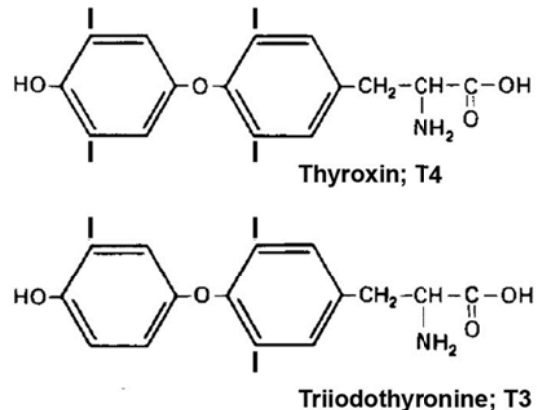


Part 3: Thyroid Gland and Antithyroid Drugs

General principles

- The major hormone secreted by the thyroid is thyroxine (T_4), which is **deiodinated** in many tissues to the more potent triiodothyronine (T_3). Both are bound reversibly to thyroxine-binding globulin (TBG). Only the free (unbound) fraction enters cells and produces biological effects.
- The most important step in the process of thyroid hormone synthesis is **oxidation** (organification) of iodides by **peroxidase enzyme** to produce molecular iodine, which then attaches to tyrosine to form mono- and diiodotyrosine. T_4 is formed by **coupling** of 2 diiodotyrosines, and T_3 by coupling of diiodotyrosine with mono-iodotyrosine.
- T_4 secretion is stimulated by thyroid-stimulating hormone (TSH). In turn, TSH secretion is inhibited by T_4 , forming a negative feedback loop.
- The gland synthesizes $T_4 > T_3$ (20:1) but T_3 is 4-times more potent than T_4 .
- Most of the circulating T_3 is derived from peripheral deiodination of T_4 . *converted to T_3 by Deiodinase enzyme in cytoplasm of cells.*
- **B-blockers** and **corticosteroids** inhibit peripheral conversion of T_4 into T_3 .

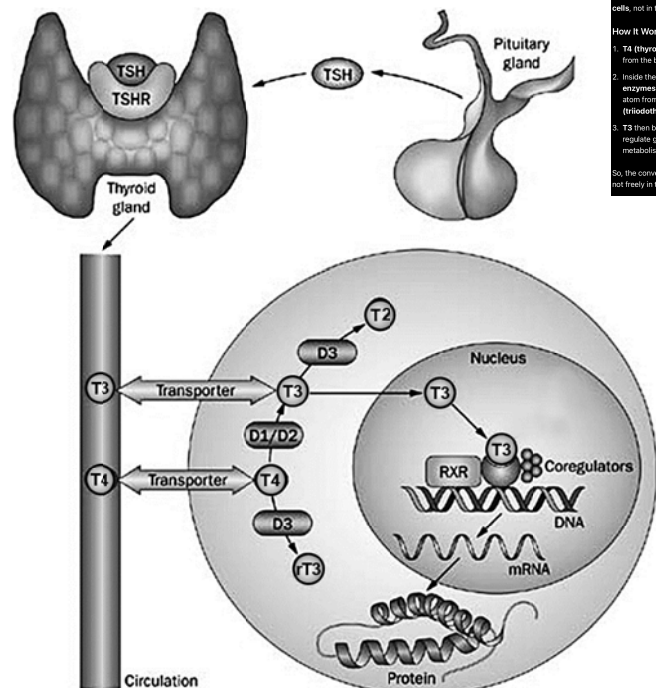


Preparations of thyroid hormones

- **L-thyroxine:** a synthetic sodium salt of T_4 that maintains normal T_4 and T_3 levels ($t_{1/2}$ is 7 days).
- **Liothyronine:** a synthetic sodium salt of T_3 ($t_{1/2}$ is 1 day).

Mechanism of action

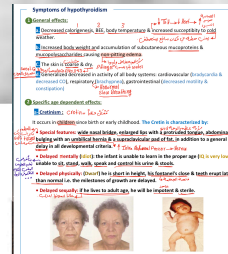
- T_3 & T_4 diffuse through the cell membranes and bind to cytoplasmic receptors then transported to the **nucleus and mitochondria**, where it interacts with many **DNA receptors (genes)** and affect their function.
- Most of T_3 & T_4 receptors are found in pituitary, liver, kidney, heart, sk ms.
- T_3 & T_4 are responsible for optimal growth and development.



Hypothyroidism (myxedema)

- Hypothyroidism in infants leads to **cretinism** (myxedema with physical and mental retardation).
- It is treated by replacement with **L-thyroxine (T4)**. The therapeutic goal is 'normalization' of the TSH level.
- Children require more T4 than adults to maintain optimal physical and mental development.
- T3 (Liothyronine) is **not used for replacement therapy** because L-thyroxine (T4) can maintain normal T4 and T3 levels, and also because **T3 has shorter $t_{1/2}$** .

normal TSH in BV is 0.5-5 mIU/L
أنا أعطيت الـ L-thyroxine
عشرات أمشاط الـ TSH level
أبقى معلمي لو خلاصه عايسيت
الـ 0.5-5 mIU/L
حدوداً. صعدا الزهر ريجناج 15D
أرنا 3 عشرات أسبل لعالنتية
سأله الـ L-T4 بلطيف في
شغله ..



A girl with hypothyroidism before and after treatment

Myxedema :

It occurs in **adults**. The patient is characterized by:

- The patient hates winter and is susceptible to cold.
- Mental functions are **depressed**: he is **apathetic & drowsy** with a prolonged reaction time.
- A special husky voice & absent outer 1/3 of the eye brows.
- Sexual functions are **depressed** due to slight atrophy of the gonads.

Laboratory findings:

Hyperthyroidism (thyrotoxicosis)

Definition: It is a clinical syndrome results from high levels of thyroid hormones.

Clinical types

Graves' disease:

- It is autoimmune disease in which there are abnormal **antibodies** (thyroid stimulating immunoglobulins) activates TSH receptors in the thyroid gland.

- The gland is diffusely enlarged and soft.

- The treatment is usually **medical**.

Toxic multinodular goiter: treatment is usually **surgical**.

Less common types: e.g. subacute (de Quervain's) thyroiditis. It is due to **viral** infection.

Toxic Multinodular Goiter (TMNG) is caused by continuous TSH stimulation or genetic mutations, leading to abnormal cell division in the thyroid, forming hyperactive nodules that secrete excessive thyroid hormones (T3 and T4), resulting in thyroid enlargement (goiter) and hyperthyroidism.

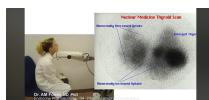
uncontrolled
TSH, No Feed
T4, وتبصلوا تغوز
لعالها عتال بلطال

Clinical picture

- Most manifestations of hyperthyroidism resemble **sympathetic overactivity** because thyroxine increases sensitivity of adrenergic β -receptors to circulating catecholamines.
- There are tachycardia, arrhythmia, sweating, lid lag, **exophthalmos**, etc.
+ loss of weight. only with Graves.D

Investigations

- Measuring serum T3, T4, and TSH (**the most important test**): T4 is $\uparrow$ and **TSH is $\downarrow$** .
- Assay for positive anti-thyroid antibodies: 90% +ve in Grave's disease.
- Thyroid scan for tumors.**



BTW
أنا أحسن بلادي وعيتم امتصاصه من الـ Thyroid Scan الـ
الغدة صغرت بصفة نهج Scan - لو لغيت حمزة مارا
زنها بخالها، لروا ان الـ T4 و T3 صعدا الـ Cold Nodule
مطلعت سود بارد. صعدا بأخاف نزيه فمعت بنوت بنوت
لنزم أسبل Scan.

Management

There are **2** main lines for treatment:

- **Medical treatment:** mainly for Grave's disease.
- **Surgical thyroidectomy:** mainly for multiple nodular goiter

MEDICAL TREATMENT (ANTITHYROID DRUGS)

1. Thiouracil drugs (thioamides) "PTU" (Carbimazole – Methimazole – Propylthiouracil)



Pharmacokinetics

- Methimazole is the active metabolite of carbimazole.
- The $t_{1/2}$ of propylthiouracil is 1.5 hr while the $t_{1/2}$ of methimazole is 6 hrs.
- The short $t_{1/2}$ of these drugs has little effect on their effect because they are selectively accumulated in the thyroid.
- Propylthiouracil is preferable during pregnancy because it does not cross placental barrier (because it is strongly bound to plasma protein).

And not secreted in breast milk.

Mechanism of action

- They inhibit **oxidation** of iodides into iodine by inhibiting peroxidase enzyme. Consequently, they inhibit **iodination** of tyrosine and **coupling** of iodotyrosine to form iodothyronines.
- Propylthiouracil also inhibits the **peripheral conversion** of T4 into T3.
- Clinical response appears after 3-4 weeks till the stored hormones are depleted from the gland (but **propylthiouracil has faster effect**, so it is used in **thyrotoxic crisis**).

Summary:
• PTU mainly works inside thyroid cells to block hormone production.
• It also enters peripheral cells' cytoplasm to inhibit T4 to T3 conversion.

Doses and duration

- **Carbimazole (Neomercazole):** start with 30 mg/d till reach euthyroid state (after ~4-8 weeks) then maintain on 15 mg /d for 12-18 months (until the gland undergo spontaneous remission).
- **Propylthiouracil:** start with 300 mg/d for 4-8 w then 150 mg/d for 12-18 months.

Adverse effects

- **Agranulocytosis & bone marrow depression (<1%):** it is the most dangerous side effect but it is usually reversible (see chapter Blood).

Hypothyroidism with increased size and vascularity of the gland due to ↑ TSH.

- Hypothyroidism of the infant (**fetal goiter**) if given during pregnancy (less common with PTU).



لذلك الـ PTU أعطيه لا Pregnancy عشان فإيصير عند الـ F. Goiter Hypo.T.J.I infant

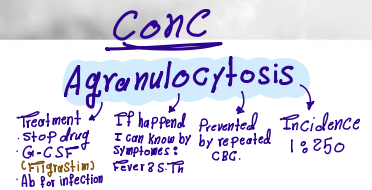
In patient of hyperthyroidism, an antithyroid drug was given to reduce the size of thyroid gland before surgery? The drug could be

Propylthiouracil
Thioamides
Iodides
2.4K answered

Explanation
Other antithyroid drugs increase the size of thyroid gland. They decrease synthesis of thyroid hormones. Carbimazole has negative feedback, it decreases increase which increase the synthesis of thyroglobulin and also size of follicular cells.

(علاج الوحيد)

- ! **Hepatotoxicity** that may be fatal (*more with propylthiouracil*).
- ! **Hypersensitivity reactions**: may require stopping of the drugs.
- ! There is **50-68%** incidence of **relapse**. *يعني بمجرد إيقاف الدواء لا يرجع الغدة إلى Hyperactivity (رجعت ربما لعادتها القديمة).*



Precautions during thiouracil treatment

- ! Therapy with thiouracil drugs should continue for **1-2 years** and should be **stopped gradually** (to prevent relapse). *كل فترة بأطلب منه CBC صورة الدم (Complete blood Count) لغياب مكونات الدم*
- ! **Agranulocytosis** is prevented by **repeated WBC count** and by observing early manifestations of the disease (sore throat & fever). *→*
- ! If used during **pregnancy**, propylthiouracil is the drug of choice.

Agranulocytosis is a severe condition characterized by a dangerously low number of granulocytes (a type of white blood cell, including neutrophils, eosinophils, and basophils) in the blood. This leads to a high risk of severe infections. Key Points: - Definition: Marked reduction or absence of granulocytes, especially neutrophils (neutropenia). - Causes: - Drug-induced (e.g., PTU, methimazole, clozapine, carbimazole). - Autoimmune diseases. - Bone marrow disorders (e.g., aplastic anemia, leukemia). - Infections (e.g., viral infections like HIV).	Symptoms: - High fever. - Sore throat. - Mouth ulcers. - Frequent or severe infections. Diagnosis: - CBC (Complete Blood Count) → Shows a severe drop in neutrophils (<500 cells/mm³). Treatment: - Stopping the causative drug. - Granulocyte colony-stimulating factor (G-CSF) to stimulate WBC production. Granstim. - Antibiotics for infections. Why is it Dangerous? Since neutrophils are the body's first line of defense against infections, their absence leaves the body highly vulnerable to life-threatening infections.
--	--

2. Radioactive iodine

Radioactive iodine is an effective **oral** treatment for **thyrotoxicosis** caused by **toxic multinodular goiter**. It is relatively '**safe**' and has largely replaced surgery (unless there is huge gland causing pressure symptoms).

Mechanism of action

- ! The isotope usually employed is ¹³¹I with a t_{1/2} of **8 days**. *• لو صار تدمير زيادة بسبب High dose من الRAI معصبي Hypo-T, أعطيه replacement T4.*
- ! Radioactive ¹³¹I is selectively accumulated in the thyroid tissue (normal or metastatic) and emits **β rays** that destroy the gland. *• صاعطيه single dose وتكون orally. ممنوع يقرب من حد لمساواة 5D لمدة 5D. حق بترينضم بال Radiation "جسمك بيتور". الRAI حيتنا كثر في الThyroid ثم يطلق الB-Rays وصمناخذ 6-12 weeks لتدمر جزء من الغدة.*
- ! **Delayed hypothyroidism** is the **main adverse effect** (80%); the majority of patients will require **thyroxin supplementation** after 5 years.

Contraindications

- ! **Pregnancy and lactation**: ¹³¹I crosses placental barrier and excreted in milk. *Teratogenic*
- ! **Age < 16 years** for fear of delayed malignant changes and gonadal damage. *Infant Goiter.*
- ! **Thyroid eye disease (exophthalmos; ophthalmopathy)**: radioiodine may worsen the condition. *• له يعني (بعد دعت المريض) يلي عنده Grave's D معافا exophthalmos من نصا حيت بد سوء العين.*

3. β-blockers (Propranolol)

- ! It controls sympathetic overactivity e.g. **tachycardia** and **arrhythmia**. *• الβ2 يلي في الBrain معصبي Blocking إصا فصعينام طبيعياً.*
 - ! It ↓ **insomnia**, and tremors (blocks central and peripheral β₂ receptors).
 - ! It inhibits peripheral conversion of T₄ to **T₃**. *• الβ2 يلي في الBrain معصبي Blocking إصا فصعينام طبيعياً.*
- N.B.** If propranolol is **contraindicated**, give **diltiazem** to control tachycardia and arrhythmia (other CCBs are less effective). *• B.Asthma مع Hyper-T حذر Cardiotoxic.*

SURGICAL TREATMENT: subtotal thyroidectomy

P.S
اليود بنسبة عالية جداً
يؤدي لتثبيط عمل الغدة
الدرقية وكذلك النخامية
(Thyrotropes).
تغلب الـ

Indications

- Failure of the medical treatment.
- Multinodular goiter with tracheal compression.
- Presence of malignancy.

CONC
أ. فضيت المغازنة.
B. وقفت الـ secretion
+ وقفت التعيين TSH

Preparation of patient before operation

6w Carbimazole
High dose of KI
منذ الـ Thyroid

- Carbimazole: 30mg/D, 6 weeks before the operation to reach euthyroid state.

- Potassium iodide: 10-14 days before operation to ↓ size and vascularity of the gland (see below). (Wolff-Chaikoff Effect).

- Propranolol: to control HR and cardiac arrhythmia.
- Sedatives (diazepam): to ↓ anxiety.

يعني خلصت المغزونات
وهنا معمم في الـ Goiter عن أستطيع عمل ectomy.
Amiodarone is an anti arrhythmic drug, 40% of it is (I), so it inhibit thyroid function (i.e. It has Wolff-Chaikoff Effect).
لماذا أت دواء فيه يود بنسبة عالية
وصعب الـ inhibition of Thyroid
أنه يعمل Wolff-Chaikoff Effect

Iodides

- Potassium iodides or Lugol's iodine, 5 drops twice daily is given 10-14 days before surgery in order to:
 - Iodides inhibit synthesis and release of T4 & T3 from the gland by inhibiting the proteolytic enzymes that release T4 & T3 from thyroglobulin (the main mechanism).
 - They inhibit release of TSH leading to ↓ size and vascularity of the gland.
- Improvement in thyrotoxic symptoms occurs within 2-7 days, but if therapy with iodides is continued (>2-4 weeks), the beneficial effects disappear and manifestations of hyperthyroidism reappear (iodine escape).

Adverse effects

- Iodides are secreted in saliva, nasal, and lacrimal secretions causing **metallic taste** and **irritation** of the salivary glands, mucous membranes and gastric mucosa. They increase lacrimal and nasal secretions.

- Iodine escape** if used > 2-4 weeks. > 14D

- Iodides increase intraglandular stores of iodine, which may **impair** uptake of **thiouracil drugs** or **radioactive iodine** by the gland. So, during preoperative preparation, they must be given **after thiouracil drugs** (or radioactive iodine), **not before them**.

- Allergic reactions: skin rash, drug fever, etc.

لأنه اليود
يغز عبر العرق
أحياناً.

الأسباب:

- 1- Any Infection. (Medical Crisis)
 2- Vigorous Palpation.
 3- not well-prepared for surgery. (Surgical Crisis)
- عيات ال Hyper.T3 لوصف
 معاه دمر برد ممكن برخل
 عندي من Storm
 طبعاً ال Hyper.T3 في البان
 481 ، بيضهوم بعدوما
 ويؤولوا صيها نقصا (في نفس فقط)
 Storm . اليعن ممكن يوقى ال Storm
 صعيح الدكتور بلاري T4 ، T3 ملين صوا.

Thyrotoxic crisis (thyroid storm)

It is a sudden severe exacerbation of the manifestations of thyrotoxicosis due to sudden release of T3 & T4 (medical emergency). It is a common postoperative complication if the patient was not well-prepared.

Manifestations

- ↑ Heat وحرارة عالية
 -! High fever with vomiting and sweating.
 -! Tachycardia, arrhythmia, acute heart failure, and shock.
 -! Convulsions, coma, and even death from heart failure.

Management

- 1-! Intravenous fluids and Paracetamol to control dehydration and fever. (Antipyretic)
 N.B. Aspirin must be avoided, because salicylate displaces bound T4 and T3, and also because of its uncoupling effect on oxidative phosphorylation renders the metabolic state even more severe. (High dose of Aspirin cause it, then mit metabolise O2 and Glu but produce little ATP with high heat.)
 2-! Propranolol (1-2 mg slowly i.v. or 40 mg oral /6 h) to control arrhythmia. Esmolol is a short-acting β-blocker can be also given by i.v.i. If β-blockers are contraindicated give diltiazem by i.v. infusion.
 4-! Potassium iodides: 10 drops orally/day to block hormone release and peripheral conversion of T4 to T3.
 3-! Propylthiouracil: 250 mg/6 hrs orally to block hormone synthesis. It acts more rapidly than other thiouracil drugs. (+ T4 -> T3)
 5-! Hydrocortisone: 100 mg i.v./6-8 h to elevates BP and reduces toxemia. It also blocks peripheral conversion of T4 to T3.
 -! Plasmaphoresis in severe cases to reduce circulating thyroxin.

uncoupling
 ↓ ATP
 ↑ حرارة

Management of myxedema coma

Myxedema coma is an end state of untreated hypothyroidism. There is progressive weakness, hypothermia, hypoventilation, hypoglycemia, hyponatremia, water intoxication, shock, and death. It carries high mortality and is a medical emergency.

Management

- 1-! Hospitalization (ICU): artificial respiration may be required.
 2-! L-thyroxine (T4): 400 µg i.v. initially, followed by 50 µg daily orally. Intravenous T3 can be used.
 3-! Hydrocortisone: 100 mg i.v./ 6-8 h because the patient usually has associated adrenal insufficiency.
 -! Intravenous fluids with caution to avoid excessive volume overload.

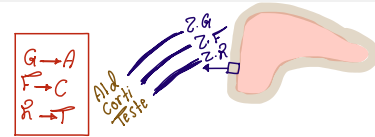
عجز
 لواحاج ييني
 شانه قلبه ضعيف الارتفاع وممكن
 يكون معاه أصلاً Pulmonary Edema
 علازم الزرع حاد عجز يكون.

Part 4: Adrenocortical Steroids

- Classification:**
- **Glucocorticoids:** have mainly anti-inflammatory action.
 - **Mineralocorticoids:** have mainly Na & water retaining action.
 - **Sex hormones:** are mainly anabolic.

All of them are from cortex
and have steroid nucleus so
all of them is Adrenocorticoid.

Glucocorticoids



	Anti-inflam potency	Na ⁺ retention potency	Duration of effect
Short-acting glucocorticoids: Cortisone	0.8	0.8	
Hydrocortisone (cortisol)	1	1	8-12 h
Prednisone and Prednisolone	4	0.5	<u>12h</u>
Methylprednisolone	5	0.1	
Intermediate-acting glucocorticoids:			
Triamcinolone → Has toxic effect.	5	0.1	12-36 h
Paramethasone	10	0.01	<u>24h</u>
Long-acting glucocorticoids:			
Dexamethasone	30	0.01	<u>48 h</u>
Betamethasone → النوع الوحيد الذي لا يعمل بال Plasma-P بشكل كبير ويكون Free	30	0.01	
Aldosterone:	0.3	3000	

- Hydrocortisone (cortisol) is the natural (endogenous) glucocorticoid.
- Equivalent dose means 20 mg of hydrocortisone = 5 mg of prednisolone.
- Steroids with high anti-inflam action (e.g. dexamethasone) are better used for inflammatory conditions e.g. **rheumatic fever**, while those with high Na & H₂O retention (hydrocortisone) are better used for treatment of hypotension and **shock** states (they also have rapid action).

Pharmacokinetics

- All glucocorticoids are completely & rapidly absorbed by **all routes**.
- 75% of hydrocortisone is bound to plasma globulin, 15% to albumin.
- Plasma t_{1/2} varies according to type (60-90 min for hydrocortisone). However, the effect of glucocorticoids is **prolonged** due to its effect on gene functions.
- **Metabolism** is by the **liver** and **excretion** is by the **kidney**.

Reduction then conjugating with
Glucuronic acid then in urine...

Mechanism of action

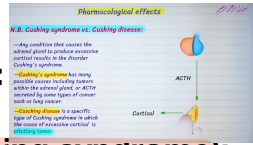
Corticosteroids bind first to cell surface receptors then to cytoplasmic receptors

oral
inhalation
injection

الستيرويدات
التي ترتبط بال
البروتينات
مثل Albumin
أو Globulin
تتسبب Displacement
وهو نوع من
Drug-Drug Interaction

أنا لو أعطيت حقنة Cortisol زب ياني فيه
جسمك وحيت بعد ساعة وضعت صلاحته تركيزه
عليك، كنت لسه ال Effect موجود ل 12h
لشدة بيكونت دخل ال Tissues واشغل ال Gene.

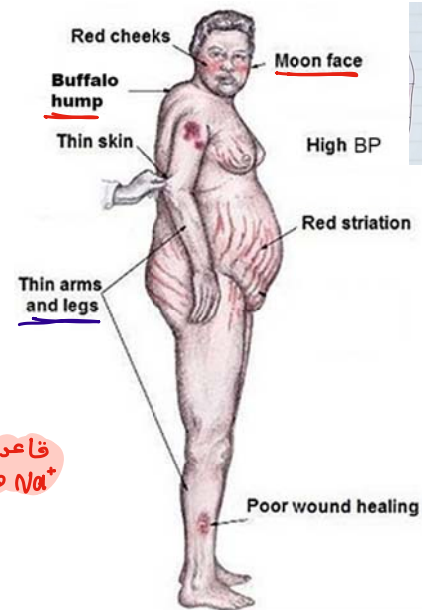
(carriers), then transported to the **nucleus**, where it interacts with many **DNA receptors** (steroid response elements) and affect their function.



Pharmacological effects:

■! On metabolism: (Cushing syndrome):

- ! Carbohydrate metabolism: hyperglycemia (↓ peripheral glucose utilization).
- ! Protein metabolism: Catabolic effect → ↓ muscle mass and thin limbs.
- ! Fat metabolism: ↑ lipolysis with redistribution of fat (moon face & buffalo hump).
- ! On water and electrolyte balance: Na^+ & water retention and hypokalemia. → قاعدة غ أي دواء بيجيس Na^+ صبيح K^+ والبس صبيح.



■! Anti-inflammatory and anti-immunological effects:

- ! They inhibit B cell function → ↓ antigen-antibody reaction.
- ! They inhibit T cell functions → ↓ inflam mediators and cytokine release.
- ! They inhibit macrophage activity and stabilize lysosomal membranes.
- ! They inhibit mast cells → ↓ histamine release and capillary permeability.
- ! They inhibit phospholipase A2 enzyme → ↓ synthesis of PGs & LTs.

■ **CNS effect:**
أول فابتاحده بيجيس
بالسعادة (Euphoria)
كنت بعدها صبيح بالكشاب
(Depression).

■! On CVS: Hypertension due to:

- ! Na^+ & water retention. - Reduces PGs. (PGE_2 , VD)
- ! Increase sensitivity of BV and heart to circulating catecholamines.

■ on Eye: ↑ IOP
يعني Glaucoma

هو نتص BP يؤدي لتصب تروية.

■! Anti-shock effects: due to:

- ! Hypertensive and CVS effects (mention them).
- ! Anti-inflammatory action (mention them).

Anaphylactic Shock vs. Septic Shock		
Feature	Anaphylactic Shock	Septic Shock
Cause	Severe allergic reaction (IgE-mediated)	Systemic infection (bacteria, fungi, viruses)
Mechanism	Massive histamine & cytokine release → vasodilation, increased permeability, bronchoconstriction	Widespread infection → excessive inflammatory response → cytokine storm, vasodilation, capillary leakage
Trigger	Allergens (food, drugs, insect stings)	Bacterial toxins (e.g., endotoxins, exotoxins)

BP severe Hypo. T severe Hypo. T

■! Hematological effects:

- ↑ RBCs and neutrophils and ↓ lymphocytes and eosinophils.
- ↑ coagulation factors and blood cholesterol.

mitosis

Apoptosis

TRNEP

صمو بينود Platelet
وصمو ليس من عوامل
التخثر، لكنه مهم في
التخثر.

■! On growth: Growth retardation, which is not prevented by growth hormone.

■! On bone: ↓ bone matrix and ↑ Ca^{2+} excretion (osteoporosis).

Collagen بيسر ال

↓ Intestinal absorption of Ca^{2+} , PO_4^{3-} (Anti-VD3)

↑ Excretion of these ions.

Administration

- ! Drug administration should follow the **circadian rhythm**: A double dose is given in the morning, and a single dose is given in the afternoon.

Administration (in chronic use)

Ad Addison's Disease
تست بأعطاء Cortisol وبيد أخرى
Prednisolone (منه مشتق)

Equivalent dose means 20 mg of hydrocortisone = 5 mg of prednisolone (based on the relative anti-inflam potency).

Drug administration should follow the **circadian rhythm**:

A double dose is given in the **morning**, and a single dose is given in the afternoon.

Alternate-day therapy is clinically effective with minimal effect on the hypothalamic-pituitary-adrenal axis. In this therapy, **double the dose** of short- or intermediate-acting glucocorticoids is administered every other day.

Glucocorticoids should be stopped **gradually** after long term administration.

Therapeutic uses

❗ **Inflammatory disorders:** e.g. iridocyclitis, neuritis, dermatitis, etc.

❗ **Autoimmune disorders:** e.g. vasculitis, rh fever, rh arthritis, hemolytic anemia, nephrotic syndrome, ulcerative colitis, etc.

Allergic disorders: e.g. anaphylactic shock, urticaria, eczema, bronchial asthma, allergic conjunctivitis, etc.

❗ **Malignancy:** e.g. lymphoma, leukemias, multiple myeloma, etc.

❗ **Shock and hypotension.....Why?**

❗ **Organ transplantation:** as immunosuppressive to prevent graft rejection.

❗ **Cerebral edema:** dexamethasone is used after brain surgery to minimize inflammatory edema associated with tissue injury.

❗ **Acute hypercalcemia:** to enhance Ca^{2+} excretion.

❗ **As replacement therapy in acute and chronic adrenocortical insufficiency (Addison's disease).** → Hydrocortisone

N.B. Acute adrenocortical insufficiency (acute Addisonian crisis):

–! Prolonged corticosteroid therapy produces feedback inhibition of ACTH and inhibition of endogenous cortisone secretion. When exogenous corticosteroids are suddenly stopped, **severe hypotension and shock occurs.**

–! **Management:**

–! i.v. fluids (saline).

–! Hydrocortisone **100 mg i.v./8h** until the patient is stable.

–! ACTH: **0.5 mg i.m.**

❗ **Stimulation of lung maturation in the fetus:**

Lung maturation in the fetus is regulated by fetal secretion of cortisol. When delivery is anticipated **before 34 weeks of gestation**, **betamethasone** is given to reduce the incidence of **respiratory distress syndrome** in the infant.

Betamethasone is chosen because its maternal protein binding is less than other steroids, allowing increased transfer across the placenta to the fetus.

Adverse effects

Most of these side effects occur after **long duration** of therapy:

(أنت it is عامة)

كل أعراض ال Cancer
يكون ضمن العلاج
Dexamethasone
كل أدوية ال Cancer تعمل
وال Cortisol يتلوه.

Toxicity
Neusea + vomiting

Hydrocortisone
عشاشات بدني أنا
Na-H₂O Re.T
شوك ال Shock يعني
↓BP
تقصي شديدا

Dexa / Beta
methasone

ضربة في الدماغ
Truma
Cell injury
في ال Brain
Inf. response
يعني VD ورشح الماء
Dexamethasone

34 - 35 ال surfactant
يكون كاف ل منع ال RDS.

Normal Gestation
(38-40 w) → ال surfactant يكون كاف
من ال اسبوع 3 وما بعده.

في حالات
الولادة قبل ال 34 w، الحل في
3 أيام:

1. 12mg Beta.m
2. 12mg Beta.m
3. الولادة

- ! **Iatrogenic Cushing syndrome:** occurs if doses up to 100 mg hydrocortisone are used daily for > 2 weeks. It is characterized by moon face, buffalo hump, thin limbs, osteoporosis, hypertension, DM, edema, etc.
 - ! **Immune suppression** leading to flaring of infections (especially viral and TB).
 - ! **Hypertension** due to salt & water retention
 - ! **Hyperglycemia.**
 - ! **Peptic ulcer:** due to prolonged inhibition of gastroprotective PGs.
 - ! **↑ IOP (Glaucoma):** due to ↓ aqueous humor drainage.
 - ! **Osteoporosis.**
 - ! **Growth retardation** in children.
 - ! **Skin atrophy & hypopigmentation** after prolonged topical use.
 - ! **Sudden withdrawal** after prolonged administration causes **acute Addisonian crisis**.
 - **Teratogenic in early gestation weeks** → May (100:1) causes cleft palate.
- Contraindications**

Absolute

- ! **Presence of infections:** especially viral infection and TB. → مريض ال TB، I. I. لو أخذ → Cortisol مش هيكمل أسبوع ويوت.
- ! **DM.**
- ! **Hypertension & heart failure:** they cause salt and water retention.
- ! **Peptic ulcer:** they ↓ synthesis of PGE₂ and I₂ that protect the stomach.
- ! **In early pregnancy:** may cause cleft palate.

Relative

N.B. Uses of corticosteroids in presence of T.B:

- ! TB meningitis: to prevent adhesions.
- ! TB of the suprarenal gland: to replace hypofunction.
- ! Miliary TB: to ↓ TB toxemia.

| Mineralocorticoids

1. Natural mineralocorticoids: Aldosterone

Physiological actions: It binds to specific intracellular receptors in the DCT to inhibit Na⁺ excretion (hyponatremia) and stimulates K⁺ and H⁺ excretion (hypokalemia).

2. Synthetic mineralocorticoids:

- ! **Deoxycorticosterone acetate (DOCA):** it has mainly mineralocorticoid effect.
- ! **Fludrocortisone:** it has both gluco- and mineralocorticoid effects.