypoglycemia
- Hyperpigmentation

Diagnosis

Clinical:

- History and examination (B.P)

Biochemical:

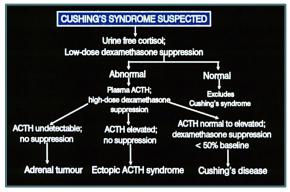
- Low Na & high K, fasting hypoglycemia, elevated serum urea, elevated plasma Renin & ACTH levels**, low Cortisol,** **High 17 – OHP, High androgens** especially testosterone level, Low Aldosterone (in salt losing types only).

Treatment

Hydrocortisone, Fludrocortisone, During adrenal crisis (intravenous hydrocortisone), IVF D5 0.9% saline, In vomiting or diarrhea (parental therapy is indicated), Medical Alert: bracelet.

L48- Adrenal Disorders

Hypercortisolism (Cushing Syndrome)

	Clinical	Biochemical	Anatomical
Approach	**- Rounded "moon" facies** with a plethoric appearance, **truncal obesity** with prominent supraclavicular and dorsal cervical fat pads **"buffalo hump"**, distal extremities and fingers are slender, muscle wasting and weakness, the skin is thin and atrophic, with poor wound healing and **easy bruising, purple striae** may appear on the abdomen, **hypertension,** renal calculi and osteoporosis. - **Hyperpigmentation** is common in the ectopic ACTH.	• High cortisol • High ACTH (ACTH dependent) and low if (non-ACTH dependent). • 24hrs for UFC • 1MG DST • Midnight salivary cortisol 	**If ACTH:** • **high: MRI pituitary** • **low: history then CT adrenals** Small tumors may be difficult to detect and selective venous sampling may be needed. In some cases, more detailed isotope scanning and **arteriography or venography may be needed.**
Treatment	**- Adrenal tumors**: **adenomas** are successfully treated by **adrenalectomy,** when adrenal cancer cannot be fully resected or there is metastatic disease that can't be identified, give mitotane. **- Ectopic ACTH syndrome:** therapy is directed at **removal of the tumour.** **- Cushing's disease:** Trans-sphenoidal surgery with selective removal of the adenoma is the treatment of choice.		

Conn's Syndrome

Causes	• Primary hyperaldosteronism: Adenoma, usually unilateral, of the glomerulosa cells of the adrenal cortex, rarely adrenal carcinoma, Bilateral adrenal hyperplasia; idiopathic AH, Indeterminate hyperaldosteronism, Dexamethasone suppressible hyperaldosteronism.	
Clinical and Lab. findings	• Secondary HTN, High Na, high Cl, high Aldosterone, Alkalosis and low K (episodic weakness, Paresthesias, transient paralysis, tetany, nephropathy with polyuria and polydipsia)	

Biochemical Investigation	**Screening test:**
	• aldosterone/renin ratio
	  ○ If high: do confirmatory test
	  ○ If low: look for secondary causes
		Confirmatory test:
		• Saline infusion test
		• Oral salt loading test
		• Captopril test
		• Fludrocortisone suppression test

Treatment	Adenoma → Surgical resection	Adrenal hyperplasia → Spironolactone

Pheochromocytoma

Clinical Features	50% are silent. (NO symptoms), Isolated or part of MEN type II A or MEN type II B, Episodic (spells): sweating, palpitation, headache, Typical symptoms are **(Secondary HTN,** Young age < 40, 3 anti-HTN medications, Resistant HTN and Accelerated HTN.

Investigation	• **Biochemical:** The best initial test is the level of free **metanephrines in plasma**, 24 hr urine collection of Metanephrines(2X) (Confirmatory Test).
	• **Anatomical:**
	  ○ CT scan = MRI
	  ○ MIBG if: Paraganglioma, Young, Large size, malignant features
	  ○ Genetic Tests

Management	**before the surgery we need to:** • **Control HTN**: α-blocker2 then B-Blocker, Ca-blockers: can be used • **Salt loading:** Oral NaCl for 3 days Or IVF 0.9% saline 1-2 days before surgery • **Surgical removal:** Surgical tumor resection with early ligation of venous drainage is the treatment of choice.

L49- Parathyroid disorders

Hyperparathyroidism

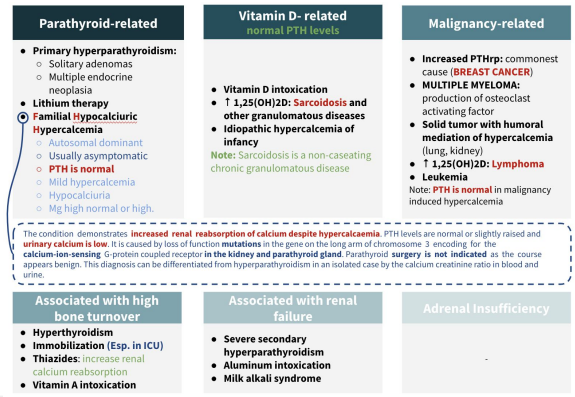
General info

- Excessive production of PTH
- A single adenoma occurs in about 80% of patients with primary hyperparathyroidism.
- Four glands hyperplasia account for 15-20% of cases.

Clinical features

- Classic presentation: Stones, Bones, Abdominal groans and Psychic moans
- The most common presentation: Asymptomatic hypercalcemia
- Osteitis fibrosa cystica (In advanced disease) is a cystic bone spaces filled with brown fibrous tissue (“ brown tumor” consisting of osteoclasts and deposited hemosiderin from hemorrhages; causes bone pain).

DDX of hypercalcemia



Diagnosis

- **Lab:** ↑ Calcium, ↓ Phosphorus, ↑ PTH; when this combination is present in an asymptomatic patient then further investigation is usually unnecessary.
- **24-hour urinary calcium or single calcium creatinine ratio** should be measured in a young patient with modest elevation in calcium and PTH to exclude familial hypocalciuric hypercalcaemia
- **Plain X-ray of hands** can be diagnostic showing **subperiosteal bone resorption** usually on the **radial surface of the distal phalanx with distal phalangeal tufting** as well as **cysts** formation and generalized osteopenia
- Preoperative localization of the abnormal parathyroid gland(s): **Thallium 201 – Tehcnichum99m scan (subtraction study) and sestamibi scan** (85-95% sensitivity)

Treatment

- If patient is symptomatic (lithiasis, osteoporosis, pancreatitis) surgery (Parathyroidectomy) is indicated.
- **During surgery the surgeon identifies all four parathyroid glands (using biopsy if necessary) followed by:**
  - The **removal of the enlarged parathyroid, not all the 4 glands** (In case of **adenoma**)
  - Or **3 1/2 glands** in case of multiple glandular **hyperplasia**. (You can easily live with half a parathyroid gland)
- **Medical treatment:** cinacalcet (Calcimimetic agent) can be used if patient has high surgical risk e.g. elderly and dialysis patients

Secondary hyperparathyroidism

- Physiological compensatory hypertrophy of all parathyroids because of chronic hypocalcaemia.
- Causes: chronic kidney disease (Most common),

Tertiary hyperparathyroidism

- The development of apparently autonomous parathyroid hyperplasia after long-standing secondary hyperparathyroidism, most often in renal failure.

L49- Parathyroid disorders *(cont.)*

Hypoparathyroidism

General info	• **Deficient secretion of PTH** which manifests itself biochemically by **hypocalcaemia**, **hyperphosphatemia diminished or absent circulating iPTH** and clinically the symptoms of **neuromuscular <u>hyperactivity</u>**.
Causes	• **The most common causes are autoimmune or post-surgery** (Thyroidectomy) **Other causes:** • **Chronic hypomagnesaemia** • **"Polyglandular autoimmune syndrome Type 1 (AKA "Hypoparathyroidism – Addison's disease – mucocutaneous candidiasis (HAM) syndrome")":** In children (2-4y/o) and In this sequence (moniliasis "mucocutaneous candidiasis" → hypoparathyroidism →hypoadrenalism)

Clinical features	• The rate of decrease in serum calcium is the major determinant for the development of neuromuscular complications.
	• **Paresthesia and numbness around mouth, hands and feet and laryngeal stridor**
	• **Tetany (if severe acute hypocalcemia, usually post-surgical)**
	• Hyperventilation and carpopedal spasm
	• **Prolonged QT interval** in the ECG
	• **Posterio-lenticular cataract** in long standing hypocalcemia due to deposition of calcium phosphate.
	• **Signs of latent tetany :**
	  ○ **Chevostek sign:** Contraction of facial muscles on tapping on zygomatic arch
	  ○ **Trousseau sign:** Carpopedal spasm when inflating sphygmomanometer 20 mmHg above systolic BP
	  ○ Extrapyramidal signs (due to basal ganglia calcification): Parkinsonism usually occur in old individuals, if a young pt presented with Parkinsonism suspect hypocalcemia

Diagnosis	• In the **absence of renal failure** the **presence of hypocalcaemia with hyperphosphatemia** is virtually diagnostic of hypoparathyroidism. • **Undetectable serum iPTH confirms the diagnosis** or it can be detectable if the assay is very sensitive.
Treatment	**Acute and severe <u>with tetany</u> (emergency):** • Give 10 cc of 10% **calcium gluconate parenterally** slowly and under ECG monitoring (careful in patients on digoxin) **Chronic hypocalcemia:** • The mainstay of treatment is a combination of oral **calcium (1-2gm daily)** with pharmacological doses of **vitamin D (Calcitriol or alfacalcidol)** or its potent analogues. • Phosphate restriction in diet may also be useful with or without aluminum hydroxide gel to lower serum phosphate level. always give active vitamin D because low PTH leads to decreased conversion of vitamin D to its active form at the kidney level.

Osteoporosis

- A common metabolic bone disease characterized by low bone mass. It most often affects thin postmenopausal women with risk doubling after 65 years of age. Men are also at risk for osteoporosis, but the diagnosis is often overlooked. Commonly asymptomatic until fractures occur.
- Exam may reveal hip fractures, vertebral compression fractures (loss of height and progressive thoracic kyphosis), and/or distal radius fractures (Colles fracture) following minimal trauma
- **Diagnostic test: DEXA** (Osteoporosis: Bone mineral density (T-score) is 2.5 standard deviations (SDs) less than normal. Osteopenia: T-score between 1 and 2.5 SDs below normal.)
- **Lifestyle modifications:** Adequate calcium and vitamin D intake (supplementation can be used for prevention), smoking cessation, avoiding heavy alcohol use, and weight-bearing exercises.
- **Best initial treatment: Bisphosphonates** (eg, alendronate, risedronate, ibandronate, zoledronic acid) are used in the treatment of osteoporosis, not osteopenia.

L50 - Dyslipidemia

◄ Lipoproteins

- **Particles that transport** transport the digestion products of dietary fat to the liver and peripheral tissues.
- **Types:**

	Chylomicrons	VLDL	IDL	LDL	HDL
Source	intestine	Liver	VLDL remnant	VLDL & IDL	intestine, liver
Atherogenicity	Not atherogenic (doesn't cause MI) but causes **pancreatitis**	+	+	+++	**Anti-atherogenic**

- **HDL** cholesterol is able to go and **remove cholesterol from the atheroma.**
- **Which one has the most atherogenic effect? Small dense LDL.**
- **Pathways:**

Pathway	Lipoprotein	Function	Enzyme
Exogenous (post-prandial)	Chylomicrons	Transport fats from the intestine to the liver	**Intestinal lipoprotein lipase**
Endogenous	VLDL → IDL	VLDL released to blood stream to form IDL	**Endothelial lipoprotein lipase**
Endogenous	IDL → LDL	Hepatic lipase breakdown IDL to form LDL → LDL carries fat & cholesterol to the cells	**Hepatic lipase**
Reverse cholesterol transport	HDL	**Nascent HDL*** carry fat and cholesterol from blood vessels (Periphery) to the liver.	

*** if you want to inject HDL, you inject nascent HDL because it is empty of cholesterol.**

◄ Hereditary causes of hyperlipidemia

- **Familial (Primary) hypercholesterolemia:**
  - **Dominant mutation in LDL receptor,** resulting in elevated levels of LDL at birth and throughout life.
  - **Heterozygous → Premature CAD (ages 30-50),** high risk for atherosclerosis, tendon xanthomas**,** tuberous xanthomas, xanthelasmas of eyes and arcus senilis (In younger ppl, it's called arcus juvenilis).
  - **Homozygous → CAD (before age 18),** total absences of LDL receptors.

- **Familial Combined Hyperlipidemia:**
  - Autosomal dominant.
  - **Raised cholesterol AND triglyceride** concentrations in association with a typical family history.
  - Increased secretions of VLDLs
  - **Fibrates** are the treatment of choice since these reduce both cholesterol and triglyceride concentrations.

- **Dysbetalipoproteinemia:**
  - Recessive.
  - Binding-defective form of apoE (which usually plays important role in metabolism of chylomicron and VLDL → High VLDL and chylomicrons).

◄ Primary hypertriglyceridemia

- **LPL deficiency** → hepatosplenomegaly, abd. cramps and **pancreatitis** at young age.
- **Apo C-II deficiency** → abd. cramps and pancreatitis.
- **Familial hypertriglyceridemia** → unknown enhanced hepatic TG-production, abd. cramps, pancreatitis and retinal vein thrombosis.

L50 - Dyslipidemia

◀ Secondary Hyperlipidemia

- **Secondary hypercholesterolemia (↑↑LDL)**
  - **Hypothyroidism**
  - **Anorexia nervosa**
  - **Pregnancy**
  - **Biliary obstruction PBC**
- **Secondary hypertriglyceridemia (↑↑VLDL)**
  - **Diabetes mellitus**
  - **Obesity**
  - **Uremia, dialysis**
  - **Alcohol** → **↑↑Chylomicrons**

◀ When to check lipid panel?

Different Recommendations:

- **Adult Treatment Panel (ATP III)** → Beginning at age 20, every 5 years.
- **US preventive services task force**→
  - **Women ≥ 45 years, Men ≥ 35** → **Total** and **HDL** cholesterol every 5 years.
  - If total cholesterol > 200 or HDL<40 → a fasting panel should be obtained.
  - **Cholesterol screening** → **Begin at 20 years in patients with a Hx of** → Multiple cardiovascular risk factors, DM, Family Hx of (Elevated cholesterol levels & Premature cardiovascular disease).

◀ Treatment

Goal of treatment:

- **Non-LDL** → To **prevent coronary heart disease outcomes** (MI & coronary death).
- **Triglyceride** → To prevent **pancreatitis** and may be CHD outcomes.

Non-medical treatment:

- **Lifestyle modification, Low-cholesterol diet, Exercise, Alcohol and Smoking cessation.**

Medication:

- **Statins** →
  - **HMG CoA reductase inhibitors.**
  - **Low intensity** → lowers LDL by <30%, **Medium intensity** → lowers LDL by 30 - 50%, **high intensity** → lowers LDL by >50%.

Stepwise approach:

1. Life style modification.
2. Does this patient have established coronary artery disease? (Had MI...)
   ✓ **If yes?** High intensity statin! except if pt is old >75.
3. Is his LDL more than 190?
   ✓ **If yes?** High intensity statin! No need for further questions
4. Has DM? More than 40 years?
   ✓ **If yes?** High intensity statin!
5. Anything other than that (2,3,4), we apply the 10 year risk assessment (done by websites & applications):
   - **If its less than 5%** → No need for meds
   - **Between 5%-7.5%** → needs moderate intensity statin.
   - **More than 7.5%** > needs High intensity statin.

- **Best to prevent CAD/MI : Statins (reduce LDL).**
- **Best to prevent Pancreatitis: Fibrate (reduce TGs)**

◀ Hypertriglyceridemia treatment

- **TG = <2** → No risk for anything, no treatment, lifestyle modification
- **TG = ≥2 to <5:** Use **statins** + omega-3 for CVS protection.
- **TG = ≥5 to <10: fibrate** to prevent pancreatitis,

L51- Thyroid disorders

◄ Hypothyroidism

◄ Causes

Primary	Secondary	Tertiary	Other
1- Hashimoto's thyroiditis (most common) 2- **RAI therapy** 3- Subtotal thyroidectomy 4- Excessive iodine intake 5- Subacute thyroiditis 6- **Iodide deficiency** 7- Congenital 8- Drugs: (lithium, amiodarone, antithyroid drugs)	1- pituitary adenoma 2- pituitary ablative therapy 3- pituitary destruction	Hypothalamic dysfunction	Peripheral resistance to thyroid hormones

◄ clinical presentation

•**Common features:**
-Easy fatigability, **coldness**, weight gain, **constipation**
-**Cool dry skin**, puffy face, hoarse husky voice,

•**GI tract:**
- **Chronic constipation**, ileus

•**CVS:**
- **Bradycardia, Decreased output**
- low voltage ECG, cardiomegaly, pericardial effusion

•**Renal:**
-Impaired GFR, water intoxication

•**Pulmonary:**
- Shallow slow respiration
- Respiratory failure

•**Anemia:**
-Impaired HB synthesis
- Iron/ folate deficiency
-Pernicious anemia

•**Neuromuscular:**
-Muscle cramps, paresthesia, muscle weakness, carpal tunnel

•**CNS:**
- lethargy, depression, agitation
-**Decreased concentration**

•**Reproduction:**
-Anovulatory cycles
-Menorrhagia

◄ Diagnosis

- **Serum TSH (initial test), high levels with clinical features confirms primary hypothyroidism**
- **Free T4 (confirms hypothyroid state)**
- **in Hypothyroidism (high TSH, Low free T4)**
- **Anti thyroid peroxidase (TPO) antibodies**

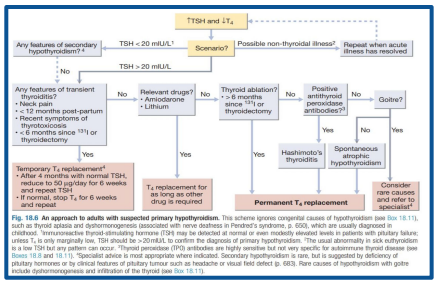


Fig. 18.6 An approach to adults with suspected primary hypothyroidism. This scheme ignores congenital causes of hypothyroidism (see Box 18.11), such as thyroid aplasia and dyshormonogenesis (associated with nerve deafness in Pendred's syndrome, p. 650), which are usually diagnosed in childhood. Immunoreactive thyroid-stimulating hormone (TSH) may be detected at normal or even modestly elevated levels in patients with pituitary failure; unless T_4 is only marginally low, TSH should be >20 mIU/L to confirm the diagnosis of primary hypothyroidism. [a]The usual abnormality in sick euthyroidism is a low TSH but any pattern can occur. [b]Thyroid peroxidase (TPO) antibodies are highly sensitive but not very specific for autoimmune thyroid disease (see Boxes 18.8 and 18.11). [c]Specialist advice is most appropriate where indicated. Secondary hypothyroidism is rare, but is suggested by deficiency of pituitary hormones or by clinical features of pituitary tumour such as headache or visual field defect (p. 683). Rare causes of hypothyroidism with goitre include dyshormonogenesis and infiltration of the thyroid (see Box 18.11).

◄ Treatment

- **Thyroid replacement (Levothyroxine T4)**
- **follow up for serum free T4 and TSH**

◄ Complications

1- myxedema coma 2- myxedema and heart disease 3- hypothyroidism and neuropsychiatric disease

◄ Treatment of myxedema coma

-Acute medical emergency
-Three main issues: 1- Co2 retention and hypoxia 2- Fluid and electrolyte imbalance 3- Hypothermia
-if myxedema with heart disease, start treatment slowly then gradually increase it

Recommendations for the treatment of myxedema coma			
hypothyroidism	**loading dose of Levothyroxine** then daily maintenance	**hypocortisolemia**	intravenous hydrocortisone daily
hyponatremia	mild fluid restriction	**hypothermia**	blankets and **not active warming**
hypoventilation	intubation and mechanical ventilation	**hypoglycemia**	glucose administration
hypotension	**cautious volume expansion** with crystalloid or whole blood	**Precipitating event**	identification and elimination by specific treatment (eg: Antibiotics)

L51- Thyroid disorders

◄ Hyperthyroidism and Thyrotoxicosis

◄ Causes of thyrotoxicosis

1-**Diffuse toxic goiter (graves' disease)** 2- Toxic adenoma (plummer disease) 3- subacute thyroiditis
4- Hyperthyroid phase of Hashimoto's 5- Thyrotoxicosis factitia 6- others (Struma ovarii, TSH secreting pituitary adenoma, pituitary resistant to T3 and T4, metastatic thyroid carcinoma)

◄ Clinical features

•Cardiorespitatory:
-Dyspnea, Tachycardia
-**Atrial fibrillation**, high output cardiac failure

•Skin:
- **Warm with excessive sweating**
- pretibial myxedema
-pruritus, alopecia, thinning of the hair

•GI tract:
- **Diarrhoea**
- weight loss

•Eyes:
- **extraocular muscles dysfunction with** diplopia lid retraction, proptosis
-Periorbital swelling and conjunctival edema

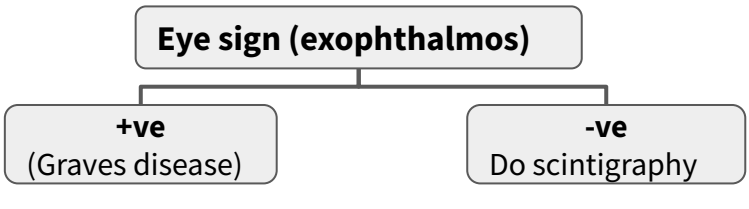
•others:
-Osteoporosis
-Irritability, anxiety, restlessness and psychosis

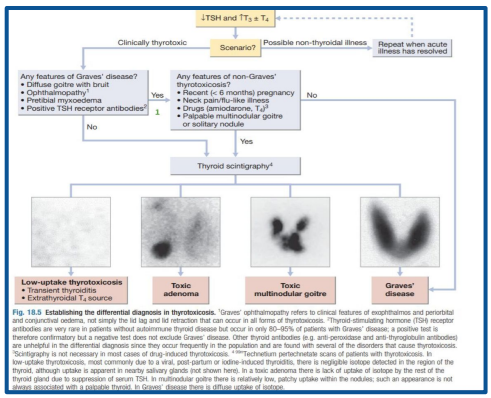
◄ Graves' disease (most common cause of Thyrotoxicosis)

-Autoimmune disease of unknown cause, affecting females more
-Most common features:
•Thyrotoxicosis •Goiter •Orbitopathy (**Exophthalmos**) •Dermopathy (**pretibial myxedema**) specific to Graves

◄ Diagnosis of Thyrotoxicosis

•Serum TSH, T4, T3 (initial test) shows: (Low TSH and High FT4)
•Thyroid stimulating Immunoglobulins (specific for and confirms Graves)
•Scintigraphy (RAI scan):
- Graves: Hot (diffuse increase uptake)
-Thyroiditis: Cold (reduced uptake)





◄ Treatment

1- **Antithyroid drug therapy** (propylthiouracil, carbimazole) should be started along with Beta blockers before iodine therapy or surgery to prevent thyroid storm
2- **Radioactive Iodine therapy** (^{131} Iodine is the most commonly used)
3-**Surgical Thyroidectomy** (subtotal thyroidectomy) when there is large goiter or failure of the previous two modalities

◄ Complications

1- **Thyroid storm** (precipitated by stress, infection or surgery)
Treatment: •Antithyroid drugs •Steroids •Beta blockers and fluids •Ipodate sodium

2- **Orbitopathy**
Treatment: •Steroids

3- in pregnancy
Treatment: - First trimester: Propylthiouracil
-Second and third trimesters: Carbimazole
- always keep T4 levels at the upper normal range

52- Obesity

Definition

Abnormal or excessive fat accumulation in adipose tissue, to the extent that health is impaired.

Surrogate measures of adiposity

BMI:
Obese = BMI ≥ 30kg/m^2.
Relatively reliable except in:
Extremes of age or height & Very fit individuals with muscular build

Population	Risk of metabolic complications of obesity	
	Increased	Substantially Increased
Caucasian (WHO)		
Men	>94 cm (37 in)	>102 cm (40 in)
Women	>80 cm (35 in)	>88 cm (35 in)
Asia (IASO/IOTF/WHO)		
Men		>90 cm
Women		>80 cm
China (WGOC)		
Men		>85 cm
Women		>80 cm

WHO recommended definition of obesity (2000)		
Classification	BMI(kg/m2)	Risk of comorbidities
Underweight	< 18.5	Low (but risk of other clinical problems increased)
Normal range	18.5 - 24.9	Average
Overweight (Pre-obese)	>25.0 25-29.9	Mildly increase
Obese (BMI >30)		
Obese Class I	30-34.9	Moderate
Obese Class II	<35-39.9	Severe
Obese Class III	>40.0	Very severe

Waist circumference (measure of visceral obesity):
The easiest way to assess obesity is by measuring the narrowest circumference midway between the lower border of the ribs and the upper border of the iliac crest.

Others: Ideal body weight, Anthropometric measures & Weight, in children: Growth Charts

Central Obesity

Central or visceral obesity is associated with more metabolic disease and complications:
- DM2 - Hypertension - Dyslipidemia

Measured by:
- Waist circumference - Waist:hip ratio - MRI - Single CT Slice(L4/L5) - DEXA
Waist:hip ratio of >1.0 in men and >0.9 in women is associated with ↑ risk of morbidity & mortality

Regulation of Appetite

Orexigenic factors (↑ Appetite):
- Ghrelin: Increase with hunger decrease with eating, Secreted primarily by the stomach and duodenum, and acts on hypothalamus to stimulate appetite

Anorexigenic factors (↓ Appetite):
- GLP-1 - Insulin - Leptin: Leptin from adipocytes acts on hypothalamus to decrease food intake and stimulate energy expenditure

Etiology & Pathogenesis:
- **Multifactorial**
- Biochemical/Dietary/behavioral/ Psychosocial/Genetic.
- Imbalance between energy intake and energy expenditure:
Calories consumed > calories used

Factors predisposing to obesity:
- Sedentary lifestyle - Diet (Overeating)
- Cessation of smoking - Sleep deprivation

Complications of Obesity

Metabolic:
- Cardiovascular (↑ BP, LDL & TGs ↓HDL, Impaired glucose tolerance & DM, Metabolic syndrome):
AACE recommends weight loss of 5% to 10% to reduce CVD risk

- DM2: Greater risk of developing T2D with higher BMI

- Others: NAFLD, Cancers (esophagus, colon, rectum, liver, gallbladder, pancreas) Infertility, Gout, Thrombosis & Gallstones.

Mechanical:
- Lung function: Reduced lung volume and vital capacity due to ↓ chest wall compliance.

- GERD & its complications: Barrett's esophagus, Erosive esophagitis and Adenocarcinoma.

- Obstructive sleep apnea: Weight gain increases severity of obstructive sleep apnoea

- Impaired physical function

Mental:
Anxiety, Depression, Suicidality & ↓ self esteem

Obesity and mortality:
Life expectancy ↓ as BMI ↑.
Obese patients are at risk of early death, mainly from diabetes, coronary heart disease (Major cause) and cerebrovascular disease.
- Weight reduction reduces this mortality and therefore should be strongly encouraged

52- Obesity

Screening

1. BMI measurement 2. Waist circumference 3. Evaluation of overall medical risks

Management

1. Lifestyle intervention: (Most important recommendation)

- Initial goal: 10% weight loss
- Rate of weight loss: Slow 1-2 pounds (0.5-1kg) per week, as rapid weight loss is associated with rapid weight gain, gallstones and electrolyte abnormalities.
- Aim for 4-6 months for weight loss, average is 8-10 kg loss
- After 6 months, weight loss is difficult due to Ghrelin & leptin effect + ↓ energy requirements

Physical Activity:
Start slowly, Avoid injury, increase intensity & duration gradually.
Increases body fitness, improves cardiopulmonary function, reduces stress, maintain weight loss & prevents weight regain

Long –term goal: 30-45 min or more of physical activity daily, 5 or more days per week

Diet therapy:
Indicated for all with BMI > 30 and those with BMI 25- 30 with comorbidities.
- Teaching about food composition (fat, CHO & protein) & calorie content by reading labels
Training: In selection of low fat, low carb foods.
Increase fruits & vegetables.
- Atkins diet: Good for short term under the supervision of a physician, but not for the long term.

2. Pharmacotherapy:

Indications:
- **BMI > 30**
- BMI 27-30 with comorbidities
- not for cosmetic weight loss

Used only when 6 months trial if weight & exercise fail to achieve weight loss

Note: Drugs can be used in the short term (up to 3 months) as an adjunct to the dietary regimen, but they do not substitute for strict dieting.

Liraglutide:
- GLP-1 receptor agonist
- loss of 15-18% of original weight maximum.

Simaglutide
- GLP-1 receptor agonist
- loss of 20-22%% of original weight maximum.

Orlistat:
- lipase inhibitor, reduces absorption of dietary fat
- Lowers Cholesterol (4-11%) & LDL (5-10%)
- loss of 8-10%% of original weight maximum.
- IMP side effect; Diarrhea

3. Surgical intervention (Bariatric surgery):

Indications:
- **Have BMI > 40**
- **BMI > 35 with comorbidities like**
  - **diabetes, sleep apnea, osteoarthritis, cardiomyopathy**
- **BMI 25-29.9 with WC > 102 cm in male and >88 cm in women**
- Age 18-60 & Psychologically stable
- **It can be used as a first-line option for individuals with a BMI > 50kg/m^2.**

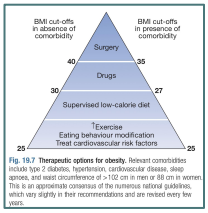


Fig. 19.7 Therapeutic options for obesity. Relevant comorbidities include type 2 diabetes, hypertension, cardiovascular disease, sleep apnoea, and waist circumference of >102 cm in men or 88 cm in women. This is an approximate consensus of the numerous national guidelines, which vary slightly in their recommendations and are revised every few years.

Types:

1. **Restrictive-type of surgery:**

Which restrict the ability to eat, for example:
- Adjustable gastric banding
- Vertical banded gastroplasty
- **Sleeve gastroplasty**

2. **Malabsorptive and restrictive**

Which reduce the ability to absorb nutrients, for example:
- **Roux-en-Y gastric bypass**

Gastric bypass causes more weight loss than sleeve gastrectomy, but sleeve gastrectomy is faster to do and with less malabsorption complications