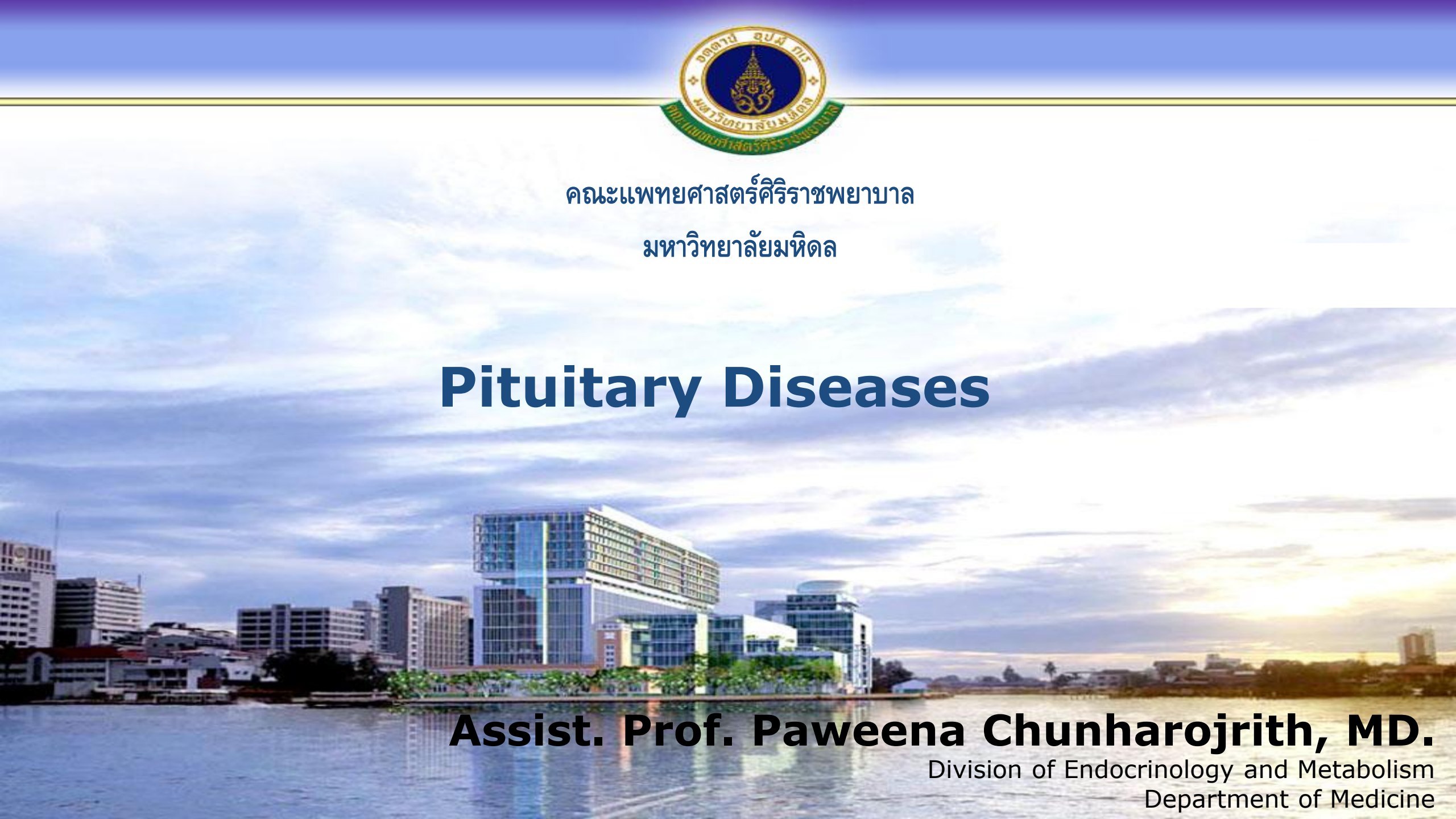


คณะแพทยศาสตร์ศิริราชพยาบาล

มหาวิทยาลัยมหิดล

Pituitary Diseases

Assist. Prof. Paweena Chunharojrith, MD.

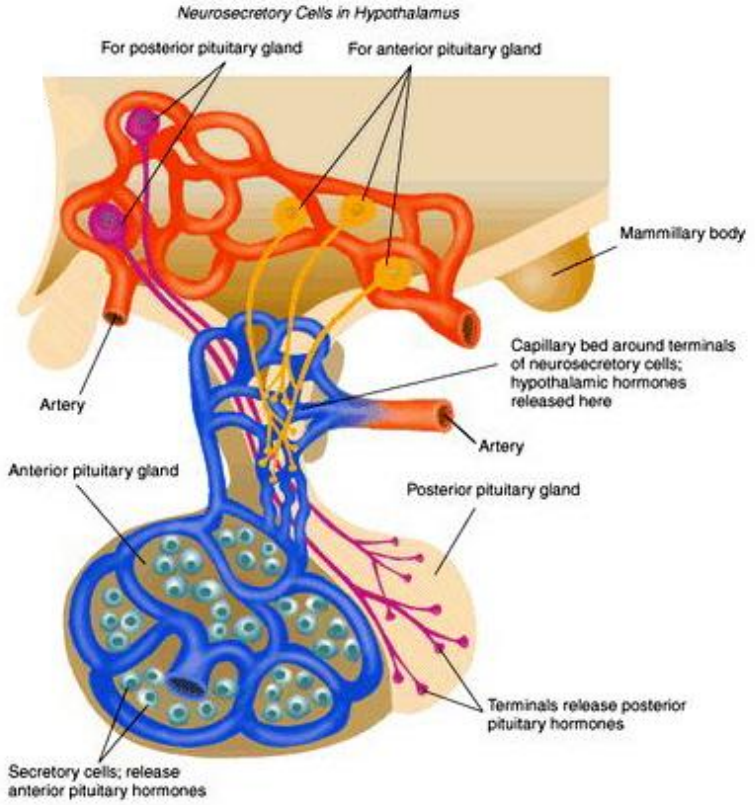
Division of Endocrinology and Metabolism

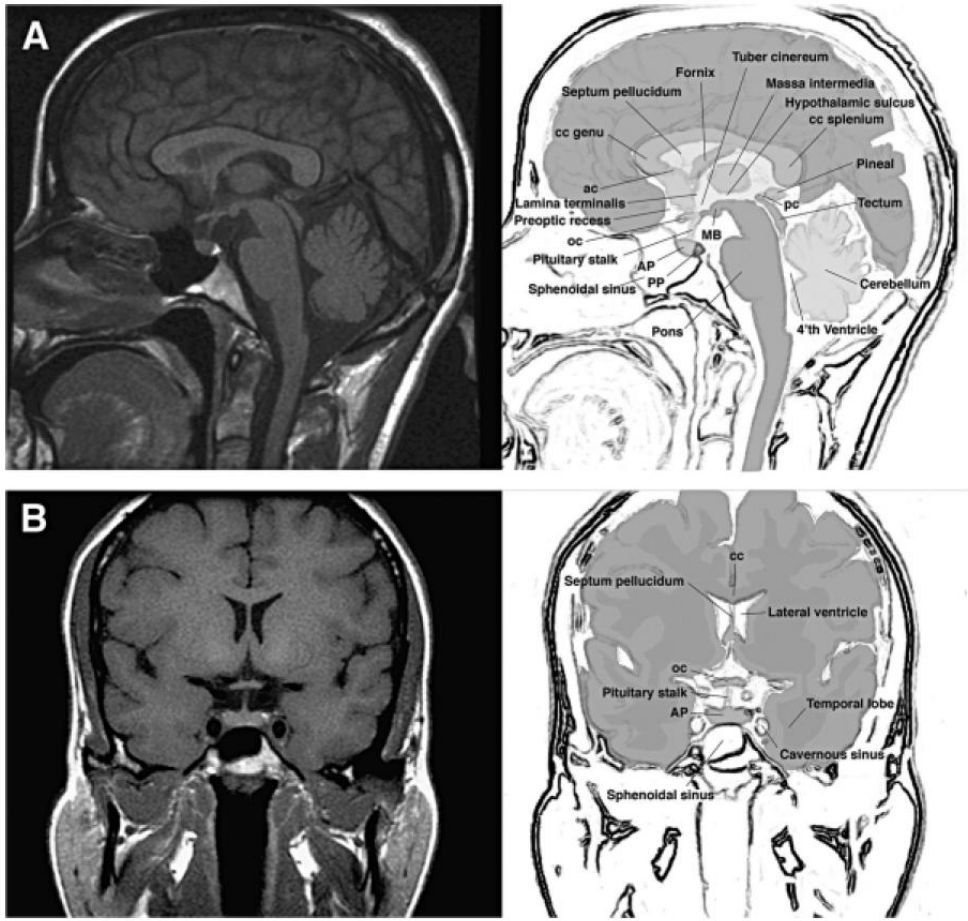
Department of Medicine

Outlines

- Pituitary gland anatomy and function
- Presentation of sellar lesions
- Pituitary tumors
  - Functioning:
    - Prolactinoma
    - Acromegaly
    - Cushing’s disease
  - Nonfunctioning
- Pituitary apoplexy

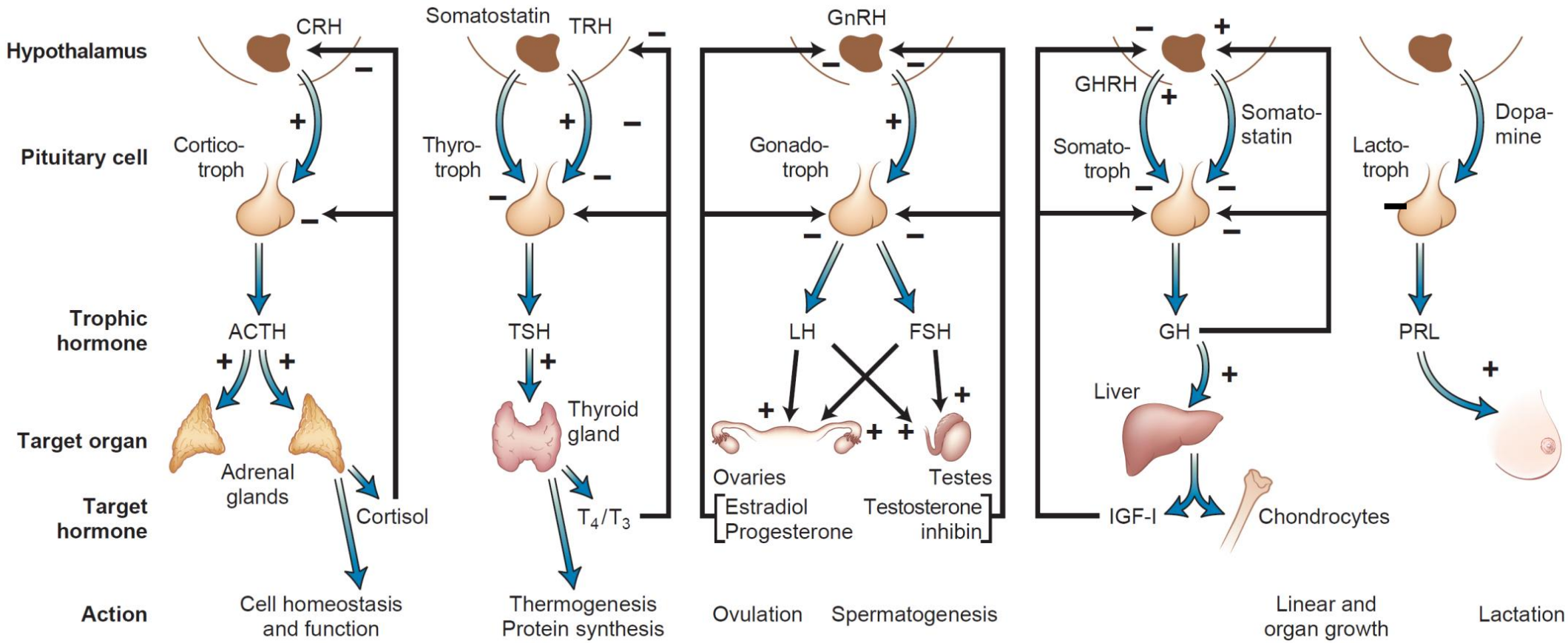
Pituitary gland





Williams textbook of Endocrinology 14th ed; 2020 p 236-302

Hypothalamic-pituitary axis



Williams textbook of Endocrinology 14th ed; 2020 p 184-235

Diseases of the pituitary and hypothalamus

- **Pituitary tumors (adenomas)**: Micro- (<10 mm) vs. macro- (≥ 10 mm)
- **Rathke's cleft cyst**
- **Other sellar tumors**: Meningioma, Germ Cell Tumor, Chordoma, Pituicytoma, Glioma, Metastases (lung,breast), Lymphoma
- **Hypothalamic (suprasellar) tumors**
  - Pituitary tumor with supra-sella extension
  - Craniopharyngioma
  - Meningiomas, germ cell tumor, other primary brain tumors
  - Metastatic tumors
- **Surgery/Radiation** (pituitary-hypothalamus)
- **Ischemic necrosis**
  - Postpartum (Sheehan syndrome), severe shock, sepsis
- **Hemorrhage** (apoplexy)
- **Infectious diseases**: tuberculosis, pituitary abscess
- **Infiltrative diseases**: sarcoidosis, histiocytosis, IGg4 related hypophysitis, chronic lymphocytic hypophysitis

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Presentation of sellar lesions

Hormonal abnormalities

Hyperfunction:

- Galactorrhea
- Gigantism/Acromegaly
- Cushing's disease
- Hyperthyroidism

Hypofunction:

- Growth hormone deficiency
- Hypogonadism
- Amenorrhea/infertility
- Adrenal insufficiency
- Hypothyroidism
- Diabetes insipidus

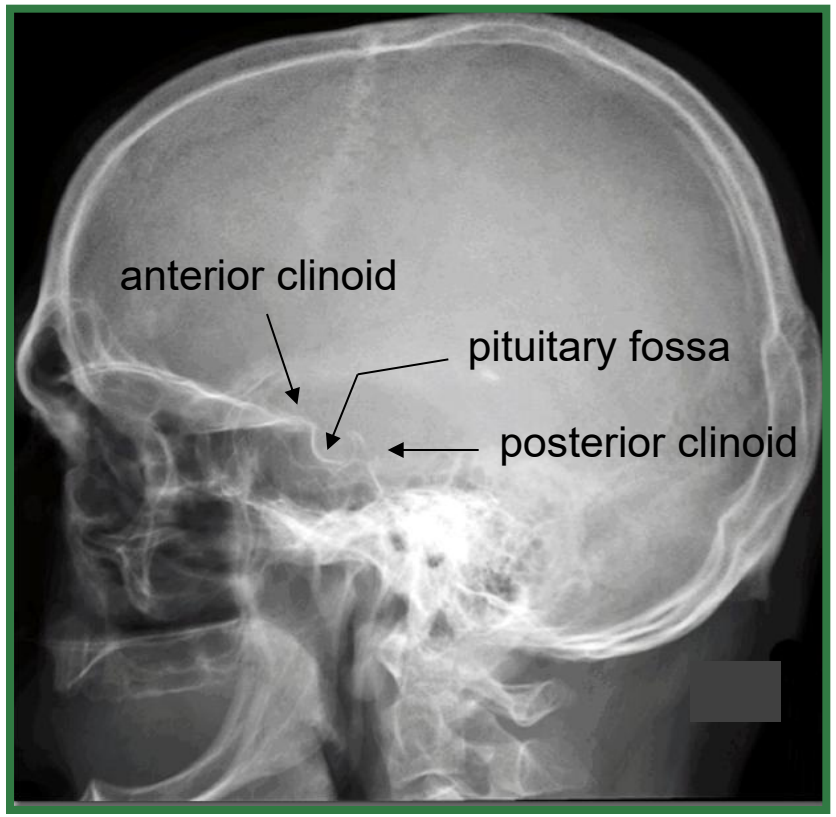
Neurologic symptom (mass effect)

- Visual field defect (bitemporal hemianopia)
- Visual diminution
- Optic atrophy
- Diplopia
- Trigeminal neuralgia
- Facial hypoesthesia

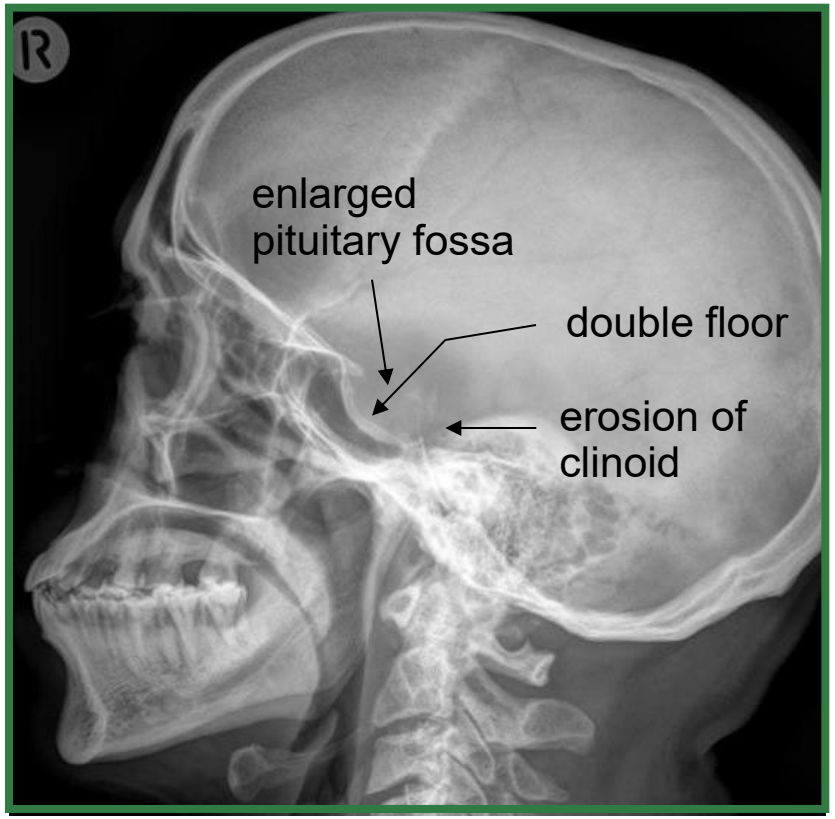
Incidental findings

- Radiological abnormality
  - Plain skull x-ray
  - CT scan
  - MRI scan

Skull x-ray

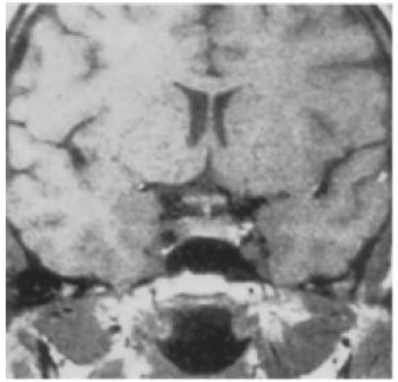


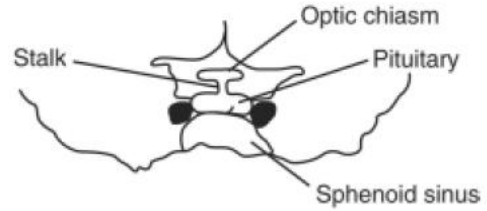
NORMAL

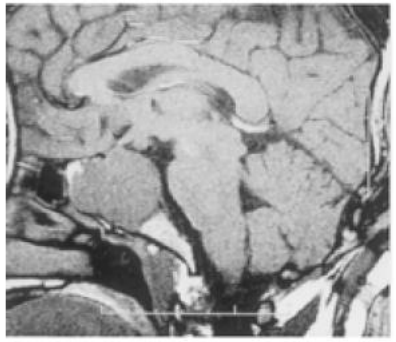


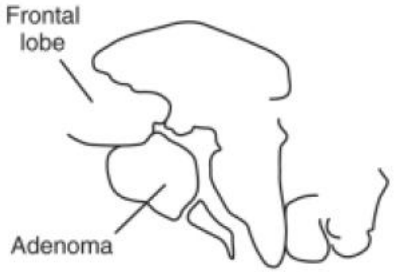
PITUITARY
MACROADENOMA

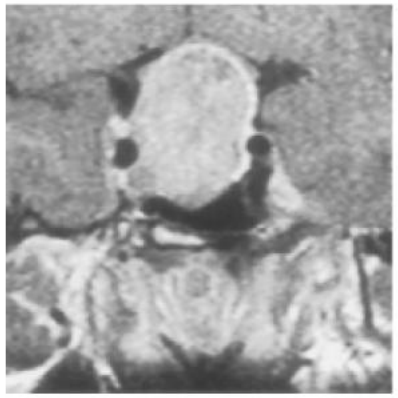
MRI scans: pituitary protocol

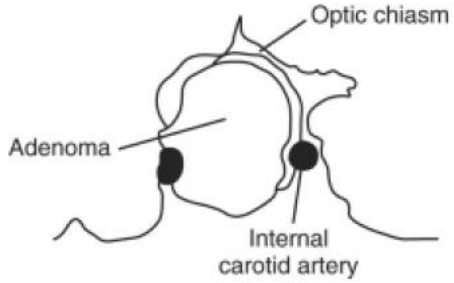












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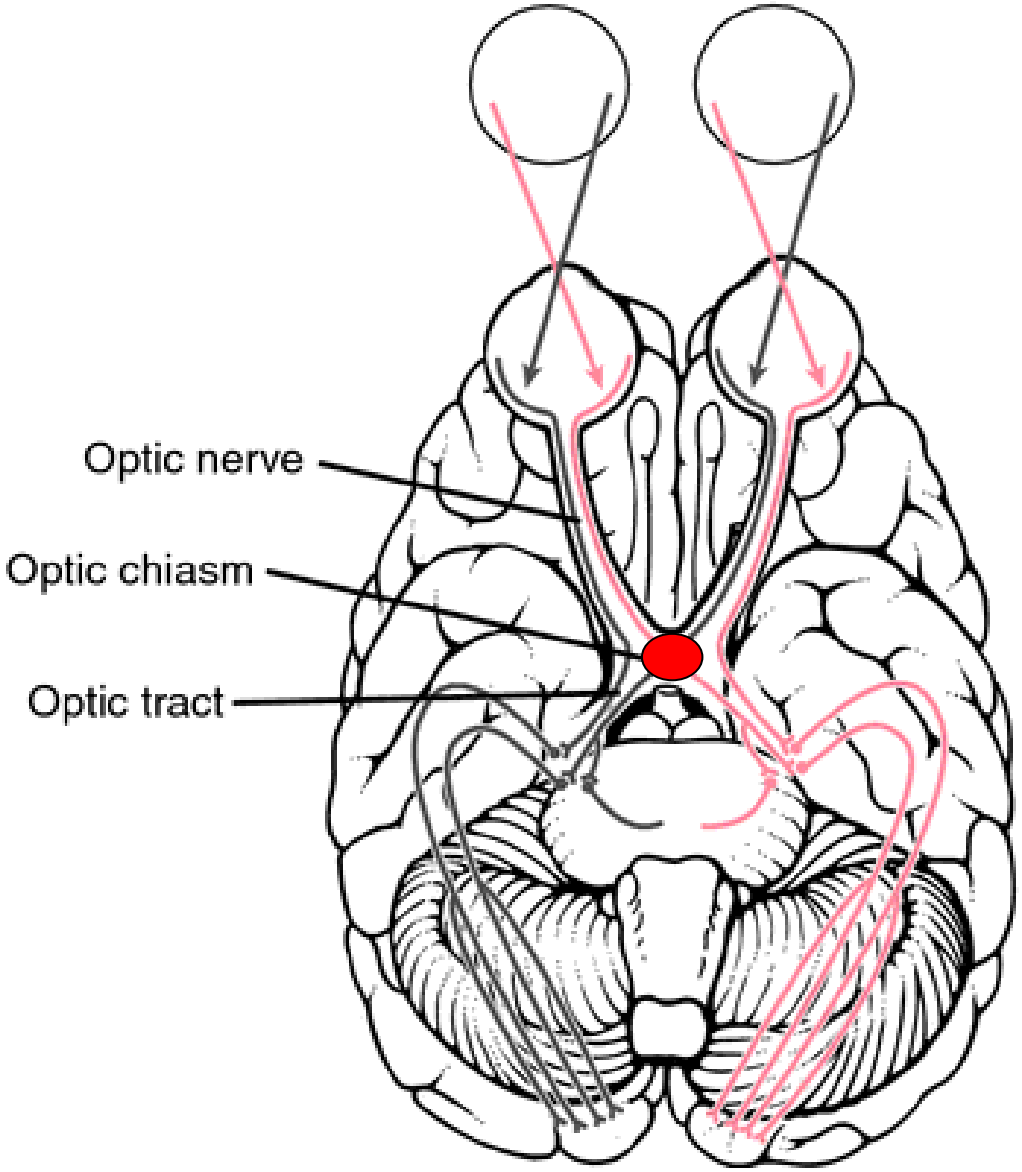
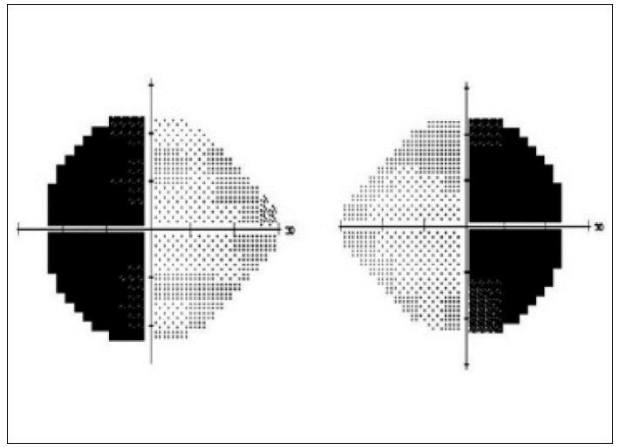
Bitemporal hemianopia





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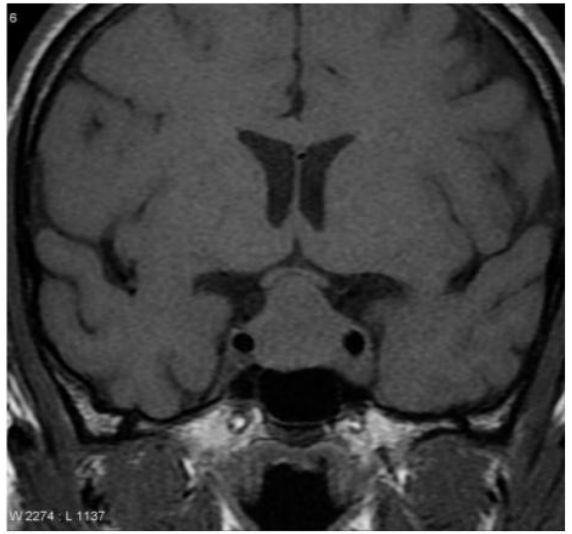
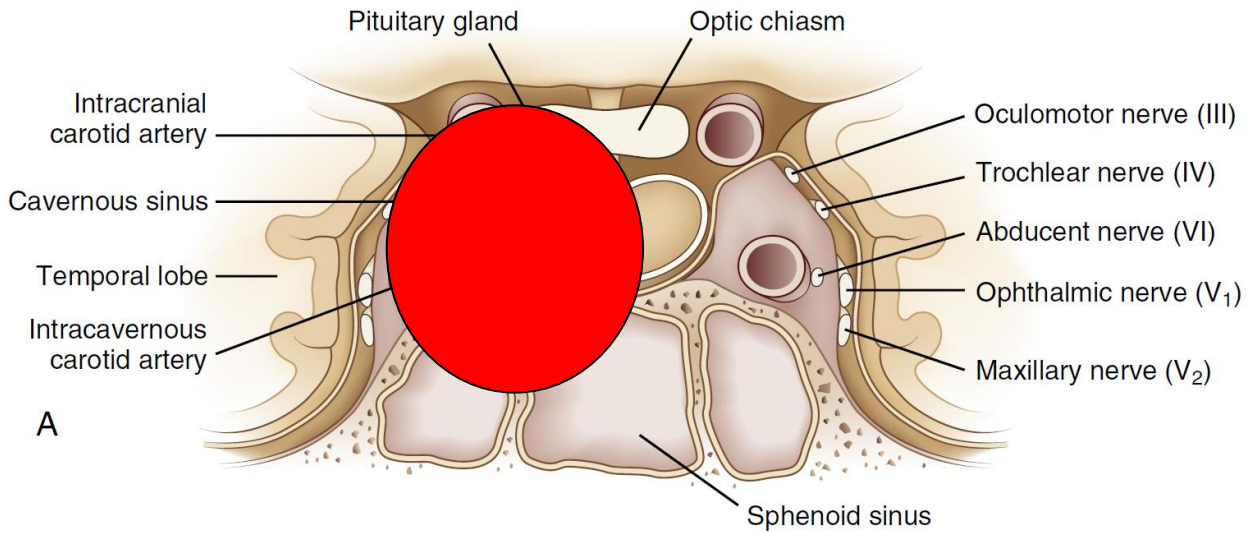


Cavernous sinus syndrome

- Chemosis
- Conjunctival edema
- Proptosis
- Exophthalmos
- Ophthalmoplegia
- Ptosis
- Trigeminal sensory loss
- Loss of facial sensation V1 and V2



Williams textbook of Endocrinology 14th ed; 2020 p 236-302

Spectrum of pituitary adenomas

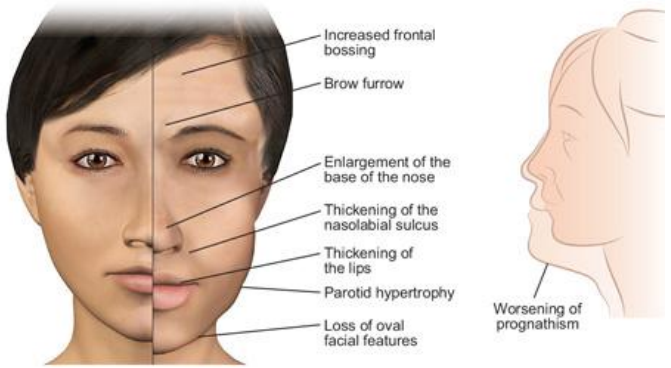
Clinically obvious	• Typical physical features of excessive hormonal hypersecretion
Clinically subtle	• Subtle physical features of excessive hormonal hypersecretion
Clinically silent	• Elevated of serum concentration of pituitary hormone but not even subtle clinical manifestation
Silent	• Type of adenoma identify only by immunostaining: normal serum concentration of hormone

Spectrum of pituitary adenomas

Clinically obvious	Functioning pituitary adenoma
Clinically subtle	
Clinically silent	Clinically Nonfunctioning pituitary adenoma
Silent	

Clinically silent somatotroph tumor

Classification	Acromegalic features	Serum IGF-1	GH immunostaining
Clinically obvious			
Clinically subtle			
Clinically silent			
Silent			



Pituitary adenoma classification

Functioning adenoma

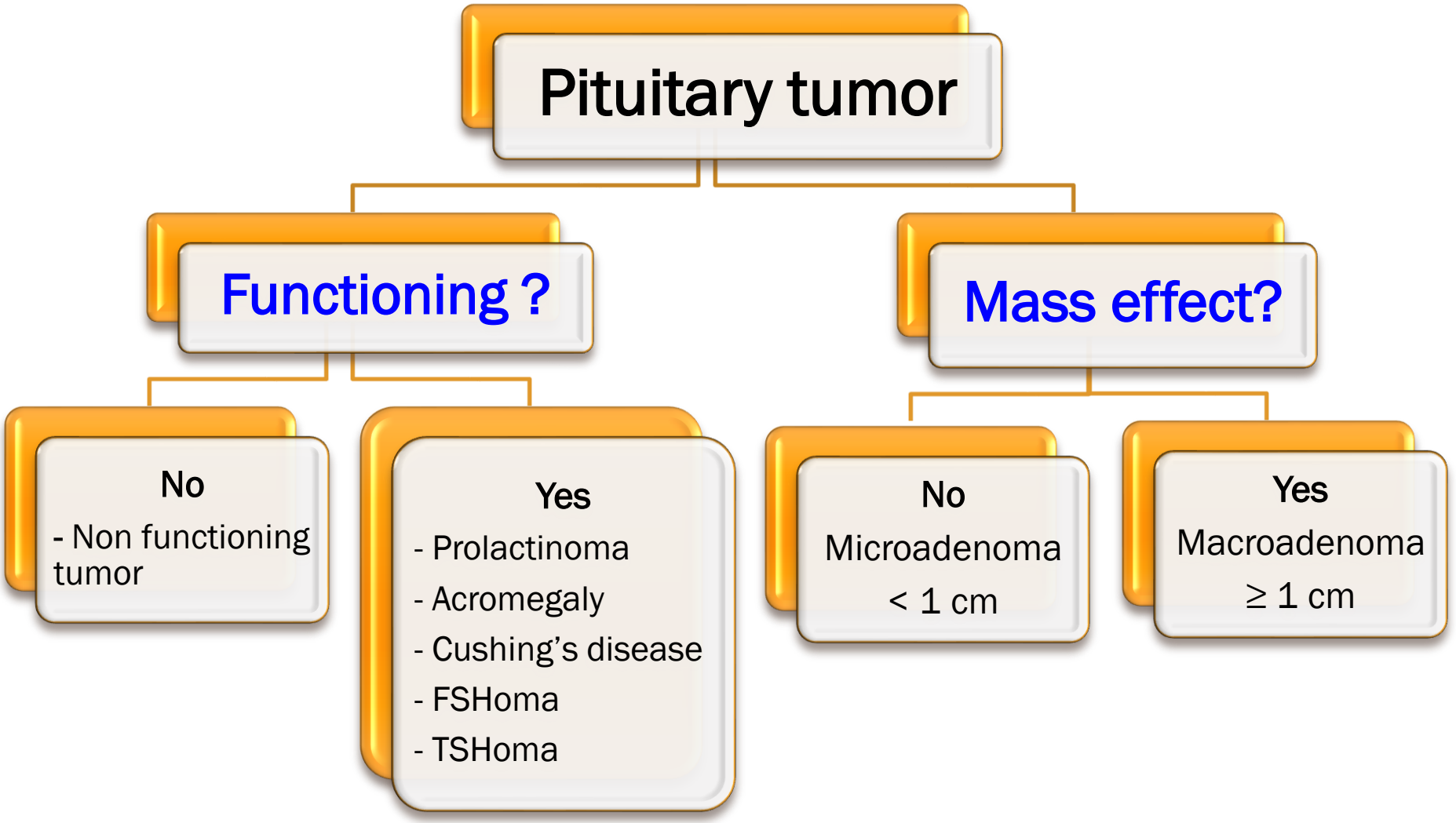
- **Produce & Secret Hormone**
- Lactotroph adenoma: PRL
- Somatotroph adenoma:GH
- Corticotroph adenoma:ACTH
- Gonadotroph adenoma:FSH/LH
- Thyrotroph adenoma:TSH

Clinically nonfunctioning adenoma

- **May or may not produce hormone**
- **No hormone secretion**
- Null cell adenoma
- Silent gonadotroph adenoma:FSH/LH (most common)
- Silent somatotroph adenoma:GH
- Silent corticotroph adenoma:ACTH

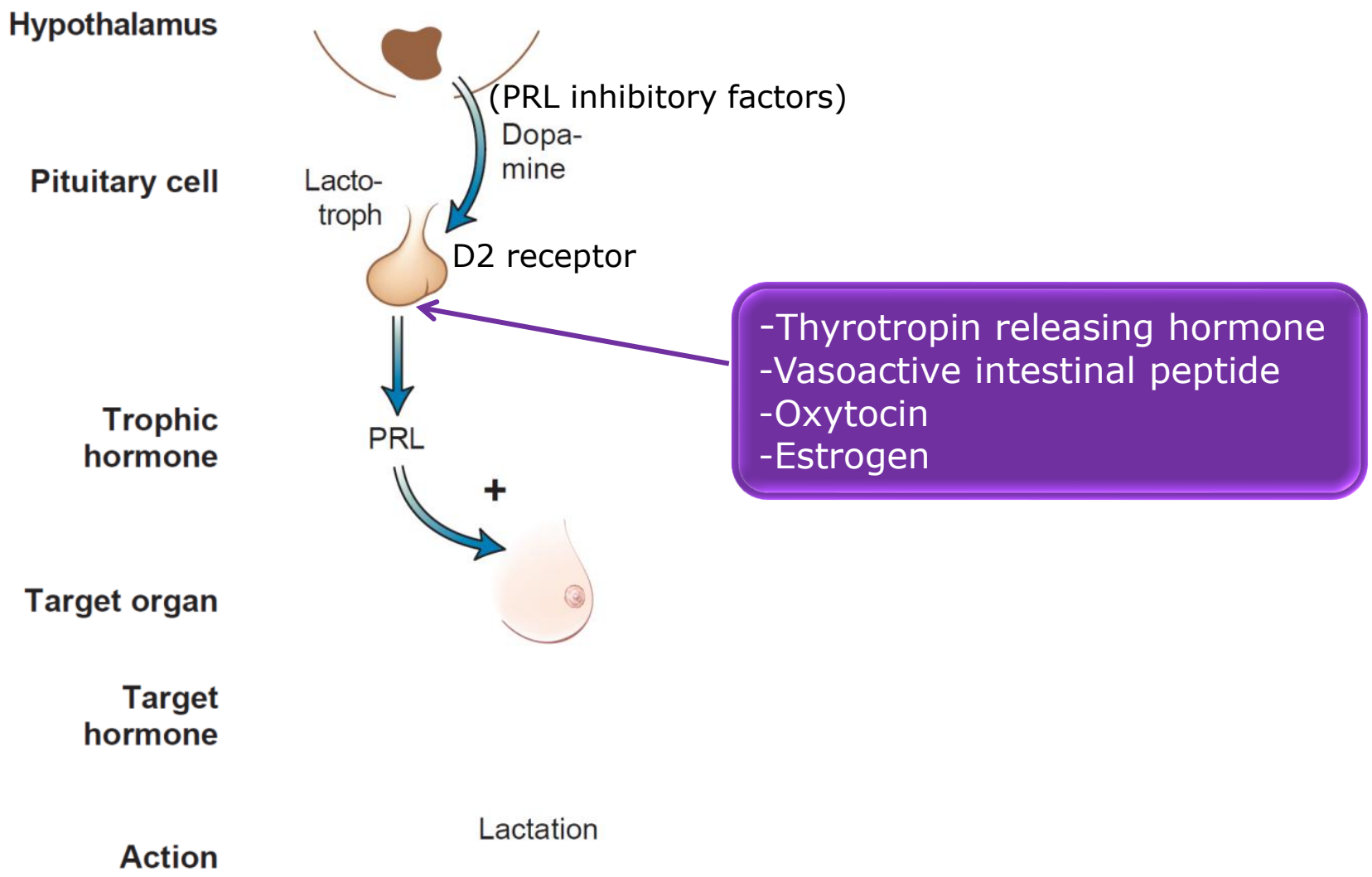
Williams textbook of Endocrinology 14th ed; 2020 p 236-302

Pituitary tumor



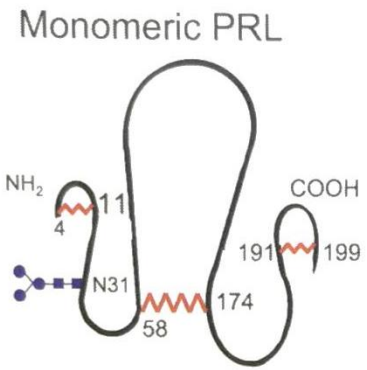
Prolactinoma

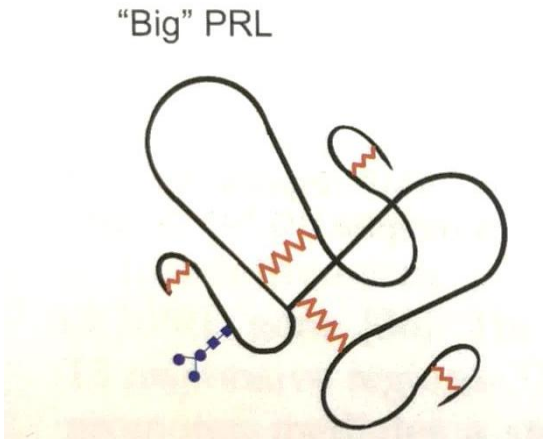
Hypothalamic-pituitary-mammary axis

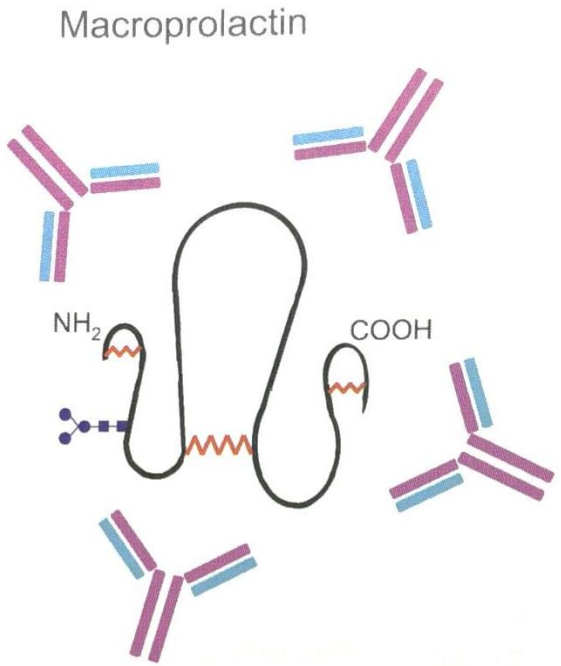


Prolactin proteins in the serum

Type of PRL	Size	Distribution
Monomeric PRL	23 kDa	85-95%
Big PRL	50-60 kDa	10%
Macroprolactin	150 kDa	5%







Causes of hyperprolactinemia

Physiologic

Pathologic

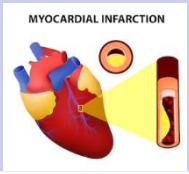
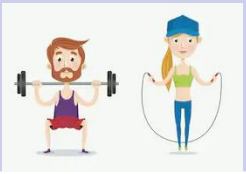
- Systemic diseases
- Hypothalamic diseases
- Pituitary diseases
- Neurogenic
- Ectopic prolactin production

Macroprolactinemia

Drug induced

Idiopathic

Causes of hyperprolactinemia

Causes	
Physiologic	**Pregnancy (PRL levels 200-500 ng/ml)**
• Pregnancy; lactation; stress; sleep; coitus; exercise; venipuncture	    
Pathologic	
Systemic diseases • **Primary hypothyroidism**	**PRL levels are usually < 100 ng/ml** -Mild elevation of PRL (40% overt, 22% subclinical) -An increase in TRH levels, which in turn stimulates PRL secretion; reduced PRL clearance; decreased sensitivity to the suppressant effect of dopamine on PRL synthesis
• **Adrenal insufficiency**	-Glucocorticoids have a suppressible effect on PRL gene expression and PRL release
• **Renal insufficiency**	-30% CKD, 80% on HD, Correction of renal failure by transplantation results in normoprolactinemia, sometimes within days - Decreased clearance and increased production of PRL as a result of disordered hypothalamic regulation of PRL secretion.
• **Cirrhosis**	-16-100% in alcoholic cirrhosis, 5-13% in nonalcoholic cirrhosis

Importance of cannulated prolactin test in the definition of hyperprolactinaemia

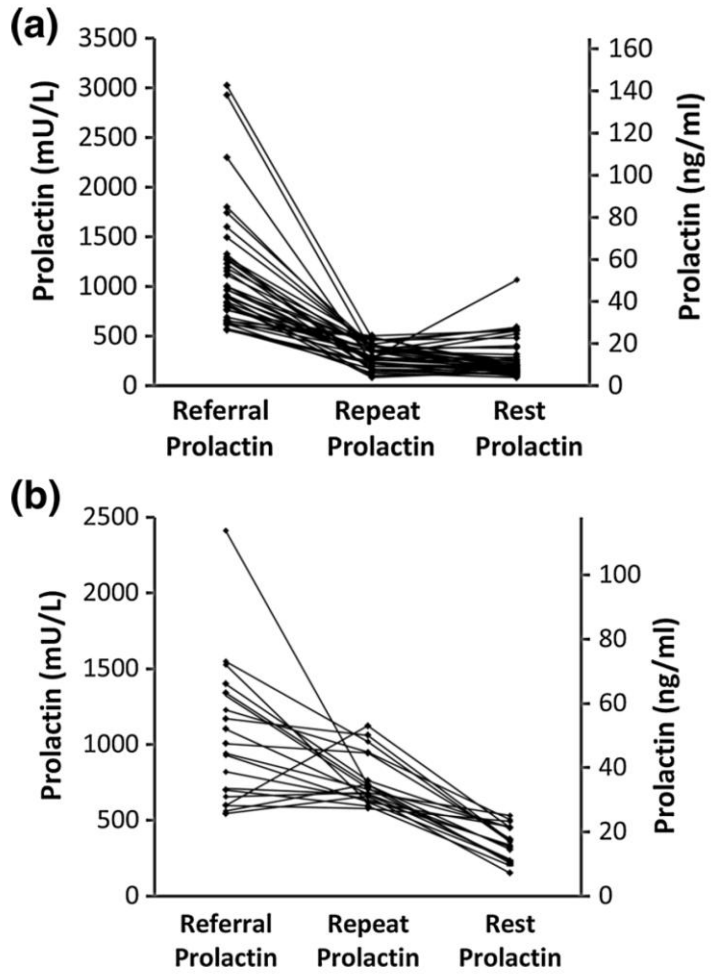


Fig. 2 Normalisation of serum prolactin concentration **a** with repeat (n = 41) and **b** following 120-min rest (n = 23)

Pituitary 18, 319–325 (2015).

- Stress (for example, due to venipuncture) can induce a twofold to fourfold rise in serum levels of prolactin that lasts for <1 h.
- Repeated or cannulated prolactin venipuncture sampling for testing is recommended with serum levels of prolactin less than five times ULN or if an influence of stress is suspected.

Nat Rev Endocrinol. 2023 Dec;19(12):722-740.

Causes of hyperprolactinemia

Causes	
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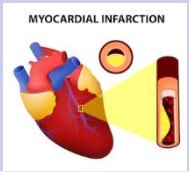
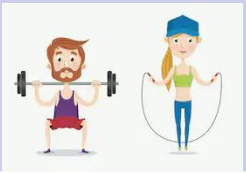
• Pregnancy; lactation; stress; sleep; coitus; exercise; venipuncture	    
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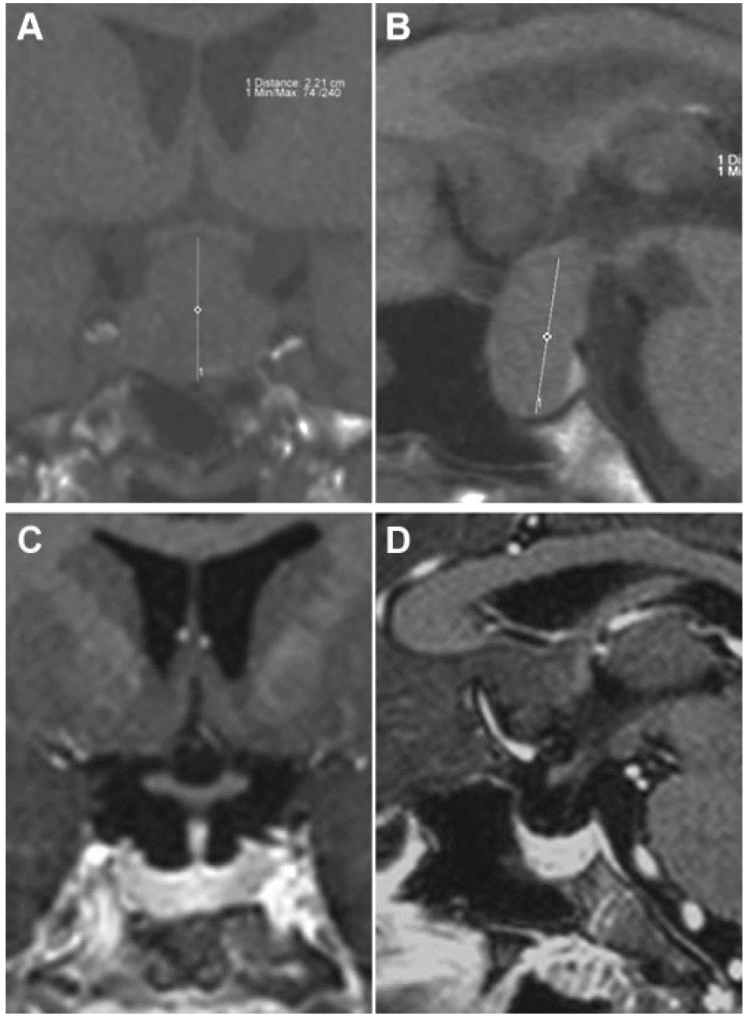
Primary hypothyroidism

- A 23-yr-old Romanian girl presented with a 7-month history of polymenorrhea, fatigue, headache, slowed mentation, and weight gain. She had facial and peripheral edema, dry skin, and fine scalp hair. Bradycardia and pericardial effusion at echocardiography were observed.
- Hormonal tests revealed a severe primary hypothyroidism
- TSH, 1578 U/ml; free T4, 0.3 ng/ml)
- **Mild hyperprolactinemia (113 ng/ml)**
- Partial ACTH deficiency



J Clin Endocrinol Metab, January 2011, 96(1):22–23

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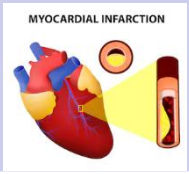
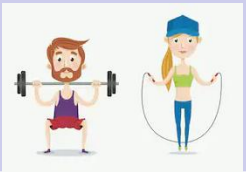
• Pregnancy; lactation; stress; sleep; coitus; exercise; venipuncture	    
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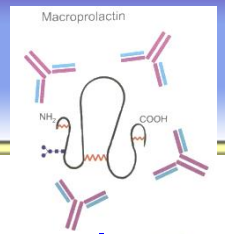
Causes of hyperprolactinemia

Causes	
• **PCOS?**	-30% in PCOS -a consequence of elevated estrogen levels and dopaminergic tonus reduction
• **Pseudocyesis**	
• **Epileptic seizures**	
Hypothalamic diseases • **Tumors** • **Infiltrative disorders** • **Metastasis** • **Cranial radiation** • **Rathke's cleft cysts**	Craniopharyngiomas, dysgerminomas, meningiomas Histiocytosis, sarcoidosis
Pituitary diseases • **Pituitary tumors** • **Infiltrative disorders** • **Metastasis** • **Lymphocytic hypophysitis** • **Empty sella syndrome** • **Stalk disorders**	**Prolactinomas**; acromegaly; TSHoma; Cushing's disease; Large NFT

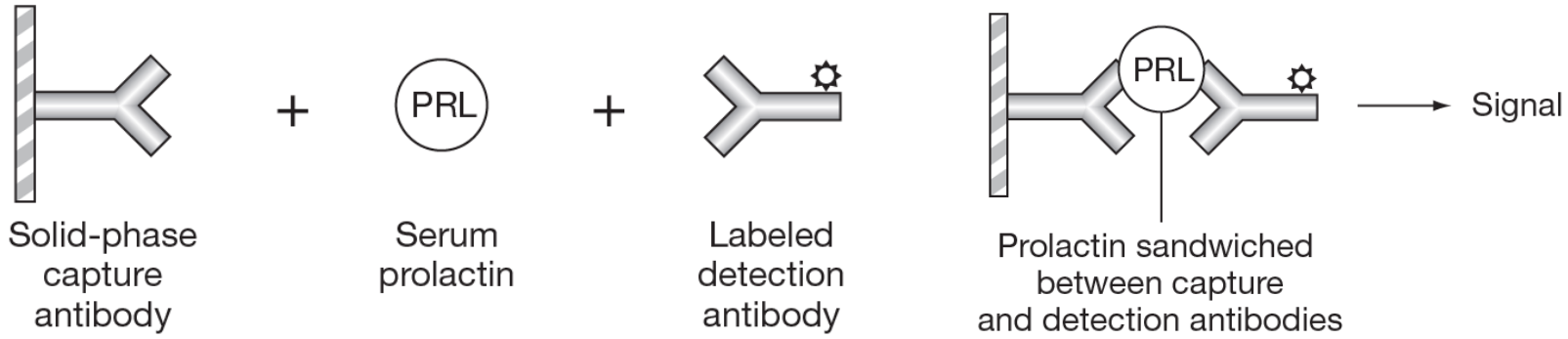
Causes of hyperprolactinemia

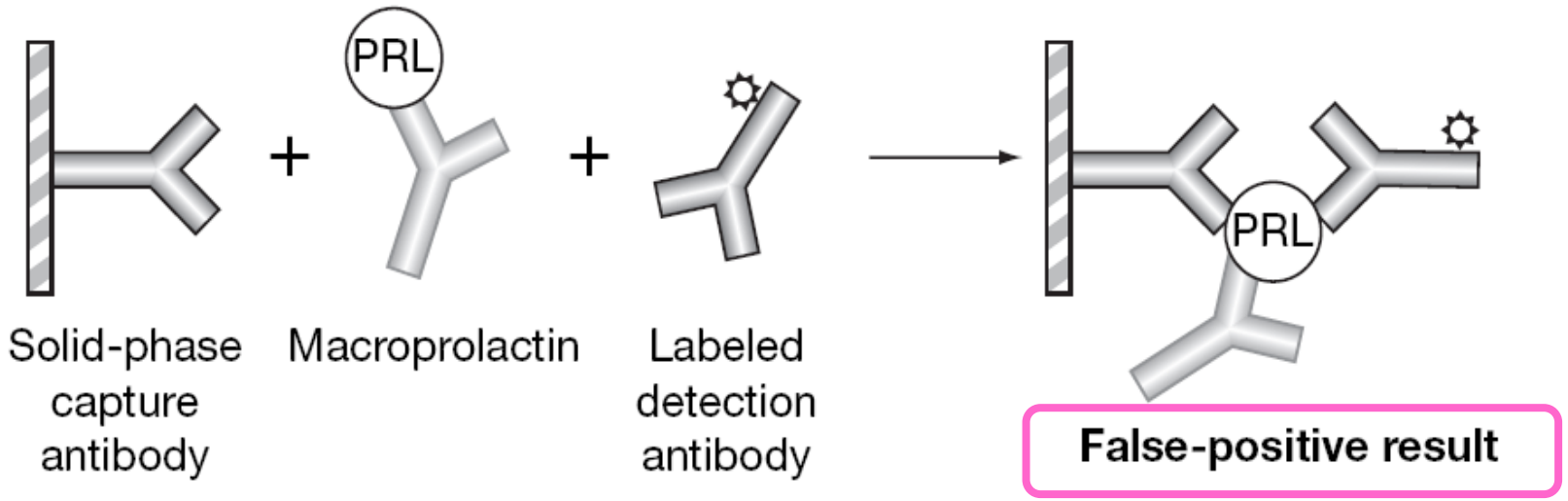
Causes	
Neurogenic • **Chest wall lesions** • **Spinal cord injury** • **Breast stimulation**	 Burns; breast surgery; thoracotomy; nipple rings; herpes zoster; etc.) Cervical ependymoma; tabes dorsalis; extrinsic tumors; etc. Reflex release of PRL, in part, by afferent neural pathways going through spinal cord.
Ectopic prolactin production	Renal cell carcinoma Ovarian teratomas Gonadoblastoma Non-Hodgkin lymphoma Uterine cervical carcinoma Colorectal adenocarcinoma
Macroprolactinemia	PRL levels are usually < 200 ng/ml+ lack symptoms
Drug induced	PRL levels are usually < 100 ng/ml Metoclopramide, risperidone, and phenothiazines can lead to prolactin levels > 200 ng/mL
Idiopathic	In one-third of the patients with IH, elevated PRL levels will resolve, and in one-half of patients, PRL levels will remain stable

Macroprolactin



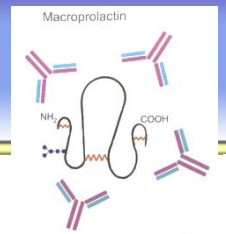
A two-site immunometric assay for prolactin



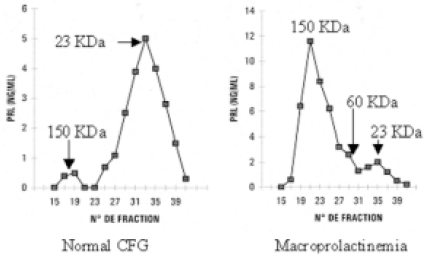


Nat Clin Pract Endocrinol Metab. 2007 Mar;3(3):279-89; JCEM.2011:96(2);273–288

Macroprolactinema



- Proportion of macroprolactinemia in hyperprolactinemic populations in most studies varies between 15 and 35%
- The gold standard method to assess macroprolactinemia is gel-filtration chromatography.



Normal CFG Macroprolactinemia

- An alternative acceptable method is polyethylene glycol (PEG) precipitation.
  - Macroprolactinema only: recoveries < 40%, when the level of nonprecipitated PRL is within the normal range
  - Monomeric PRL: recoveries > 60%

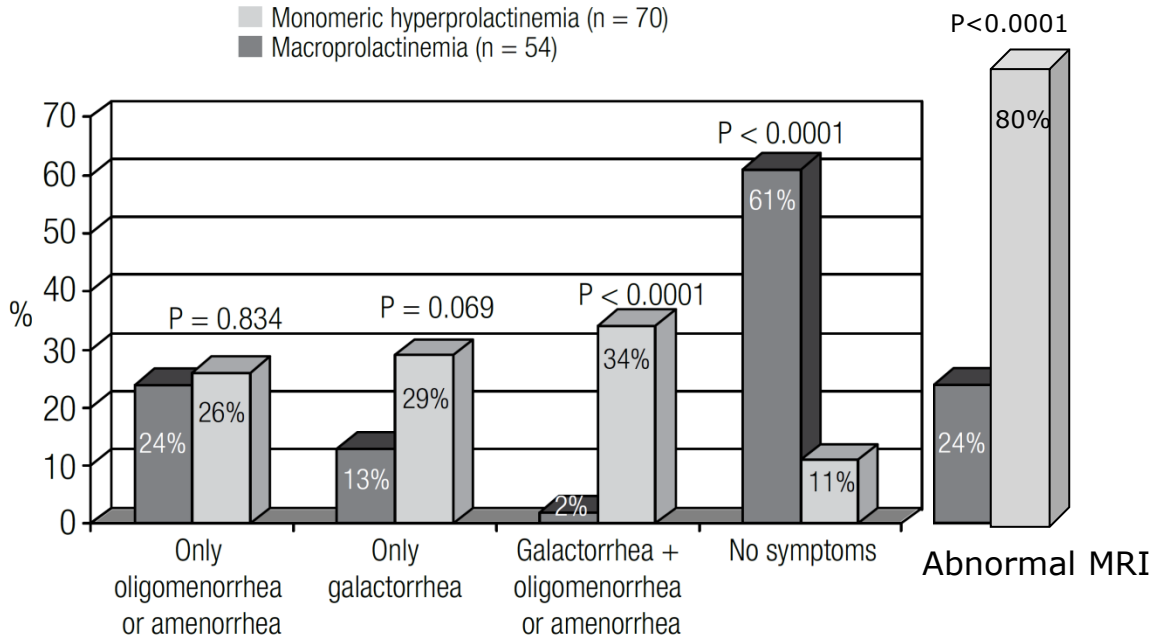
=30/100* 100

Percent recovery = (amount of substance recovered on purification ÷ amount of substance originally taken) × 100

Macroprolactinema

Clinical relevance

- It has been mostly suspected when hyperprolactinemic patients do not present the typical symptoms and/or evidence of a pituitary tumor on MRI
- However, many patients with macroprolactinemia can have nonspecific symptoms and neuroradiological abnormalities



Minerva Endocrinol. 2007;2(2):79-86.

Causes of hyperprolactinemia

Causes	
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Macroprolactinemia	PRL levels are usually < 200 ng/ml+ lack symptoms
Drug induced	PRL levels are usually < 100 ng/ml Metoclopramide, risperidone, and phenothiazines can lead to prolactin levels > 200 ng/mL
Idiopathic	In one-third of the patients with IH, elevated PRL levels will resolve, and in one-half of patients, PRL levels will remain stable

Drug-induced hyperprolactinemia

- Neuropeptides
  - Thyrotropin-releasing hormone
- Drug-Induced Hypersecretion

  Dopamine Receptor Blockers
  - Phenothiazines: chlorpromazine, perphenazine
  - Butyrophenones: haloperidol
  - Thioxanthenes, Risperidone
  - Metoclopramide, domperidone

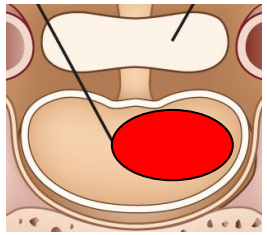
  Dopamine Synthesis Inhibitors
  - α-Methyldopa

  Catecholamine Depleters
  - Reserpine
- Cholinergic Agonists: Physostigmine
- Antihypertensives: Labetolol, Reserpine, Verapamil
- H2 Antihistamines: Cimetidine, Ranitidine
- Estrogens (increased transcription of PRL gene)
  - Oral contraceptives (controversial)
  - Oral contraceptive withdrawal
- Anticonvulsants: Phenytoin
- Neuroleptics: Chlorpromazine, Risperidone, Promazine, Promethazine, Trifluoperazine, Fluphenazine, Butaperazine, Perphenazine, Thiethylperazine, Thioridazine, Haloperidol, Pimozide, Thiothixene, Molindone
- Opiates and Opiate Antagonists
  - Heroin
  - Methadone
  - Apomorphine
  - Morphine
- Antidepressants
  - Tricyclic antidepressants: chlorimipramine, amitriptyline
  - Selective serotonin reuptake inhibitors: fluoxetine

Williams textbook of Endocrinology 14th ed; 2020 p 236-302

Prolactinoma: Clinical features

↓ GnRH



↑ Prolactin

Oligo/Amenorrhea
Infertile

Osteoporosis

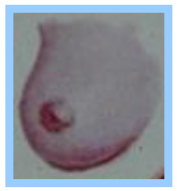
Decreased libido
Impotence
Infertile

↓ Ovarian function

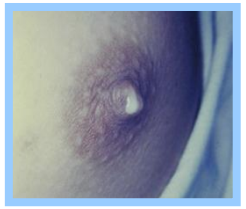
Female

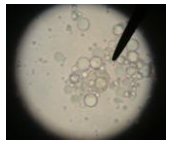
↓ FSH / LH Male

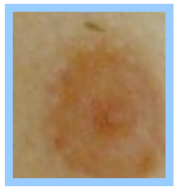
↓ Testicular function



Female







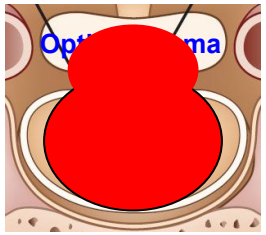
Male

No Galactorrhea

1. Hyperprolactinemia

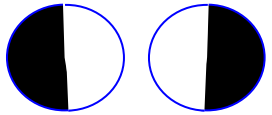
Prolactinoma: Clinical features

↓ GnRH



↑ Prolactin

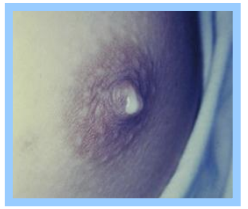
Headaches
Cavernous sinus syndrome

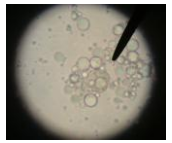


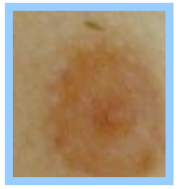
Bitemporal hemianopia

Hypopituitarism → ↓ FSH / LH → ↓ GH → ↓ ACTH → ↓ TSH

Female







Male

No Galactorrhea

2. Mass effect

Macroprolactinoma

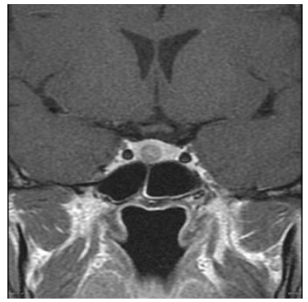
Diagnosis of prolactinoma

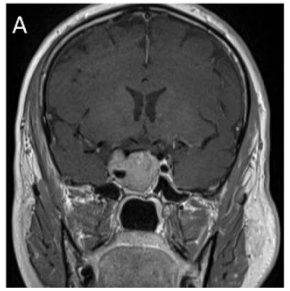
- Exclude other causes of hyperprolactinemia
- **Prolactin levels**: serum prolactin levels generally parallel tumor size
  - > 250 ng/ml: prolactinoma is likely (exclude risperidone and metoclopramide)
  - > 200 ng/ml: prolactinoma is more probable than other diagnoses. Nat Rev Endocrinol. 2023 Dec;19(12):722-740.
  - > 500 ng/ml:Dx macroprolactinoma
- MRI pituitary shows pituitary adenoma

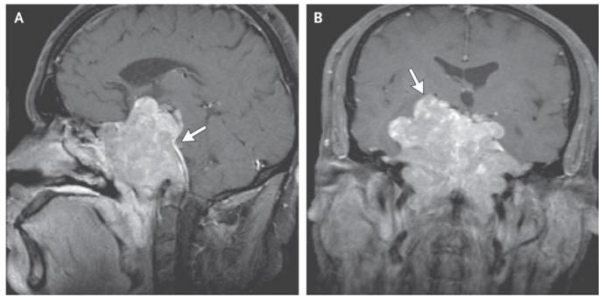
Shlomo Melmed et al. J. Clin. Endocrinol. Metab. 2011 96: 273-288.

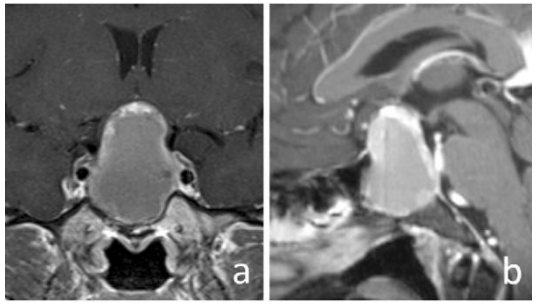
Classification of prolactinoma

Prolactinoma	Size	Prolactin level (ng/ml)	Tumor growth rate
Microprolactinoma	< 1 cm	>ULN-250	Low
Macroprolactinoma	≥ 1 cm	>250	High
Giant prolactinoma	> 4 cm	> 1,000	High
Cystic prolactinoma	Cystic part ≥ 50%	variable	-





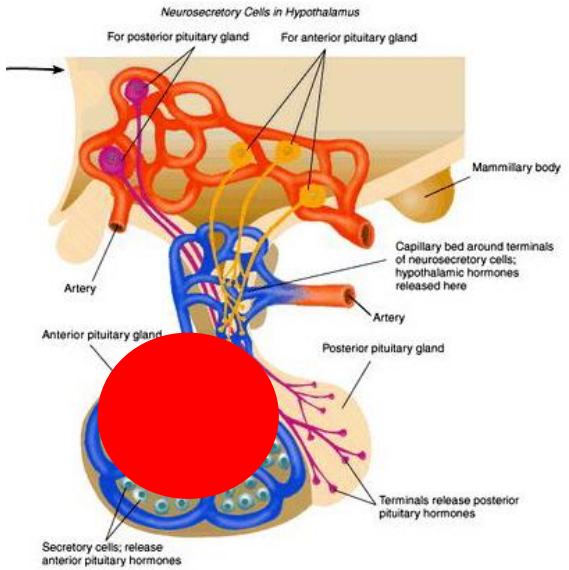




A. Wong et al. Journal of Clinical Neuroscience 22 (2015) 1562–1567

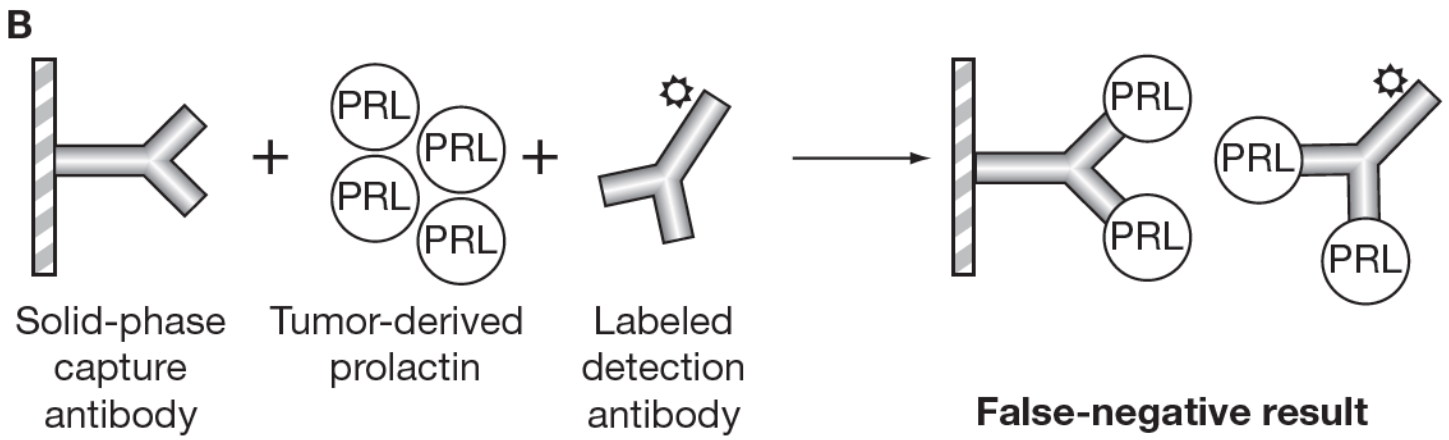
Pituitary macroadenoma with mild elevated prolactin levels

- A discrepancy between a very large pituitary tumor and a mildly elevated prolactin level
  - Macroprolactinoma with hook effect
  - Non functioning pituitary tumor with stalk compression
  - Cystic macroprolactinoma

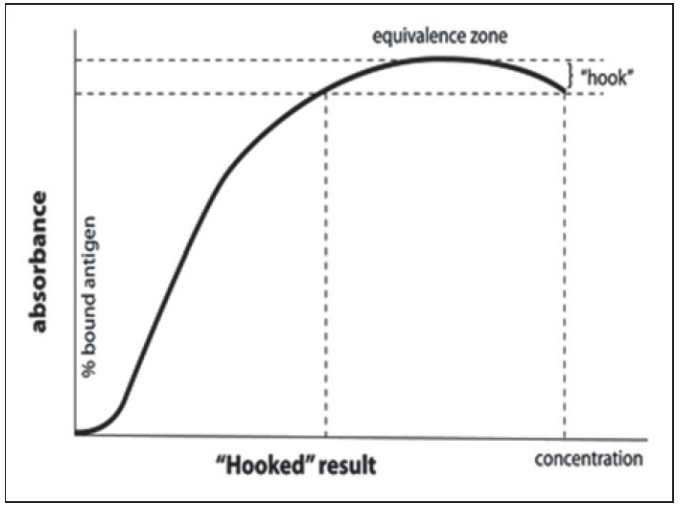


Hypothalamic pituitary dopaminergic pathway

Hook effect



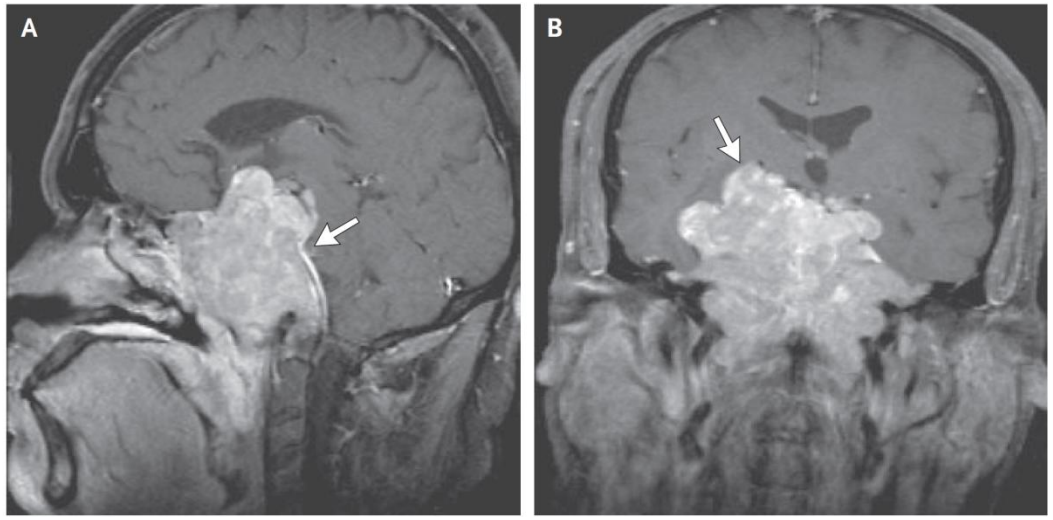
Dilution of serum sample (1:100) to eliminate hook effect in pituitary macroadnoma and a mildly elevated prolactin level[1]



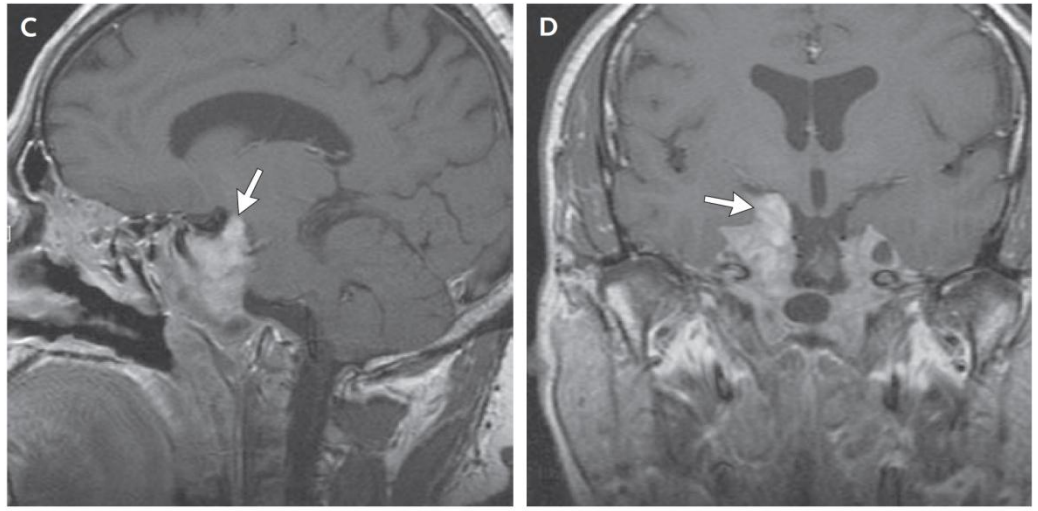
In patients with **giant adenoma** and typical features of hyperprolactinaemia but **normal or slightly elevated** serum levels of prolactin, samples should be **re-measured after 1:100 dilution** to exclude a high-dose hook effect (strong).[2]

Nat Clin Pract Endocrinol Metab. 2007 Mar;3(3):279-89;[1] JCEM.2011:96(2);273–288;[2] Nat Rev Endocrinol. 2023 Dec;19(12):722-740.

Pituitary macroadenoma with hook effect



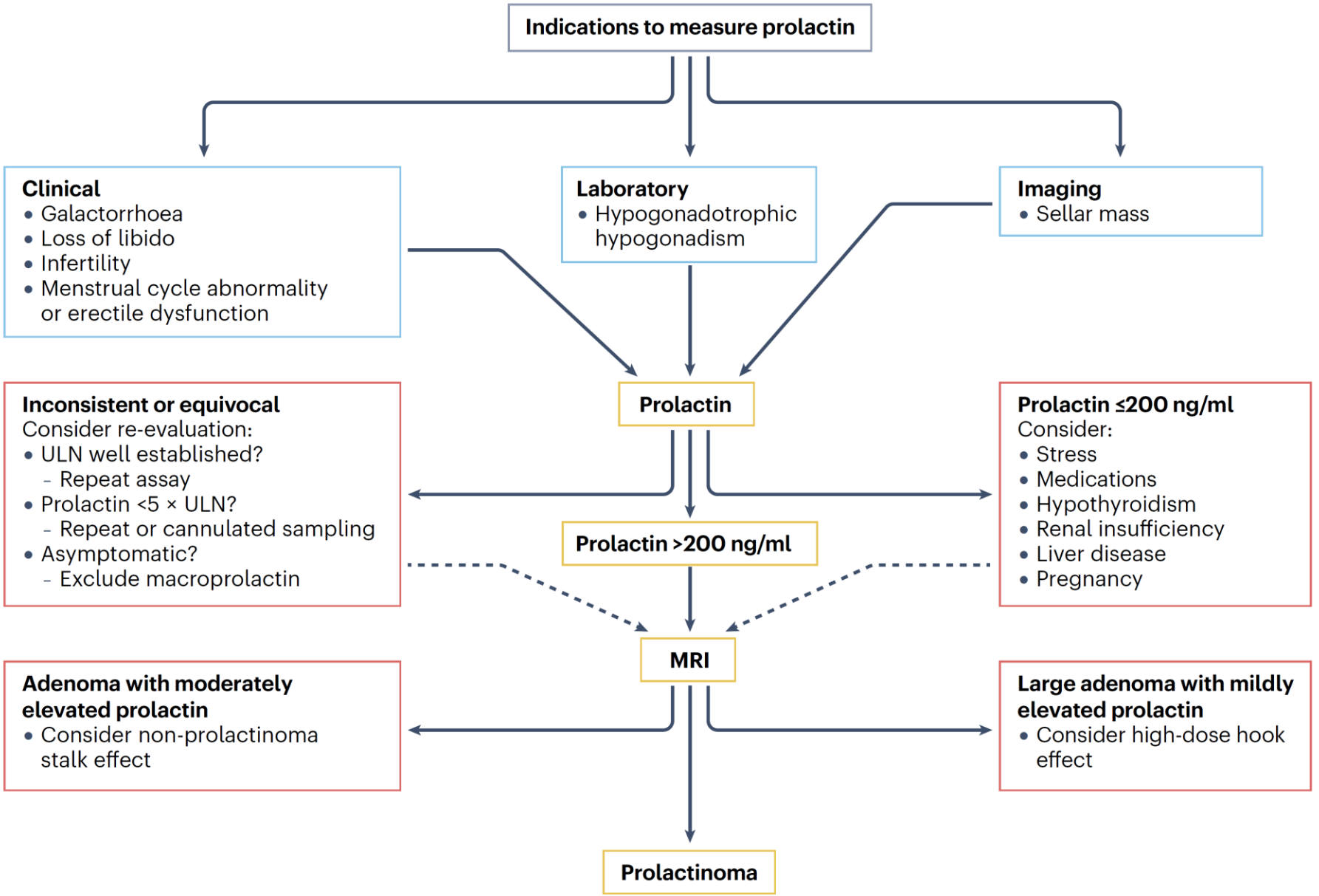
40 months



A 32-year-old man with left hemiparesis, severe headache and impaired hearing loss

- Pituitary macroadenoma (5.6x7.9 cm)
- Prolactin level 7.3 ng/ml
- Prolactin level (dilute 1:1000) 122,260 ng/ml
- Transnasal biopsy: lactotroph adenoma and positive for prolactin
- 4 days after cabergoline treament: prolactin level 10,823 ng/ml
- 3 wks, prolactin level 772 ng/ml and neurologic symptoms had resolved.

Mohammed Ahmed. N Engl J Med 2010; 363:177

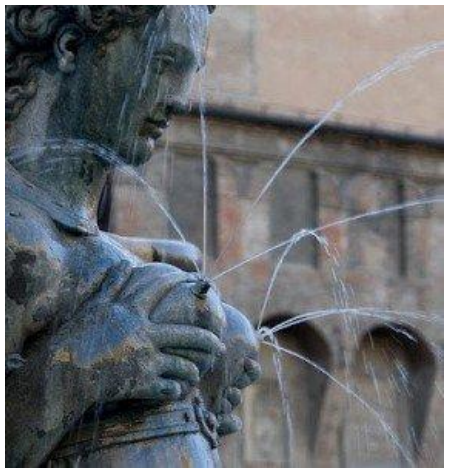


Nat Rev Endocrinol. 2023 Dec;19(12):722-740.

Indication for treatment

- Macroprolactinoma
- Microprolactinoma
  - Amenorrhea
  - Osteoporosis
  - Bothersome galactorrhea
  - Male hypogonadism
  - Increased size
  - Need fertility

The goals of treatment
- To normalize prolactin levels
- To restore gonadal function
- To reduce tumor mass effect
- To preserve residual pituitary function
- To prevent disease recurrence or progression



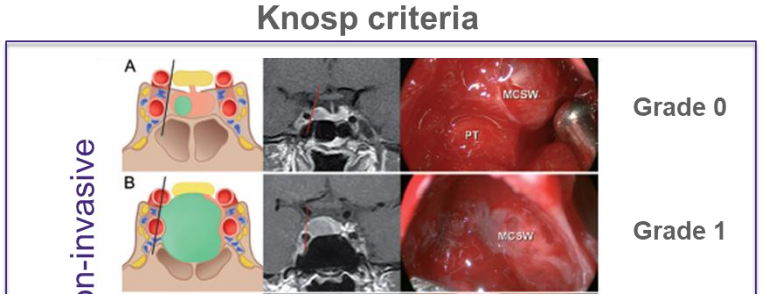
Shlomo Melmed et al. J. Clin. Endocrinol. Metab. 2011 96: 273-288.

Treatment of prolactinoma

Surgery

For microprolactinomas and well-encased macroprolactinomas (Knosp grade 0 and 1), the curative potential and risks of surgery should be discussed with patients in a multidisciplinary setting prior to medical treatment initiation (strong). Nat Rev Endocrinol. 2023 Dec;19(12):722-740

Dopamine agonists is the first therapeutic option in patients both with micro- and macroprolactinoma



Medication

Radiation

Dopamine Agonists

Table 1. Effects of bromocriptine on PRL normalization and tumor shrinkage

Study	Patients, *n*	Dose, mg/day	PRL normalization cases, *n*	Eugonadism[a] cases, *n*	Tumor shrinkage[b], cases
Seppälä et al. [20]	14	5	12	8	–
Carter et al. [21]	22	–	7	9	–
Thorner et al. [26]	12	2.5–7.5	12	12	–
Beckers et al. [28]	29	50–150 (LAR)	28	8	14
Merola et al. [29]	22	2.5–15	15	13	10
Total	99	–	74 (74.7%)	50 (50.5%)	24 (47%)[c]

Using cabergoline in preference to other dopamine agonists because it has higher efficacy in normalizing prolactin levels, as well as a higher frequency of pituitary tumor shrinkage

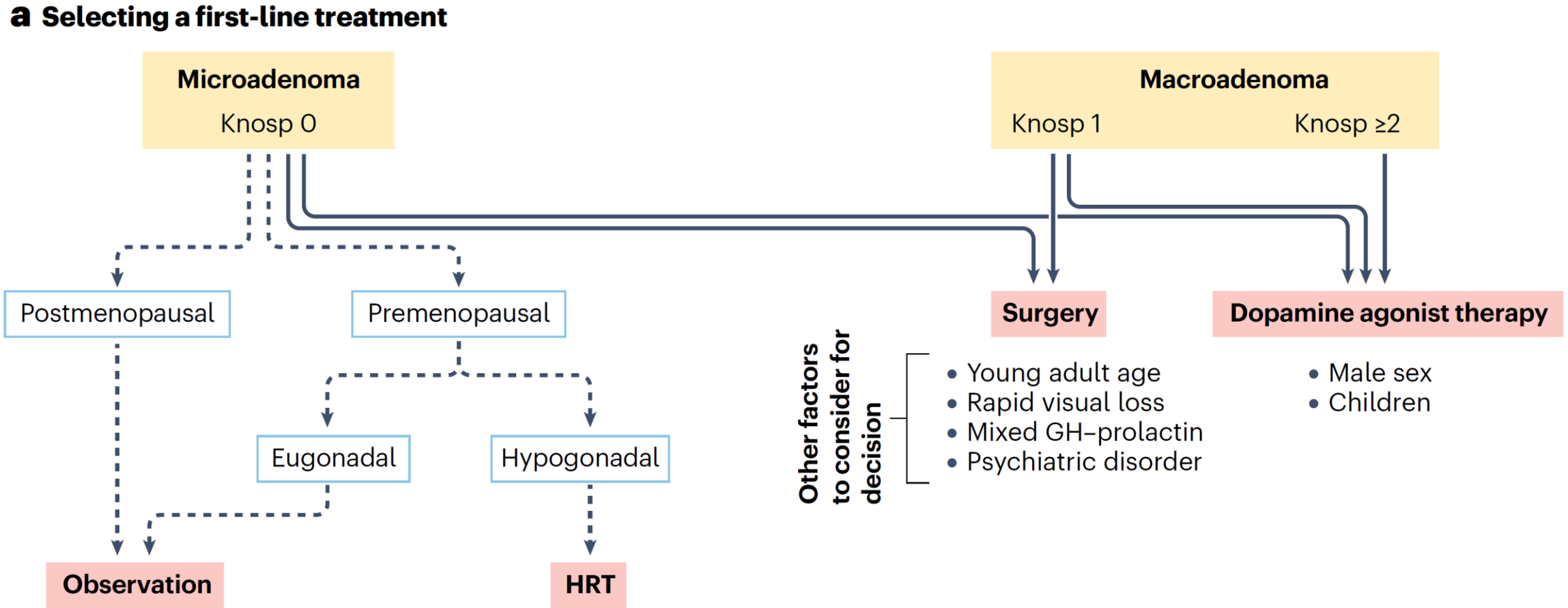
Study	Patients, *n*	Dose, mg/week	PRL normalization cases, *n*	Eugonadism[a] cases, *n*	Tumor shrinkage[b] cases, *n*
Wenster et al. [58]	223	0.25–2	186	201	–
Colao et al. [59]	23	0.5–3	19	21	14
Colao et al. [60]	110	0.25–3.5	88	94	93
Total	356	–	293 (82.3%)	316 (88.8%)	107 (80.4%)[c]

[a] Defined as restoration of regular menstrual cycles, pregnancy, and/or a normal libido or potency. [b] Defined as a reduction >25% of the baseline volume. [c] Calculated based on 133 patients with available data about pituitary imaging.

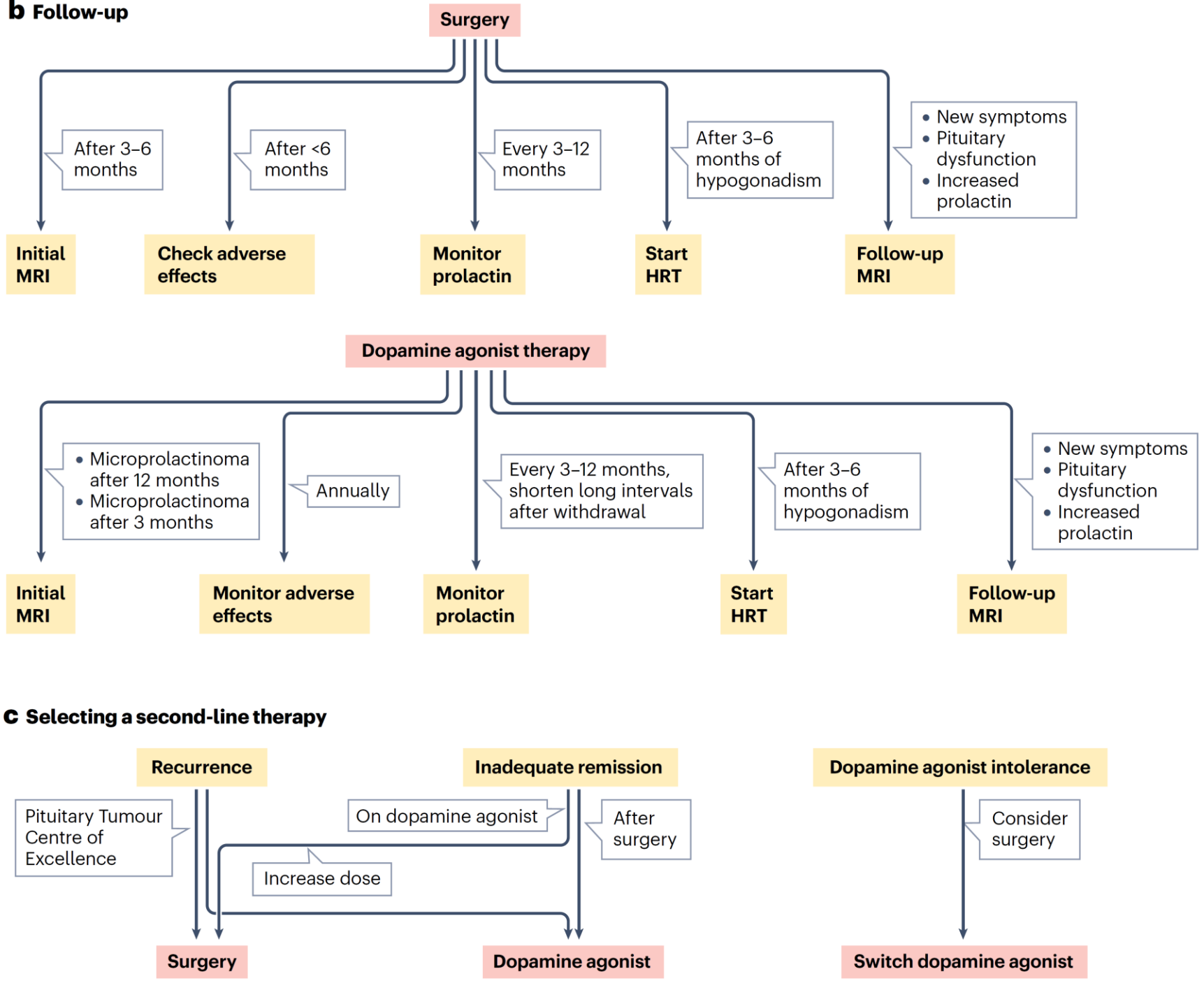
Renata S. Auriemma, et al. Neuroendocrinology 2019;109:34–41
Shlomo Melmed et al. J. Clin. Endocrinol. Metab. 2011 96: 273-288.

Bromocriptine VS Cabergoline

	Bromocriptine	Cabergoline
Action	An ergot derivative with potent dopamine receptor agonist activity	An ergoline D2 agonist with high affinity for D2 receptors
Administration	**2–3 times daily**	**only once or twice weekly**
Dose	**starts at 0.62–1.25 mg/day and is increased by 1.25 mg every week, up to 30 mg/day**	**0.25 to 3 mg/wk**
Side effects	**GI**: nausea, vomiting, constipation, reflux, dyspepsia **Neurological**: headache, dizziness, dyskinesia, confusion **CVS**: postural hypotension, syncope **Other**: muscle cramps, psychosis, nasal stuffiness, digital vasospasm and dry mouth	Less frequent and less severe
Cost	**Low**	**High**



Nat Rev Endocrinol. 2023 Dec;19(12):722-740.



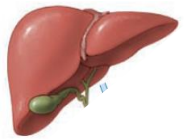
Nat Rev Endocrinol. 2023 Dec;19(12):722-740.

Acromegaly

GH-secreting pituitary adenoma

↑ Growth hormone

↓



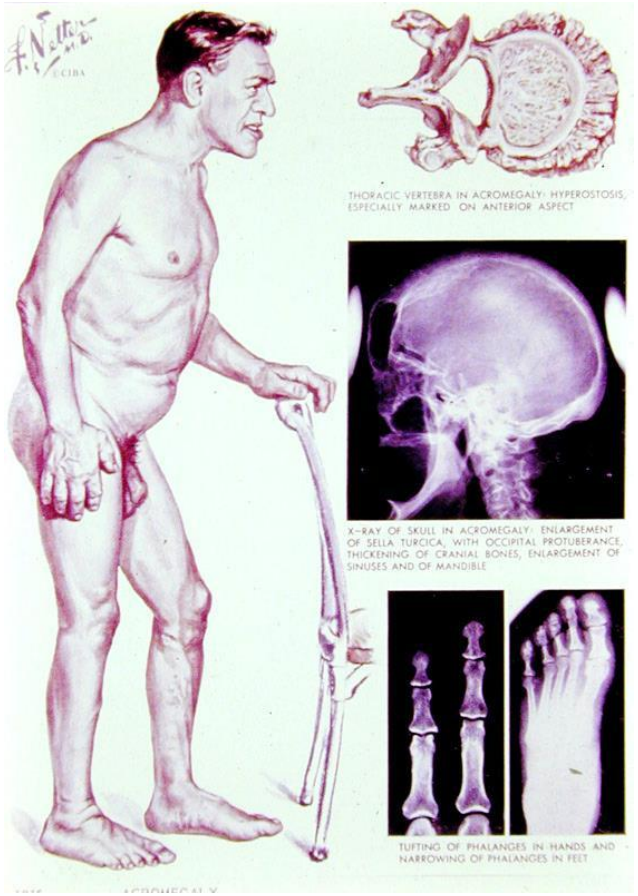
↓

↑ IGF-1

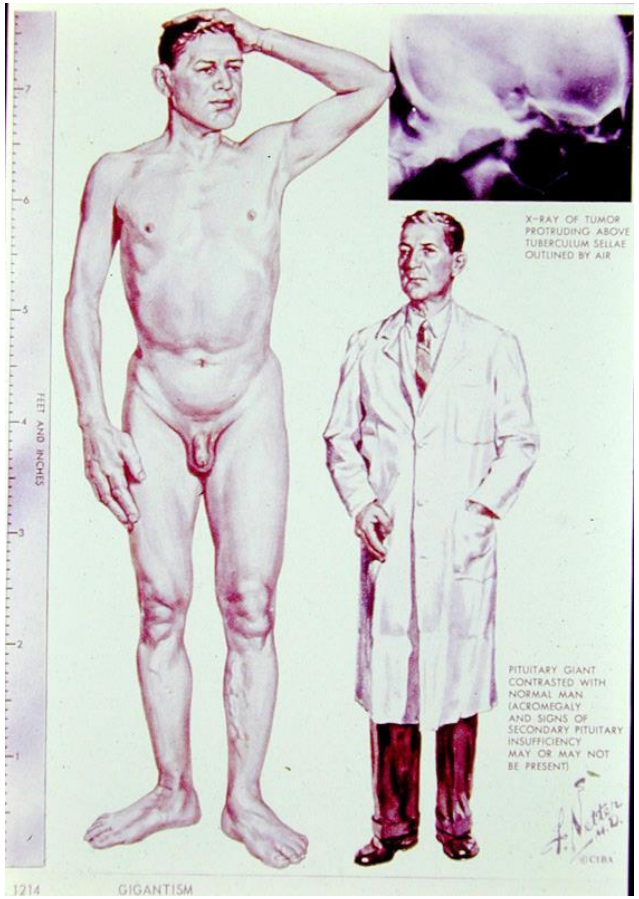
↓

ACROMEGALY

GIGANTISM

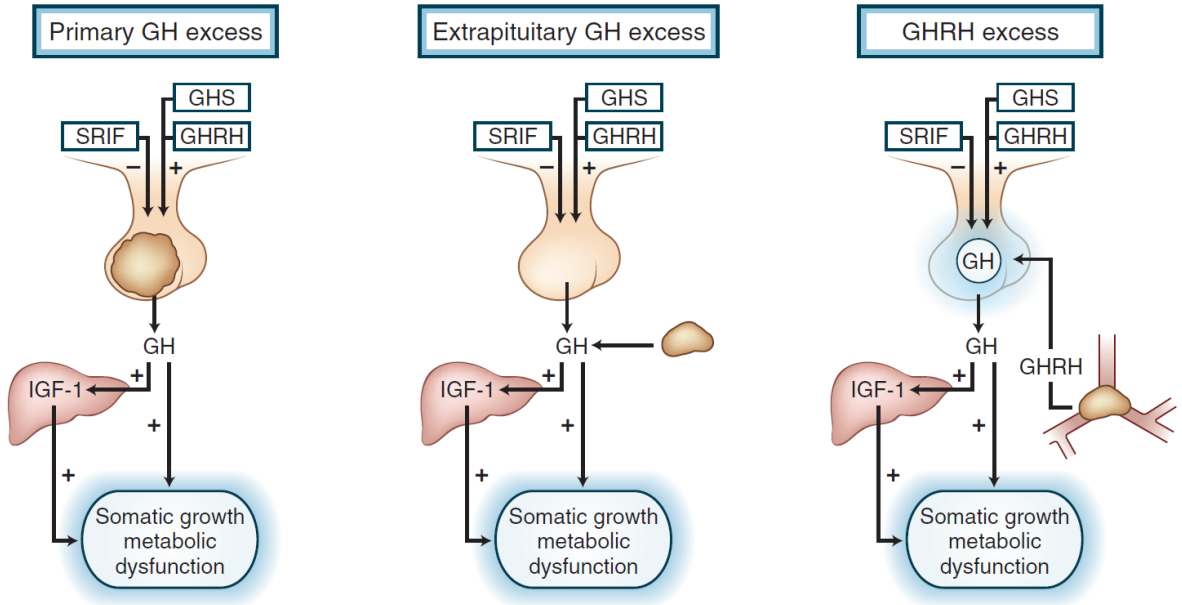


ACROMEGALY



GIGANTISM

Causes of GH excess



Pituitary adenoma
Densely granulated GH cell
Sparsely granulated
Mixed GH cell and PRL
Mammosomatotroph cell
Acidophil stem cell
Plurihormonal
Silent somatotroph

Pituitary carcinoma

Ectopic

Familial syndromes
Multi-endocrine neoplasia-type I
McCune-Albright syndrome
Familial acromegaly
Carney complex

Pancreatic islet cell tumor
Lymphoma

Iatrogenic

Central
Hypothalamic tumor

Peripheral
Bronchial carcinoid
pancreatic islet cell tumor
small cell lung cancer
adrenal adenoma
medullary thyroid carcinoma
pheochromocytoma

Williams textbook of Endocrinology 14th ed; 2020 p 236-302

Acromegaly

Williams textbook of Endocrinology 14th ed; 2020 p 236-302

1977

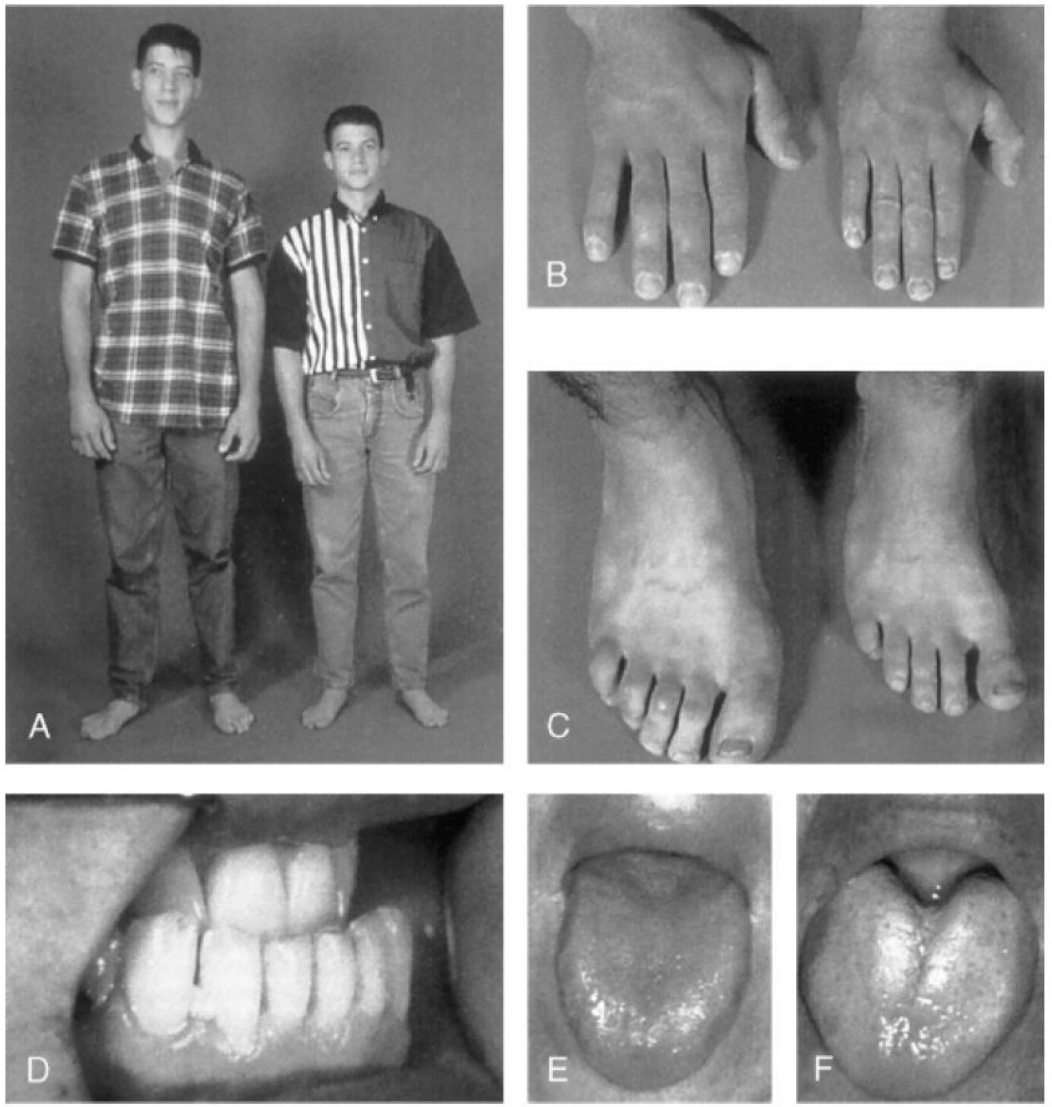
1981

1983

1988

Molitch ME. Endocrinol Metab Clin North Am. 1992;21(3):597–614.

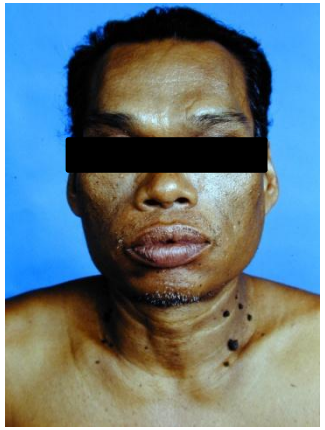
Acromegaly

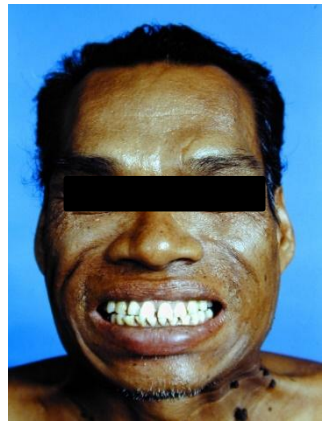


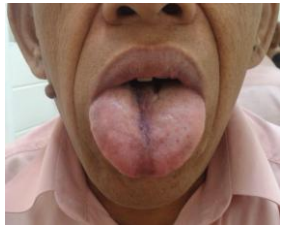
Williams textbook of Endocrinology 14th ed; 2020 p 236-302

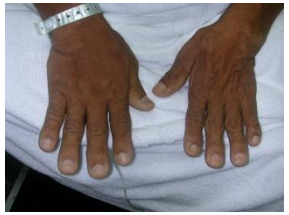
Somatic Effects

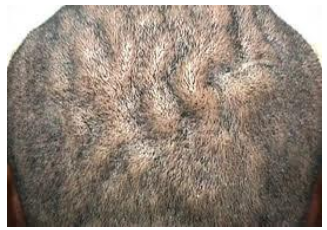
- **Acral Enlargement :** Thickness of hand and feet soft tissue
- **Cardiovascular**
  - Asymmetric septal hypertrophy
  - Cardiomyopathy
  - Congestive heart failure
  - Hypertension
  - Left-ventricular hypertrophy
- **Musculoskeletal**
  - Acroparesthesia
  - Arthralgias and arthritis
  - Carpal tunnel syndrome
  - Gigantism
  - Hypertrophy of frontal bones
  - Jaw malocclusion
  - Prognathism
  - Increased spacing of teeth
  - Proximal myopathy
- **Pulmonary**
  - Narcolepsy
  - Sleep apnea—central and obstructive
  - Sleep disturbances
- **Skin**
  - Hyperhidrosis
  - Oiliness
  - Skin tags
  - Cutis verticis gyrata
  - Acanthosis nigricans
- **Colon** : Polyps
- **Visceromegaly**
  - Kidney
  - Liver
  - Prostate
  - Salivary gland
  - Spleen
  - Thyroid
  - Tongue









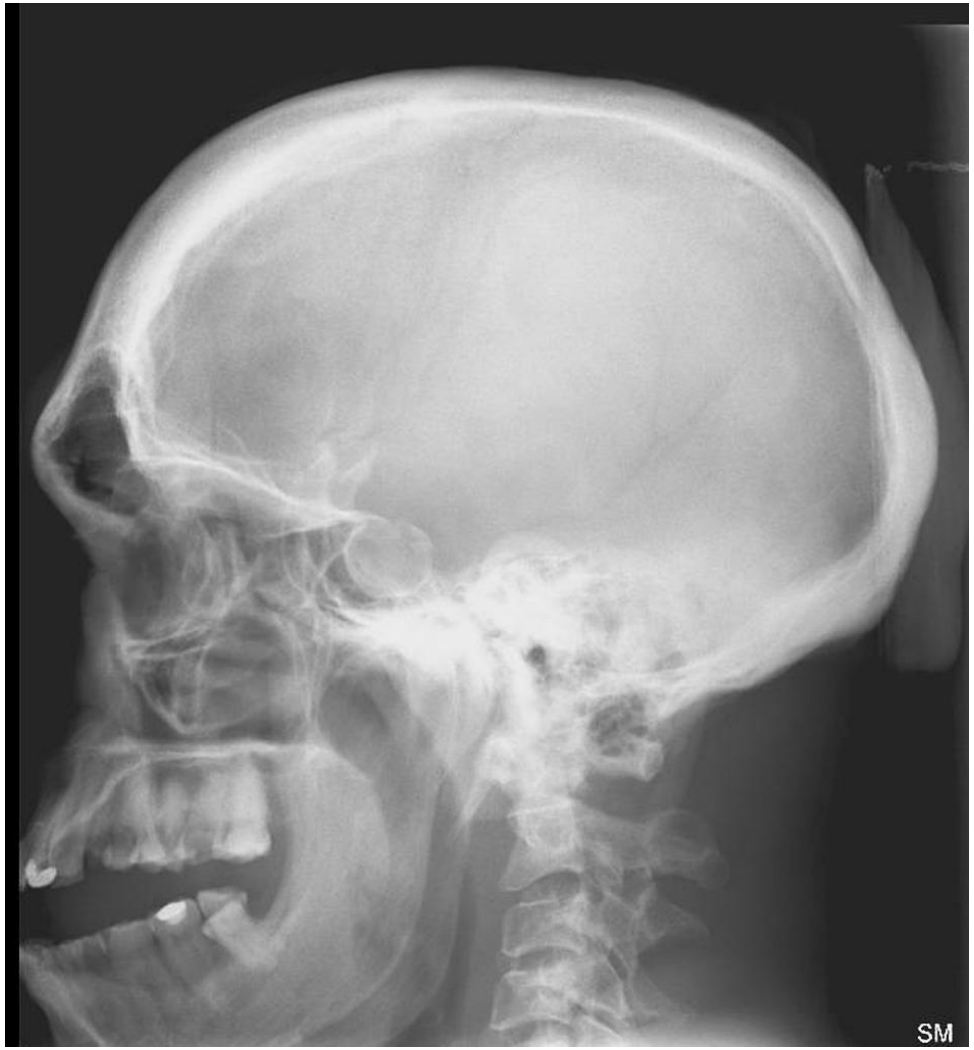


Endocrine And Metabolic Effects

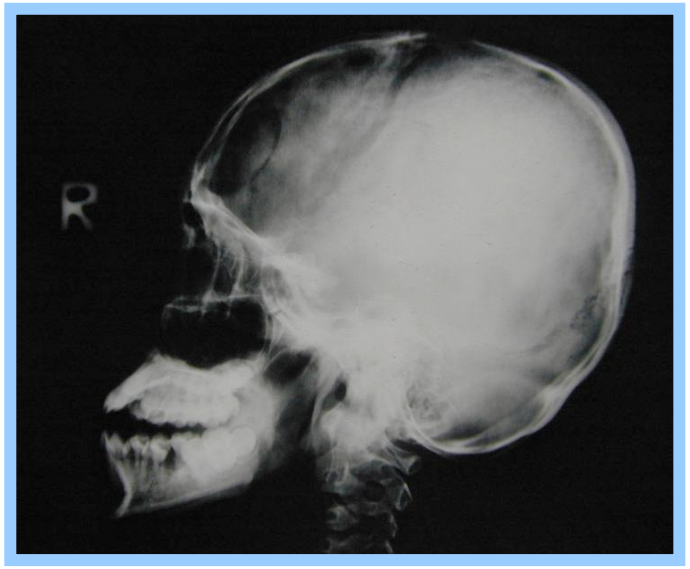
- **Carbohydrate**
  - Diabetes mellitus
  - Impaired glucose tolerance
  - Insulin resistance and hyperinsulinemia
- **Electrolytes**
  - Increased aldosterone
  - Low renin
- **Lipids :** Hypertriglyceridemia
- **Minerals**
  - Hypercalciuria, increased 1,25(OH)2D3
  - Urinary hydroxyproline
- **Reproduction**
  - Decreased libido, impotence, low sex hormone–binding globulin
  - Galactorrhea
  - Menstrual abnormalities
- **Thyroid**
  - Goiter
  - Low thyroxine-binding globulin
- **Multiple endocrine neoplasia type 1**
  - Hyperparathyroidism
  - Pancreatic islet cell tumors

Radiographic features

ACROMEGALY

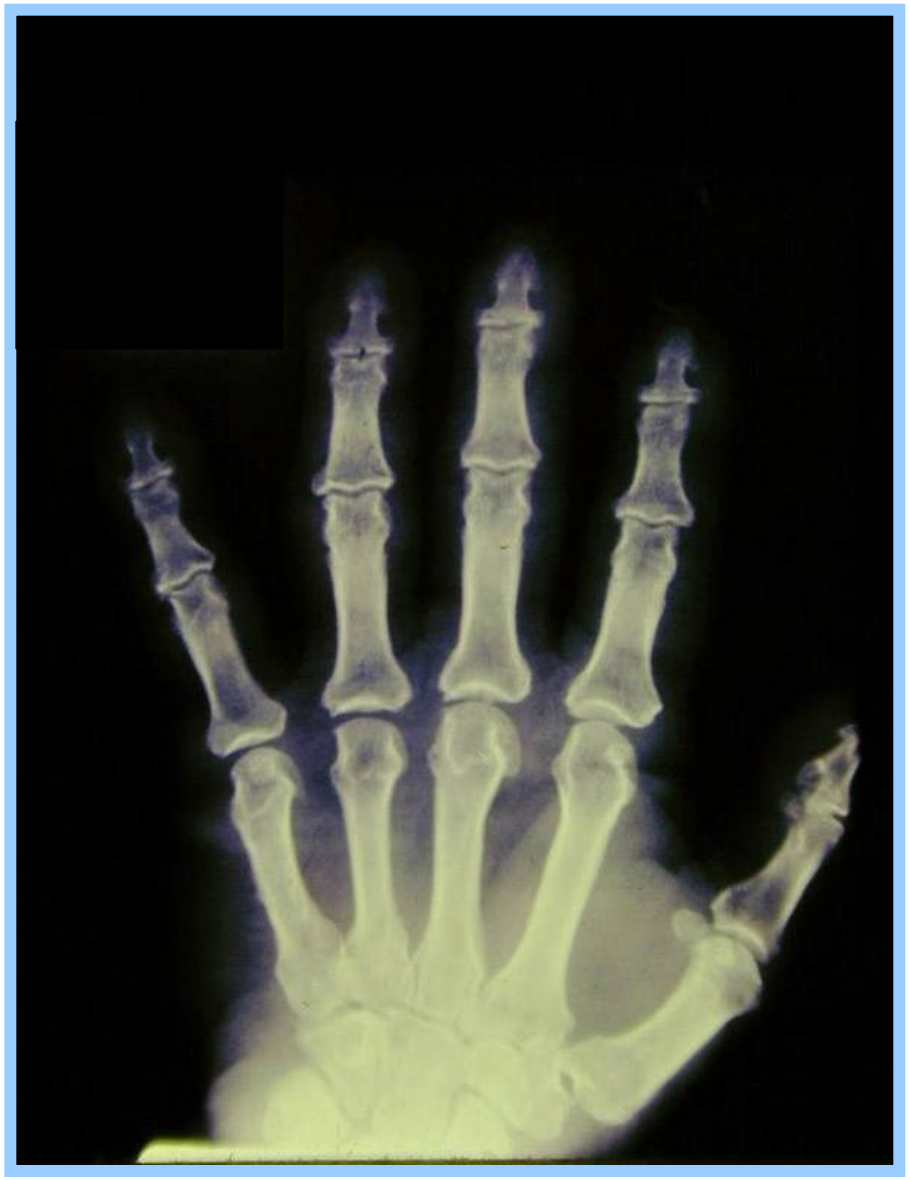


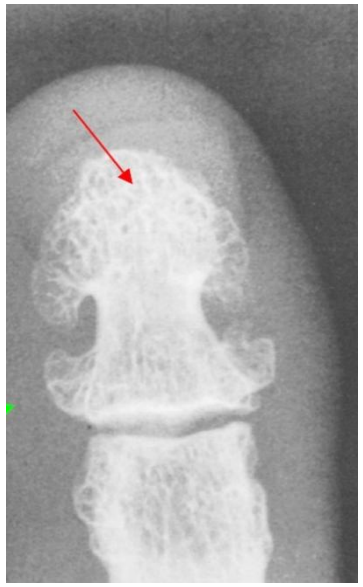
NOT ACROMEGALY

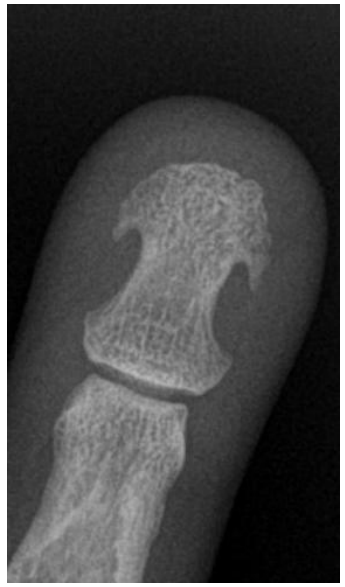


Calvarial thickening
Enlarged sinuses
An enlarged sella turcica
Prognathic jaw

Acromegaly : Changes in bone and soft tissue

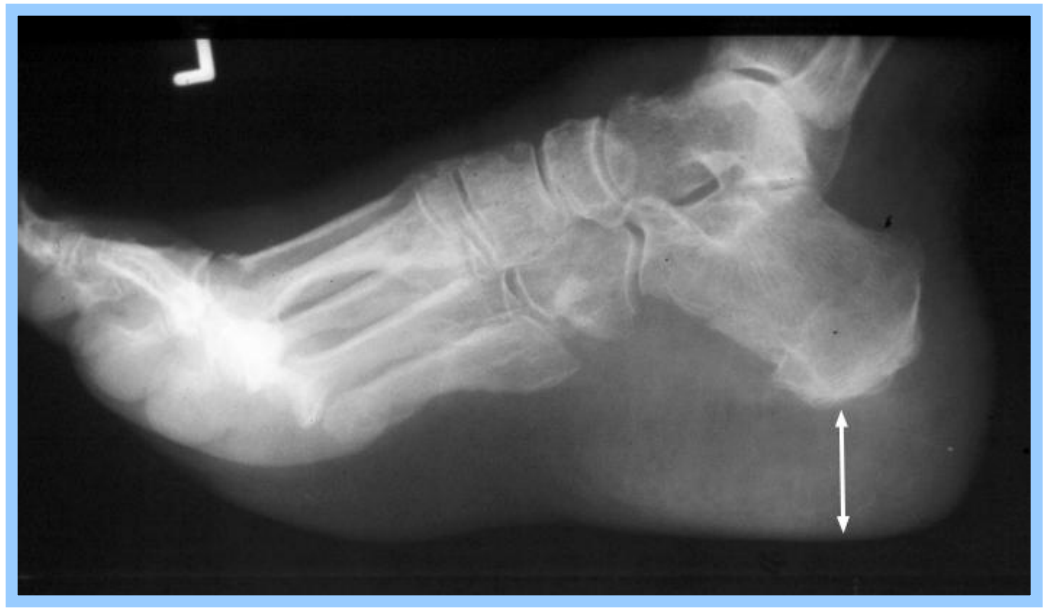


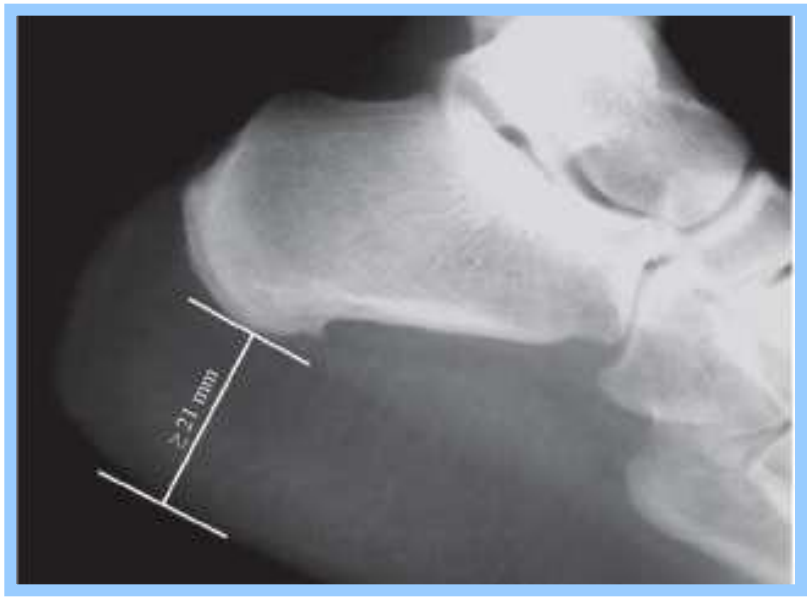




- Enlarged bones and soft tissue shadow
- Spade like terminal tuft or arrow head distal phalanges
- Widening of MCP joint space

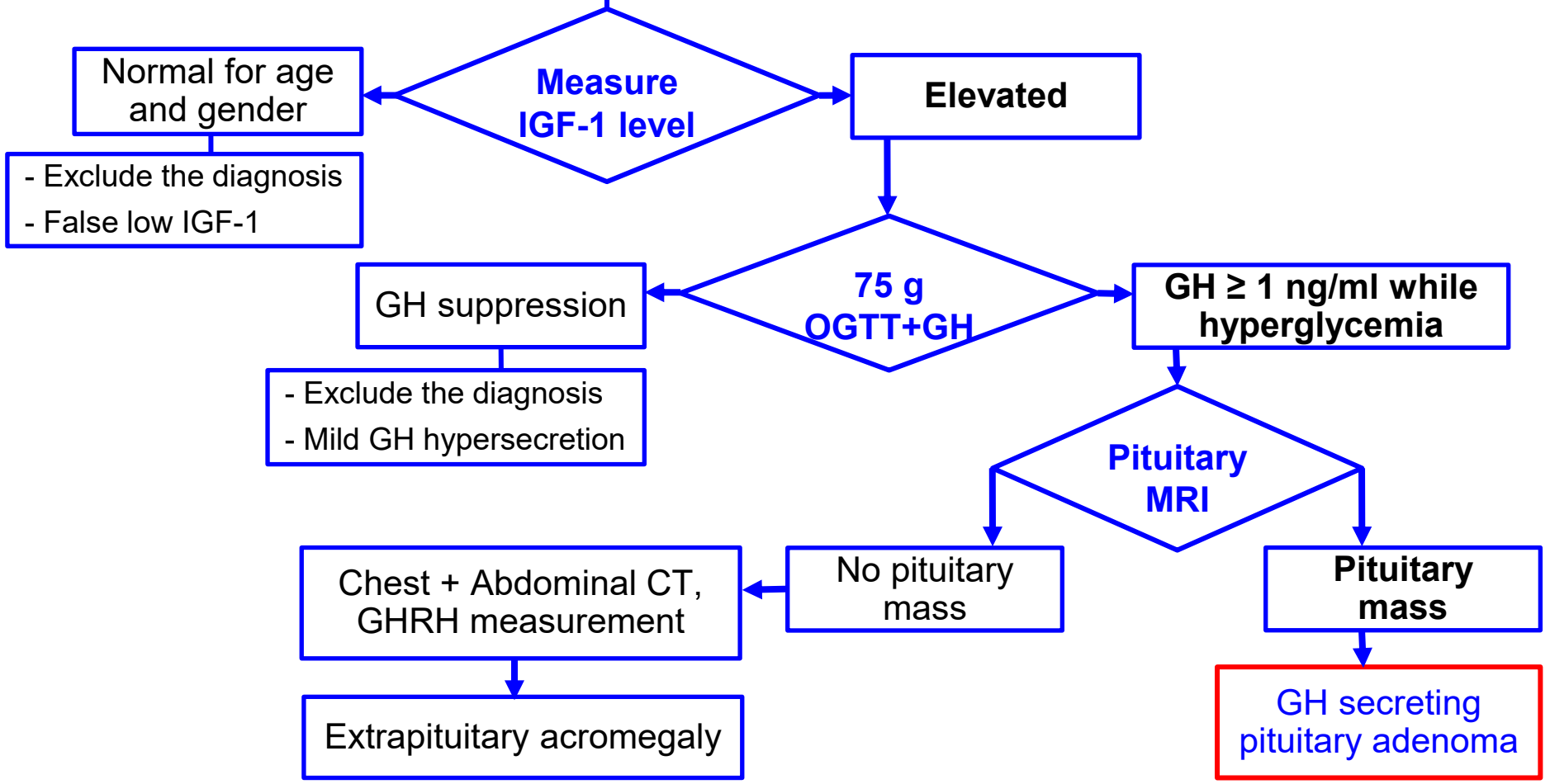
Acromegaly: Heel pad thickness





Patients

- With typical clinical manifestation of acromegaly: acral and facial features
- Without typical clinical manifestation of acromegaly: sleep apnea syndrome, T2DM, debilitating arthritis, carpal tunnel syndrome, hyperhidrosis and HT
- Pituitary incidentaloma



J Clin Endocrinol Metab, 99(11):3933-3951

Evolution of criteria for acromegaly diagnosis and evaluation of therapeutic efficacy

	Diagnosis	Therapeutic efficacy target
1st Acromegaly consensus [3] 1999	IGF-I elevated for age and sex Confirm with random GH ≥ 0.4 µg/L *or* IGF-I elevated for age and sex Confirm with GH > 1 µg/L during OGTT	IGF-I normalized for age and sex GH < 1 µg/L during OGTT
7th Acromegaly consensus [4] 2010	IGF-I elevated for age and sex *and* Random GH elevated	Random GH < 1 µg/L GH < 0.4 µg/L during OGTT
Endocrine society guidelines [5] 2014	IGF-I elevated for age Confirm with GH > 1 µg/L during OGTT	IGF-I normalized for age Random GH < 1 µg/L
14th Acromegaly consensus (this publication)	IGF-I > 1.3 × ULN for age *and* Characteristic clinical signs of disease For equivocal results, IGF-I measurements can be repeated, and OGTT might additionally be useful	IGF-I normalized for age

- BMI-based GH nadir cutoffs of **< 0.4 µg/L** for BMI **< 25** kg/m2 and **< 0.2 µg/L** for BMI **≥ 25** kg/m2 can be considered.
- Cessation of oral estrogen therapy 4 weeks prior to OGTT may avoid its effects on the GH axis.

Pituitary. 2023 Nov 3. doi: 10.1007/s11102-023-01360-1.

Limitation of IGF-1

Table 2. Factors influencing GH and IGF-I concentration

Influencing factor	GH	IGF-I	Remarks	References (examples)
Obesity	↓	↔↓	Decreased GH secretion (possibly through low ghrelin concentrations). Normal IGF-I bioactivity.	(26,28)
Fasting	↑	↓	Decreased metabolic clearance of GH, hepatic GH resistance.	(55,81)
Malnutrition	↑	↓	Decreased IGF-I secretion, lack of IGF-I feedback and, thus, increased GH secretion.	(56)
Anorexia nervosa	↑	↓	Hepatic GH-resistance, reduced IGF-I bioactivity.	(28)
Stress (acute)	↑	↔	Stimulation of GH secretion.	(82)
Exercise	↑	↔	Stimulation of GH secretion.	(82)
Sleep	↑	↔	Increased GH secretion in slow-wave sleep (deep sleep).	(83)
Glucose intake	↓	↔	Decreased GH secretion.	(26)
Type 1 Diabetes mellitus	↑	↔↓	Hepatic GH-resistance.	(57)
Type 2 diabetes mellitus	↓	↔↓	Hepatic GH-resistance.	(58)
Chronic renal failure and uremia	↔↑	↔↓	Reduced renal GH degradation and GH resistance. IGF-I bioactivity is reduced due to elevated binding protein concentrations.	(59)
Liver disease	↑	↓	Reduced IGF-I production, increased GH secretion through negative feedback mechanism and hepatic GH resistance.	(61)
Hypothyroidism	↓	↓	Decreased GH secretion in long term hypothyroidism.	(64)
✓ Hyperthyroidism	↓	↑	Decreased GH secretion. Increased IGF binding proteins and therefore reduced IGF-I bioactivity.	(64)
Acute critical illness	↑	↓	Hepatic GH-resistance.	(62)
Systemic inflammation	↑	↓	Hepatic GH-resistance.	(63)
Oral estrogens	↑	↓	Hepatic GH-resistance.	(26)
✓ Testosterone	↔ (↑)	↑	No changes in long-term therapy (> 6 weeks).	(65)
Biotin intake*	↓	↓	depends on susceptibility of specific assay used, GH and IGF-I can be falsely low.	Personal observation (unpublished)
Pegvisomant	↑↓↔	↓**	Influence of pegvisomant on GH dependent on assay used (see Table 1).	(11)
✓ Pregnancy	↑↔	↑	GH cross reactivity dependent on assay used (see Table 1).	(11)

GH: growth hormone; IGF-I: insulin-like growth factor I; ↓ decreased; ↔ unchanged; ↑ increased. *Applies only, if biotin-streptavidin system is used. **Therapeutically desired effect.

Schilbach K, Bidlingmaier M. Arch Endocrinol Metab.2019,63(6):618–629.

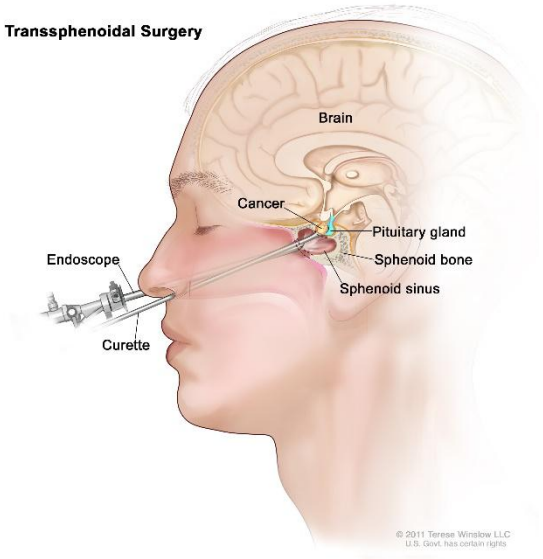
Assess comorbidity and mortality risk

- Comorbidity
  - Hypertension
  - Diabetes mellitus
  - Cardiovascular disease
  - Osteoarthritis
  - Sleep apnea
- Screening for colon cancer with colonoscopy at diagnosis
  - Repeat colonoscopy
    - every 5 yrs: polyp or elevated IGF-1
    - every 10 yrs: no polyp and normal IGF-1
- A thyroid ultrasound (palpable thyroid nodule)
- Hypopituitarism and replacing hormone deficits

JCEM 2014, 99(11):3933-3951.

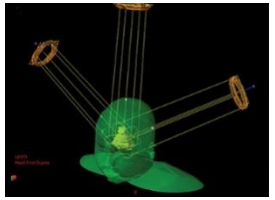
Management of acromegaly

Surgery



Medication

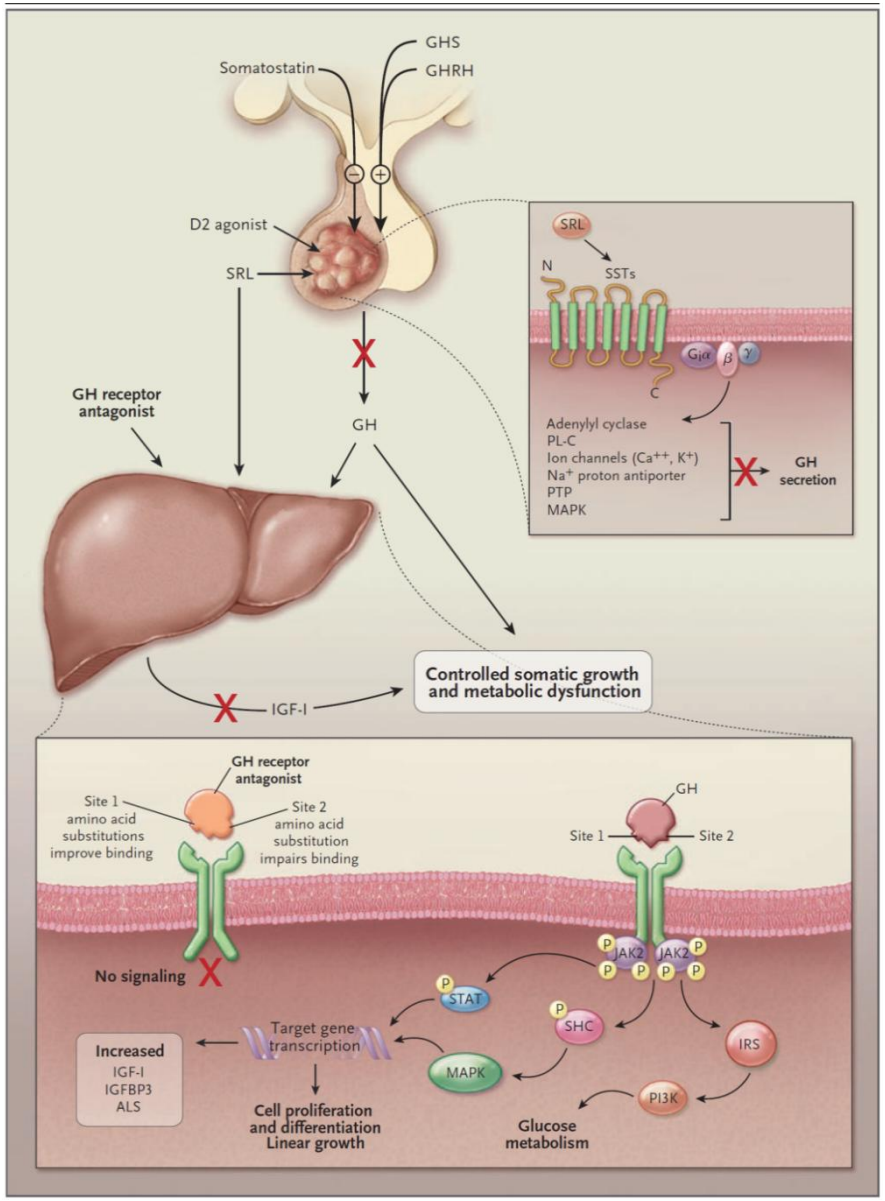
Radiation



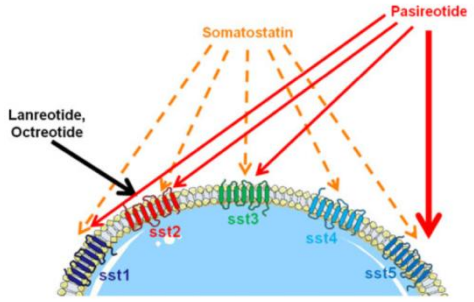
Postsurgical remission

	GH	IGF-I	
Endocrine Society 2014			
Remission	A random GH < 0.14 ng/ml	Normalized IGF-1 value	At 3 months postoperatively
Control of acromegaly	A random GH < 1 ng/ml	Normalized IGF-1 value	At 3 months postoperatively
Acromegaly Consensus Group 2020			
Remission	GH nadir <0.4 ng/ml during OGTT		Ultrasensitive assays
Control of acromegaly	A fasting GH < 1 ng/ml	Normalized IGF-1 value *[Values slightly higher than a standard cut-off for age-adjusted normalization(e.g.,within 1.2–1.3 × ULN) may be considered sufficient for control of Acromegaly](DR)*	At least 3 months postoperatively
Pituitary Society 2020			
Remission		Normalized IGF-1 value	**At 6 weeks** postoperatively
Acromegaly Consensus Group 2025			
Control of acromegaly	GH nadir <0.4 ng/ml during OGTT predicts long term remission	Normalized IGF-1 value	At 3 months postoperatively

Receptor target of medications

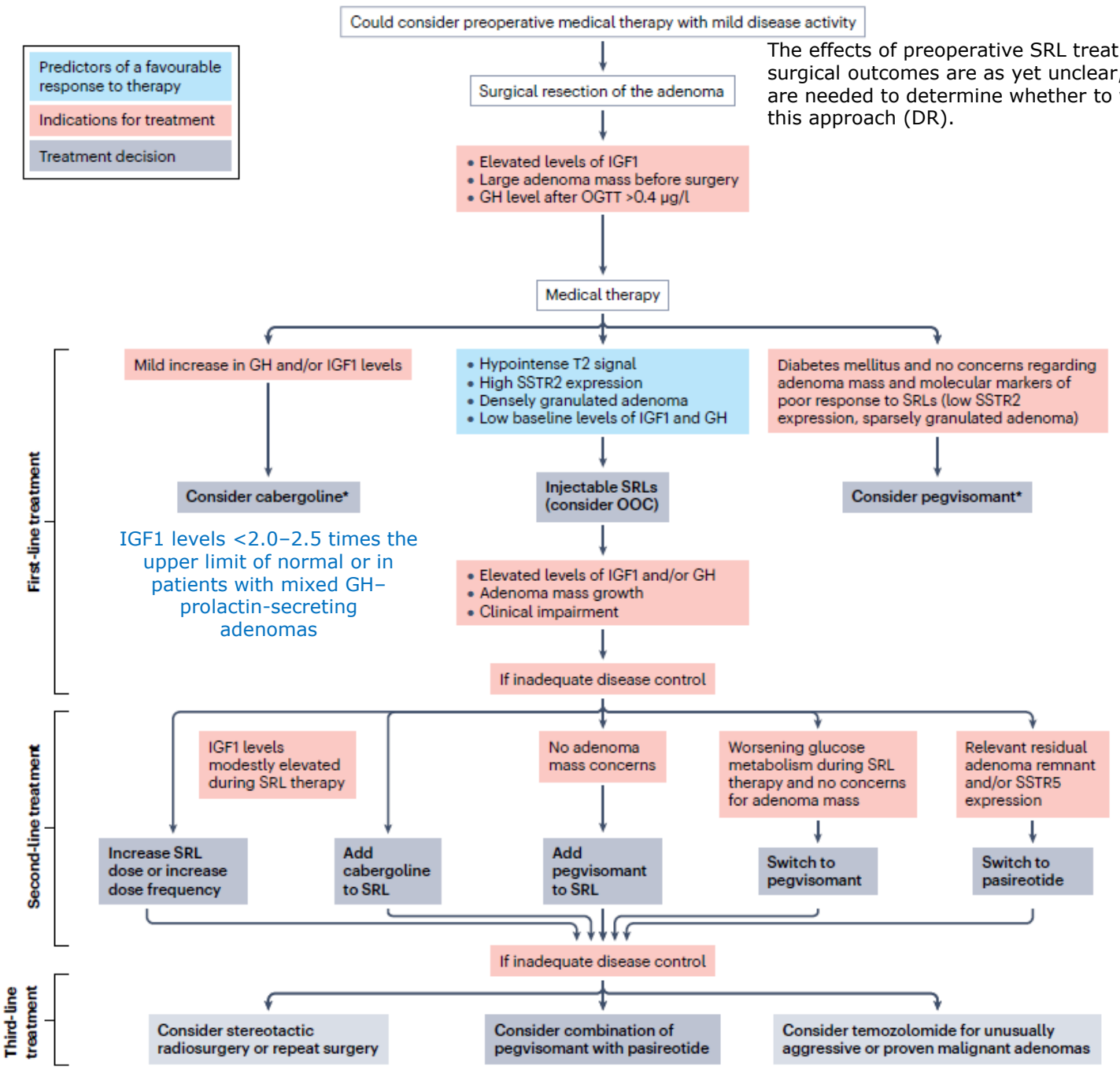


Drug	Dose
Somatostatin receptor ligands (SRL)	
First generation	
- Octreotide	50-400 μg SC q 8 h
- Octreotide LAR	10-40 mg IM q 4 wks
- Lanreotide	30 mg IM q 2 wks
- Lanreotide autogel	60-120 mg SC q 4 wks
Second generation	
- Pasireotide LAR	20, 40, 60 mg/month
GH antagonist	
- Pegvisomont	10-40 mg SC daily
Dopamine agonist	
- Cabergoline	1-4 mg orally q wk



NEJM 2006; 355:2558-2573.
Nat Rev Dis Primers. 2019.21;5(1):20. doi: 10.1038/s41572-019-0071-6.

The effects of preoperative SRL treatment in improving surgical outcomes are as yet unclear, and more studies are needed to determine whether to widely recommend this approach (DR).



Melmed S, et al. Nat Rev Endocrinol. 2025;21:718–737

*Cabergoline or pegvisomant might be considered in these selected patients as a possible first-line treatment

Cushing’s disease

Cushing's syndrome : Etiology

- Exogenous Cushing's syndrome
- Endogenous Cushing's syndrome

Endogenous Cushing's syndrome : ACTH-dependent

ACTH-secreting pituitary tumor (Cushing's disease)

Ectopic ACTH syndrome / Ectopic CRH syndrome

Macronodular adrenal hyperplasia (MAH)

Endogenous Cushing's syndrome : ACTH-independent

Adrenal adenoma

Adrenal carcinoma

Primary pigmented nodular adrenal hyperplasia (PPNAD)

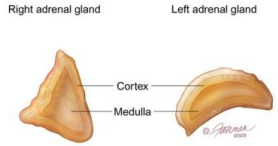
Carney's complex (PPNAD + mesen tumor-atrial myxoma + spotty skin pigmentation + other tumors: breast, tetes, pituitary (GH))

McCune-Albright syndrome

ACTH independent macronodular adrenal hyperplasia (AIMAH)

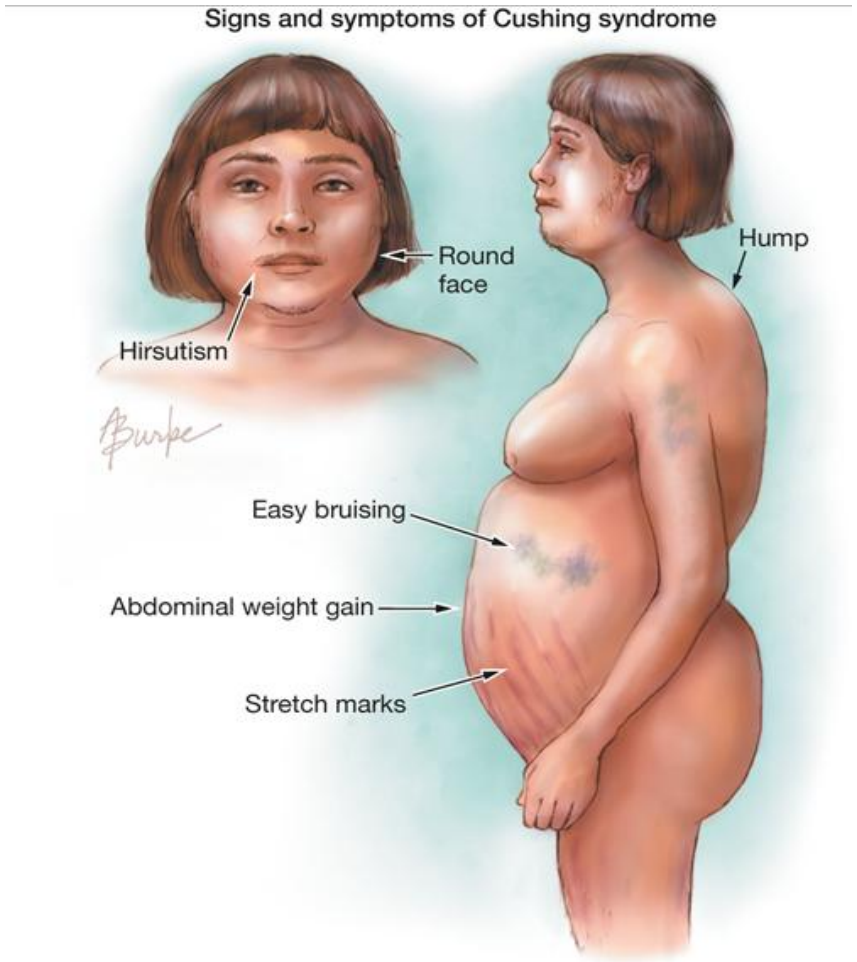
Cushing's disease

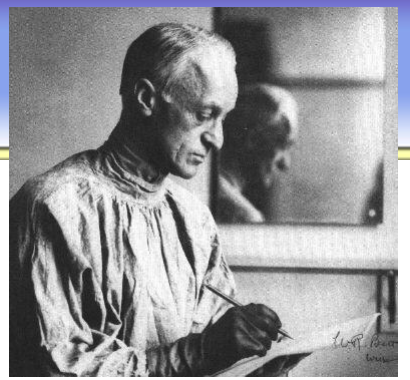
↑ **ACTH**

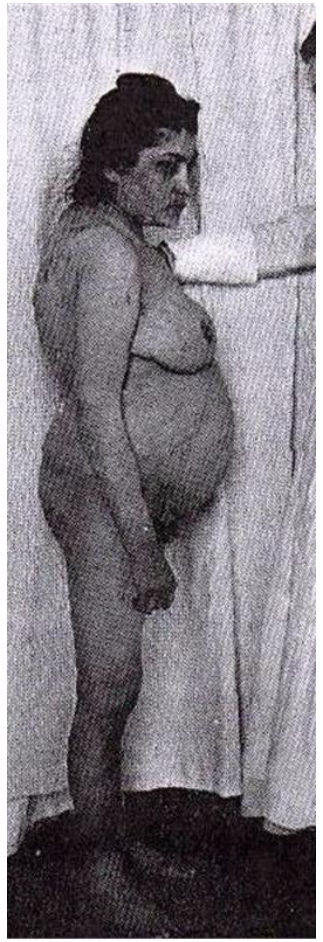


↑ **Cortisol**

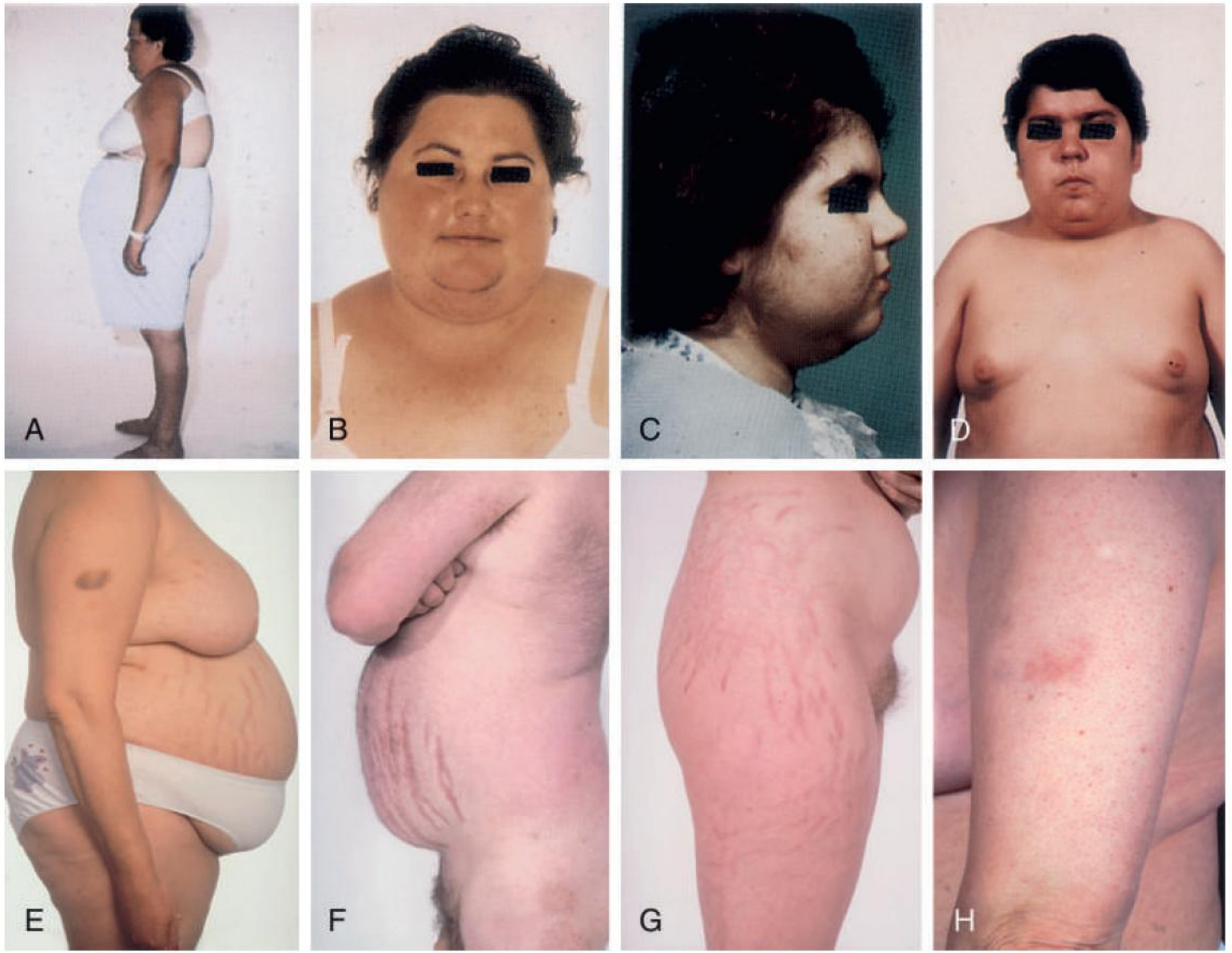
Cushing's disease







Bull Johns Hopkins Hosp. 1932;50:137–195.



Williams of Endocrinology textbook.14th;2020 p 480-541

Clinical features of Cushing's syndrome

Frequent and nonspecific for Cushing syndrome, %	Frequent and Cushing syndrome specific, %
Recent weight gain, 70-95	Round face, ≤90
Plethora, 70-90	Osteopenia or osteoporosis and fragility fractures, ≤80
Oligo or amenorrhea, 70-80	Muscle weakness, 60-80
Depression, 50-80	
Hypertension, 60-90	
Hirsutism, 50-75	
Sleep disorders, ≈60	
Dyslipidemia, 40-70	
Decreased libido, 25-90	
Cognitive impairment (exact prevalence unknown)	
Vitamin D deficiency (exact prevalence unknown)	
Less frequent and nonspecific to Cushing syndrome, %	**Less frequent and Cushing syndrome specific, %**
Kidney stones, ≤50	Dorsocervical fat pad, ≈50
Diabetes, ≈30	Purple striae, <50
Atherosclerosis, ≈30	Easy bruising, ≈50
Acne, <50	Thin skin, ≈40
Hair loss, 30	Unusual infection

The best discriminate features

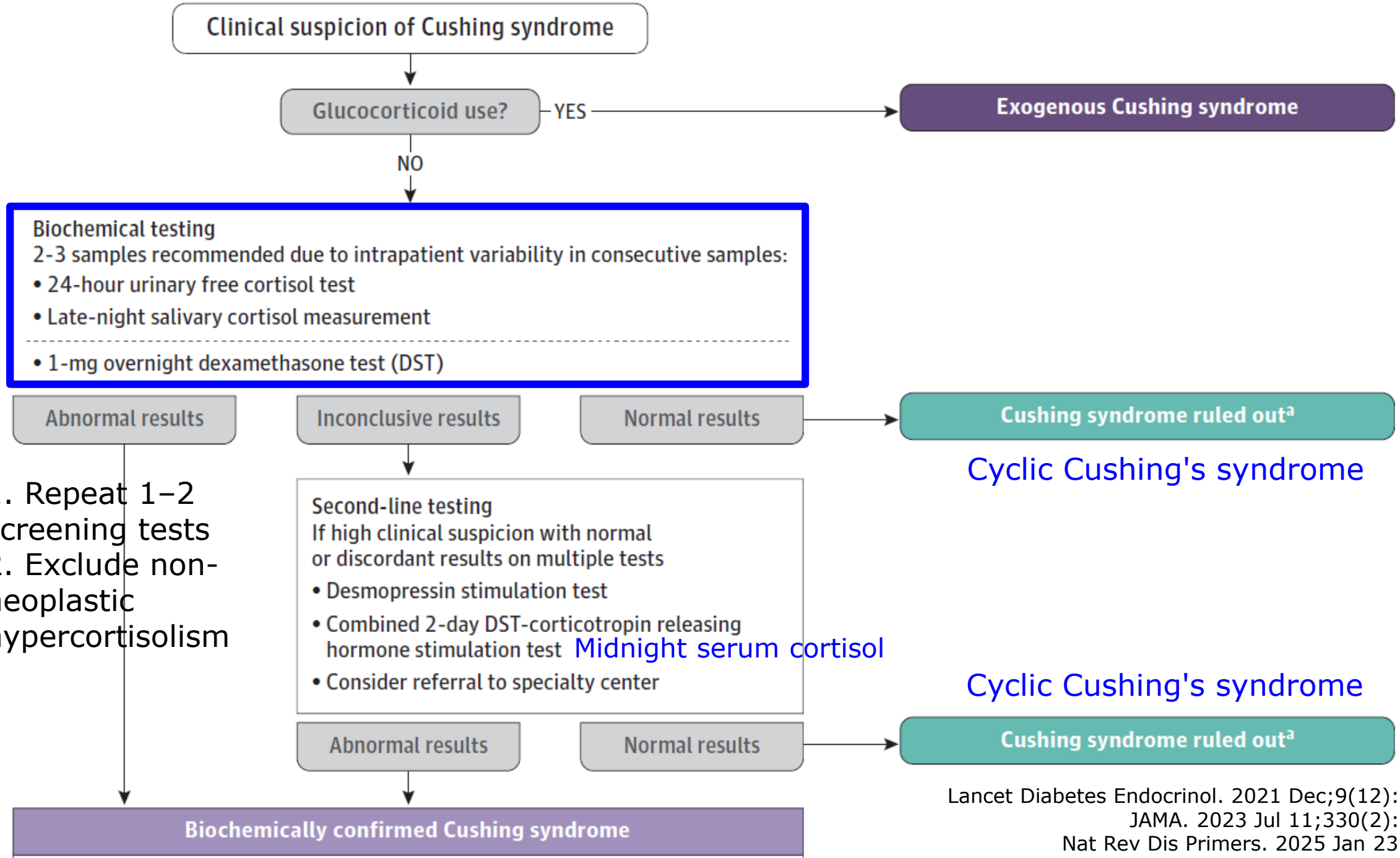
- Easy bruising
- Facial plethora
- Proximal muscle weakness
- Striae (reddish purple > 1cm)
- In children, weight gain with decreasing growth velocity

J Clin Endocrinol Metab, 2008, 93(5):1526–1540
JAMA. 2023 Jul 11;330(2):170-181.
Nat Rev Dis Primers. 2025 Jan 23;11(1):4.

Glucocorticoid excess evaluation

- Patients with unusual features for age (*e.g.* osteoporosis, hypertension)
- Patients with multiple and progressive features, particularly those that are more predictive of Cushing's syndrome
- Children with decreasing height percentile and increasing weight
- Patients with adrenal incidentaloma compatible with adenoma.

J Clin Endocrinol Metab, 2008, 93(5):1526–1540



Lancet Diabetes Endocrinol. 2021 Dec;9(12):847-875.
JAMA. 2023 Jul 11;330(2):170-181.
Nat Rev Dis Primers. 2025 Jan 23;11(1):4.

	Cutoff*	Sensitivity (%)	Specificity (%)	Advantages and instructions for testing	Disadvantages and pitfalls
Diagnosis					
1 mg dexamethasone suppression test	1·8 µg/dL (50 nmol/L)	98	81	High negative predictive value; easy for health-care provider to administer	False positives common; variable dexamethasone metabolism can confound results; oral oestrogen can increase corticosteroid-binding globulin
24-h urinary-free cortisol	Assay-specific reference range	91	81·5	Wide range for normal values	Cumbersome for patient to undertake; variability could be 50% between samples, thus 2–3 collections are needed
Late-night salivary cortisol	Assay-specific reference range	97	97·5	Easy for patient to perform; patients should be cautioned not to eat, drink, smoke, or brush their teeth for 15 min before collecting saliva samples	Intra-patient variability; cut-offs vary substantially based on reference laboratory; potential for contamination with topical hydrocortisone; not available in all centres
Monitoring for recurrence					
Late-night salivary cortisol	0·27 µg/dL (7·5 nmol/L)	75–90	93–95	In most patients late-night salivary cortisol is abnormal earlier than dexamethasone suppression test and urinary-free cortisol	Intra-patient variability; can be normal despite recurrence
24-h urinary-free cortisol	1·6 × ULN	68	100	Direct reflection of bioavailable cortisol	Approximately 50% intra-patient variability; last test to show abnormal results
Desmopressin test	Absolute cortisol increments of 7·0–7·4 µg/dL from baseline†	68	95	Earliest test to show positive results in some studies; predicts presence of corticotroph tumour; can become positive before clinical adenoma recurrence	Dynamic labour-intensive testing
1 mg dexamethasone suppression test	1·8 µg/dL (50 nmol/L)	NA	NA	Likely to be abnormal before 24-h urinary-free cortisol	Limited evidence specifically assessing utility for recurrence

ULN=upper level of normal. NA=not available. ACTH=adrenocorticotropic hormone.*Cutoffs specified are for adults. Some experts recommend using the same cutoffs for initial diagnosis and recurrence. †Some studies use ACTH absolute cutoffs or increments.

Table 1: **Laboratory tests for Cushing's syndrome diagnosis and monitoring for Cushing's disease recurrence**[12,13,158,166]

Lancet Diabetes Endocrinol. 2021 Dec;9(12):847-875.

Urine free cortisol (UFC)

False positive	False negative
• High fluid intake > 5 L/d	• Incomplete urine collection
• Hypercortisolism conditions without Cushing's syndrome	• CKD (GFR < 60 ml/min)

• Drugs increase UFC results
  • Carbamazepine (increase)
  • Fenofibrate (increase if measured by HPLC)
  • Some synthetic glucocorticoids (immunoassays)
  • Drugs that inhibit 11β-HSD2 (licorice, carbenoxolone)
	• Mild Cushing's syndrome
	  • Salivary cortisol may be more useful (UFC is less sensitive than salivary cortisol and DST)

	• Cyclic Cushing syndrome

J Clin Endocrinol Metab, 2008, 93(5):1526–1540

1-mg overnight DST

False positive responses (Nonsuppresible)	False negative responses (Suppressible)

• Drugs increase CBG
  • Estrogen
  • False positive rate 50%
  • Should withdrawn for 6 wk before testing
  • Mitotane (Tamoxifen)
	• Decrease dexamethasone clearance:
	CKD (GFR < 15 ml/min)

• Failed to take dexamethasone • Adequate plasma dexamethasone concentrations > 0.22 μg/dl	• Impair dexamethasone metabolism: Liver failure

• Accelerate dexamethasone metabolism by induction of CYP 3A4
  • Phenobarbital
  • Phenytoin
  • Carbamazepine
  • Primidone
  • Rifampin
  • Rifapentine
  • Ethosuximide
  • Pioglitazone
	• Impair dexamethasone metabolism by inhibition of CYP 3A4
	  • Aprepitant/fosaprepitant
	  • Itraconazole
	  • Ritonavir
	  • Fluoxetine
	  • Diltiazem
	  • Cimetidine

• Decrease dexamethasone absorption	
• Hypercortisolism conditions without Cushing's syndrome	

J Clin Endocrinol Metab, 2008, 93(5):1526–1540

Late-night salivary cortisol

- Indications
  - Screen or confirm the diagnosis of CS
- Procedure
  - Collect a saliva sample on two separate quiet evenings between 23:00 – 24:00 at home
  - Saliva is collected either by passive drooling into a plastic tube or by placing a cotton pledget (salivette) in the mouth and chewing for 1–2 min.
  - Food was not to be eaten in the 2 hours before sample collection, and they were to avoid brushing teeth, smoking, and drinking alcohol or coffee during that time.

J Clin Endocrinol Metab, 2008, 93(5):1526–1540

Conditions associated with hypercortisolism in the absence of Cushing's syndrome

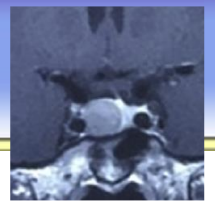
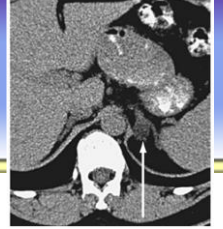
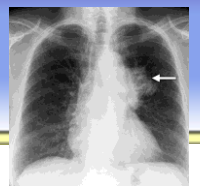
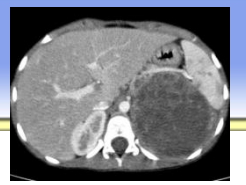
- **Some clinical features of Cushing's syndrome may be present**
  - Pregnancy
  - Depression and other psychiatric conditions
  - Alcohol dependence
  - Glucocorticoid resistance
  - Morbid obesity
  - Poorly controlled diabetes mellitus
- **Unlikely to have any clinical features of Cushing's syndrome**
  - Physical stress (hospitalization, surgery, pain)
  - Malnutrition, anorexia nervosa
  - Intense chronic exercise
  - Hypothalamic amenorrhea
  - CBG excess (increased serum but not urine cortisol)

J Clin Endocrinol Metab, 2008, 93(5):1526–1540

Differential diagnosis of Cushing syndrome

	Exogenous	ACTH dependent		Adrenal tumor	
		Cushing disease	Ectopic ACTH	Adenoma	Carcinoma
Rate of development	rapid	slow	slow - rapid	slow - rapid	rapid
Pigmentation	no	yes / no	yes / no	no	no
Androgen excess	no	no	no	no	No / yes
Basal serum cortisol	low	high	high	high	high
24-hour UFC	low	high	high	high	high
Basal plasma ACTH	low	high	very high	low	low
Low-dose DST		non-supp	non-supp	non-supp	non-supp
High-dose DST		supp or non-supp	non-supp	non-supp	non-supp

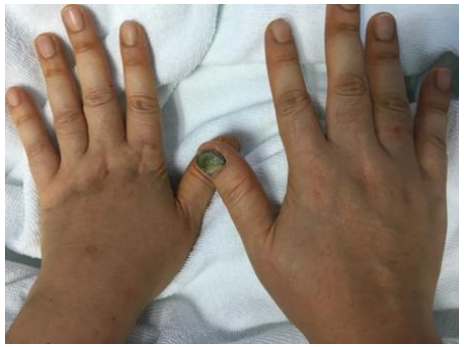
DST = dexamethasone suppression

	Cushing's disease	Adrenal adenoma	EAS (malignant)	ACC
Onset	Slow	Slow	Rapid (<3 mo)	Rapid (<3 mo)
Typical features of CS	+++	+++	+/-	+/-
Metabolic manifestations of glucocorticoid excess - Hypertension with hypokalemia and metabolic alkalosis	+ (10-15%)	+	+++ Rapid and progressive (>95%)	+++ Rapid and progressive
- Diabetes (poor control)	+	+	+++	+++
Hyperpigmentation	++/-	-	+/-	-
Androgen excess	-	-	-	+

High mortality rate

Strategy for the differential diagnosis of CS



Measure ACTH

- **ACTH-independent (primary adrenal disease)** ≤10 pg/ml
  - **Adrenal gland imaging**
    - Unilateral lesion → Adenoma or carcinoma
    - Bilateral lesions → PBMAH, iMAD or PPNAD Or two adenomas (both or only one functional)
- **Indeterminate** 10–20 pg/ml
- **ACTH-dependent** ≥20 pg/ml
  - **Pituitary MRI**
    - No lesions or <8 mm → **6-9 mm** → **BIPSS** and/or **8-mg DST ± Desmo ST**
    - Lesion ≥8 mm → **≥10 mm** → **8-mg DST ± Desmo ST**

8-mg DST ± Desmo ST → CD Ectopic ACTH

Lancet Diabetes Endocrinol. 2021 Dec;9(12):847-875.
JAMA. 2023 Jul 11;330(2):170-181.
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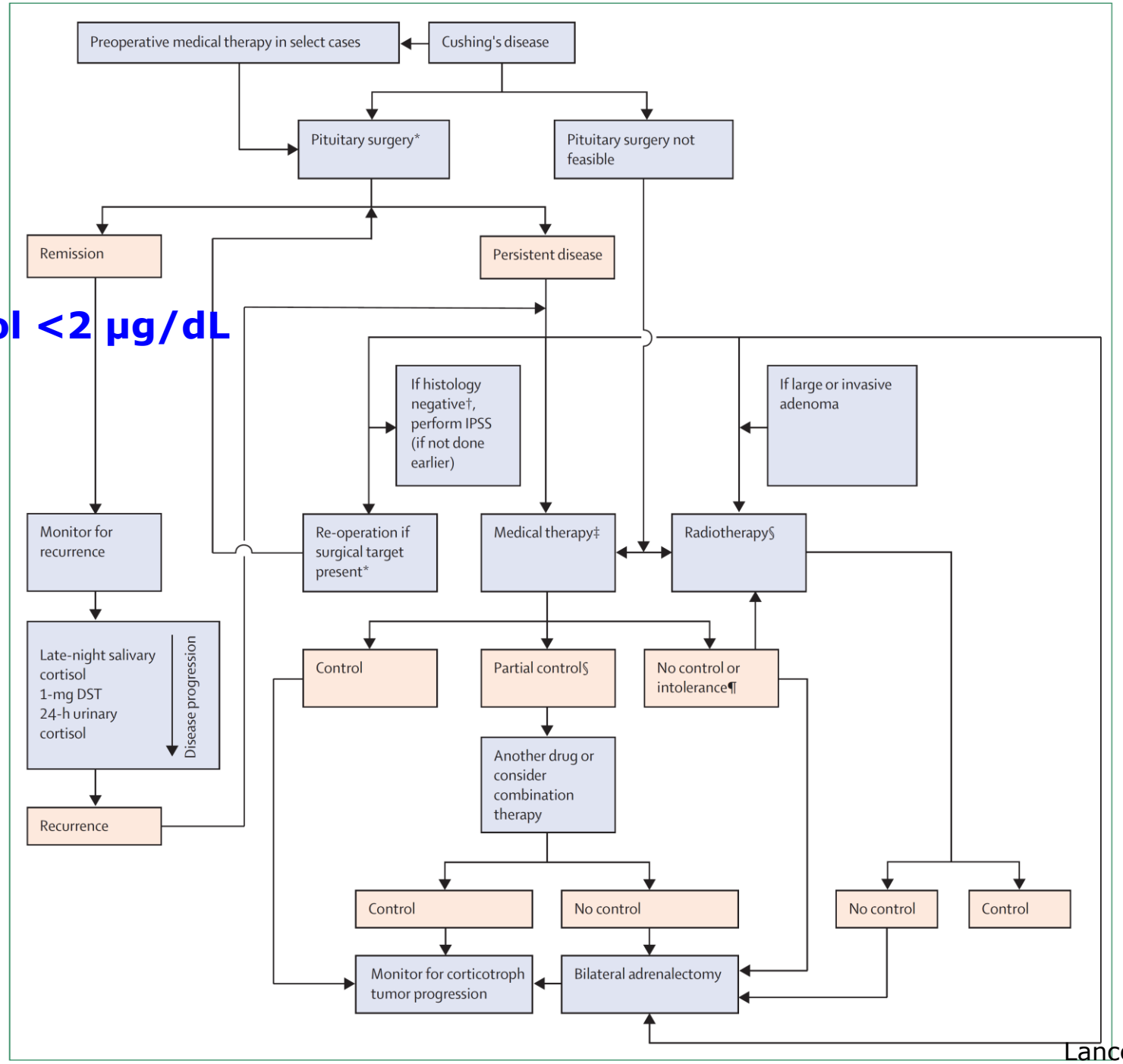
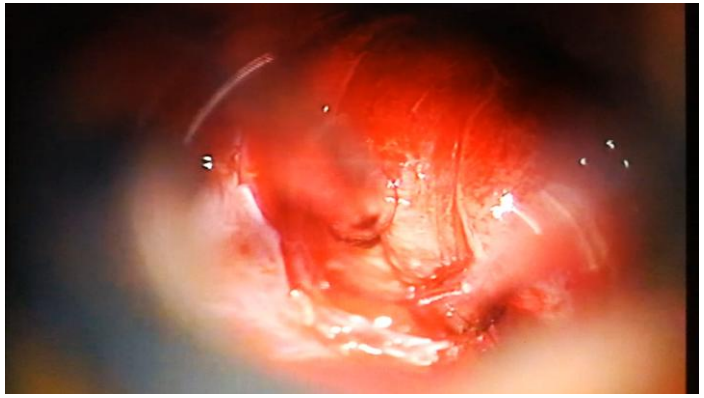
Cortisol <2 µg/dL



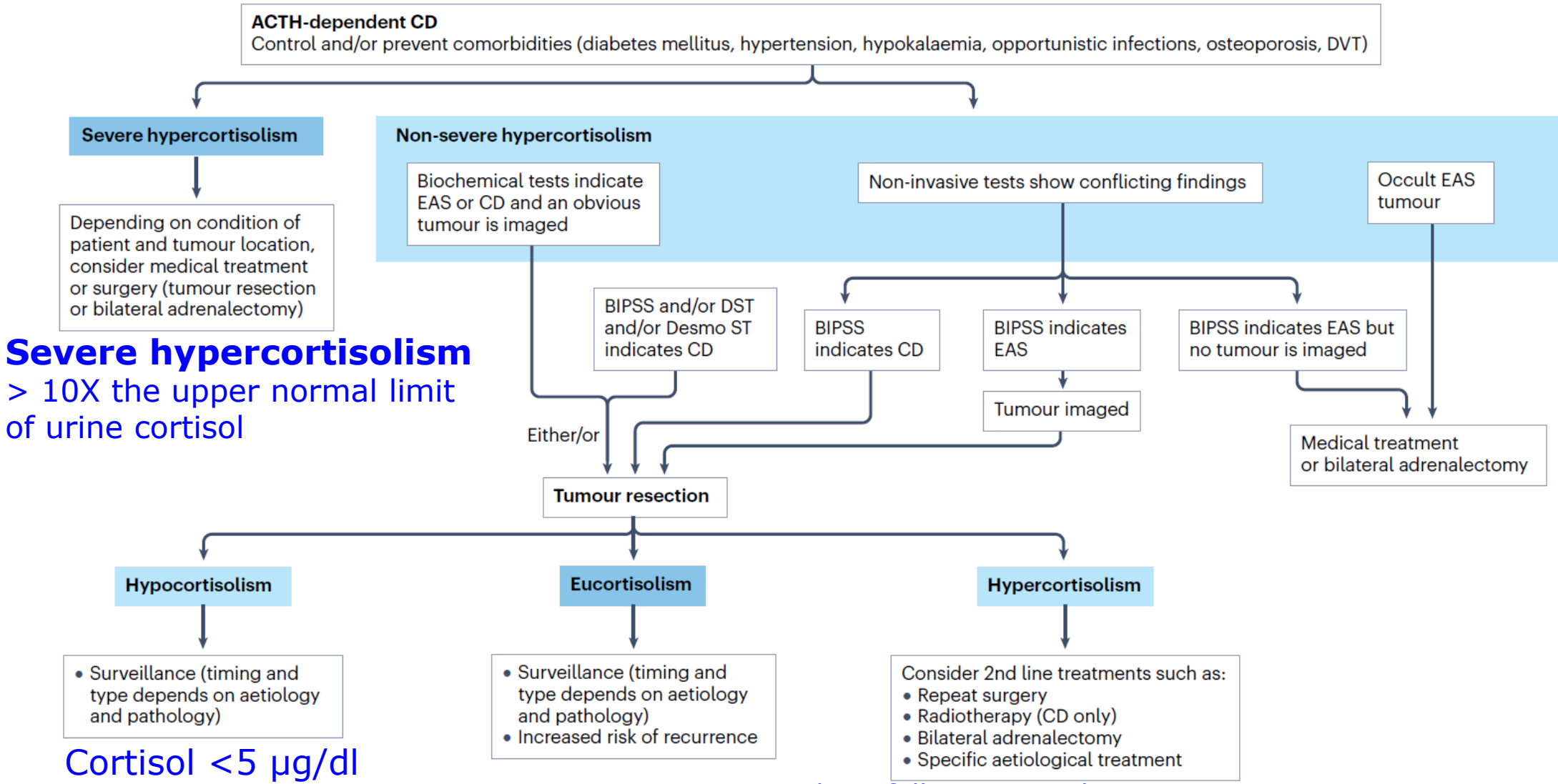


Use of the tumor pseudocapsule to achieve complete excision

Lifelong monitoring for recurrence of Cushing's disease

Lancet Diabetes Endocrinol. 2021 Dec;9(12):847-875.

Management of ACTH-dependent CS



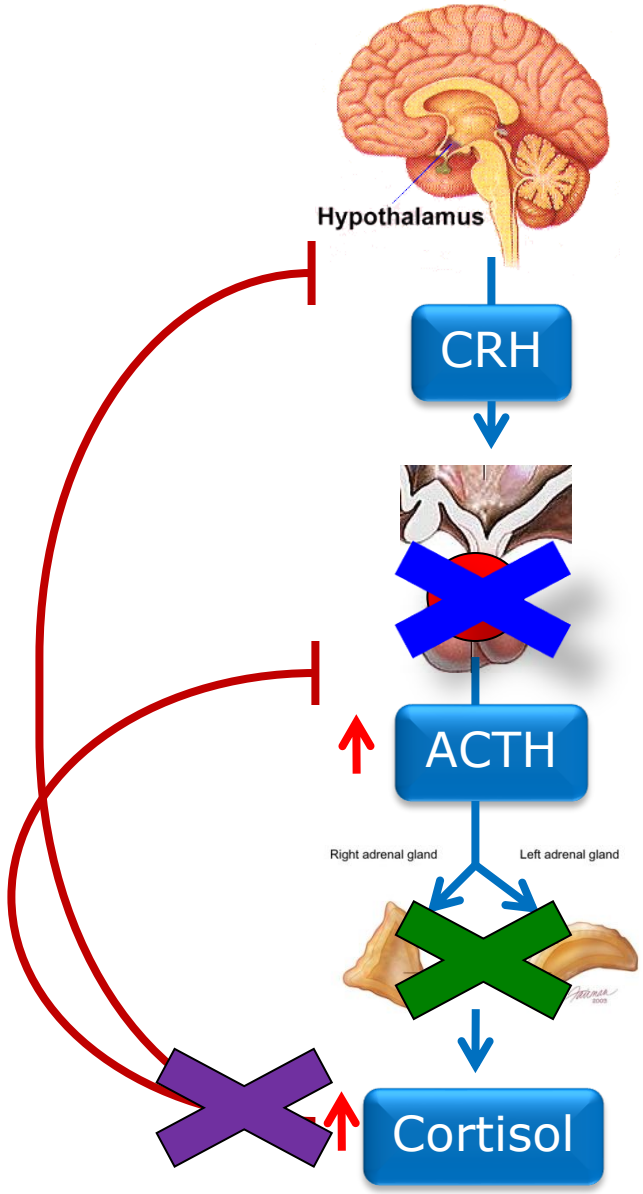
Severe hypercortisolism
> 10X the upper normal limit of urine cortisol

Cortisol <5 µg/dl
(ACTH <15 pg/ml)

Remission in patients without full corticotroph suppression
(mild hypercortisolism or previous medical treatment)

Nat Rev Dis Primers. 2025 Jan 23;11(1):4.

Medical treatment of CS



Pituitary-directed

Dopamine receptor agonist
Cabergoline

Somatostatin receptor ligand
Pasireotide

Steroidogenesis inhibitors
Ketoconazole, Metyrapone, Mitotane, Etomidate, levoketoconazole, Osilodrostat

Glucocorticoid receptor antagonist
Mifepristone

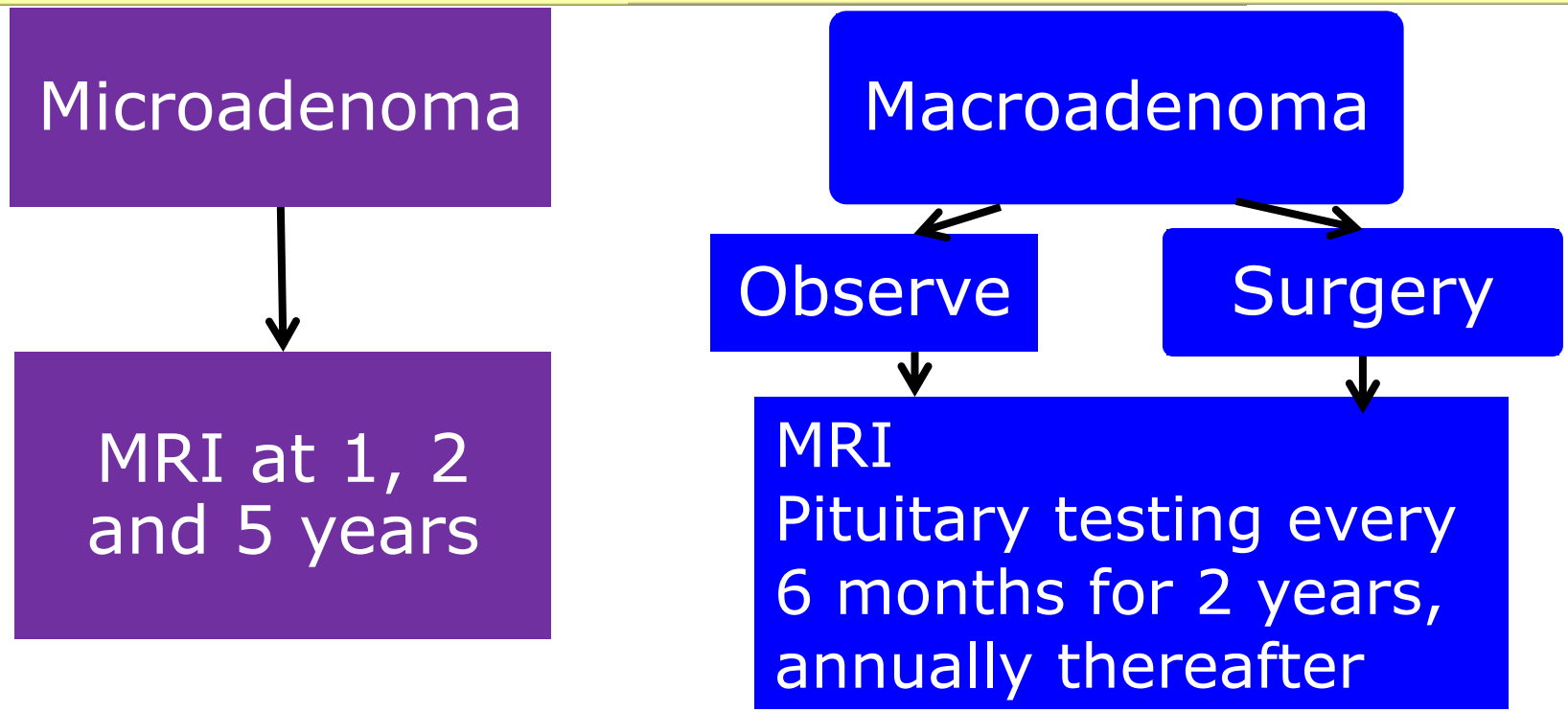
JCEM 2015, 100(8):2807-2831.

Outlines

- Pituitary gland anatomy and function
- Presentation of sellar lesions
- Pituitary tumors
  - Functioning:
    - Prolactinoma
    - Acromegaly
    - Cushing's disease
  - Nonfunctioning
- Pituitary apoplexy

Clinically nonfunctioning pituitary adenoma

Treatment of NFT



The absence of adenomatous residue

MRI is repeated annually for 5years, then at 7, 10 and 15 years.

Adenomatous remnant or suspect image,

MRI is repeated annually for 5 years and then every 2 or 3 years in the absence of progression.

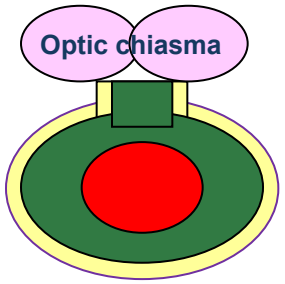
Williams of Endocrinology textbook.14th;2020 p 236-302, Annales d'Endocrinologie 76 (2015) 239–247

Treatment of NFT

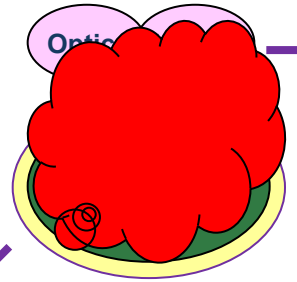
- Surgery: The first-line treatment
- Indications
  - Symptomatic macroadenoma
    - *Visual disorders*
    - *Hypopituitarism*
    - *Mass effect: headache*
  - Asymptomatic macroadenoma
    - The kinetics of progression on two successive MRI scans
    - The decision is made on an individual basis

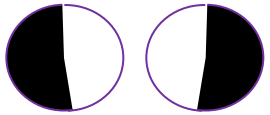
Williams of Endocrinology textbook.14th;2020 p 236-302, Annales d'Endocrinologie 76 (2015) 239–247

Pituitary apoplexy (pituitary hemorrhage)



Intratumor bleeding





Bitemporal hemianopia

Headache
(sudden headache)
Stiff neck

PRL

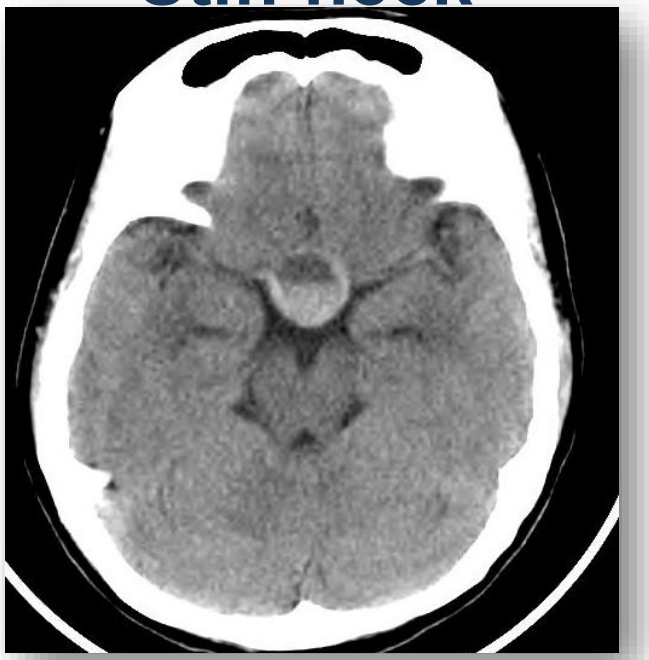
Hypopituitarism

FSH / LH

GH

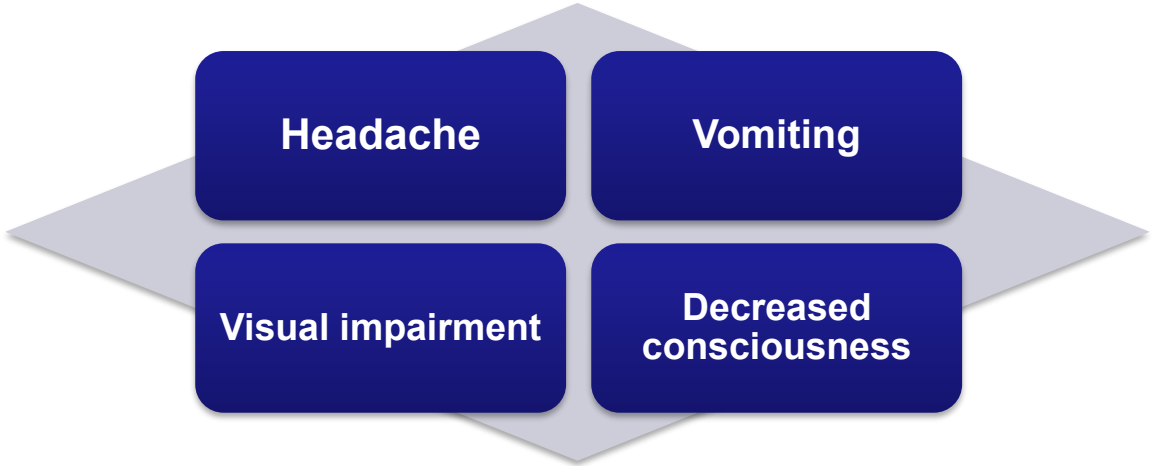
ACTH
TSH

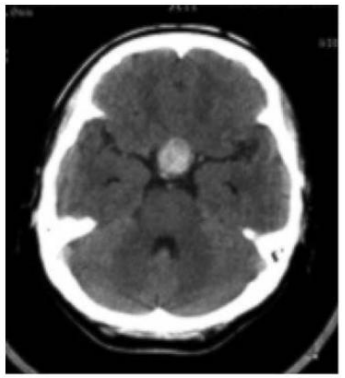
Adrenal Insufficiency (Hypotension)



Pituitary apoplexy (pituitary hemorrhage)

- Pituitary apoplexy is a rare but life-threatening medical emergency.



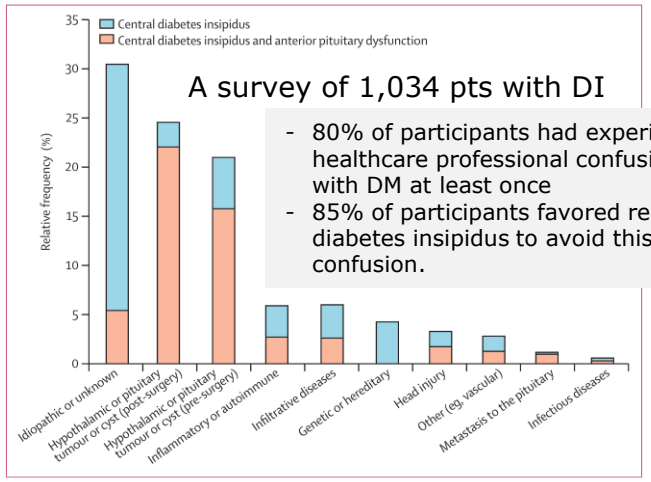


- **Adrenal crisis management**
  - Blood for cortisol
  - Do not wait for laboratory results
  - Hydrocortisone 100 mg IV push then 200 mg IV drip in 24 hr

Changing the Name of Diabetes Insipidus

Arginine vasopressin deficiency (AVP-D)
for central etiologies

Arginine vasopressin resistance (AVP-R)
for nephrogenic etiologies



A survey of 1,034 pts with DI

- 80% of participants had experienced a healthcare professional confusing DI with DM at least once
- 85% of participants favored renaming diabetes insipidus to avoid this confusion.

***Figure 1:* Causes of central diabetes insipidus**
The proportion of participants with isolated central diabetes insipidus cases and proportion with combined central diabetes insipidus and anterior pituitary dysfunction due to each clinical cause.

Lancet Diabetes Endocrinol 2022; 10: 700–09

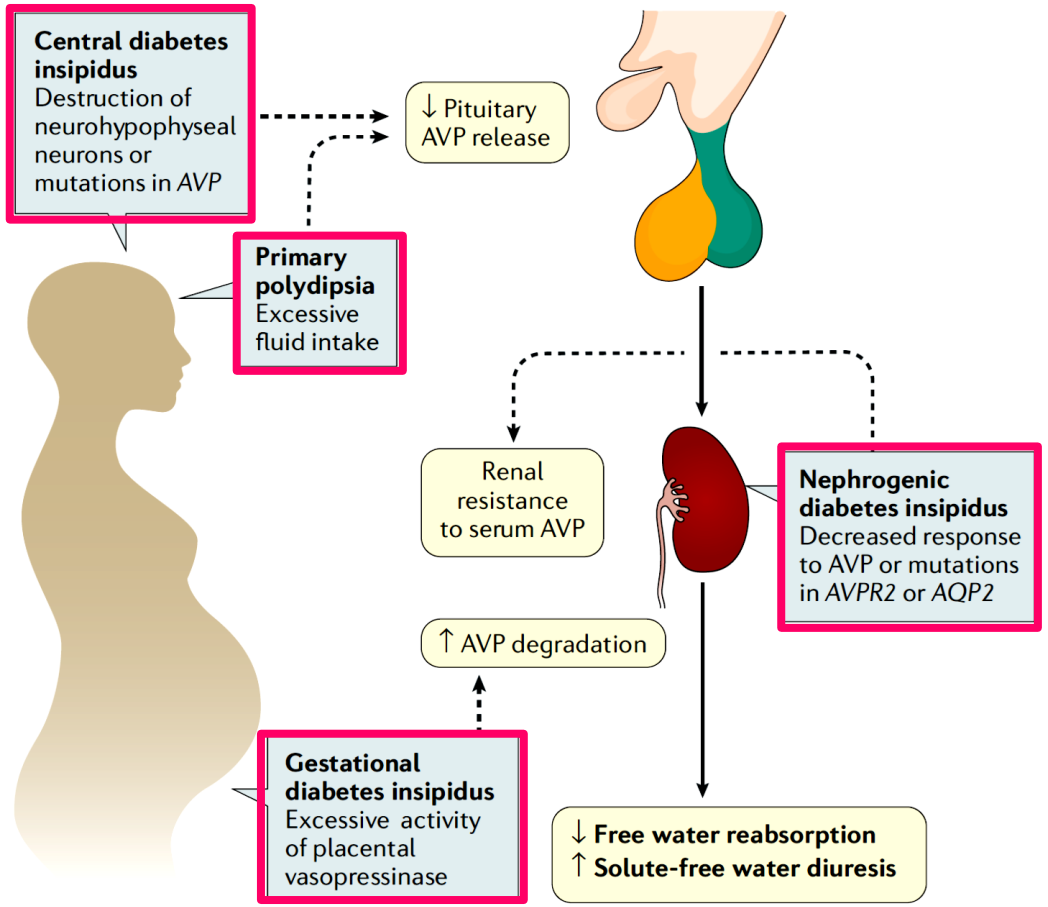
The transition period
- Using the terms AVP-Deficiency (cranial DI) and AVP-Resistance (nephrogenic DI) in manuscripts and chapters

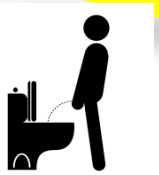
1. Endocrine Society
2. European Society of Endocrinology
3. Pituitary Society
4. Society for Endocrinology
5. European Society for Pediatric Endocrinology
6. Endocrine Society of Australia
7. Brazilian Endocrine Society
8. Japanese Endocrine Society

The Journal of Clinical Endocrinology & Metabolism, 2023, 108, 1–3

Polyuria–Polydipsia Syndrome

- **Polyuria**: High output of hypotonic urine (>50 ml/kg/24 h)
- **Polydipsia** of more than 3 L a day





Urine output and Sp.gr. (Urine osmolality <800 mOsm/Kg)

Fluid intake

The differential diagnosis of polyuria polydipsia syndrome

- **Central diabetes insipidus**
- **Nephrogenic diabetes insipidus**
- **Primary polydipsia**
- **Gestational diabetes insipidus**

Christ-Crain. M., et al. Nat Rev Dis Primers. 2019 Aug 8;5(1):54. doi: 10.1038/s41572-019-0103-2.

Etiology of Polyuria–Polydipsia Syndrome

Basic defect	Acquired causes	Hereditary causes
Central DI		
Deficiency in AVP synthesis or secretion SARS-CoV2	• Trauma (surgery and deceleration injury) • Neoplasia (craniopharyngioma, meningioma, germinoma and metastases) • Vascular (cerebral or hypothalamic haemorrhage and infarction or ligation of anterior communicating artery aneurysm) • Granulomatous (histiocytosis and sarcoidosis) • Infectious (meningitis, encephalitis and tuberculosis) • Inflammatory or autoimmune (lymphocytic infundibuloneuro-hypophysitis and IgG4 neurohypophysitis) • Drug or toxin exposure • Osmoreceptor dysfunction (adipsic DI) • Others (hydrocephalus, ventricular or suprasellar cyst, and trauma and degenerative diseases) • Idiopathic	• Autosomal dominant: *AVP* mutations • Autosomal recessive, type a and b: *AVP* mutations • Autosomal recessive, type c: *WFS1* mutations • Autosomal recessive, type d: *PCSK1* mutations • X-linked recessive: gene unknown
Nephrogenic DI		
Reduced renal sensitivity to antidiuretic effect of physiological AVP levels	• Drug exposure (lithium, demeclocycline, cisplatin, etc.) • Hypercalcaemia or hypokalaemia • Infiltrating lesions (sarcoidosis, amyloidosis, multiple myeloma, etc.) • Vascular disorders (sickle cell anaemia) • Mechanical (polycystic kidney disease and urethral obstruction)	• X-linked: *AVPR2* mutations • Autosomal recessive or dominant: *AQP2* mutations
Primary polydipsia		
Excessive fluid intake at a diminished set point	• Dipsogenic[a] (idiopathic or similar lesions as with central DI) • Psychosis intermittent hyponatraemia–polydipsia (PIP) syndrome • Compulsive water drinking • Health enthusiasts	NA
Gestational DI		
Increased enzymatic metabolism of circulating AVP hormone	Pregnancy	NA

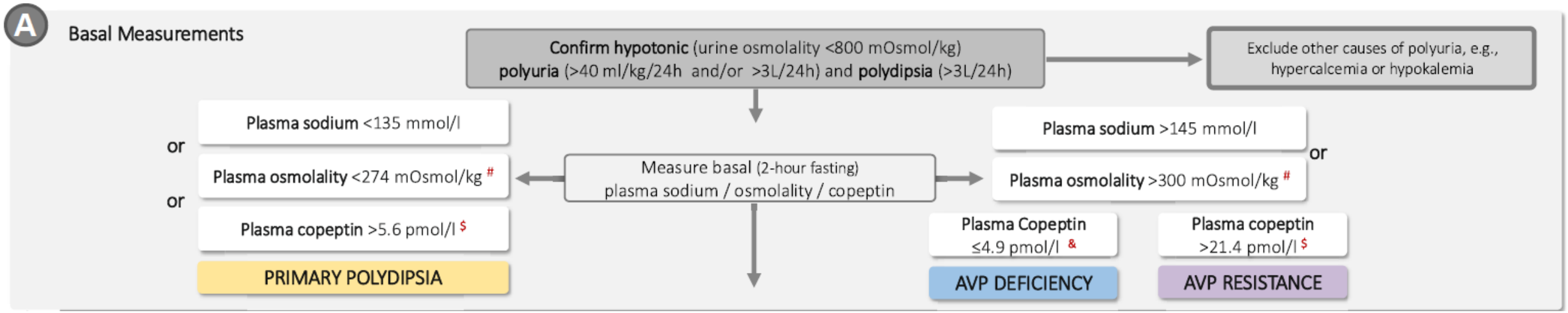
[a]Downward resetting of the thirst threshold. AVP, arginine vasopressin; DI, diabetes insipidus; NA, not applicable.

Clinical symptoms of Central Diabetes insipidus

- **A sudden onset of symptoms**
- **A preference for cold drinks**
- **Drinking at night**
- **The presence of nocturia**
- **The presence of thirst**

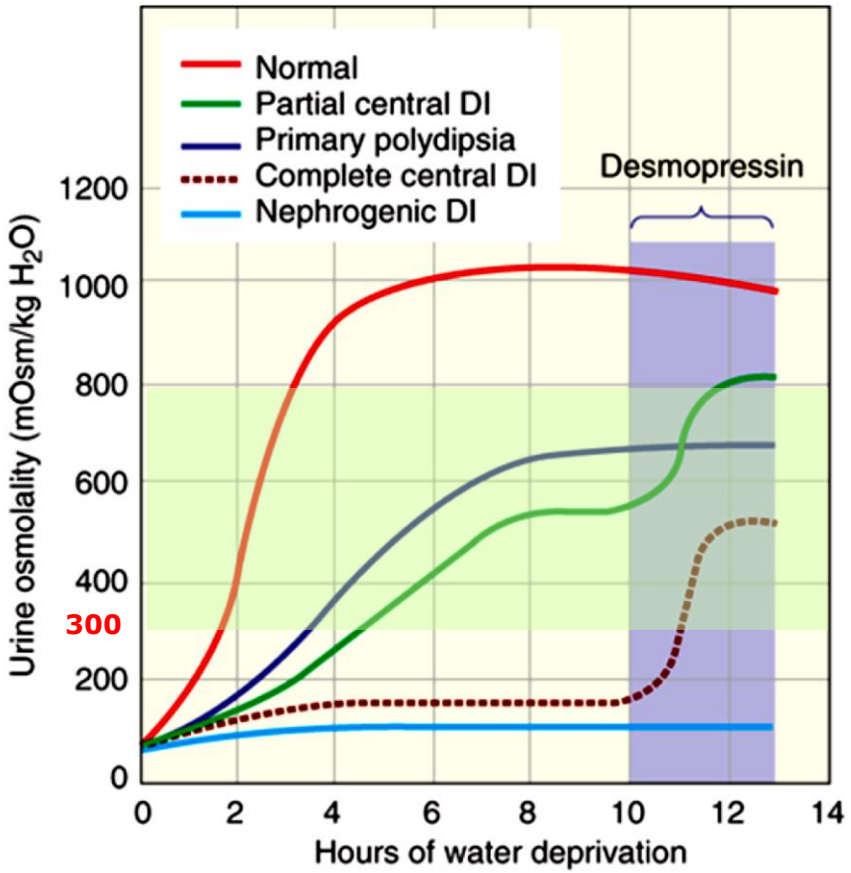
Refardt J. Best Practice & Research Clinical Endocrinology & Metabolism 34 (2020) 101398
Christ-Crain. M., et al. Nat Rev Dis Primers. 2019 Aug 8;5(1):54. doi: 10.1038/s41572-019-0103-2.

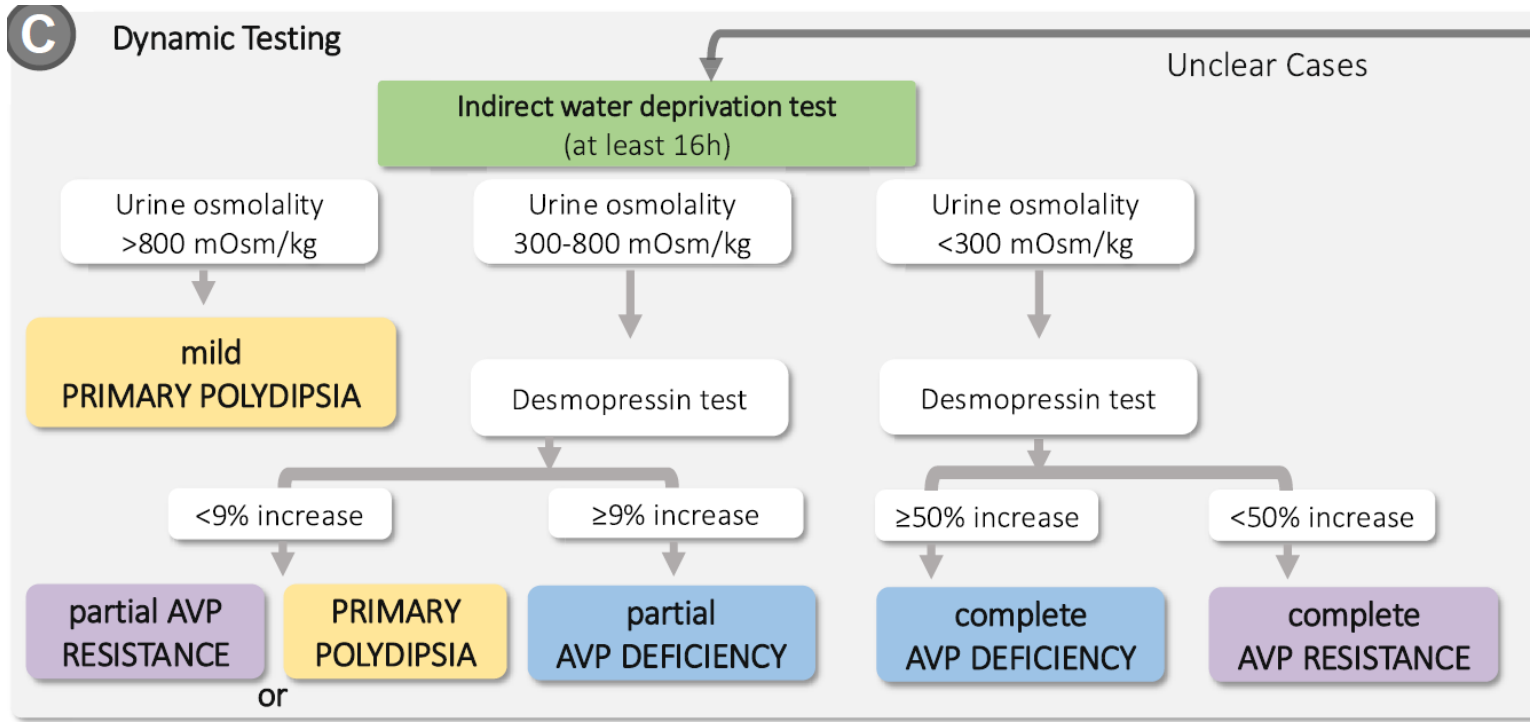
Polyuria–Polydipsia Syndrome



Atila C, Refardt J, Christ-Crain M. The Journal of Clinical Endocrinology & Metabolism, 2026, 111, 922–937.

Water deprivation test





Atila C, Refardt J, Christ-Crain M. The Journal of Clinical Endocrinology & Metabolism, 2026, 111, 922–937.

Take home message

- Prolactinoma
  - Amenorrhea is the most common symptom of prolactinoma
  - Medication is the first line of treatment
- Rule out acromegaly in patients
  - With typical clinical manifestation of acromegaly: acral and facial features
  - Without typical clinical manifestation of acromegaly: sleep apnea syndrome, T2DM, debilitating arthritis, carpal tunnel syndrome, hyperhidrosis and HT
  - Pituitary incidentaloma

Take home message

- Rule out Cushing’s syndrome in patients
  - With unusual features for age (e.g. osteoporosis, hypertension)
  - With multiple and progressive features, particularly those that are more predictive of Cushing’s syndrome
  - The diagnosis of Cushing's syndrome is often long delayed and can be difficult to make.
- Nonfunctioning pituitary tumor
  - Pituitary functions and VF should be assessed in macroadenoma.
- Pituitary apoplexy

Practicing and perfecting the art of medicine demands recognition.

Thank you