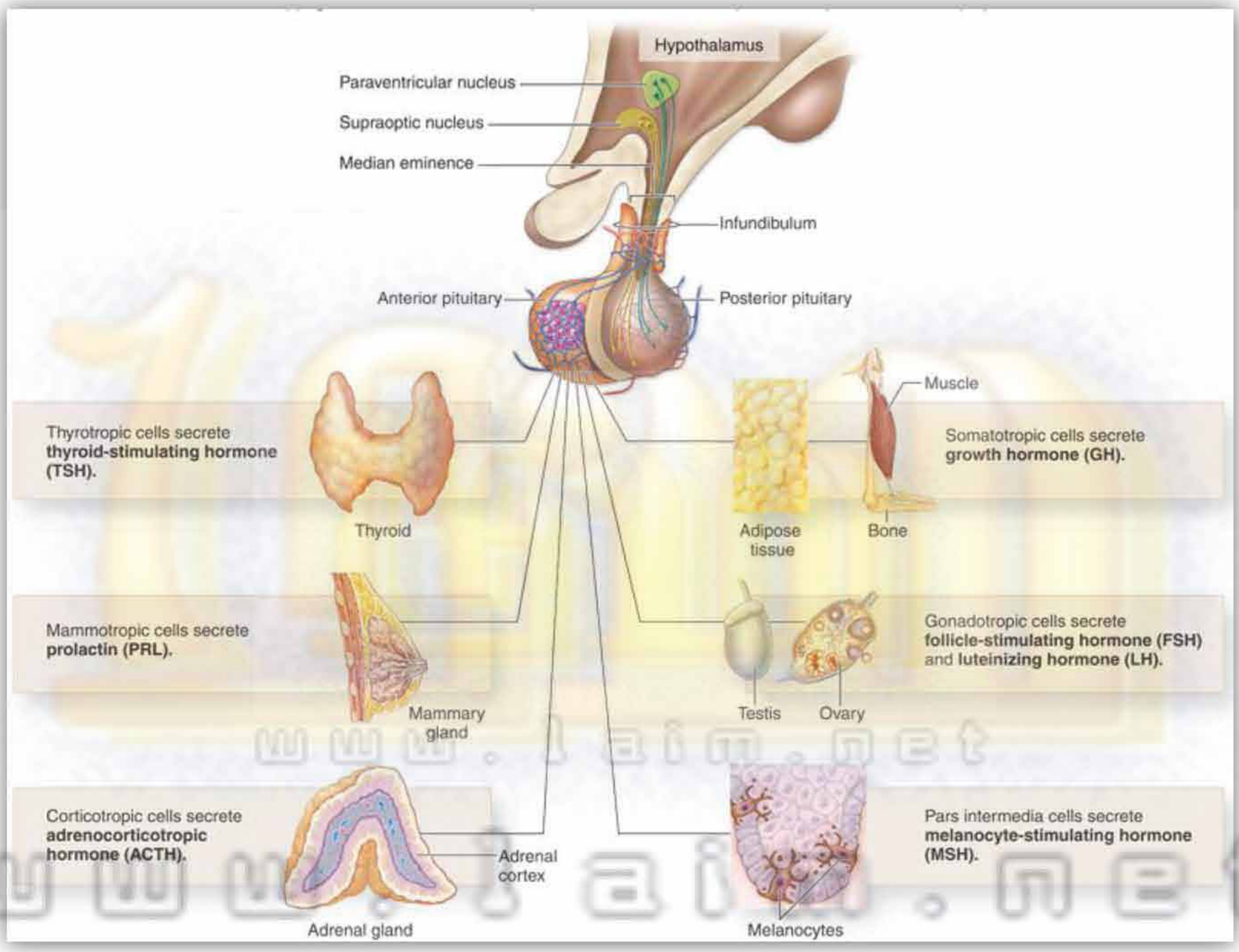
ENDOCRINE



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Index:

Pituitary Gland:

- Acromegaly.
- Diabetes Insipidus.
- SIADH.
- Pan-hypo-pituitirism.

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Thyroid Gland:

- Grave's D.
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Para-Thyroid Gland:

- Hyper-parathyroid.
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- Tetany.

Diabetes Mellitus.

Pituitary Gland

DD of Tall Stature:
1) hypogonadism.
2) Familial.
3) Marfan $.
4) Racial.
5) Klinefelter's $.
6) Cerebral Gigantism. (Sotos $)

Ant. pituitary

↑ GH

Child *"pituitary hyper-plasia"* → **Gigantism**

Over-Growth of Skeleton & Soft t.
- Tall Stature > 190 cm.
- Too Strong / Intelligent / Sexual precocity.
- "Acromegaly in late life"

Adult *"pituitary Adenoma"* → **Acromegaly**

↑ Prolactin

hyper-prolactinemia
- **Females** → Amenorrhea-Galactorrhea $ Sub-fertility.
- **Males** → Impotence loss of libido

Post. pituitary

↓ ADH

DI → Water Diuresis *"poly-uria"*

↓ Urine ↑ plasma Osmolarity.

↑ ADH

SIADH → Water Intoxication

Dilutional Hyponatremia
↑ Urine ↓plasma Osmolarity

GH

Invest.

Imaging
- X-Ray
  1) **Skull** → widening of sella turcica + ↑PNS.
  2) **hands** → Tuffing of T. phalynges (mushroom app.)
  3) **heel** → ↑ thickness of heal pad.
- CT / MRI on pituitary

LAB
1) ↑ GH after Glucose inf.
2) ↑ Somato-medicn C. "IGF-1"
3) ↑ BS. "DM"

Treatment

Medical "Only given till Surgery"
- Dopamin Agonsit → Bromocriptin
- Somatostatin Analogue → Octerotide

Surgery "of Choice"
- Trans-sphenoidal
- Radioth. "Recurrence /Sterilization"

prognosis:
1) Tissue & Sk. Changes are permanent even after surgery.
2) DM dt exhausted pancreas

Hyper-Prolactinemia

1)	phys.	Lactation – pregnancy – Stress.
2)	Tumor	Preventing (-) stimuli from hypoth.
3)	Metabolic	1ry hpo-Thyroidism (↑TSH → ↑TRH → prolactin) CRF dt ↓ excretion.
4)	Drugs	phenoth. / Metoclopraide / Haloperidol.

Invest
1) ↑ S. Prolactin.
2) CT / MRI on sella turcica.

Treatment:
1) Dopamine ⊕ → Bromocriptine. (Parlodel)
2) Surgery. (Transphenoidal)

SIADH

1) Old = Br. Carcinoma. (para-malig. $ of Small CC)
2) Young=TB – Sarcoid – legionella.
3) HIV – Lymphoma.

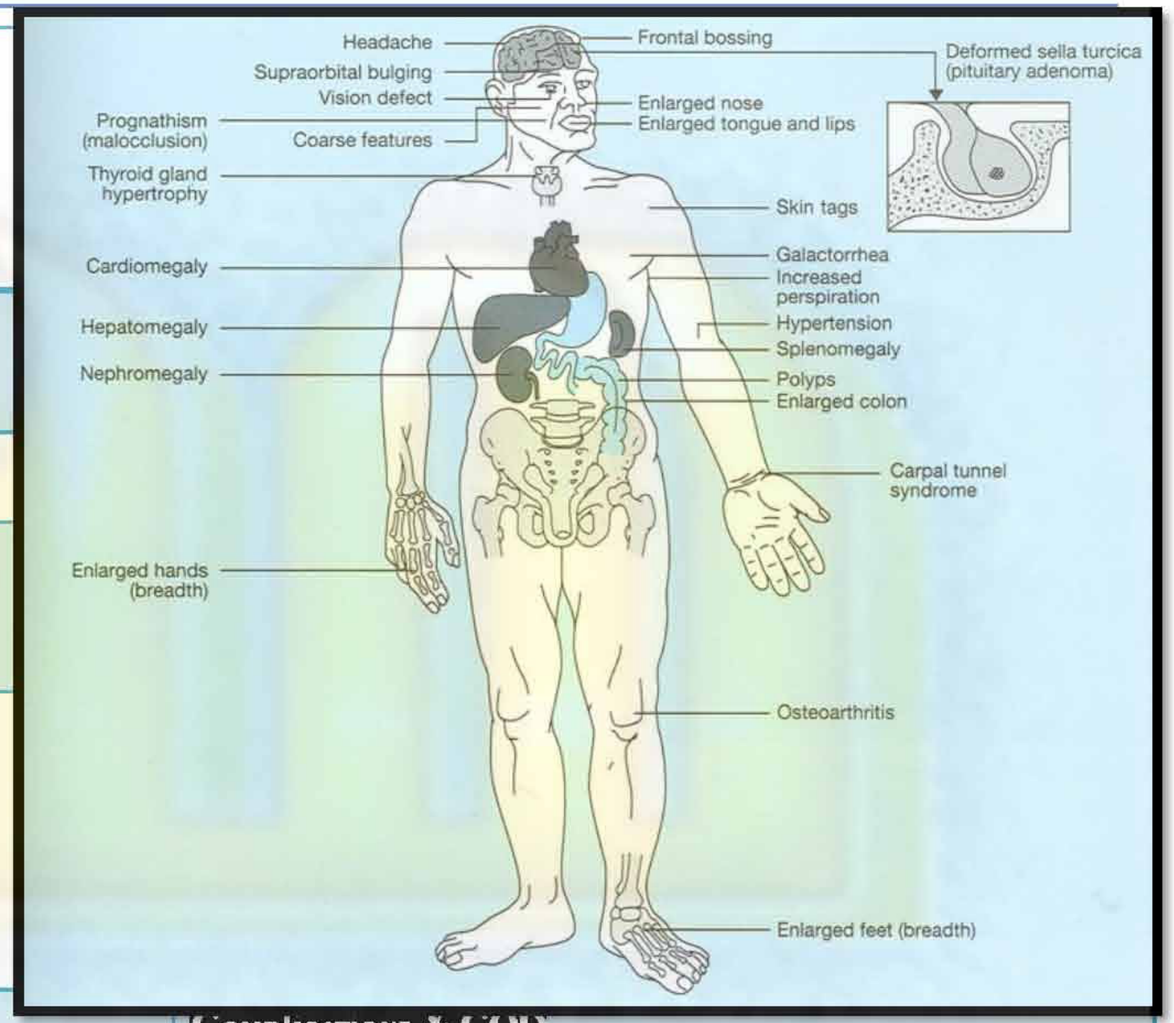
Invest.:
1) ↓ NA & Osmolarity.
2) Urine Osmolarity > plasma

Treatment:
1) Water restriction.
2) Democlocyclin.

(↓ sensitivity of kidney tubules to ADH)

Acromegaly

1) Facies	**Ape like… (Old photographs):** • Big skull. • Prominent supra-orbital ridge. • Ear + Nose ++ dt cartilaginous ++. • Proganthism → wide separated teeth + large tongue.
2) Hand – Feet & Joints	• Hand & feet ++ → **Spade hands.** • OA + Crepitus in knee joints.
3) Viscera	HSM + Cardiomegaly + ↑ lung size.
4) Endocrinal	• **↑ prolactin** → (-) FSH / LH → Infertility & Impotence. • **DM** GH is diabetogenic. • **Thyroid ++ but no hyper-function.**
5) Neuro	• Carpel Tunnel $. • Diabetic Neuropathy. • Pit. Tumors → pr. manifest. • Emotional instability. – hyper-somnolence.
6) Other	• Tiredness – ms. weakness. • Lx hypertrophy → hollow sounding voice. • ↑ Vit. D → hyprcalcuria → Renal Stones . • **DM → hyper-insulinemia → HTN due to:** a) Na + H_2O retention. b) ⊕ Sympathetic. c) Atherogenic.



Complications & COD

1) Colonic polyps → Cancer colon.
2) Dm → HTN.
a) CVS.

Activity of the Disease:

1) ↑GH > 10 ng after glucose infusion.
2) ↑ P → dt ↑Re-absorption by GH.
b) ↑ Sweating → DD.

↑P:
1) RF.
2) Hypo-PTH.
3) Acromegaly dt ↑GH.

Diabetes Insipidus

- Hypothalamic DI
  - Head injury.
  - Surgery.
  - Vascular.
  - Tumor.
  - Chest Granuloma. (TB - Sarcoidosis - Histiocytosis X)
- Nephrogenic DI
  - Heridetary
    - X-LR
  - Aquired
    - SCA.
      - sickle cell nephropathy: sickeling in medulla → hypoxic / hyper-tonic → Ischemia → Renal tubules
    - Hyper-calcemia.
    - Hypokalemia
    - Lithium. "TTT. of Manic depressive"

Cl./P of DI

- **poly-uria** (>2000 ml/24 hrs.) **poly-depsia.**
  - Urine Analysis
    - ↑ Sp. Gravity
      - if +ve sugar in Urine
        - DM
    - ↓ Sp. Gravity, ↓ Osmolarity
      - Water Deprivation for 8 hrs.
        - Good Response
          - if ↑ Sp. Gravity to N. ↑ Urine Osmalality
            - Compulsive Water Intake
              - 1) psychogenic. 2) Anti-Cholnergic. (Dry mouth) 3) Coffee.
        - No Response
          - ↓ Sp. Gravity ↑ plasma + ↓ Urine Osmolality
            - DI
              - "Desmopressin Test"
                - Good Response
                - Hypothalamic DI
                - TTT. by Desmopressin "IM / Nasal Spray / Oral" (↑ Factor 8)
                - Bad Response
                - Nephrogenic DI
                - TTT. is to ↑ senstivity of Renal Tubules to ADH
                - Thiazide "paradoxical although it is Diuretic"
                - CBZ
- DI may be masked
  - dt associated ↓ Cortisol
    - DI appears on start of Cortisol Th. dt ↑GFR

CT / MRI on sella turica.
CXR ... Granuloma.

Hypo-Pituitarism in Adults

(Simmond's Disease)

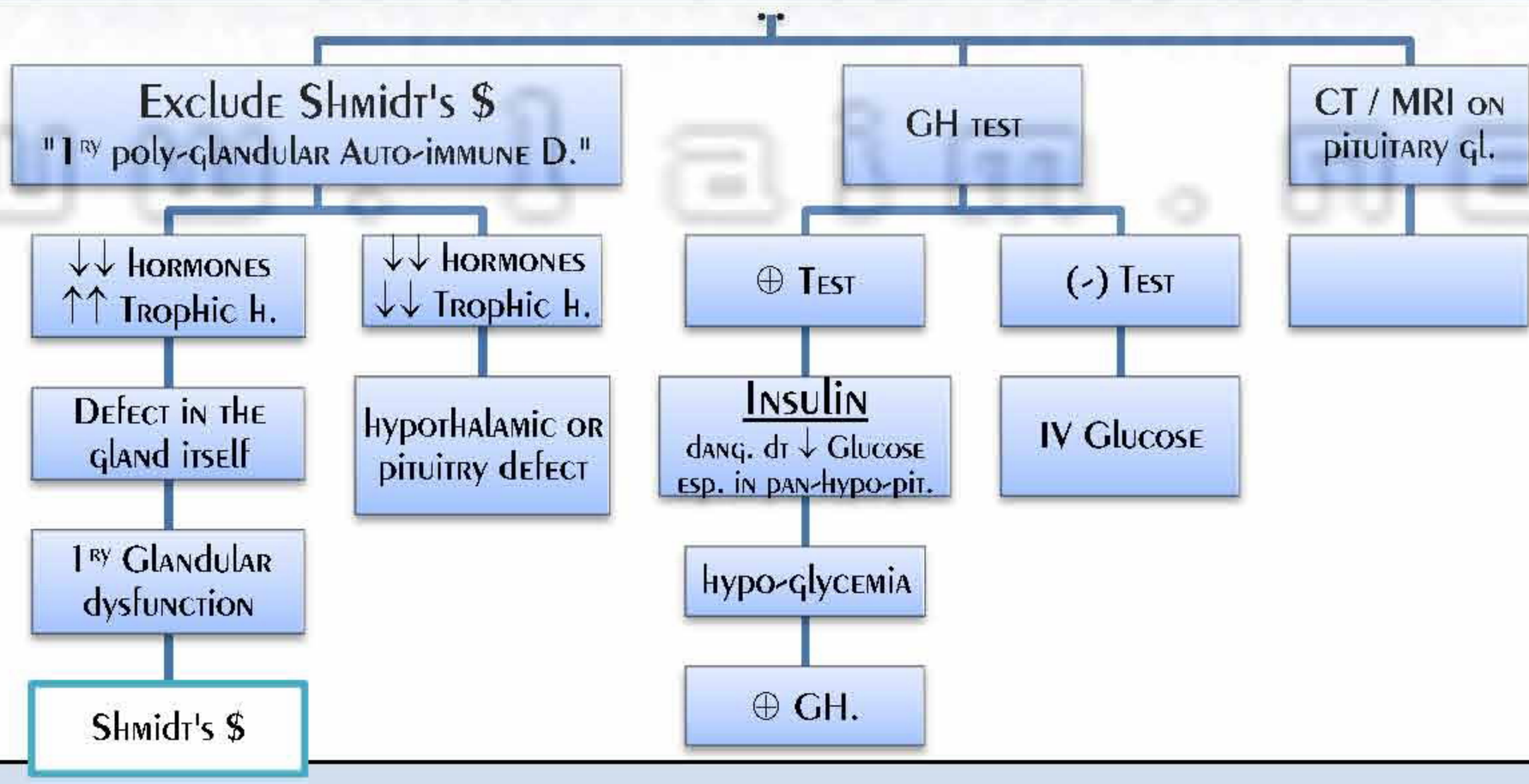
Etiology = DVT CIN:

1) Vascular → Infarction in Ant. Pituitary = Sheehan's $
   (due to post-partum hge → marked ↓↓ bl. Supply to pituitary gl. W has been doubled in size during pregnancy → Ischemic Injury)
2) Tumor in pituitary.
3) Surgery. (hypo-physectomy)
4) Inflam. → TB – Sarcoidosis.

Cl./P ⇒ Multiple ↓ Hormones:

1) ↓ GH in adult → wrinkling aground eyes & mouth + easy fatigue → "pre-mature senility"
2) ↓Gonado tropin → ↓ Gonadal h. → loss of libido – Impotence - Amenorrhea.
3) ↓ TSH → ↓Thyroid h. → see later. (apathy – bradycardia….)
4) ↓ ACTH → ↓Adrenal h. → hypo-glycemia – hypotension –tiredness.
   - *Long-Standing → Alabaster Skin = pallor + hairless … dt ↓ACTH.*
   - *Acute hgic infarction in pit. Adenoma → Auto hypophysectomy → Pituitary Apoplexy → sever headache + Acute hypo-pituitirism + pr. on Optic Chiasma … Ophthalmo-plegia.*

Investigations for hypo-pituitarism



Treatment = Replacement Th.

1) Thyroxine. (100-150 μ gm) *"Given e Steroids as Thyroxin → ↑Cortisol Turnover → **Adrenal Crisis**"*
2) Steroid → (Initiation of ttt. May unmask DI)
   - Prednislone → 7.5 mg (5 + 2.5)
   - Hydro-cortisone → 30 mg (20 + 10)
3) Gonadal

   - *↓Cortisol → ↓GFR → No poly-uria → mask DI.*
   - *Start of TTT. → ↑GFR → poly-uria → unmask DI.*

Hypo-Pituitarism in Childhood

Pituitary Dwarfism

- **Causes**: ↓ GH - ↓GH-RH - ↓ IGF.
- **Cl./P:**
  1) Dwarfism.
  2) Fasting hypo-glycemia.
  3) hypogonadfism.
- **Invest**: ↓ GH & (-) Insulin ⊕ Test.
- **TT**.: GH Injectio + Thyroxin + Gonadal h.

Froehlich's $

Obesity
hypogonadism.
Dwarfism.
DI - Polyphagia.

Laurence Moon Biedl $

as Froehlich's $

- polydactly.
- Skull deformiites
- Retinitis Pigmentosa.
- MR.

Adrenal Gland

- **Cortex**
  - **Hypo-function**
    - 1RY Chronic Adrenal Insuff.
      - Addison's D.
        - Causes:
          - Auto-immune. (90%)
          - TB. "miliary" (10%)
          - HIV.
          - Ketoconazole → medical Adrenalectomy.
        - If Adrenal insuff. is dt hypo-pituiterism → 2RY Adrenal insuff. NOT Addison's D.
  - **Hyper-function**
    - ZG
      - ↑ Aldosterone
        - Conn's $
          - Uni-lat. = Adenoma
          - Bi-lat. = hyperplasia.
    - ZF
      - ↑↑Cortisol
        - Cushing $
          - ACTH dependant
            - *pituitary Adenoma*
              - Basophilic μ Adenoma
                - Cushing D. "M/C Cause"
                - 1) No ICT.
                - 2) Bi-lat. Adrenal hyperplasia.
            - *para-Malignant $*
              - Ectopic ACTH
                - Carcinoid Tumor as in Br. Carcinoma (Small CC)
          - Non-ACTH dependant
            - Adrenal Tumor
              - Uni-lateral
                - Adrenal Carcinoma
              - Bi-lateral
                - Adrenal hyper-plasia
            - Exogenous Steroid
              - Cushinoid picture
    - ZR
      - Androgens
        - Cong. Adrenal hyperplasia
          - see NBs
- **Medulla**
  - ↑↑ CA
    - **Pheocromocytoma**
      - "May be part of MEN 2
      - Arise from Chromafin cells or Sympathatic Chain"
      - **5 Ps**
        - Bouts of HTN inbet. Normal
        - **P**ressure. (↑BP)
        - **P**ain "headache"
        - **P**alpitation. (HR)
        - **P**allor. (VC)
        - **P**anic. (tremors / Sweating)
        - + No Apprehension to diff. from GAD
        - • CA in bl. / VMA in Urine. (in 24 hr. period)
        - • CT / MRI Abdomen.
        - • Radio-Isotope.
          - α blockers 1st to control HTN then ββ to control Tachycardia to avoid unopposed α ⊕ → Refractory HTN. Then **Surgical Removal**

Addison's Disease

"1ry Chronic Adrenal Insufficiency"

Conn's $

"1ry Hyper-Aldosteronism"

↓ Cortisole / Aldosterone

- ↓Na / ↑K
  - ↓ Na
    - Orthostatic hypotention in early cases (SBP < 110)
    - also dt ↓ senstization of T. to CA
  - ↑ K
    - Diarrhea
    - Ms. Weakness "Asthenia":
    - Also due to: hypo-glycemia. hypotenstion.
- ↑ ACTH
  - Hyper-pigmentation
    - "dt ↑ ACTH on melanocytes + Destruction of medulla → shift of tyrosin metabolism to melanin instead of CA"
    - persistent Tanning after sun exposure "early sign"
    - Palmar creas. Friction & Exposed areas. Buccal mucosa. Scars after onset of D.

↑ Aldosterone

- ↑ Na
  - hypokalemic HTN "not sever"
    - No edema dt
      - Aldosetrone escape ph.
        - ↑↑↑Aldosteron → loss of kidney response.
      - hypo-kalemic Nephropathy
        - *poly-uria*
- ↓ K
  - CNS
    - Apathy
  - PNS
    - Motor
      - ms. Weakness
    - Sensory
      - Parathesia
    - Autonomic
      - Constipation & abd.Distention. Arrythmia

Management of Addison's D.

- Invest.
  - Addison's $
    - Hormonal
      - ↓ Cortisole.
      - ↓ Aldosterone.
      - ↑ ACTH.
      - Rapid ⊕ Test
      - *All of the above are Normal in 2ry Adrenal insuff.*
    - Non-hormonal
      - ↓ Na
      - ↑ K
      - ↓ Glucose
      - Eosinophilia
  - of the Cause
    - CT / MRI Abdomen + ABs aginst Adrenal gl.
- Treatment
  - Replacement Th. "Diet = ↑Salt + CHO + pr."
    - Cortisone
      - Prednisone 7.5 mg (5+2.5)
      - Hydr-Cortisone 30 mg (20+10)
      - ↑ Dose during Stress to avoid Addisonian Crisis
    - Aldosterone
      - Fludro-Cortisone "AcitoninH"

Management of Conn's $

- Invest.
  - Conn's $
    - Hormonal
      - ↑ Aldosterone
      - ↓ Renin
      - 1ry indep. on Renin
    - Non-hormonal
      - ↑ Na
      - ↓ K
  - of the Cause
    - CT / MRI Abdomen
- Treatment
  - Unilateral Adenoma
    - Surgical removal.
  - Bi-lateral Hyper-plasia
    - Spironolactone up10 400 mg "used as Anti-HTN only in this case"
    - ↓
    - If Tender Gynaecomastia
    - ↓
    - Amiloride

Cushing's $ = ↑ Cortisol

1) **Metabolic**	• CHO → Diabetogenic. → *poly-depsia / poly-urea* • Fat → *lipolysis* → ↑*FFA* → *Dyslipidemia / Re-distrib.* • Protein → *catabolism.*		
2) **Ms.**	→ px. myopathy (sign not a symptom)	3) **GIT**	→ PU – Pancreatitis.
4) **Bone / Ca**	Osteoporosis → rib fracture. ↓ linear growth → short stature.	5) **Renal**	→ Na-retention - ↓ K polyurea (K diuersis) – polydepsia.
6) **CNS**	→ depression.	7) **Endocrinal**	→ hypo-gonadism.
8) **Eye**	→ Cataract / 2^{ry} Glaucoma.	9) **Immune supp.**	→ recurrent infections.
10) Skin:		11) **CVS**	→ 2^{ry} HTN dt (↑CA permissive effect + Salt & H_2O ret.
a) Thin skin → cig. Paper. b) Rupture → stria rubra. c) Delayed healing → scars ahyper-pig. d) Hyper-pig. → localizing. e) Plethora dt polycythemnia. f) Hirsutism + Acne e no Comedons.	g) Re-distribution of fat • Face → moon face. • Trunk → trunkal obesity. • Inter-scapular → buffalo hump. NB: buttock → hollow Limbs → thin.		

Addisonian crisis on top of	Diagnostic criteria of Conn's $.	Diagnostic criteria. Of Cushing
• Stress • Infection • Trauma.	• Diastolic HTN + no edema. • ↑ Aldosetrone. • ↓ Rennin.	• 30-40 ys. • Female > males • See below.

Diagnostic flow Chart for a pt. suspected to be Cushing's $

When to Suspect Cushing?!

1) ↑ BS + ↑NA + ↓ K.
2) Blood → ↑ RBCs.
   → ↑ Neutrophils.
   ↓ Eosinophils.
   ↓ Lymphocytes.

Dexamethazone supp. Test
small dose to (-) pituitary gl.
(0.5 mg / 6hrs. for 48 hrs.)

- supp.
  - psuedo-cushing for DD
  - **Syndrom X** (Obesity - HTN - DM - hyper-lipidemia) OCP
- No supp.
  - Cushing but where?!
  - high dose Steroid (2 mg / 6hrs. for 48 hrs.)
    - supp.
      - pituitary Basophilic μ Adenoma
      - MRI / selective venous sampling
      - Trans-sphenoidal hypophysectomy
    - No supp.
      - Undetectable ACTH dt ↑ Cortisol
        - Adrenal Tumor
        - CT abdomen
          - Adrenal Adenoma
            - Surgical Removal
            - **Nelson's $** pituitary Tumor++ after adrenalectomy → ↑ ACTH → ↑ skin pigmentati
          - Adrenal Carcinoma
            - Inoperable dt metastases
      - ↑ ACTH
        - para-malignant $ Ectopic ACTH
        - search for tumor by CT / MRI
        - Surgical Removal

Medical TTT. of Cushing's $:

1) Diet = ↑ protein + KCL Orally.
2) DM → Insulin.
3) Medical Adrenalectomy → Ketoconazole / Metyaprone.

Thyroid Gland

Hypo-Thyroidism

CIN DVT:

1) Cong. Abscence / E. defect ± Deafness. (Pendred's $)
2) Inflam. → Hashimoto's thyroiditis.
3) Neoplasm.
4) Drugs → Anti-Thyroid / Li / Amiodarone.
5) Vascular → post-partum hge.
6) Trauma → Surgery. (Thyroidectomy) ^{131}I.
7) Endemic → Iodine def..

Infancy

Cretenism

Neglected 1ry hypo-Thyroidism in Adult

Myxedema "Investigations"

of Myxedema

↓ T_3 T_4 ↑ TSH.
↑Choleterol /↑Proplactin

of Manifest.

- Anemia
  - **Normo**
    - dt Chronic D.+ ↓ Thyroxin … ↓ BM⊕"
  - **Micro**
    - Iron def. dt Menohrragea
  - **Macro**
    - Megalo-blastic dt perneicous An. "Auto-immune D."
    - Non-Megaloblastic "dt hyper-lipidemia"
- ECG.. low voltage

of the Cause

Anti-Thyroglobulin in Hashimoto's Thyrooidits.

Thyrotoxicosis

Thyroid hyper-function

Hyper-Thyroidism (Active = ↑ RAIU)

Toxic Nodular Goiter. Thyroid Adenoma. *Graves' D.*

Investigations

- **Diagnosis**
  - Thyrotoxicosis
    - ↑T_3 T_4 ↓TSH
  - Hyper-Thyroidism
    - ↑ RAIU
  - Auto-immune
    - +ve TSI
- **Others**
  - • ↓ Cholest. / Glucosuria. (lag-storage)
  - • ↑ Ca^{++} dt ↑ bone turn-over

No Thyroid hyper-function

Transient Thyrotoxicosis (Passive = ↓ RAIU)

1) Thyroidis. (Initial pahse)
2) Facticiuos.
3) Struma Ovarii. (Teratoma)
4) Hamburger Toxicosis.

MYXEDEMA

neglected 1ᵞ hypothyroidism in adult
→ *accumulation of* **MPS**
→ *binds to water* → *Thickened features.*

Myxedema → 2ry hypo-pituitirism (pituitary myxedema)

1) General	• Intolerance to cold weather. • Tiredness – week – wt. gain.
2) Face	• Bloated – puffiness • Loss of Outer 1/3 of eye brow. • Carotenemia..... (Thyroxin is ess. for conversion of Carotenes to Vit. A) • Lips & Tongue → Thickened.
3) Skin	• Dry - Thickened dt MPS. (Non-pitting)
4) Neuro	• Slow mov. + poor memory. • Vocal cords → hoarseness. • Carpal Tunnel $. • Tendon jerks hung up Reflex. • Myxedemal Madness.
5) Ms.	Px. Myopathy.
6) CVS	• ↓ HR + pericardial eff. (dt MPS) • Atherosclerosis due to (↑ TSH + hyperlipidemia) → HTN. (Diastolic) → ISHD (start low dose then ↑ gradually) → Claudicaion.
7) GIT	↓ motility → Constipation. → bact. Over-gr. In SI → Malabsorption $.
8) Genital	Menorragia. (↑TRH → ↑prolactin → (-) FSH / LH → Menohhragia → Iron def. An.)
9) **Myxedema Coma**	See NBs.
p. 27 ..... Hypo-thyroidism in pregnancy.	

DD of puffiness:

- Nephrotic / Nephritic.
- Myxedema.
- Chronic Cough. "Lower lid"
- SVC Ob.

hypothyroidism problem

- Female 30 -40 ys.
- Constipation.
- Skin changes. (Dry / Thick)

Treatment of Myxedema = L-Thyroxine

- Start low dose. (25 – 30 µgm)
- Gradually ↑ dose / 2wks upto 150 µgm to Avoid ISHD dt Atherosclerosis.
- Max. Dose = 300 µgm.

Grave's Disease

General Symptoms

- ♀ → Intol. to hot weather + Wt. loss ε Good Appetite.
- ♂ → Gynaecomastia.
- Children → Tall Stature.

"Auto-immune D. against Thyroid gl. → production of TSI (IgG) → acts as TSH → ⊕ TSH Rs → ↑ Thyroid Release"

hypothyroidism problem

- ♀ 30 -50 ys.
- Onset: Gradual Onset.
- Course: Remission / Exacerbation.
- ppt. by: Emotional Stress. Infection ε (E. Coli / Yersenia)

Triad

Thyroid Gl.	Dermopathy	Ophthalmopathy	
		Non-infiltrative	Infiltrative
• Diffuse ++. • Non-tender. • ↑ Vascularity (systolic thrill & bruit over the thyroid gl.)	1) Skin → sweaty-warm – flushed (palmar crease) dt VD. 2) Nails → onycholysis "Plummer's nails" 3) Pre-tibial myxedema → itchy swellings. 4) Grave's clubbing Thyroid acro-pachy.	1) *Staring look* → Dalrympl's. 2) *Lid Lag* → Von Graev's 3) *Infrequent blinking* → Stellwag. 4) *Fine tremors on gentle closure of UL* → Rossenbach's.	*secretion of exophthalmus subst., lymphocytic infilt. Of* Retro-orbital t. ⇓ proptosis Exophthalmus. (bi-lateral) EOM "MR" ⇓ *Weak convergence* (Moebius Sign)

Others

1) Neuro	• *Nervousness, anxiety, insomnia + Fine tremors. (No Apprehension to diff. From GAD)*
2) Ms.	- *Px. myopathy ± MG (Auto-immune)*
3) Bone	- *↑bone turnover → Osteoporosis*
4) CVS	- *↑HR → palpitations ± AF* - **hyper-dynamic circ. Dt** *(↑SBP dt ↑COP + ↓DBP dt VD)* ○ *water hammer pulse.* ○ *↑HS over PA.* • *Murmur → Hemic. Peri-cardial rub like "lerman scratch"*
5) GIT	*→ ⊕ Gasto-colic R. → hyper-defecation → wt. loss / ↑ Apetite.*

Mono-symptomatic

"one manifest. pre-dominates eg. AF "Thyro-cardia" in elderly"

➢ Treatment of Grave's D.

	Medical	Surgery	I^{131}
Indications	1) 1st attack in adults > 40 ys. 2) Before surgery → to keep the pt. Euthyroid. 3) pt. Refusing / Unfit for surgery. (pregnancy)	1) Recurrent. (after medical) 2) Poor drug compliance. 3) Huge goiter / Malignancy.	1) Recurrent after medical & surgical. 2) # of Surgery.
S/E	1) M-P rash. (common) 2) GIT upset. • prophylthio-uracil → *Agranulocystosis.* • Carbimazole → ***Fetal goiter*** *if given during pregnancy.*	1) Lx. N. palsy. 2) Transient hypo-calcemia. 3) Hypo-thyroidism. 4) Post. Op. Thyrotoxicosis.	1) ↑ Dose → *hypo-thyroidism.(Myxedema)* 2) ↓ Dose → *recurrence.* 3) # in Pregnancy / lactation / children → radiation induced Genetic cancer.
procedure	1) Diazepam → Sedative. 2) ββ → ↓Symp. Over activity. (↓ Conv. Of T_4 to T_3) 3) **Anti-thyroid** → (-) New synthesis e no effect on the already formed →effect appears after 6 wks.	1) Sub-total thyroidectomy. 2) <u>Lugol's iodine b4 surgery</u> • *↓ Vascularity → ↓ size* • *↓ Thyroxin → to be euthyroid.*	<u>I^{131} rapidly accumulates in thyroid gl.</u> *→ local β-radiation* *→ poor penetration power* *→ destroys the thyroid gl. only w out affecting the surrounding t.*
Anti-Thyroid	<u>Prophyl Thio-uracil</u>: of choice in pregnancy. <u>Carbimazole:</u> • Start 40 – 60 mg/d. • ↓ 20 – 40 mg/d • MD 5 – 20 mg/d. • Stop after 2 ys till pt. becomes Euthyroid at 5 mg/d		

Treatment of Complications

- **Thyrotoxic Crisis**
  1) Hyper-pyrexia → *cooling blankets.*
  2) Disprop. Tachycardia upto AF → *Digitalis.*
  3) Shock & Coma → *Volume expansion.*
  4) hydro-cortisone → *to Avoid relative Adrenal insuff. dt ↑ Cortisol turnover + ↓ Conv. Of T_4 to T_3)*
  5) Prophylthiouracil / Propranolol / K Iodide.
- **Dermopathy** "pretibial myxedema"
  - Topical Steroids
- **Ophthalmopathy** "Exophthalmus"
  - mild → Lubrication by Artificial tears
  - Sever → CS + supra-orbital deroofing

Hyper-thyroidism

Thyroiditis

Acute Non-Supp.
"de Quervain's Thyroidits"

- Viral.
- painfull.
- Thyro-Toxicosis & Malaise.

Lymphocytic Thyroiditis

- Auto-Immune. (Anti-Tg & Anti-microsomal)
- painless.

Hashimoto's Thyroiditis

- Auto-Immune. (M/ C Type)
  (Anti-TG & Anti-microsomal)
- 1st Hashitoxicosis → Myxedema.
- Other ass. Auto-immune D.
  1) Addison's D. "Shmidt's $"
  2) hypo-PTH - Type I DM.
  3) PBC.

Riedl's "Woody" Thyroidistis

- Chronic fibrous Tissue.
- Mediastinal $.
(Dysphadia / hoaesness)

Treatment of Thyroidits

1) Aspirin + NSAID + ββ.
2) Partial Thyroidectomy if Mediastinal $.
3) Thyroxine in hashimoto's.

Thyroid Malignancy

papillary
popular.
due to Irradiation.

Follicular
Blood borne metastasis.

Anaplastic
Old age.
Mediastinal $.

Medullary
"part of MEN II"

para-follicular C-cells → Calcitonin
"Tumor Marker"

Clinical Pathology

Hypo-Thyroidism
(↓ T_3 Uptake & FTI)

- 1ry Hypo
  - ↑ TSH. (early)
  - ↓ T_3 T_4
  - "Hashimoto's Thyroidits"
    - Anti-TG
    - Anti-microsomal
- 2ry Hypo
  - ↓ TSH
  - ↓ T_3 T_4
  - TRH ⊕ Test
    - Good Response → hypo-th. hypo-Thyroidism
    - Bad Response → pituitary hypo-Thyroidism

Hyper-Thyroidism
(↑ T_3 Uptake & FTI)

- 1ry Hyper
  - ↓ TSH
  - ↑ T_3 T_4
  - No Response to TRH ⊕
  - Grave's D.
    - TSI - TGSI - TBI Abs
- 2ry Hyper
  - ↑ TSH.
  - ↑ T_3 T_4

Pregnancy

- 1st 20 wks
  - HCG & ↑ TBG
  - ↑ Total T_3 T_4 … (-) TSH
- After 20 wks.
  - ↑ TSH

Sick Euthyroid $
Non-Thyroidal Illness

Thyroid function dist. due to sickness (Infection - Trauma - Surgery - MI)

- Acute
  - mild
    - N T_4
    - ↓ T_3
    - ↑ rT_3
    - N. TSH
  - sever
    - ↓ T_4
    - ↓ T_3
    - ↑ rT_3
    - ↓ TSH
- Recovery
  - ↑ TSH (Transiently) dt releas of stress (-) on Thyroid gl.

Follow up of TTT.

- 1ry Hypo-Th.
  - T_4 in few days.
  - T_3 in 2-3 wks.
  - TSH in 6-8 wks.
  - poor Compliance = ↑ TSH & Normal T_4
- 1ry Hyper-Th.
  - in the 1st 6 ms depend on T_4 or T_3 as TSH is still suppressed.

Other Euthyroid

- ↓TSH in Euthyroid
  - sub-Clinical hyper-Thyroidism.
  - pregnancy. (1st 20 wks.)
  - 1st 6 ms. inn TTT. of 1ry hyper-Th.
  - NTI. (Sever cases)
- ↑ TSH in Euthyroid
  - sub-Clinical hypo-Th.
  - NTI. (Recovery Stage)
- Euthyroid hyper-Thyroxinemia
  - Causes of ↑ TBG
  - NTI.
- Euthyroid hypo-Thyroxinemia
  - Causes of ↓ TBG
  - NTI.

Hyper- Para-Thyroid

	1ry Hyper-PTH	2ry Hyper-PTH	3ry Hyper-PTH
Etiology	• No hypo-calcemia. (No 2ry Cause) • hyper-active gl. → Autonomous sec. → No feedback (-) (Although Normal or high Ca)	• 2ry to hypo-calcemia. • ✓ feed back (-)	1) long-standing 2ry hyper-PTH ..... يقلب ..... 3ry 2) Autonomous sec. (hyper-plasia) → No feedback (-) (Although Normal or high Ca)
Causes	1) Adenoma → single gl. 2) hrper-plasia → 4 glands. 3) MEN = Multiple Endocrine Neoplasia.	1) CRF → ROD. 2) Mal-absorption $. 3) Rickets – Osteomalacia.	1) CRF + ↑ Ca^{++} (dr 3ry hyper-PTH + Ca Supplements) 2) Mal-Absorption $.

MEN - I "Wermer's $" → 3 Ps
- Pituitary tumor.
- Pancreatic tumor.
- PTH. (hyper)

MEN - II A "Sipple's $" → Oma
- pheochromo-cytOma.
- medullary carcinOma.
- PTH. (hyper)

MEN - II B → Oma + Marfanoid features.

Cl./P of Hyper-Calcemia = 1ry & 3ry

• BOnes	Back ace – pain – Arhtralgia – pseudo-gout Weakness - hypotonia. (tetany 3also)
• STOnes	Renal Stones - Nephrocalcinosis.
• GrOans	N V – Abd. Pain – PU – Acute Pancreatitis.
• Psychiatric Over-tOnes	Drowsiness – Depression.
• CVS	HTN (VC) + ↓ HR. (so Give CCB)

Invest. for hyper-PTH

LAB

	1ry	2ry	3ry
Urine Ca/P	↑	↑	↑
s. Ca	↑ or N.	↓ or N.	↑
s. P	↓	↑ c CRF	↑ c CRF
s. ALP	↑	↑↑	↑↑↑
PTH	↑	↑	↑

X-Ray

Bone
1) Skull → mottling. (salt/pepper)
2) long bones → Ground glass.
3) Vertebrae → Cod-fish app.
4) Teeth → loss of lamina dura to diff. from MM.

Kidney → Stones / Nephro-calcinosis

Exclude Other Causes
1) MM → electroph.
2) Thyro → T3 T4 TSH.
3) Vit. D tox. → Cortisone (-) test.
4) Sarcoidosis → Conv. E.
5) Tuomr → CT / MRI / Radio-isotope Scan.

Treatment of hyper-PTH

Tumor
- Adenoma → Surgical Removal
- hyper-plasia → Reomve 4 gl. & implant a part in the for-arm

hyper-calcemia
- 1st Aid
  - Saline.
  - Lasix.
- ↓ Ca
  - ↑ P Orally.
  - Malignancy: Calcitonin - Bisphosph.
  - Sarcoidosis: Steroid
- HD → لو غلبت

Calcium

Hypo-Calcemia

1) Hypo-Albumin. (M/ c Cause)
2) CRF.
3) Hypo & pseudo hypo-PTH.
4) Acute pancreatitis.

"dr Ca deposition in pancreatic necrotic T. although pancreatitis is caused by hyper-calcemia"

Hyper-Calcemia

↑↑ PTH

1) 1ry & 3ry Not 2ry hyper-PTH
2) Para malignant $.

↑↑ Vit. D

1) Vit. D Toxicity.
2) Sarcoidosis.

Malignancy (due to IL-1)

1) Osteolytic Metastasis
2) Miltiple Myelomoa.
3) Lymphoma. (dr Vit. D3 + IL-1)

Miscellaneous

1) Milk - Alkali $.
2) Immobilization → ⊕ BR.
3) Thiazides → ↓ Ca excreation.
4) hyper-Thyroid → ↑Bone turnover.

Phosphorus

H – K – P all ↑

or all ↓

Hypo-phosphatemia

1) ↑ loss → Renal loss→ hyper-PTH - Fanconi $.
   → GIT loss → Vomiting Diahrrea
2) ↓ Absorption → ↓ Vit. D & Malabsorption $.
3) IC shift Insulin th. in ttt. of DKA & Alkalosis.

Hyper-phospatemia

1) Hypo & pseudo hypo-PTH.
2) CRF. (↓ Excretion)
3) Acromegaly (↑ GH)
4) EC shift (Acidosis)

Other Metabolic Bone Diseaes

Osteoporosis

Slow process in Senile

All Lab are Normal

Acute Immobilization

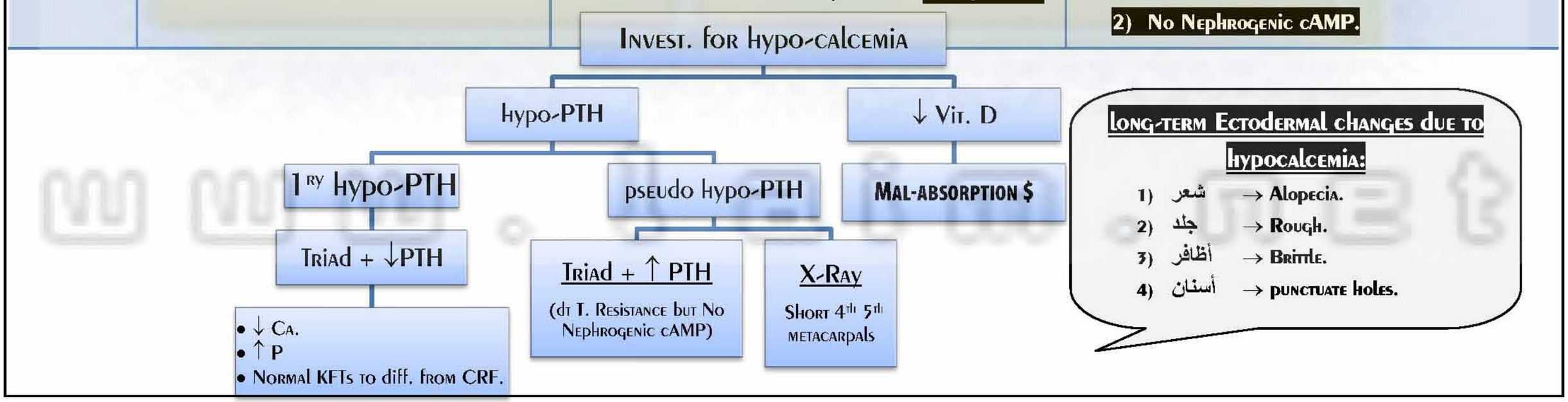
⊕ Osteoclast
↑ CA/P
↓ PTH

Paget's Diseasses

1) ↑ ALP. (10 X)
2) Ca/P .. Normal
3) ↑Bone Turnover → . … ↑hydroxy-proline.

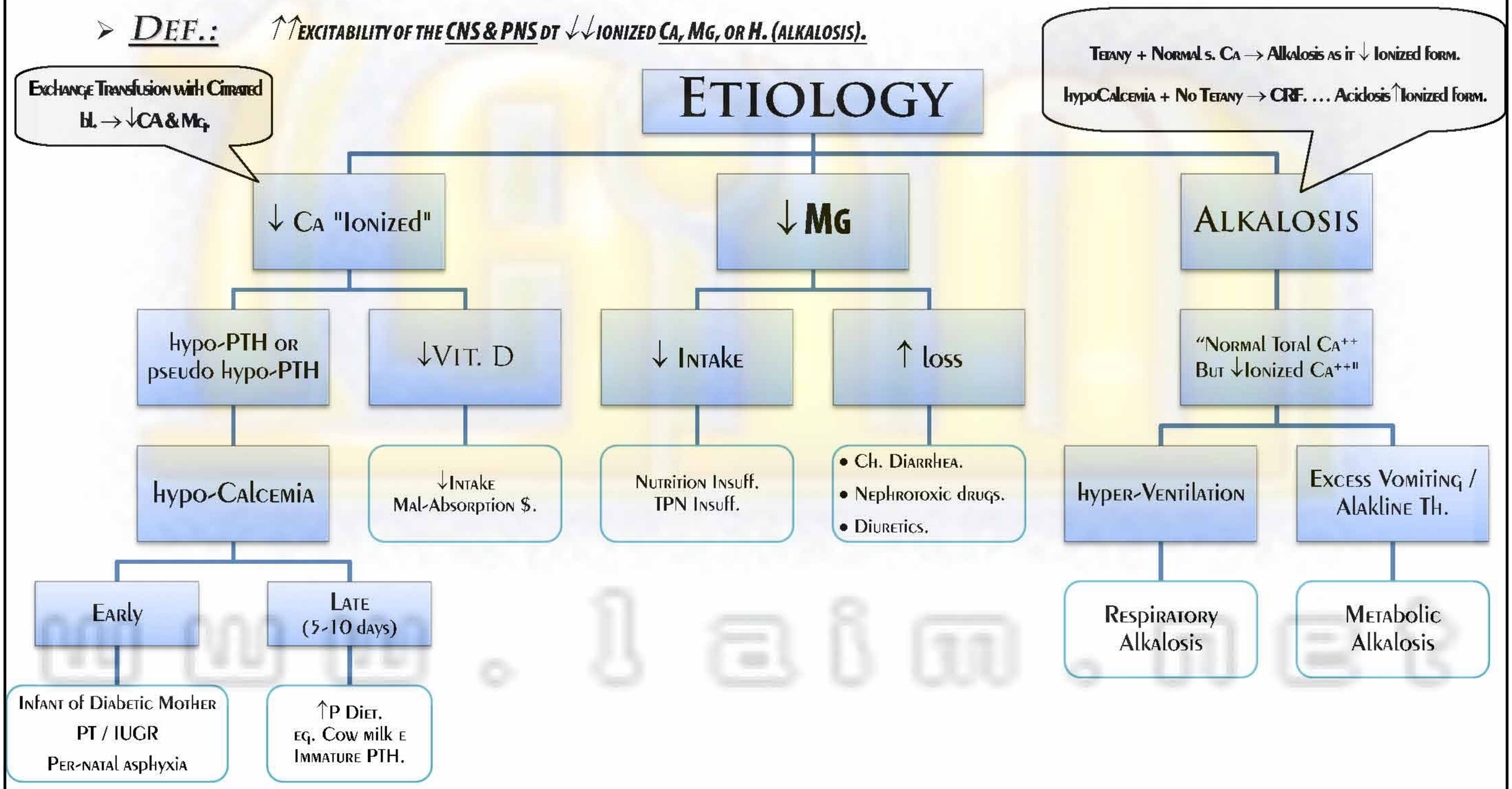
Hypo- Para-Thyroid

	Hypo-PTH	Pseudo - Hypo-PTH	Pseudo – Pseudo Hypo-PTH
Etiology	1) Idiopathic. 2) Surgical Removal -Irradiation 3) Congenital hypoplasia "Di-George $" (Absence of Thymus & PT gland)	1) Tissue Resistance to PTH. 2) No ↓ PTH.	As pseudo in Cl./P → But (Normal) Ca/P → So no Tetany.
Cl./P	Tetany.	**Tetany + Albright's Osteo-dystropthy:** أنت قصير — Short Stature. و دماغك كبيرة — Big Skull. و طخين — Obese. و أهبل — MR. X-Ray — Short 4th / 5th Meta-carpals.	Skeletal Abnormality Only
Invest.	○ Triad + ↓PTH	○ Triad + ↑PTH. + X-Ray hands + No Neph. cAMP	1) Normal (Ca/P) 2) No Nephrogenic cAMP.



Tetany

➢ **Def.:** ↑↑Excitability of the CNS & PNS dt ↓↓Ionized Ca, Mg, or H. (Alkalosis).



Cl./P of Tetany

Latent Tetany
↓Ca but > 7 mg

Provocative Tests

Chovsteck sign
⇓
Tapping the VII N. Ant. To the tragus
⇓
Deviation of angle of mouth.

Trousseau sign
⇓
↑BP > (S) Ischemia of forearm for 3mins.
⇓
"Carpal spasm"

Flexion of Wrist / MCP Joint & Extension of IP Joints.

Pernoeal sign
⇓
Tapping the peroneal N. over neck of fibula
⇓
Dorsi-flexion & eversion of the foot.

Electrical

ECG
⇓
↑↑Q-T interval.

Erb test
⇓
Ms. contraction at current < 5mA.

Manifest Tetany
↓Ca < 7 mg

CNS
↓
Convulsions
± only neonates & infants.

PNS

Motor
- **Carpo-pedal spasm**
  ⇓
  Plantar-flexion &
- **Laryngismus stridulous**
  ⇓
  Croup & cyanosis

Sensory
⇓
Para-thesia & numbness. (circum-oral) early sign

Treatment of Tetany

Emergency

ABC + …

Anti-Convalsants + O_2 in laryngismus stridulous

1) Ca Glucanate: 10% 10 ml V. slowly + Monitor ↓HR
2) Mg Glucannate.
3) Psychogenic hyper-ventilation ⇒ Re-breathing in bag.

Maintenance Th.

- Ca Intake. (Diet)
- $CaCO_3$. (OS-Cal)
- Vit. D_3 (1 α hydroxylase)

Invest. for Tetany:

1) ↓Ca Mg pH. (↓Vit. D)
2) ↓ PTH + ↓ Nephrogenic cAMP.

Diabetes Mellitus

DM is th M/C cause of:

- CRF. (ESRD)
- Amputation.
- Blindness.

	Type I	Type II
Cause	β-cell destruction *"Absolute Insulin def"*	Insulin Resistance *"Relative Insulin def."*
Etiology	**Auto-immune Abs against (ICA)** *β-cell dt Viral infection / A. Feeding* *DM occurs after destruction of > 80% of B cells*	**Obesity (visceral / central)** *→ Adipocyte secret (leptin / TNF / resistin)* *→ ↑ Insulin level.*
C-peptide	×	✓
• Age	< 30 ys – Thin	> 40 ys. – Obese
• FH	*Uncommon (5 %)*	*Common (25 %)*
• HLA ass.	HLA $DR_{3,4}$	×
• Ass. Immune D.	Thyroiditis / lupoid hepatitis / pernicious an.	×
pathology	***Insulinitis*** *"Isltes infiltrated e **lymphocytes**"*	***Islet Amyloid deposition*** *"dt **Amylin** co-secreted e insulin"*
Keto-Acidosis	***Prone*** *(Occurs without ppt. factors)*	***Un-common**...except in Stress conditions* *(infections – MI – surgery – pregnancy)*
Treatment	*Insulin ± Immunosuppressives.*	*Oral hypo-glycemics → if failed → Insulin.*
	Honey-moon phase *"In early glycimic control (insulin doses are ↓)* *dt endog. Insulin release from the residual β-cells.* *→ Then complete destruction → Absolute Insulin def."*	

MODY: TTT. by

1) *Diet.*
2) *Oral hypo-glycemics.*
3) *Insulin..*

2ry Causes of DM:

1) **Pancreatic:**
   - Ch. Pancreatitis.
   - Cystic fibrosis.
   - Hemochromatosis.
2) **Endocrinal:**
   - Cushing $.
   - Hyder-Thyroidism.

Clinical Picture of DM

- **Asymptomatic**
  - Discovered Accidently during Routine Invest.
- **Acute**
  - 3 Ps
    - poly-uria.
    - poly-depsia.
    - poly-phagia
  - DKA if Not Recognized
- **Sub-Acute**
  - Blurry Vision
- **Complications**
  - see later

NBs:

1) Onset of DM in Children → Nocturnal Enuresis.
2) Onset of DM in females → pruritis vulvae & Vaginitis.
3) DM should be suspected in:
   - Obese pt. → +ve FH of DM.
   - P. Neuropathy → Tingling & Numbness.
   - Female pt. → large babies – polyhydraminos – Un explained fetal death.

2ry Causes of hyperlipidemia

1) Endocrinal:
   - DM → ↑TG
   - Hypo-Thyroidism → ↑Cholesterol.
2) Renal:
   - Nephrotic $ → ↑ LDL & Cholesterol.
   - CRF → ↑TG.
3) Storage D → Glycogen SD. – Gaucher's D.
4) Drugs.
   - ββ (NS) → ↑ TG
   - Thiazides → ↑TG.
   - Alcohol → ↑TG
   - Steroids – OCP – Obesity.

Diabetic Complications

Acute

Infections

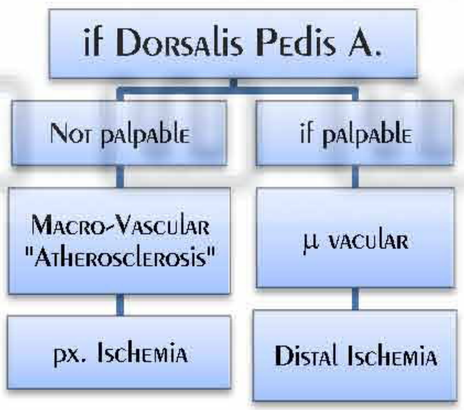
- ↓ CMI / HMI
- ↓ Vascularity.
- ↑ Org. colonization.

Comas

(C below)

Infections in

1) Skin → *staph - M-C candidiasis, furuncle / Carbuncle.*
2) GB → *Emphysematous cholocystitis.*
3) UT → *PN - emphysematous.*
4) Lung → **TB** / *pneumo-coccal.*
5) **Mucormycosis.**



Chronic

Vascular

μ-vascular ⇓

Diabetic Triopathy

1) Nephropathy (1)
2) Retinopahty (2)
3) **Neuropathy (3)**

Macro-vascular ⇓

Atherosclerosis

1) Stroke – TIA.
2) Coronary - Renal.
3) **LL ischemia.**

+ Infections
⇓
Diabetic foot

	Ischemia	Neuropathy
Symptoms	*Claudicating Rest pain*	*Painless*
Inspection	*Trophic changes*	*High arch* *Clawing of toes.*
Palpation	*Cold. Pulsless.*	*Warm. Pulse present.*
Ulcer	*Painful* *Heal & toes.*	*Painless* *Plantar.*

Skin

Non-specific

1) *Infections.*
2) *Neuropathic foot ulcers.*
3) *Xanthomas.*

Diabetic Dermatosis

1) **Necro-biosis lipoidica:**
   erythematous patch on skin of tibia → yellow → atrophy → ulcer.
2) **Diabetic Dermoapthy.**
   (pigmented pre-tibial papules)
3) **Diffuse granuloma annulare.**
4) **Acanthosis Negricans.**
   (Insulin R. & Br. Carcinoma)

Causes & Path. of DM complications

1) **Aldole Reductase** → ⊕ **Sorbitol pathway** → *(-) ATPase activity & ↓ myo-insitol + Osmosis.*
2) **Glycosylation of Collagen in BVs** → *thick wall / n. lumen* → *ischemia.*
3) It Affects: Renal Tubules - p. nerves. - Hb & plasma pr - Lens.

Other Mechanisms of Vascular Comp.:

- ↓RBCs deformability → Trental®.
- ↑Platelet agg. → Aspirin®.

Diabetic Retinopathy

"µ angiopathy of the Retinal BVs."

Duration & Control dependant

Leakage
"loss of T. junction & pericyte"

1) Aneurysm.
3) Edema.
2) Hard exudates.
"Lipid laden MQ"
3) Hge

Occlusion

1) BM → Thickening.
2) endoth → proliferation.
3) RBCs → sticking.
4) platelets → sticking.

Ischemia & Hypoxia of he Retina

Cl./P = fundus

Non - PDR

As Leakage path.

Pre-PDR

1) Arteries ⇒ attenuated.
2) Veins ⇒ beading & looping.
3) Cotton-whool spots.
4) Blot Hge.

PDR

VE-GF secretion dt severe ischemia

NV D & NV E

- Rupture: Vitreous Hge
- Fibrosis: T RD

NV I = Rubiosis Iridis

- Rupture: Hyphema
- Fibrosis: NV Glaucoma

Other Ocualr Complications

- *Lids → Styes –Xanthelasmas.*
- *Lens → Cataract.*
- *6th CN Palsy.*
- *Retina → D. retinopathy.*

Diabetic Keto-Acidosis

prophylacti c ABS

no Insulin ..... pt by (infections "mucormycosis" / trauma / **MI** / surgery)

Keto-Acidosis

- mild
  - spont. corrected by Insulin
- sever < 7
  - $NaHCO_3$

Metabolism

- ⊕ lipolysis
  - ⇓
  - ↑ FFA
  - ⇓
  - ↑ KB
    - Keto-Acidosis
      - ⇓
      - hyper-ventilation "Kussmaul br."
    - Acute Abdomen
      - ⇓
      - Nausea / Vomiting
- ↑ G Output
- ↓ G Uptake
  - ⇓
  - hyper-glycemia
  - ⇓
  - ↑ Osmolarity
  - ⇓
  - Osmotic Dieuresis "poly-uria"
  - ⇓
  - **Dehydration**
    - Coma also dr CNS (-) by KB
    - ↓ RBF
      - ⇓
      - ↓ excretion of K+/H+
      - ↓
      - hyper-kalemia / Acidosis.
    - Hemoconc.
      - ⇓
      - DVT
      - ⇓
      - Thrombo-embolism
    - Dry Skin

IV Fluids = 6L

- saline 1st
  - 3L to replace ECF
    - Isotonic 1st
    - 1/2 Tonic if.. s. Na > 155
      - not give 1st t to avoid osmotic hemolysis of RBCs.
- Glucose 5% "when BS ↓ to > 250 mg/dl"
  - 3L to replace ICF
    - to Avoid hypoglycemia
    - to support Osmolarity to avoid sudden ↓BS
      - Cerebral Edema. "Dysequilibrium $"

Insulin

Regular low dose 5U/hr.

- to Avoid hypokalemia bec.
  - low dose Insulin
    - ↓ Glucose output e minimal K uptake
    - No hypokalemia
  - high dose Insulin
    - ↑ Glucose uptake mainly e ↑K uptake
    - hypokalemia
- When BS ↓ to 250 mg/dL
  - shift to Glucose 5% (see IV fluids)

hyper-kalemia

- Initially dr Acidosis
  - ⇓
  - ↑K Outflux
  - ⇓
  - hyperkalmeia at the beginning.
- Then hypokalemia due to Insulin th. + polyuria.

K Therapy

- ↑K > 5.5
  - Don't give K
- Normal K 3.5 - 5.5
  - 20 mEq/L proph.
- ↓K < 3.5
  - 40 mEq/L
    - 20 to correct the error
    - 20 proph.

LMWH "Clexan SC"

Comas in DM

	Hypo-Glycemic Coma	DKA Coma
Insulin level	**Insulin Shock** **Over TTT. & Un-corresponding Diet.** (Insulin Shock / Oral-hypoglycemics)	**Absolute Insulin deficiency** • *Newly presenting DM.* • *Neglect the ttt.* **Relative Insulin def.** *dt Stress – Infection.*
Onset	Acute.	Gradual.
Pulse	Tachycardia + Good volume.	Weak & Rapid.
BP	↑ dt ↑ CA	↓ BP dt dehydration + acidosis.
Skin	Sweaty, pale.	Dry & inelastic. (dehydration)
breath	Normal.	Kusmmaul br. Acetone odor.
Pupils	Dilated.	Not-dilated.
Tongue	Normal.	Dry (under surface of tonge)
Urine	No sugar.	+ve sugar & acetone
IV glucose	Rapid recovery if early.	No effect.
Coma	Irritable.	Not irritable.
Temperature	Normal, hypo-thermia.	Sub-normal.

Hyper-Osmolar Coma

Minimal Insulin def.

- Can't Utilize Glucose → hyperglycemia >1000 → hyper-Osmolarity of bl. → Dehydration (Stroke - MI)
- But Can (-) Ketogenesis → No DKA

TTT.:

1) as DKA exactly.
2) Insulin. "small dose" to avoid Disequilobrium $.
3) LMWH to Avoid ...

Lactic Acidosis

Biguanides in "high dose" in Advanced Liver or Kidney or COPD

- ↑↑↑ Lactic A. → sever metabolic Acidosis
- No hyper-Glycemia No Ketosis

TTT.:

1) Stop the offending drug.
2) Rehydration
3) Isotonic $NaHCO_3$.

Invest. Of DKA:

- **Blood** → **Glucose** > *300.* **pH** < *7.25*
  ↑*Aceto-Acetic & β-OH buteric Acid.*
- **Urine** → *Glucosuria & Ketonuria.*
- **ECG** → *for hyper-kalemia.*

Investigations for DM

Don't depend on Urine Glucose in Diag. of DM due to:

- **Mild DM** → ↑BS but still below Renal Threshold., (170 mg/dL)
- ↑ **Renal Threshold:** as in Old age - long-standing DM & As → ↓GFR → ↑BS conc. > re-absorptive capacity → +ve Glucose in urine.

Urine
"Qualitative Tests by Dipstick"

- **Glucosuria**
  - "false results in (Vit. C - Aspirin)
- **Ketonuria**
  - False +ve in (pregnancy - prolonged fasting - Repeated Vomiting)

Blood

- **Glucose**
  - **LAB**
    - **BS tests** "done during TTT. to Adjust the doses"
      - **FBS** > 126
      - **PP BS** > 200 in OGTT
      - **RBS** > 200
      - On more than 1 occasion
    - **Glycosylated** "Glycemic control"
      - **Hb**
        - long-term Glycemic control for the last 6 - 8 wks & done every 3 ms (long LS 120 days)
      - **Fructosamine**
        - Short-term Glycemic control for 2 - 3 wks to diff. from (Stress or Steroid induced hyperglycemia)
  - **Self-monitor**
    - finger-prick "from side of finger not tip" for tight metabolic control
- **KB**
  - Acetone
  - β OH buteric A. replaced by pH.

OGTT

1) If border line FBS. - Unexplained μ-vascular Diabetic complications.
2) Gestational DM.
3) Abnormal OGTT.

Renal Glucosuria	Alimentary Glucosuria (Lag-Storage Curve)	Flat Response	Impaired Glucose Tol. (IGT)	Impaired Fasting Tol. (IFG)	Gestational DM
Normal BS + Glucosuria at benign ↓Renal Threshold for Glucose **Causes of ↓ R. Threshold:** • Pregnancy. • Fanconi S - RTA. • Heavy metal poison.	hypoglycemia لما ياكل يجيله Early sharp rise in G. > 200 → Renal Glucosuria but PP Glucose < FBS **Causes:** "post-Gastrectomy late Dumping S - Thyrotoxicosis - Advanced LD"	Diff. bet. peak & FBS < 20 **Causes:** (Mal-absorption - Insulinoma - Adrenal hypofunction)	• FBS < 126 but • PP (140 – 199) • Bet. Normal & DM + RF for DM Type II	• FBS 100 – 125 • PP < 140	1st detected during pregnancy in 3rd Trimester (24 – 28 wks.) & limited to it. & return to Normal at least 6 wks. from labor **Diagnosis:** • FBS > 126. • 50 gm Glucose → After 1 hr. > 140 – 150. • 3 hr. OGTT → 100 gm Glucose.

Insulin

Insulin sources

endogenous from β-cell of pancreas as pro-insulin"

- Insulin
- C-peptide = Endog. Insulin "also ↑ by SU"

secretion of Insulin

↑ by
- Oral hypo-glycemics.
- Arginine AA.
- Hyper-glycemia.

↓ by
- Thiaides. BB.
- Phenytoin.
- Somato-statin.

exogenous

- Animal Insulin
  - Beef → 3 wrong AA → Antigenic
  - Pork → 1 wrong AA → Less Antigenic
- Human Insulin
  - Semi-synth. → Modified pork insulin
  - Bio-synth. → r-DNA.

Mech. of action

Insulin ⊕ α-sub-units "binding sites"

⇒ ⊕ β-subunits "traverse CM" & have Tyrosine Kinase Activity

⇒ migration of GLUT4 to cell surface

⇒ ↑G transport to cell.

Actions

- **Rapid (Transport)** ⇓ ↑G, AA – K Uptake by cells.
  - Brian: insulin independent
  - Ms. / fat: insulin dependent
- **Gradual (Anabolic)**
  - **CHO**: ⊕ Glycogenises. (-) Gluconeo-genesis.
  - **Fat**: ⊕ lipogenesis. (-) Ketogenesis. (-) Carntine shuttle in mitochondria. Of liver.
  - **Protein**: ↓ break down. AA uptake by cells.

Insulin preparations

1)	Short acting	Regular. (Crystaline)	Neutral	SC / IV /IM & Rapid Onset →Emergencies eg DKA.
2)	Intermediate	NPH (hagedoen)	..... + protamine	SC only.
3)	Long acting	PZI	.....+ protamine +Zn	SC only.
Insulin mixture		Hymilin Mixtard	70 % NPH 30% Regular	100 Unit / ml

Indications of insulin

Therapeutic Uses

1) Type I.
2) Type II
   - a) After failure of (Diet / exercise / Oral Th.)
   - b) Critical times (surgery / pregnancy / Infection)
3) DKA – Hyper-osmolar coma.
4) Hyper-kalmeia

Diagnostic uses

Hypoth. / Hypoph. axis test.

Insulin ⊕ test for GH.

complications of Insulin therapy

special problems in DM:

- **Infection** → ↑ Insulin dose.
- **Pregnancy** → # Oral hypoglycemic → fetal hypoglycemia
  Shift from single dose to multiple doses.
- **Surgery** → ↑ Insulin dose "Regular" for tight control.

Insulin lypodyst. at site of inj.

change site of inj.

Allergy

urticaria
angiodema
anaphylaxis

1) Change insulin.
2) Anti-histaminic.
3) Topical steroids.

Action

Over TTT.

Hypo-glycemia

1) Oral sugar / candy ASAP.
2) IV G. 50% 50 ml.
3) IM Glucagon (1 mg) → ↑ G release then search for the vein.

pseudo-Insulin R.

"Somogyi ph."

Over TTT. e Insulin

⇓

mild Hypo-glycemia

⇓

⊕ Anti-Insulin h.

⇓

Rebound hyper-glycemia

Hyperglycemia w is ttt. by ↓ Insulin dose & diet control

Under TTT. due to

Insulin R.

"↑Insulin Req. > 200 U/D"

Metabolic $

1) Obesity.
2) HTN as ↑ Insulin:
   a) ⊕ Symp.
   b) Na + H_2O Retention.
   c) Atherogenic.
3) DM.
4) Hyper-lipidemia.

1) Change to human insulin.
2) Wt. reduction. Exercise.
3) ↓ fat in diet.

Salt / H_2O retention

HTN + Edema.

Dawn phenomena:

- **Dawn** → ↑**GH surge**
  → **hyperglycemia**
  → ↑ **dose of Insulin.**

causes of Insulin Resistance:

- **Pre-Rs** → Insulin Abs.
- **Receptors** → Obesity.
- **post-Rs** → failure to ⊕ TK.

Anti-Diabetic Drugs

	Hypo-Glycemics		EuGlycemics	
	Repaglinide	*sulphonyl urea*	**Biguanides**	**Acarbose**
Mech.	*As SU by ↑Insulin Release at meal times.*	***Insulin release from β-cell*** *(insulin secretagogue)* → ⊕ ATPase K channels → membrane depolarization. → open Ca channels → Insulin R.	1) ↓Intestinal G. absorption. 2) ↑conv. of G. to lactic A. 3) ↓hepatic G output. 4) Insulin senstizer.	***Competitive (-) to α- Glucosidase*** → ↓ conv. of oligo to mono-saccharide → ↓ G. absorption. → ↓PP hyper-glycemia.
S/E	غالي و أهبل	**2H + WC** 1) Hypo-glycemia → (Glabinclamide) 2) HS → Allergy. 3) Wt. gain → insulin is anabolic. 4) CVS → VC & ECG changes. *Except with Glimipride, "bec. it binds to specific Rs."*	1) **Lactic acidosis** esp. in liver & kidney D. → so give Rosiglitazone. 2) **GIT upset:** • Metallic tatse. • Dyspepsia - Diarrhea.	1) Abd. Distention 2) Flatulence. 3) Diarrhea.
Uses	Type II	Type II only	Type 1 & 2	with SU who can't tolerate Biguanides
Eg.	**Rosiglitazone: (Glustin®)** 1) *Insulin senstizer.* (PPAR-γsub-unit) 2) *↓hepatic G output.* 3) *As Biguanides but doesn't cause LA ⇒ so used in liver & renal D.*	1st Gen. "Tolbutamine" → Not potent → easily displaced from PP → many drug interactions. 2nd Gen. "see below" → 150 X potent → ↓ disp. from PP → less drug interactions	**Metformin =** **Cidophage® or Glucophage®**	1) ↓PP hyper-glycemia. 2) No hypo-glycemia / no wt. gain. 3) ↓insulin R. **Eg. Glucobay®**

1) Glipizide	short acting.	Minidiab
2) Gliclazide	Intermediate. "Good."	Diamicron
3) Glabinclamide	long acting. "Bad" → hypoglycemia in liver or kidney D.	Doanil
4) Glimipride	bind to specific Rs. →No CVS S/E. 1) On/ Off mech. • *Rapid insulin release* → ↓PP hyper-glycemia. • *Rapid shutdown* → ↓risk of hypo-glycemia 2) Long duration (24 hr.) → Given once/day → Good comp.	Amaryl

Insulin Therapy in Type I

- **Twice Daily Regimn**
  "Conventional" ..if failed
  - 0.5 → 0.8 IU /Kg
    1st 2 doses start by 15-20 U/d. & ↑ gradually to adjust the dose.
    - Best method: **Mixtard** → Twice daily
      (70% NPH + 30% Crystaline)
      - الصبح قبل الفطار 2/3 — 30 U
      - بالليل قبل العشاء 1/3 — 15 U
- **Multi SC inj.**
  "pen Injection device"
  - 75% of dose → Regular
    - Taken as the following:
      - 35% → فطار
      - 20% → غذاء
      - 20% → عشاء
  - 25% of dose → NPH or long acting
- **Infusion devices**
  - Basal infusion allover the day with Additional Meal doses infused by the pt.
- **Pancreas Transplant**
  - If renal transplant is required in Diabetic Nephropathy
    - Long-term use of Cyclosporin for Grafted Kidney & Pancreas.

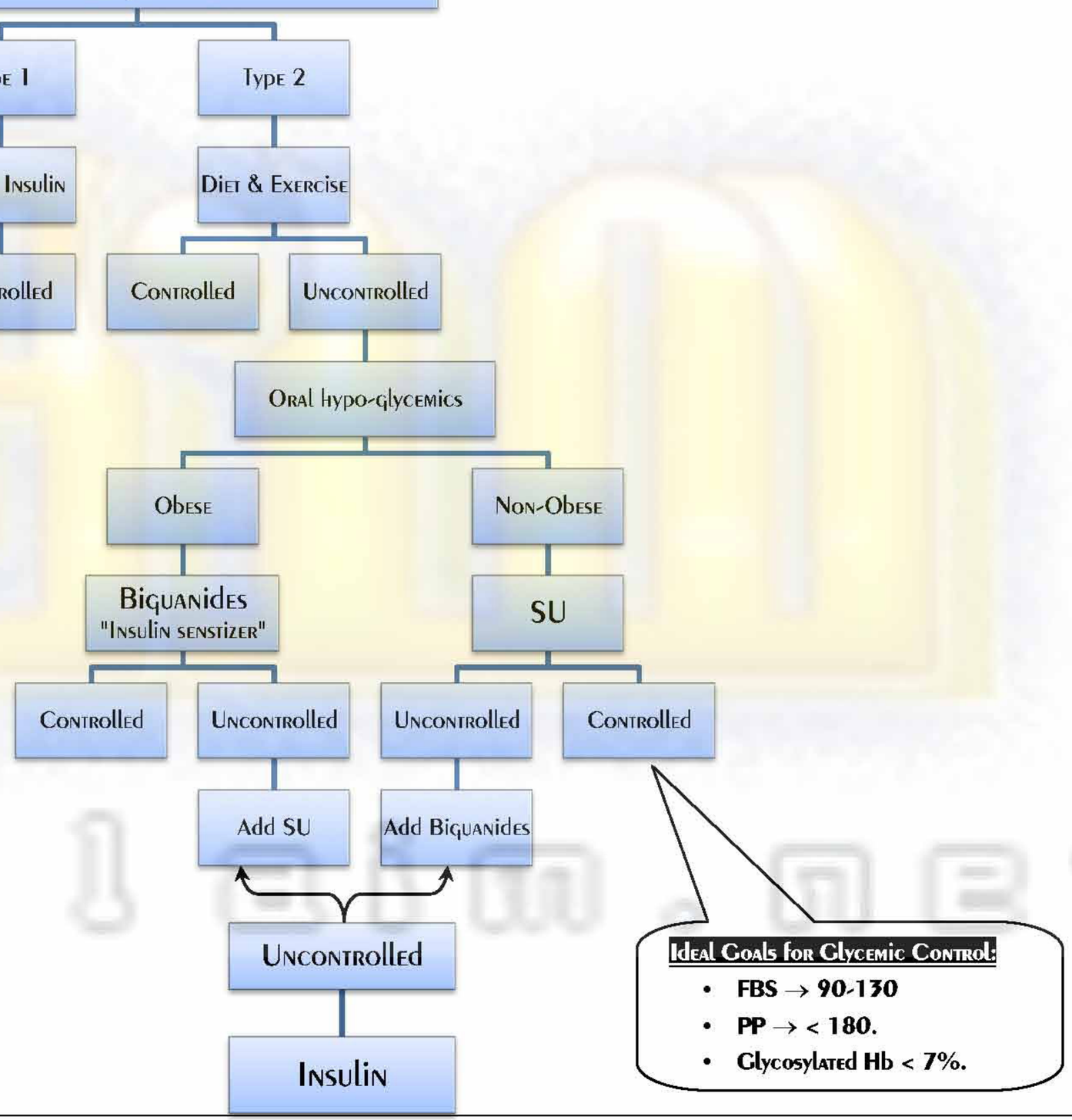
Treatment of DM

	Type I	Type II
Diet	1) M…36 Kcal / kg 2) F…34 Kcal/kg. 3) Non-nutritive sweeteners. "candril".	Obese: Metabolic $ Wt. reduction – Exercise - ↓ fat in diet.
Prev.	1) Neonatal → CM deprivation. 2) Imm. Supp. → Cyclosprins. 3) Anti-oxidant.	1) Diet control after 30 ys. 2) Metformine → Insulin sensitizer. 3) ACE-I → ↓ Insulin R. 4) Anti-oxidants.

Treatment Approach for DM p. 81

Treatment pathway for DM

"New patient"



Brittle Diabetes

"Unpredictable fluctuations of blood glucose ±ketoacidosis ±recurrent hypoglycaemic episodes"

Management of Brittle Diabetes:

1) *Hospitalization.*
2) *Insulin "Regular" at regular interval e.g every 6 hours.*
3) *Insulin pump.*
4) *Treatment of cause.*

Causes of Recurrent Hypoglycemia

1) *Over treatment with insulin.*
2) *Low renal threshold for glucose.*
3) *Endocrine causes e.g pituitary or adrenal insufficiency.*
4) *Gastroparesis due to autonomic neuropathy → early satiety so Add Motilium b4 meal by 1 hr.*
5) *Renal failure.*
6) *Uncooperative, unintelligent patient.*

Causes of Recurrent Keto-Acidosis

- *Inappropriate insulin combinations.*
- *Inter-current illness e.g unsuspected infections.*
- *Unknown etiology.*

Causes of Recurrent Hyperglycemia

As ketoacidosis + somogyi + dawn phenomena.

Hypoglycemia

Triad ⇒Whipple's triad for Diagnosis:

1) ↓*BS < 45-50 mg/dl.*
2) *Manifest. Of hypoglycemia.*
3) *IV Glucose ⇒ Good response.*

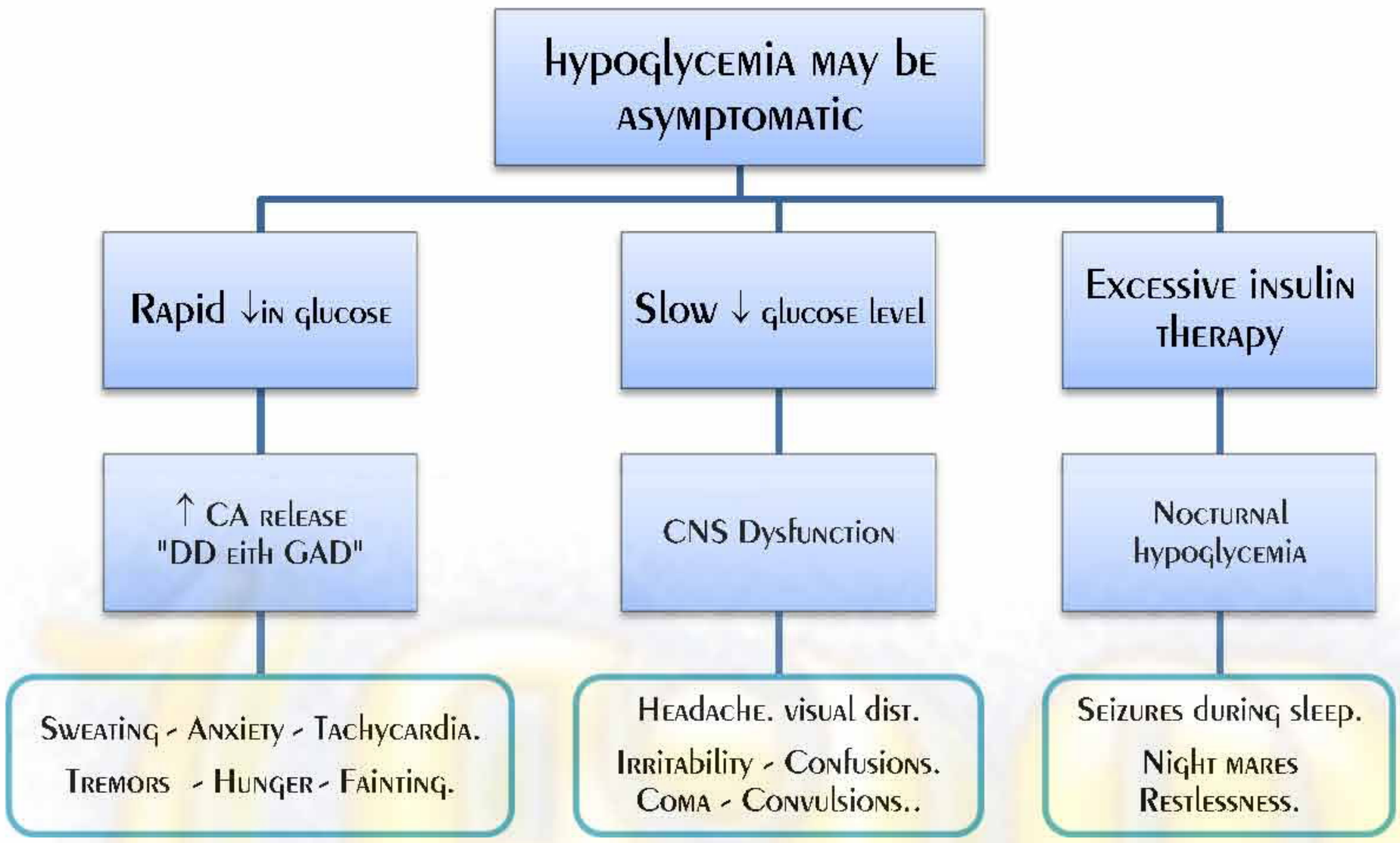
Types of Hypoglycemia

Fasting Hypoglycemia	Postprandial hypoglycemia
• **Tumor** = *Insulinoma, hepatoma.* • **sever illness** = *LCF, CRF, anorexia nervosa.* • **Drugs:** *Insulin, Oral hypoglycemic.* **↓↓ Hormonal:** *GH, Epinephrine, Cortisol.* *(Addisonn's D / Panhypopituitirism)*	• **Alimentary hypoglycemia** *eg. Dumping $ after gastric surgery.* • **Functional hypoglycemia.** • **Reactive hypoglycemia** *dt ↑↑insulin after CHO diet.* • **Galactosemia, fructose intol., ethanol.**

Important Causes of Hypoglycemia

Insulinoma	Insulin therapy	Oral hypoglycemic SU no Biguanides	Postprandial Hypoglycemia
• **HYPO-GLYCEMIA.** • **↑ INSULIN +** • **↑ C PEPTIDE.**	1) HYPO-GLYCEMIA. 2) ↑ INSULIN & 3) ↓ C PEPTIDE.	• HYPO-GLYCEMIA • ↑ INSULIN. • ↑ C PEPTIDE.	***AFTER GASTRECTOMY*** → *rapid glucose absorption* → *↑insulin, glucose metabolized rapidly but insulin remain ↑↑* → *hypoglycemia 1-2 hours PP.*
• **CT SCAN, ANGIOGRAPHY.**		SEARCH FOR HYPOGLYCEMICS IN BLOOD OR URINE.	
• **SURGICAL REMOVAL** • **(-) INSULIN = DIAZOXIDE, OCTREOTIDE.**			**TTT.** → FREQUENT SMALL MEALS. (↓CHO & ↑ PROTEIN)

Cl./P of Hypoglycemia



Grades of hypoglycemia:

- ***Mild:*** *aware of hypoglycemia, & **can** treat himself.*
- ***Moderate:*** *aware of hypoglycemia, & **can't** treat himself.*
- ***Severe:*** *Coma. recovery by IV glucose ef glucagon SC or IM.*

Treatment of severe hypo-glycemia

- *Glucose 25% then 10% infusion. Glucagon 1mg IM or SC.*
- *Then → 10% of glucose to keep the glucose level > 100 mg/dl.*

Mild to moderate cases ⇒ oral glucose or, sucrose or 100 ml. of sweet drink

Causes of Hypoglycemia in pt. taking insulin or SU?

- *Missed, delayed or inadequate diet.*
- *Errors in doses or schedule*
- *Gastroparesis (autonomic neuropathy).*
- *Other endocrine disorder e.g **Addison's disease***
- *Factitious.*
- *Unexpected or unusual exercise*
- *Poorly designed insulin regimen.*
- *Mal-absorption or dumping.*

Important Notes in Endocrine

p. 16 DD of *polyuria*

- **Renal**
  - Chronic TIN.
  - Diuretics.
  - DI. (Nephrogenic)
  - Diuretic phase. (ATN)
- **Endocrinal**
  - DM. (Osmotic Diuresis)
  - Cushing → K Diuresis.
  - Conn's → K Diuresis.
  - DI → hypothalamic.
  - hyper-PTH. (Ca Diabetis)
- **Functional**
  - Excess Water Intake.
  - Coffe - Tea - Cola.

p. 25 Myxedema Coma

Cl./P	TTT.
Confusion & Coma Stress Conditions (s. cold – Infection – Trauma)	→ IV Hydro-Cortisone + IV fluids.
• ↓↓ Thyroid H.	→ IV Tri-iodo-thyronine & ↑ Dose gradually
4 H:	
• Hypo-Thermia → VF	→ Hot bags.
• Hypo-glycemia	→ Glucose Infusion.
• Hypo-Ventilation	→ O_2 Th. + Ventilator.
• Heart - Liver - Kidney Impairm.	

p.51 Causes of Hypo-Aldosteronism

- **1ry Adrenal Insuffeciency**
  - Addison's Disease
- **2ry Adrenal Insuffeciency (hypo-pituitirism)**
  - No ↑ACTH Or ↓Aldosterne
- **Hypo-Reninemic (الأصل) Hypo-Aldosternism**
  - defect in Kidney
    - 1) D. Nephropathy.
    - 2) TIN.
    - 3) Obstructiv Uropathy.
- **Hyper-Reninemic Hypo-Aldosternosim (الأصل)**
  - defect in ZG
    - ↓ Aldosterone
    - → ↓NA ↑K
    - → ↑↑ Renin.

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Acute Adrenal Failure due to

Causes	
a) Addisonian Crisis	Stress eg. Operation, Trauma – Infections Addison's D.
b) Sudden Withdrawal of high dose of CS	dr (-) of ACTH → so gradual withdrawal to allow the regain of ACTH secretioin (so ↓10% of dose /wk.)
c) Water house friderichson $	Meningiiocooccal or pseudomonas septicemia → Adrenal hge.
d) Anti-Coagulant Th.	→ Bilat. Adrenal hge.

Cl./P	
Exaggeration Of Addison's D.: 1) Sever hypotension → Coma or Shock. 2) Sever asthenia.	
➢ Invest.	as Addison's D.
➢ Treatment	1) Saline + IV hydrocortisone (100 mg) 2) Hypo-glycemia → Glucose.

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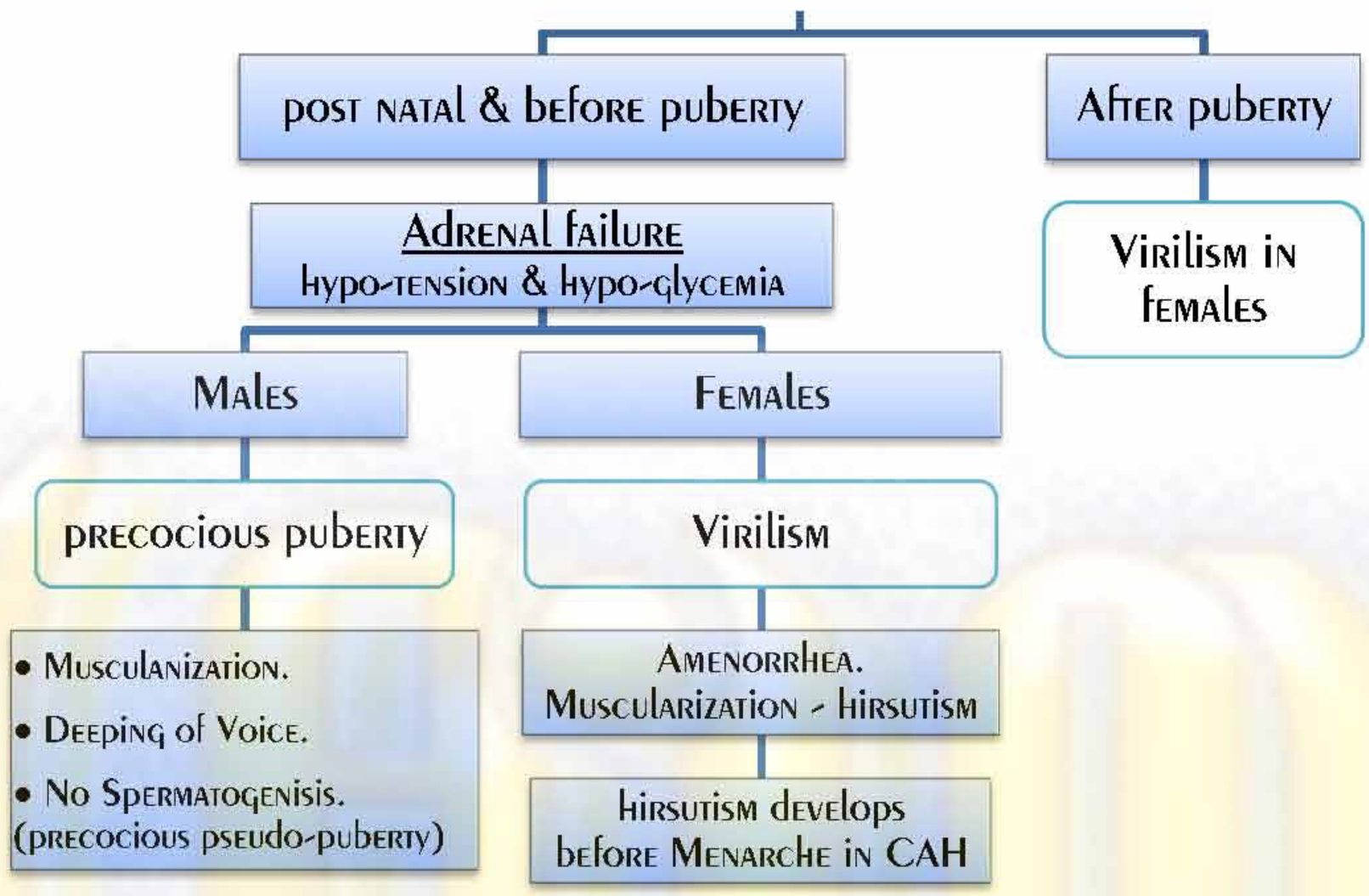
DD of Hyper-pigmentation:

1) Cushing D. (↓ACTH)
2) Familial.
3) OCP & Pregnancy.
4) Sun Exposure.
5) Hemochromatosis.
6) Addison's D.

Congenital Adrenal Hyperplasia (CAH)

- **AR = Enzymatic defect in the Cortisol synthesis pathway** dt *(↓ 21 or 11 Hydroxylase or 11 E.)*
- (↓ Cortisol → ↑ACTH → shift of steroid precursors to Androgenic H. pathway)

Cl./P of CAH



Causes of Hyper-Aldosteronism