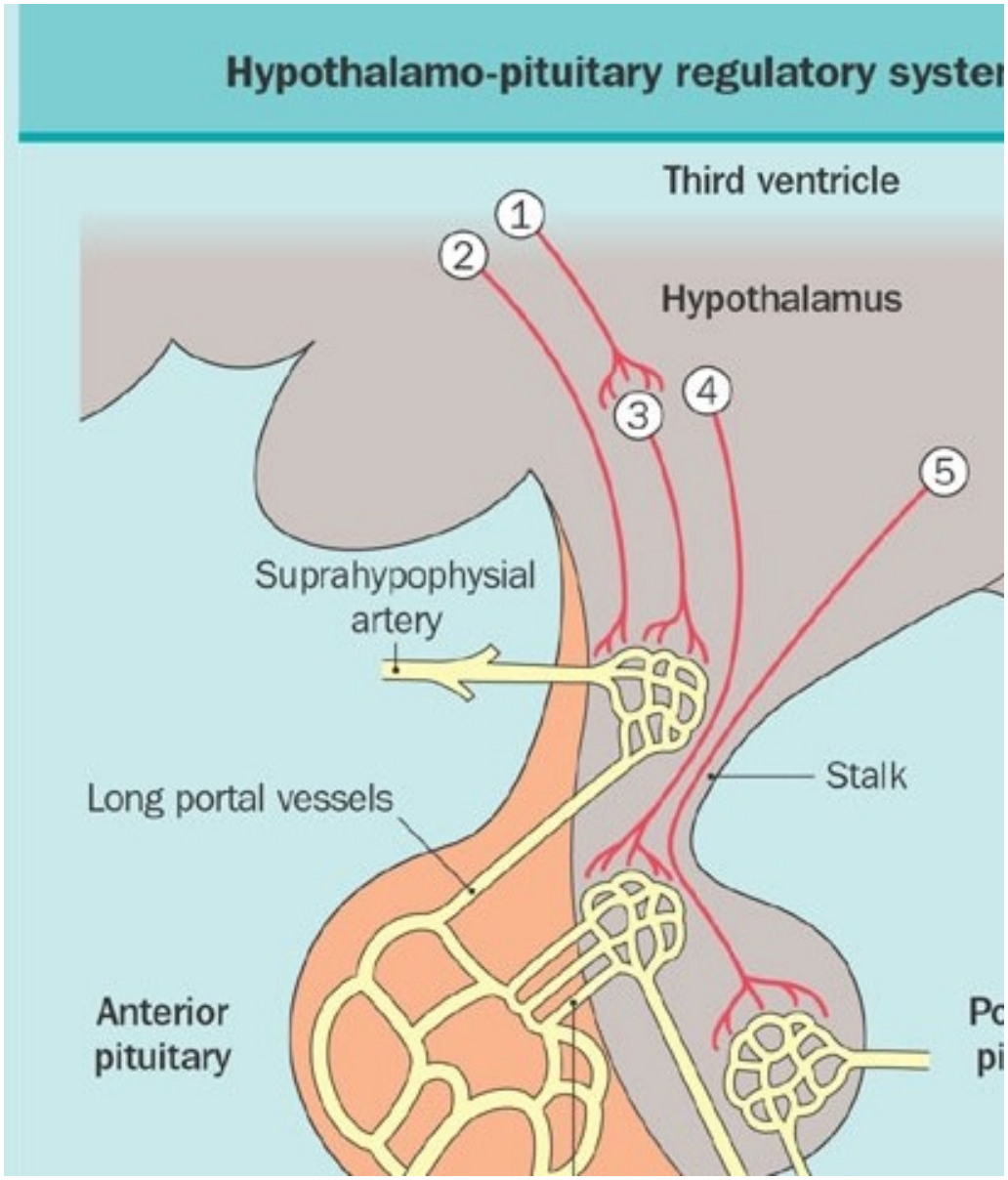
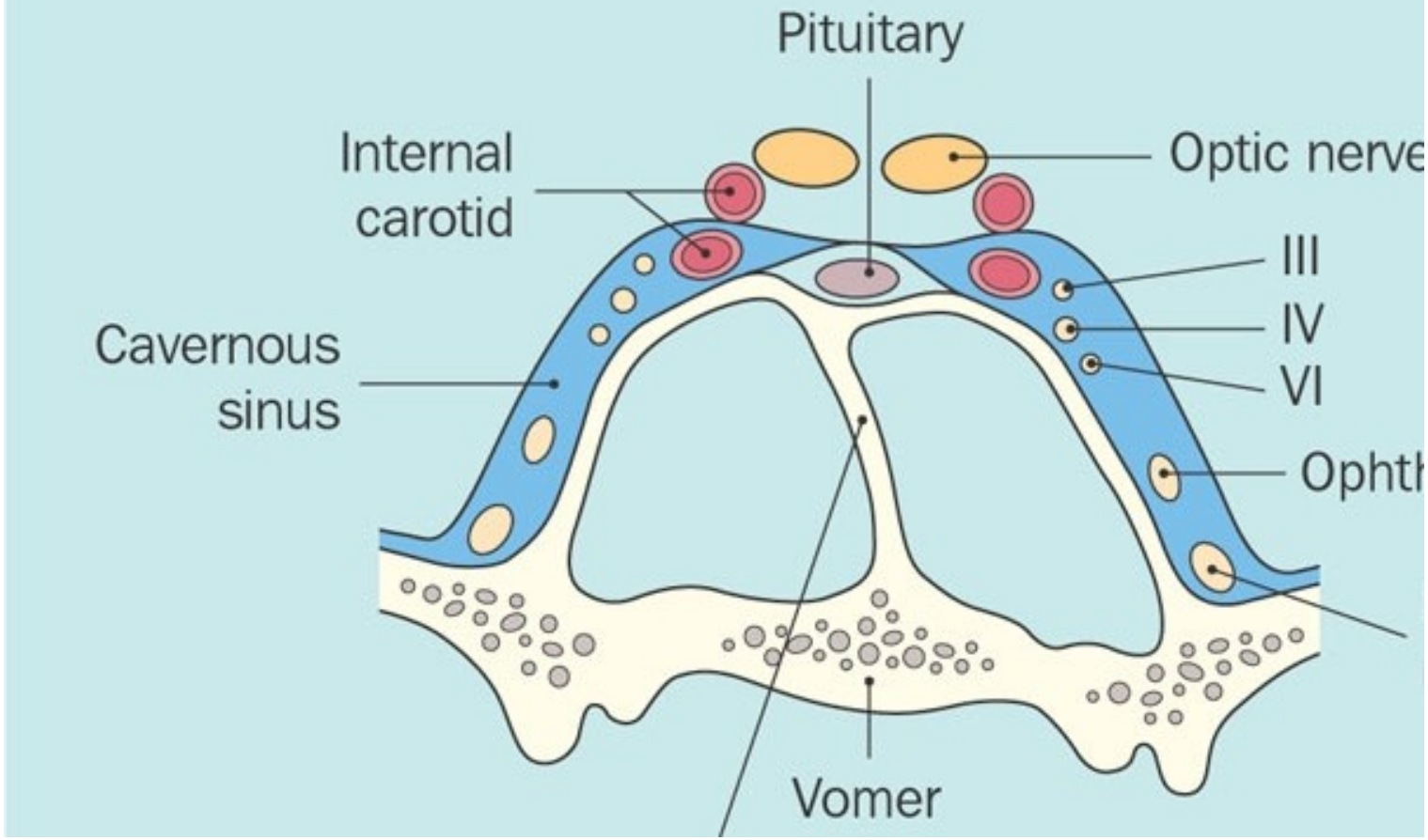
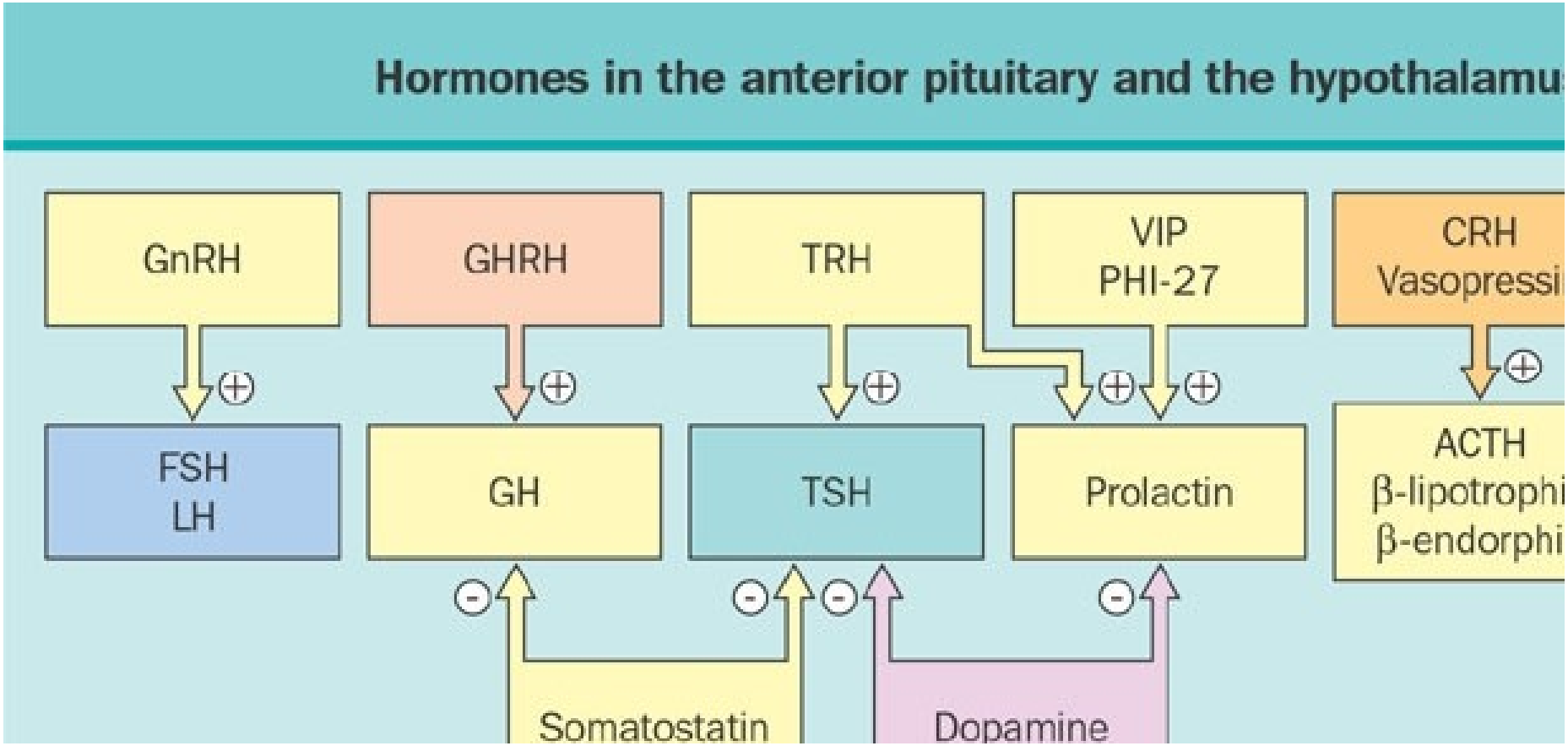
ADENOAMELE HIPOFIZARE


Hypothalamo-pituitary regulatory syste
Third ventricle
1
2
Hypothalamus
3
4
5
Suprahypophysial
artery
Stalk
Long portal vessels
Anterior
pituitary

Coronal section at the level of the cavernou




Hormones in the anterior pituitary and the hypothalamu
GnRH
GHRH
TRH
VIP
PHI-27
CRH
Vasopressi
FSH
LH
GH
TSH
Prolactin
ACTH
β-lipotrophi
β-endorphi
Somatostatin
Dopamine

TUMORILE HIPOFIZARE

10% din tumorile intracraniene la adult; 1% la copil

Clasificare

1. Izolate/sd genetice – asociaza alte manifestari endocrine/non-endocrine
2. Diametru: microadenoame < 1cm/macroadenoame > 1cm
3. Evolutie: incapsulate/invazive
4. Afinitatea tinctoriala: acidofile (GH, PRL), bazofile (ACTH, FSH, LH, TSH), cromofobe
5. Clinica: functionale (clinic secretante)/nefunctionale
6. Imunohistochimic - secretante de:

   - GH (somatotropinoame)
   - PRL (prolactinoame)
   - ACTH (corticotropinoame)
   - TSH (tirotropinoame)
   - FSH , LH (gonadotropinoame)
   - secretie mixta: ex. GH+PRL (somatomamotropinoame)
   - negativ (adenoame nule)

7. Majoritatea benigne, rar maligne (doar in prezenta metastazelor)

Clinica adenoamelor hipofizare

1. Elemente ale sindromului mecanic tumoral
2. Elemente legate de excesul hormonal
3. Elemente legate de insuficienta hipofizara

Sindromul tumoral hipofizar (1)

Cefaleea

- prin compresia durei mater de pe tavanul seii turcesti
- nacaracteristica (localizare si caracter)
- pe masura cresterii adenoamelor devine cvasipermanenta

Hipertensiunea intracraniana

- cefalee
- varsaturi (fara greata, fara efort)
- edem papilar

Sindromul tumoral hipofizar (2)

Extensie:

1. **Antero-superioara** → sindrom de compresie optochiasmatica:
   hemianopsie bitemporala
   scaderea acuitatii vizuale
   edem papilar – atrofie optica dupa 6 saptamani

2. **Laterala** → invazia sinusului cavernos
   oftalmoplegie
   ptoza palpebrala
   diplopie
3. **Superioara** → tija hipotalamo-hipofizara
   hiperprolactinemie
   diabet insipid
   insuficienta hipofizara

sindrom de hipofiza izolata

4. **Inferioara** → sinusul sfenoid → sinuzita sfenoidala + rinorahie

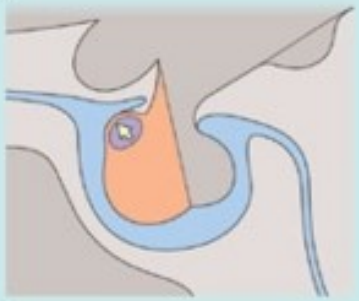
Clinical features of a pituitary tumor

Upward

a

Headaches

Stretching of dura by tumor

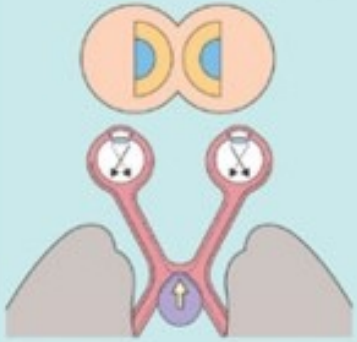


b

Hydrocephalus (rare)

Visual field defects

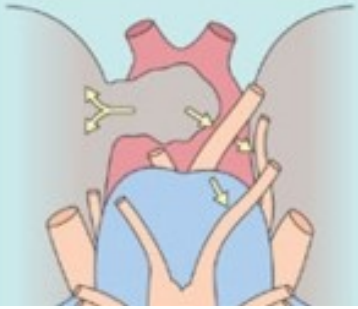
Nasal retinal fibers compressed by tumor

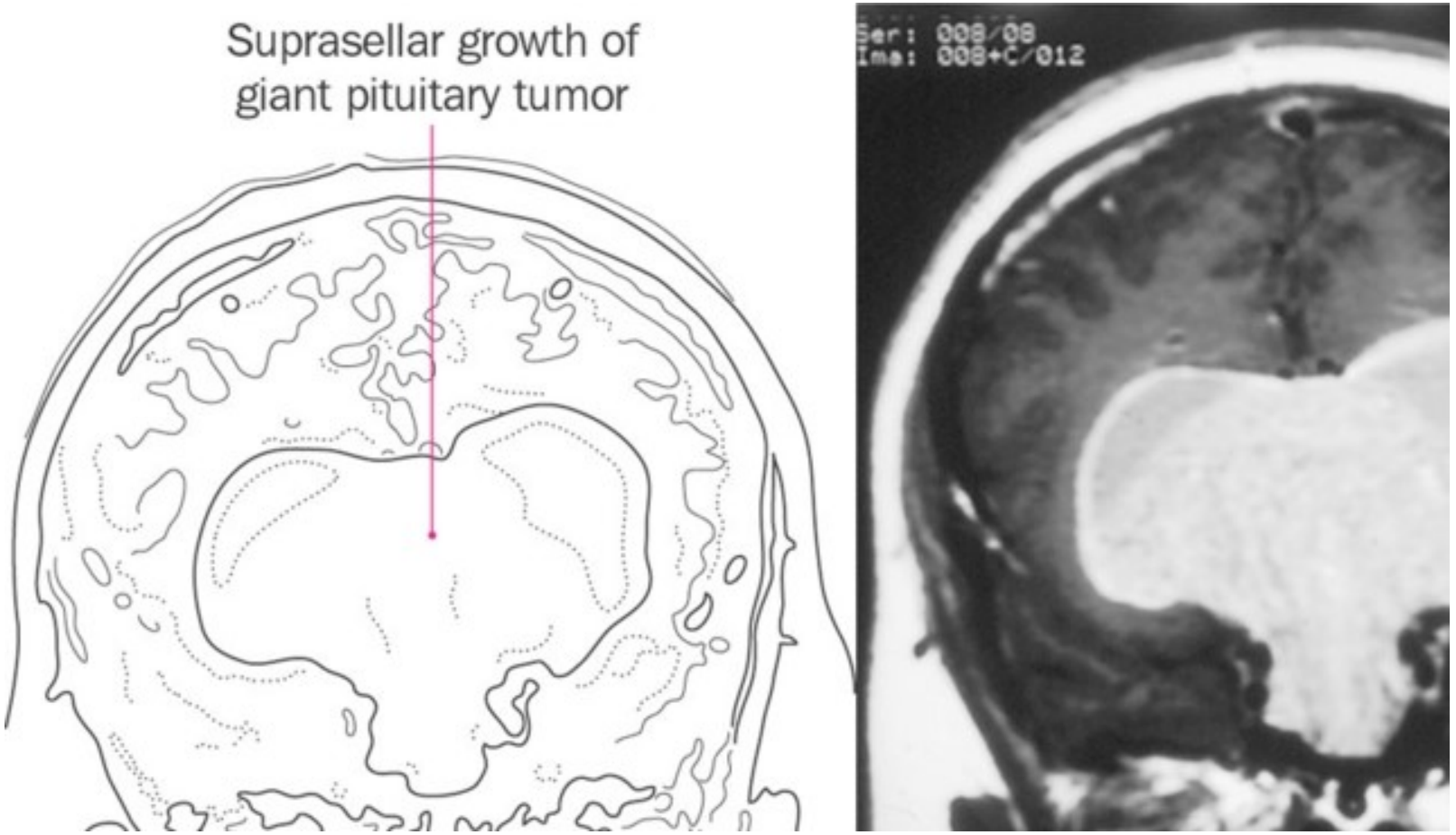


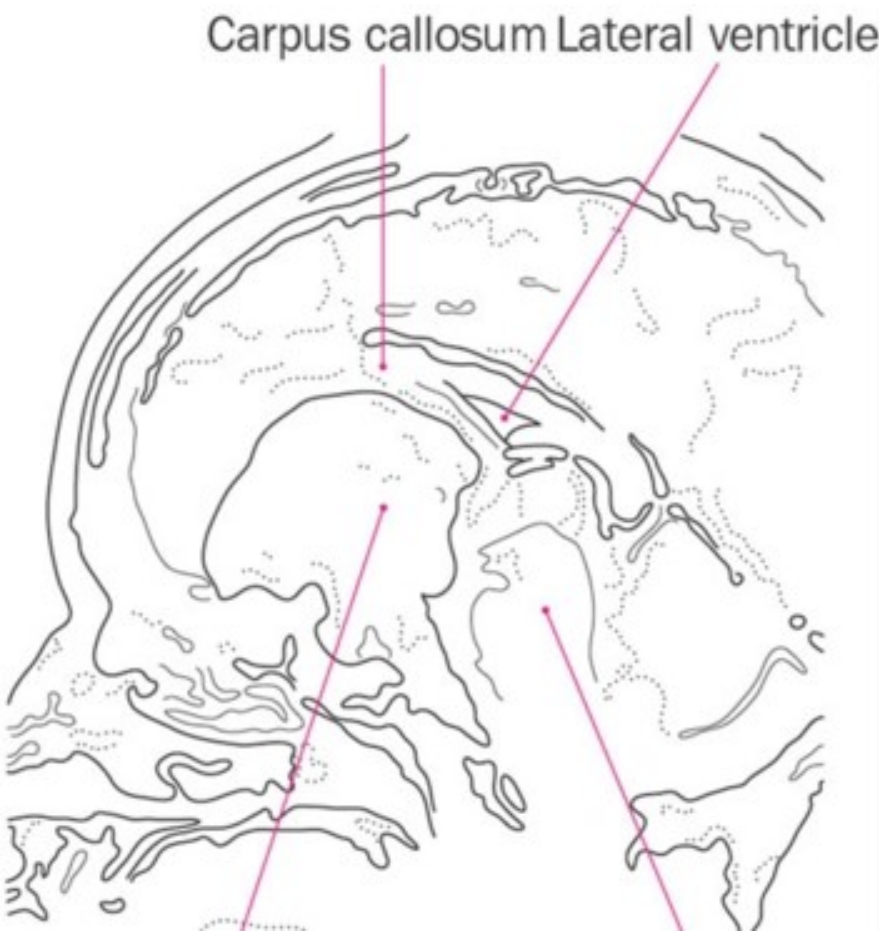
Sideways

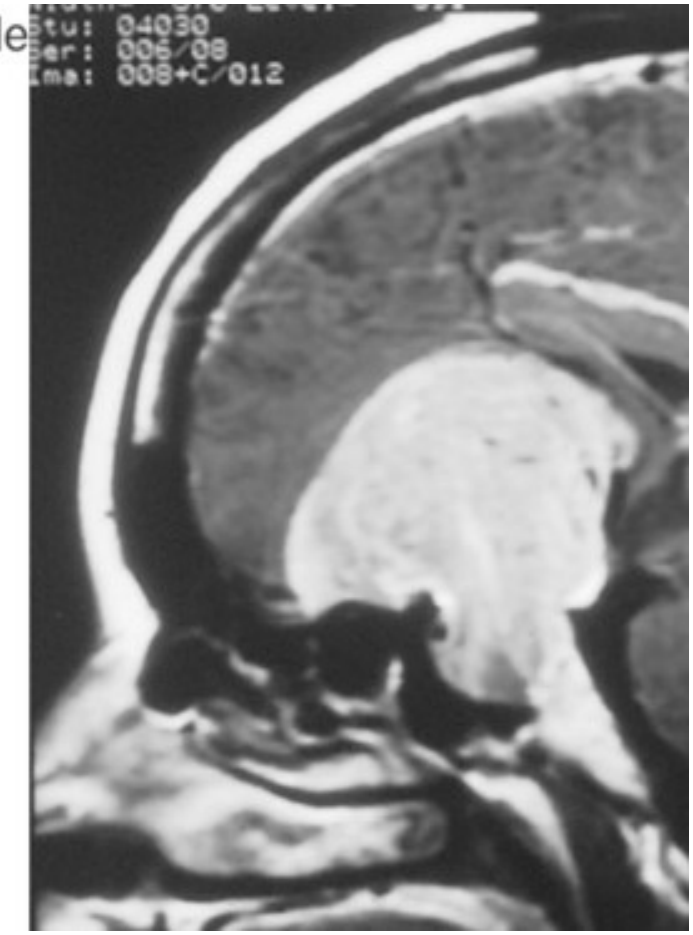
Cranial nerve palsies and temporal lobe epilepsy

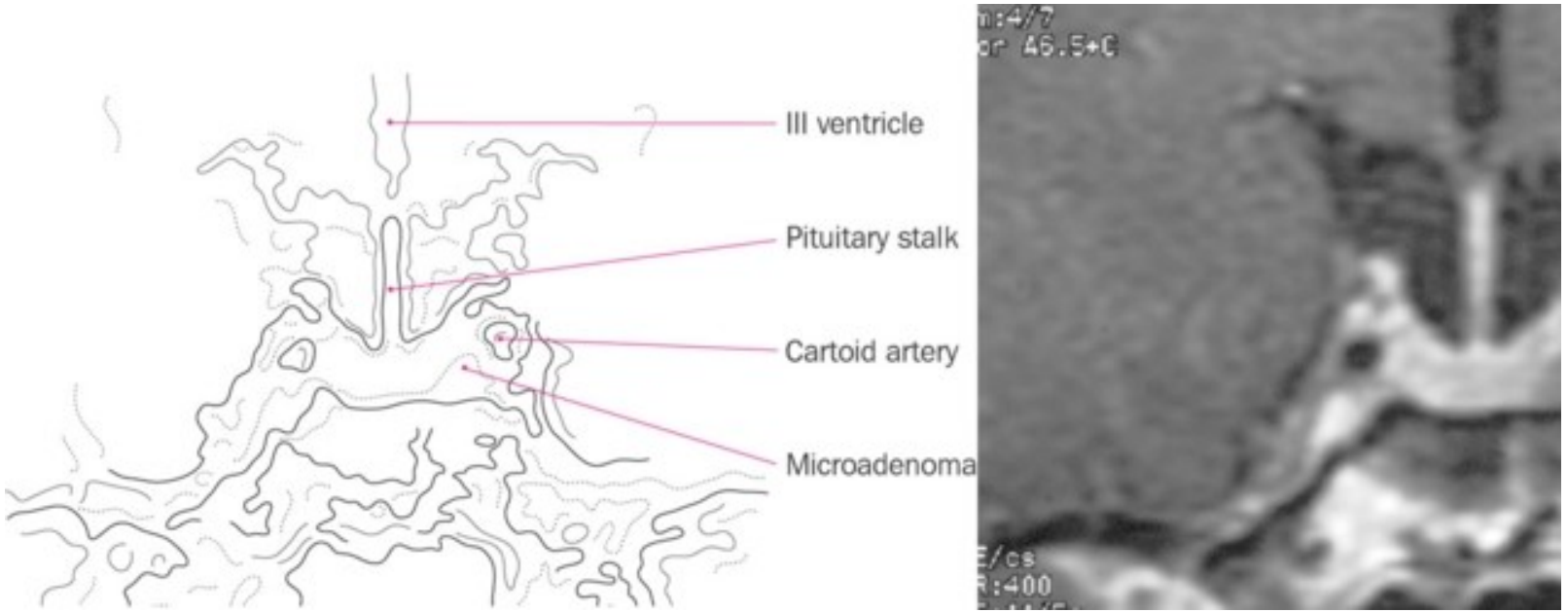
Lateral extension of tumor

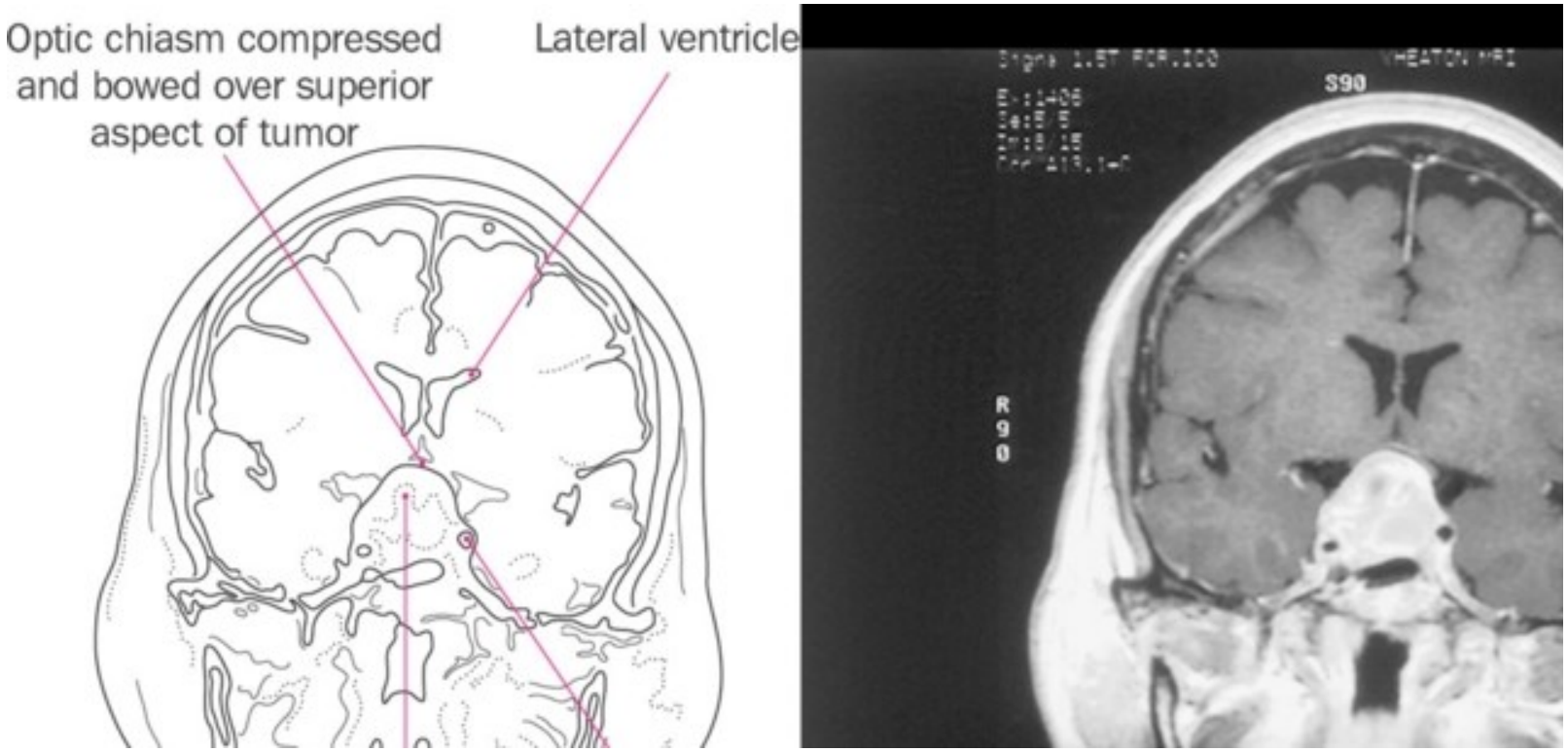



Suprasellar growth of
giant pituitary tumor
Ser: 008/08
Ima: 008+C/012

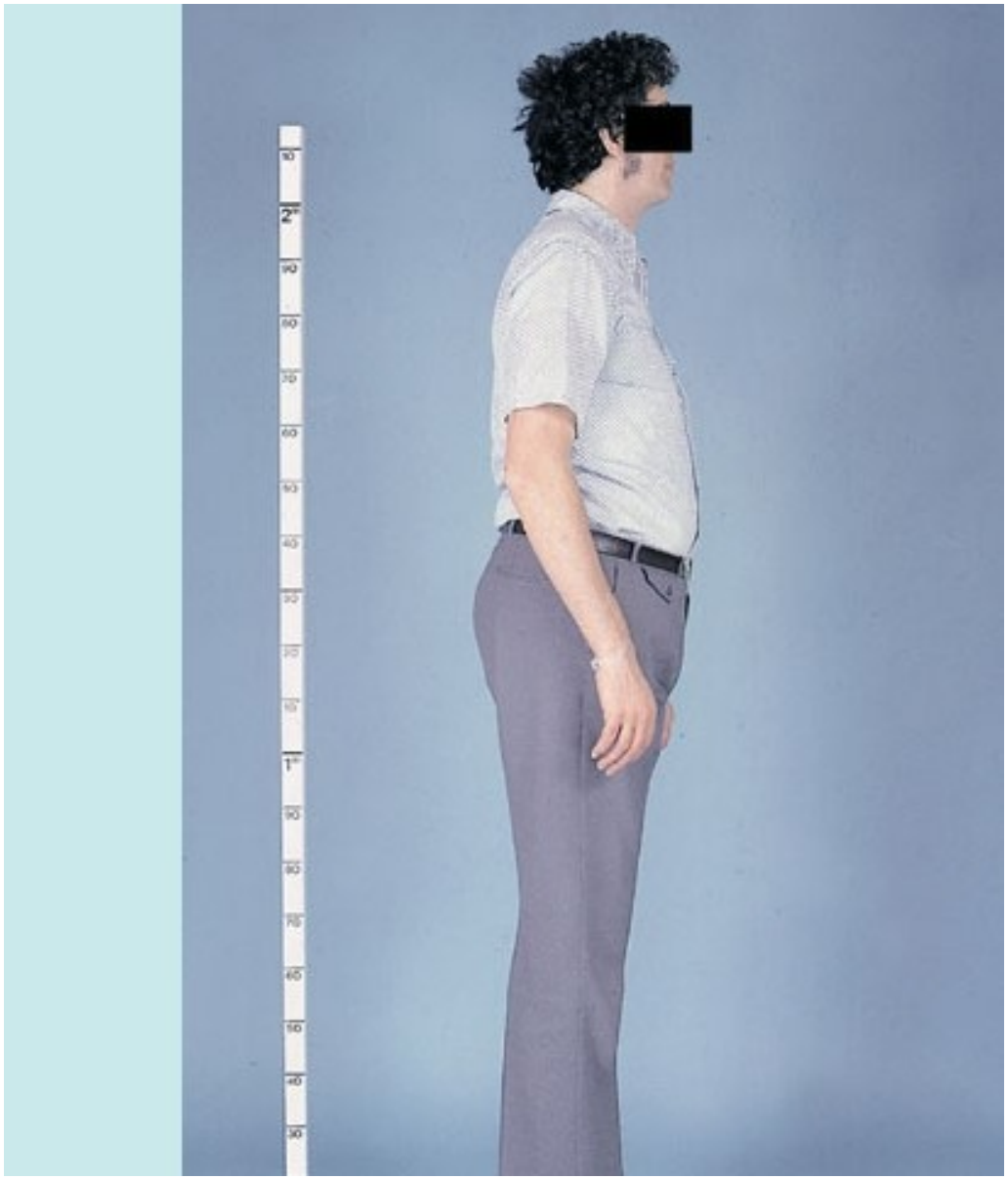

Carpus callosum
Lateral ventricle


tu: 04030
er: 006/08
ma: 008+C/012


III ventricle
Pituitary stalk
Cartoid artery
Microadenoma


Optic chiasm compressed and bowed over superior aspect of tumor
Lateral ventricle
S90
R
9
0

ADENOAME SECRETANTE DE GH



ACROMEGALIA

Definitie: sindrom clinico-biologic datorat secretiei excesive de GH la adult (dupa inchiderea cartilajelor de crestere)

Epidemiologie: ♂ = ♀, varsta medie la diagnostic = 40 ani

Etiologie:

- 99% - adenoame hipofizare: somatotrop/somatomamotrop
- 1% - secretie excesiva de GHRH - ganglocitom hipotalamic
  - tumori cu secretie ectopica de GHRH: bronsice, GI/pancreatice, carcinoid
  - secretia ectopica de GH (adenom pancreatic/neoplasm pulmonar)

Fiziopatogenie:

GH ↑ → IGF1 ↑ → modificarile somatice

GH ↑ → modificari metabolice

Anatomie patologica:

- macroadenoame > microadenoame
- pot fi mixte = celule somatotrope + lactotrofe → secretie mixta
- hiperplazie (rar) – in formele cu exces GHRH

Tablou clinic (1)

Debut insidios → diagnostic dupa 10 – 20 ani de la debut (frecvent confundata cu afectiuni reumatologice datorita cresterii de volum dureroase a articulatiilor)

<u>Extremitatea cefalica</u>:

- ↑ perimetrul frontal
- arcade sprancenoase proeminente (↑ volum sinus frontal)
- proeminenta arcadelor zigomatice
- apofize mastoide proeminente
- largirea piramidei nazale – portiunea cartilaginoasa
- prognatism → ocluzie dentara inversa
- spatii interdentare – treme, diasteme → edentatie (rupere ligg alveolo-dentar)
- macrocheilie - macroglosie
- santuri nazo-labiale accentuate
- cute frontale si occipitale

Tablou clinic (2)

Torace:

- "In butoi" - bombarea sternului
  - accentuarea cifozei dorsale

Membre:

- latirea extremitatilor - degete groase, cilindrice
  - ↑ nr la pantofi

Tegumente:

- umede, seboreice (hipertrofia gld sudoripare si sebacee)
- numeroase papiloame
- acanthosis nigricans

Aparat respirator:

- hipertrofie corzi vocale + ↑ cavitatii de rezonanta a sinusurilor → voce groasa
- apnee in somn

Tablou clinic (3)

Aparat cardio-vascular:

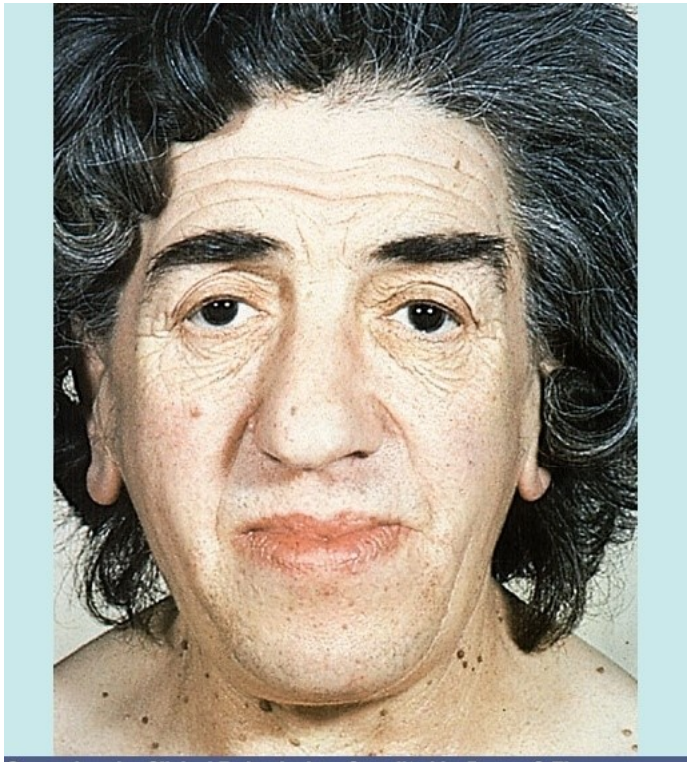
- cardiomegalie
- boala cardiaca ischemica (ateroscleroza accelerata)
- insuficienta cardiaca
- HTA sistolo-diastolica
- vase periferice ingrosate, sinuoase, varice ale mb inferioare

Aparat digestiv:

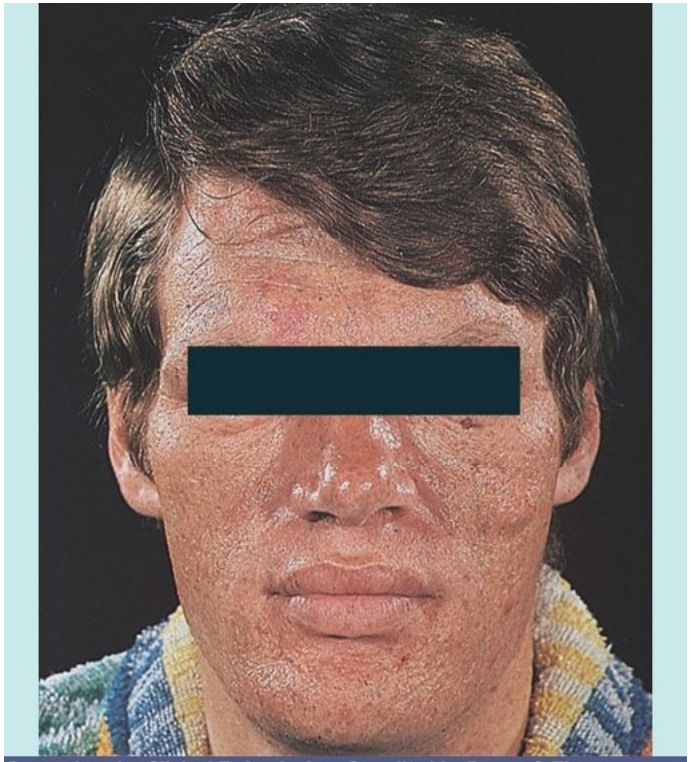
- hepatosplenomegalie
- polipi colonici cu risc ↑ de transformare maligna

Modificari endocrine:

- gusa
- insuficienta hipofizara: gonadotropa, tireotropa, corticotropa etc
- hiperprolactinemie → galactoree, tulburari de ciclu menstrual



Comprehensive Clinical Endocrinology 3e: edited by Besser & Thorner
Elsevier Science Ltd



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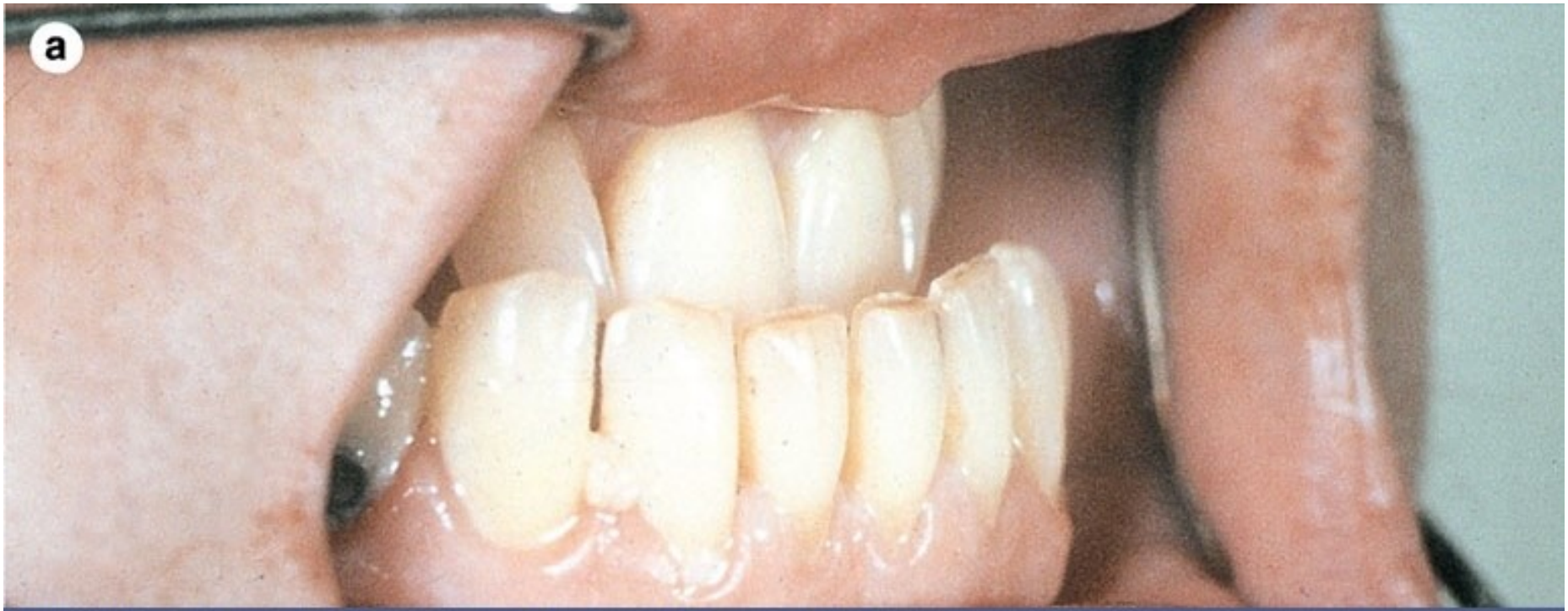

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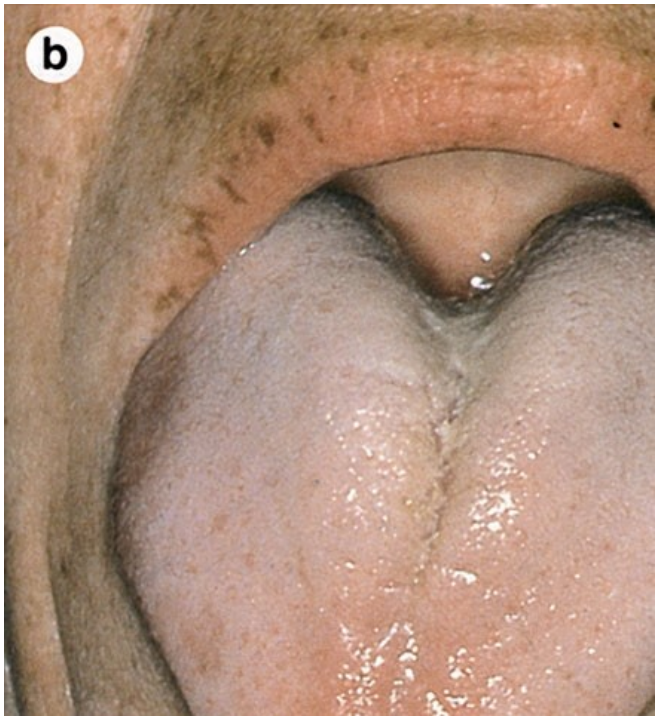
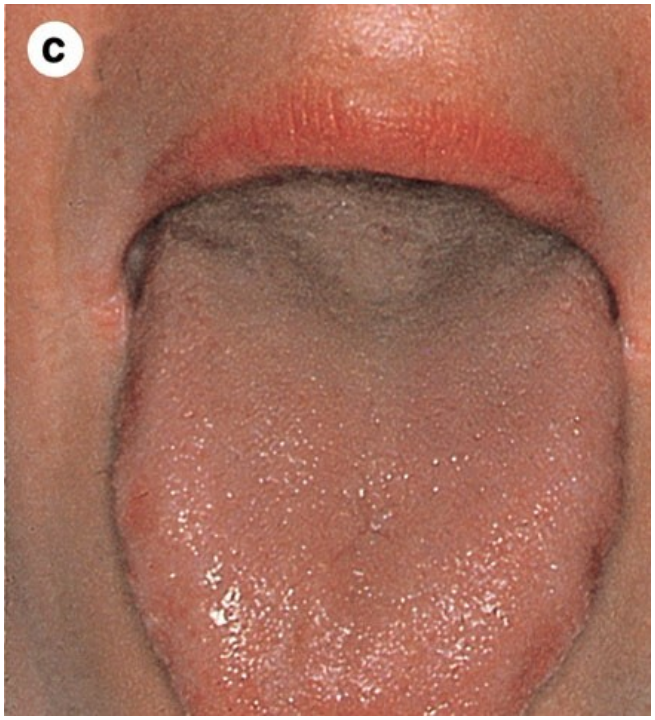

b


c

COMPLICATII

1. HTA
2. DIABET ZAHARAT sau toleranta alterata la glucoza
3. APNEE DE SOMN
4. BOALA CARDIACA ISCHEMICA
5. INSUFICIENTA CARDIACA CONGESTIVA
6. Risc crescut de POLIPI COLONICI si CARCINOM DE COLON
7. Complicatiile sdr. mecanic tumoral

Dg. paraclinic in acromegalie

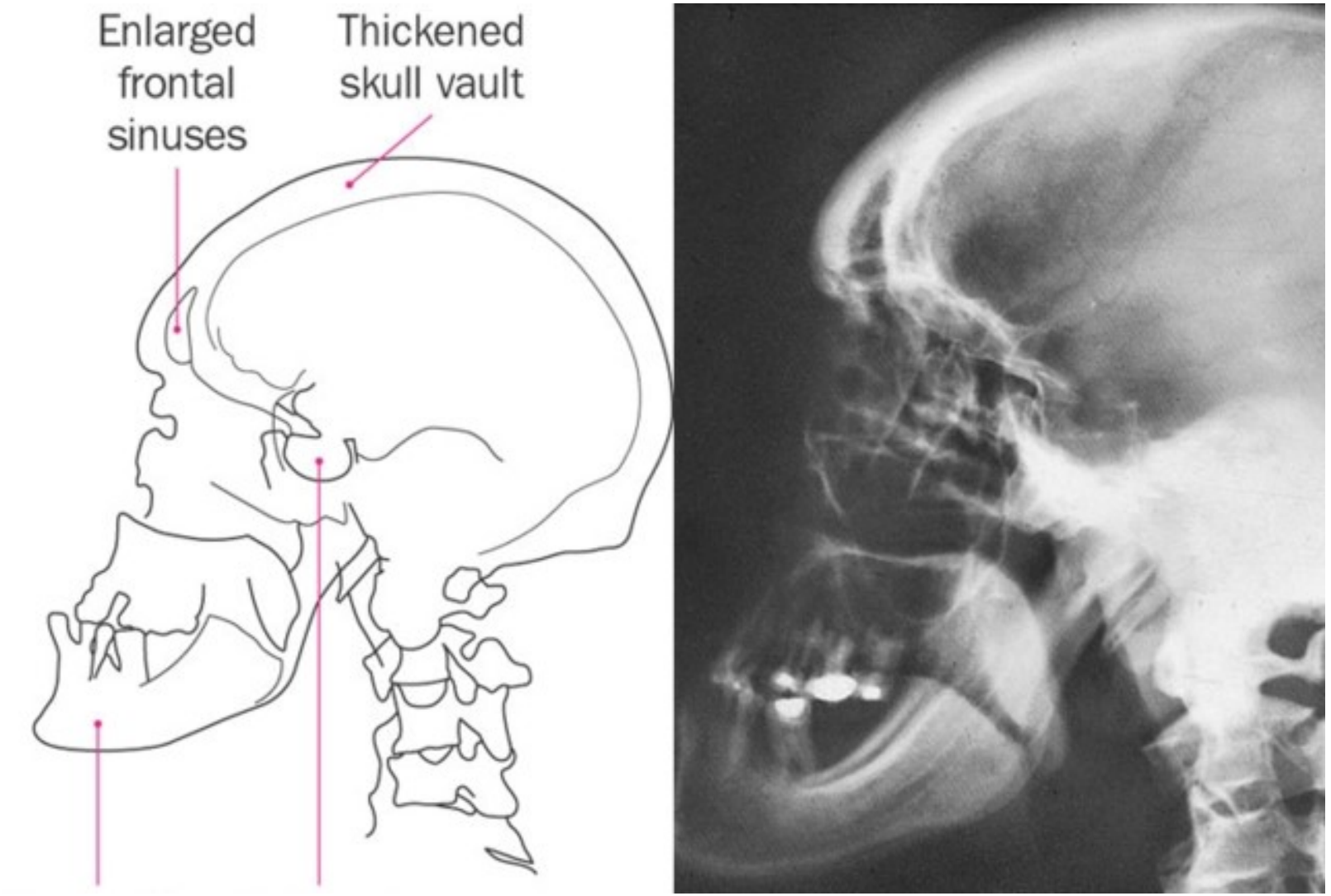
- **Testul de supresie la hiperglicemia provocata –** in acromegalie GH **NU** se supreseaza < 1ng/dl dupa administrarea de 75g glucoza

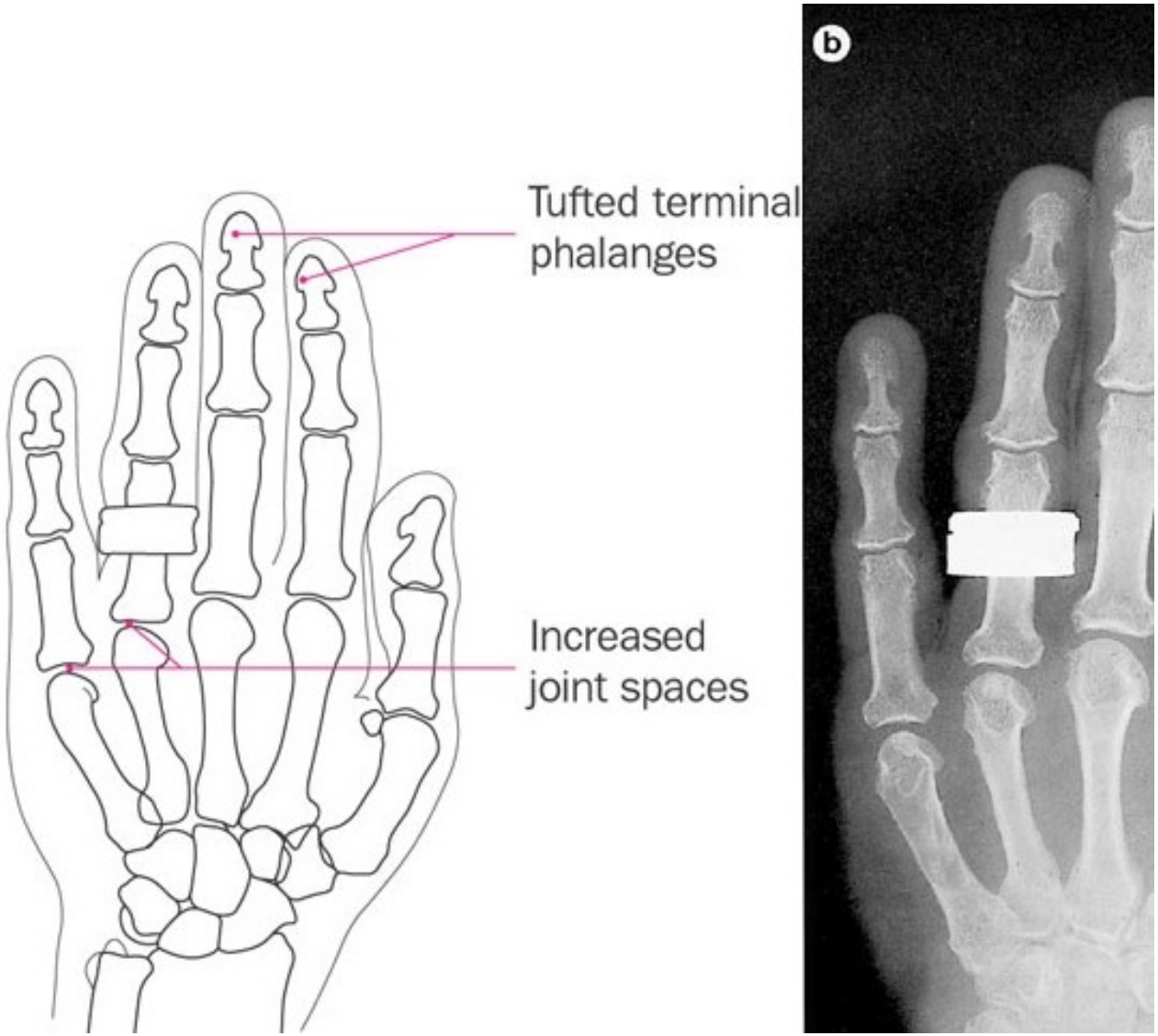
	0’	30’	60’	90’	120’
Glicemie (mg/dl)					
GH (ng/dl)					

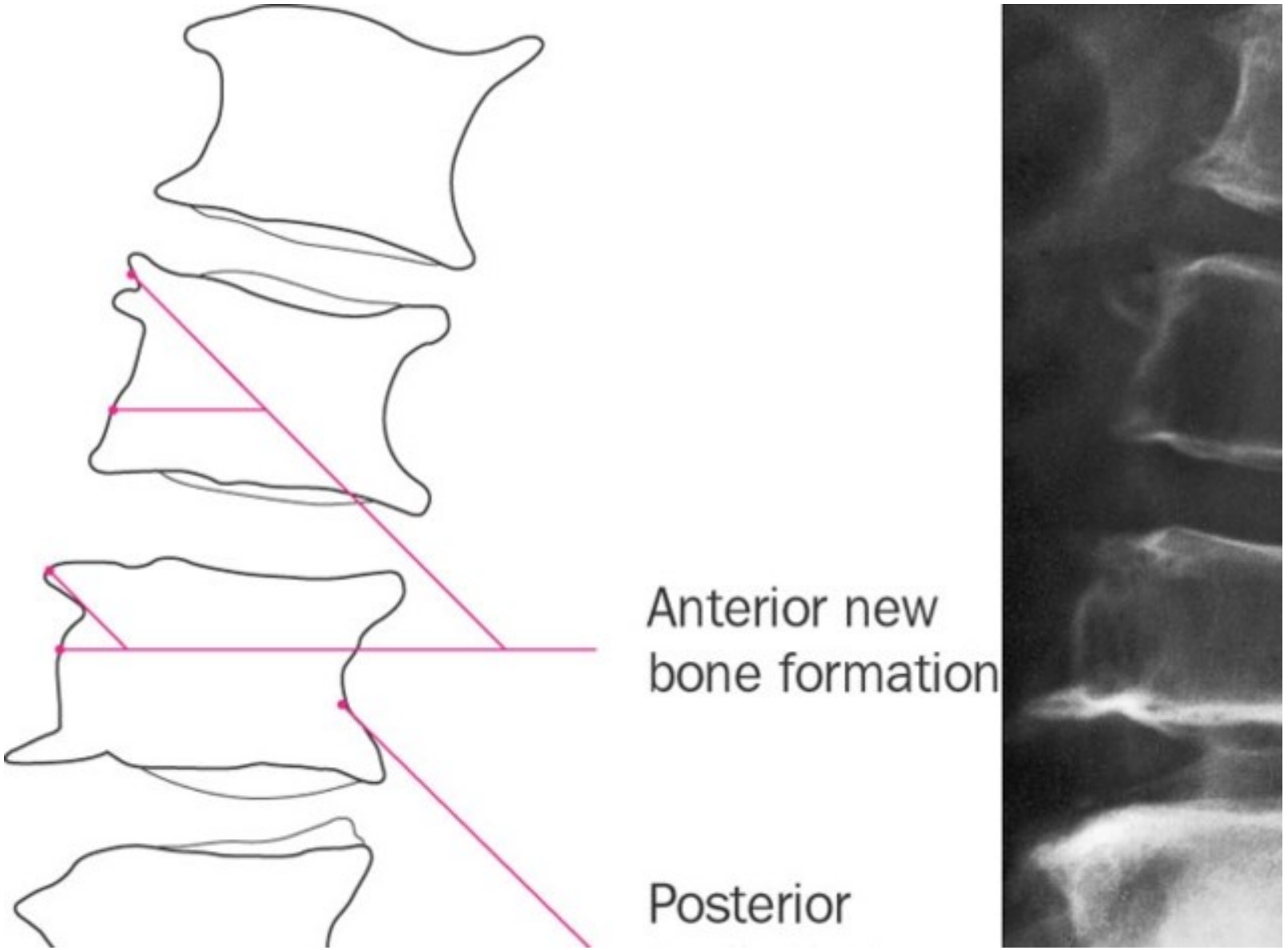
DZ – profil GH/24 ore = 4 probe GH la interval de 4 ore

- **IGF1** crescut
- **RMN/CT hipofizar (Radiografia de sa turceasca)**
- **Examen oftalmologic:** CV, AV, FO
- **EKG, ecografie cardiaca**
- **Colonoscopie**
- **Alte analize de sange:**

- **glicemie, Hb glicozilata, profil lipidic**
- **PRL, FSH, LH - T/E2, TSH - fT4, ACTH - cortizol, test de toleranta la insulina**

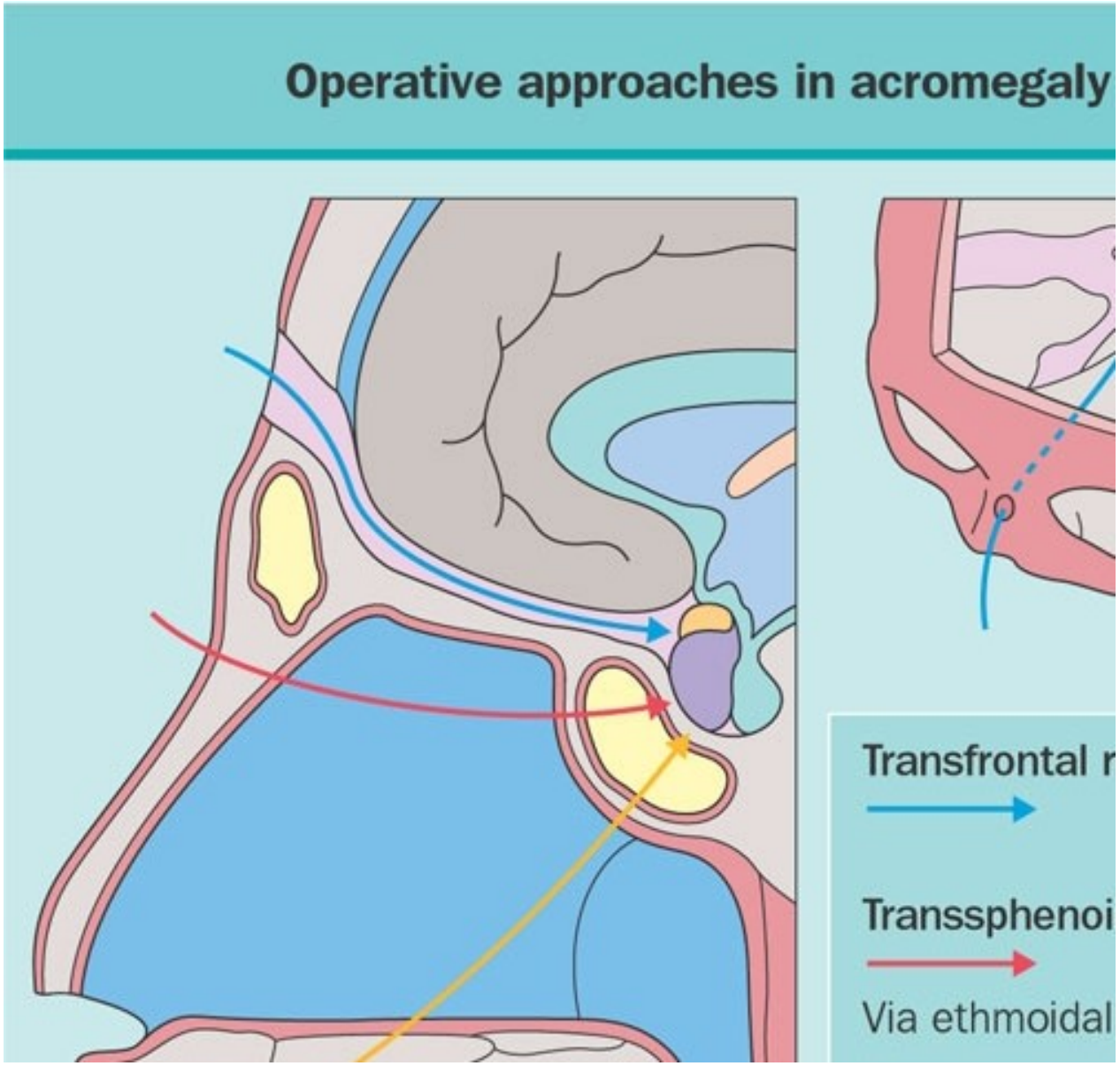

Enlarged frontal sinuses
Thickened skull vault


Tufted terminal phalanges
Increased joint spaces
b

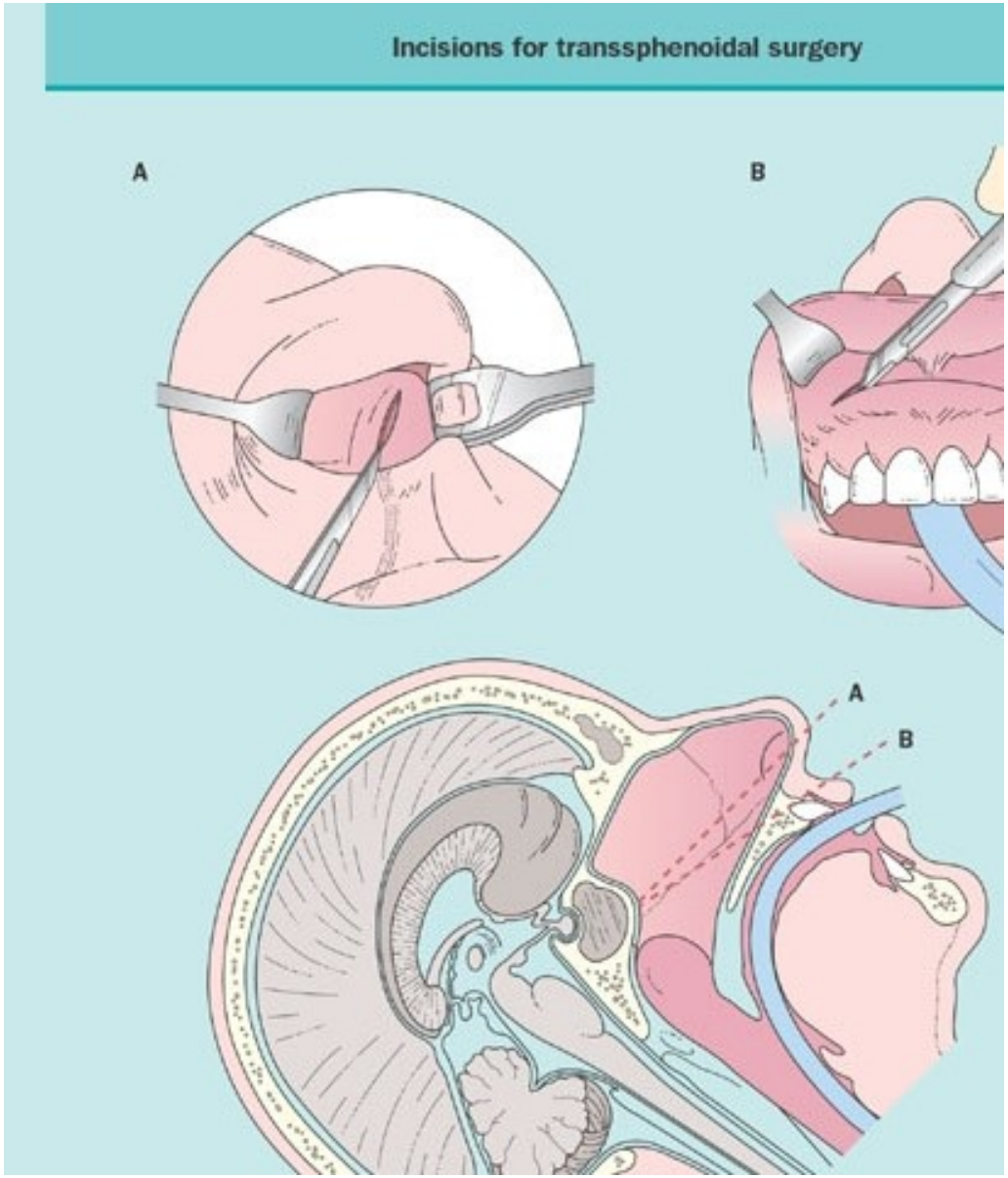

Anterior new
bone formation
Posterior

TRATAMENTUL ACROMEGALIEI

1. Chirugical: adenomectomie transsfenoidală
2. Medical:
    - Derivaţi de somatostatină: **octreotide/lanreotide**
    - Blocanţi de receptori pentru GH: **Pegvisomant**
    - Bromocriptina/Cabergolina
3. Radioterapie
    - externă de înalt voltaj
    - gammaknife


Operative approaches in acromegaly
Transfrontal r
Transsphenoi
Via ethmoidal

Incisions for transsphenoidal surgery



Complicatii postoperatorii

Hemoragia

Rinoree cu LCR

Meningita

Tulburari de camp vizual

Diabet insipid tranzitor

Insuficienta hipofizara

Complicatii post-radioterapie

Insuficienta hipofizara

Atrofie de nerv optic

Risc de neoplazie cerebrala

Tratamentul medical în acromegalie

OCTREOTID = SANDOSTATIN LAR 10-30mg/luna, im

LANREOTIDE = SOMATULINE

PR – 30mg/14 - 10 – 7 zile, im

Autogel – 60 - 120mg/4 saptamani, im

Reactii adverse:

- greata, crampe abdominale
- litiaza biliara

PEGVISOMANT = SOMAVERT 10 – 40 mg/zi, sc

Reactii adverse:

- cefalee, fatigabilitate
- cresteri ale TGO, TGP

CABERGOLINA = DOSTINEX 1 – 4mg/saptamana, oral

In tumorile cu secretie mixta GH + PRL

CRITERII DE CURABILITATE IN ACROMEGALIE

Boala remisa:

- GH in TTOG <1ng/dl
- IGF normal
- Absenta activitatii clinice a bolii

Observate fara tratament

PROLACTINOMUL

Introducere

Cea mai frecventa tumora hipofizara secretanta

♀ - microadenom > macroadenom

♂ - macroadenom > microadenom

Clinic:

♀ - post-pubertar: sindrom amenoree – galactoree

- pre-pubertar: amenoree primara fara galactoree (gld mamara nedezvoltata)

♂ - hipogonadism

Galactoreea:

- spontana/la presiune
- poate sa nu apara daca hipogonadismul este sever
- **NU** orice galactoree = prolactinom
- **NU** orice hiperprolactinemie = prolactinom

Hipogonadism – perturbarea secretiei pulsatile de GnRH

Hipogonadismul ♀

Bradimenoree → amenoree secundara/Amenoree primara

Anovulatie → infertilitate

Involutia tractului genital feminin:

- uscaciunea mucoasei vaginale
- stenoza vaginala

Scaderea masei osoase

Riduri fine

Hipogonadismul ♂

Scaderea libidoului

Tulburari de dinamica sexuala

Scaderea pilozitatii faciale si corporale

Infertilitate

Adipozitate ginoida

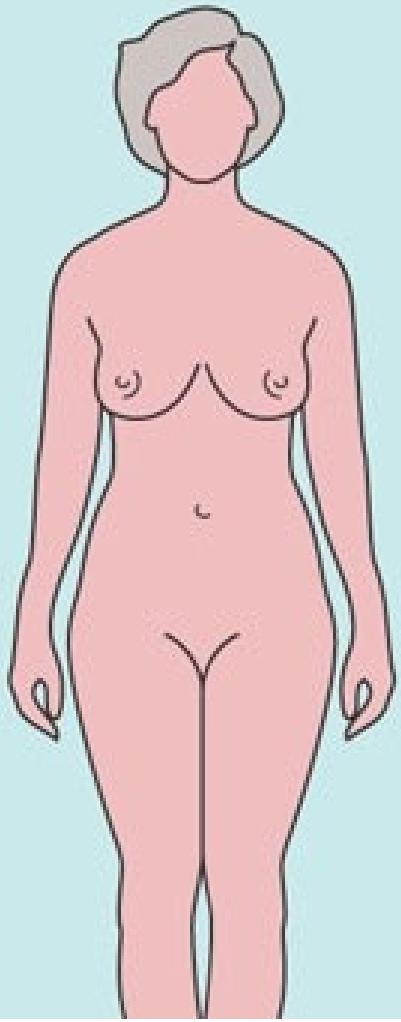
Ginecomastie

Scaderea masei osoase

Riduri fine

Clinical manifestations of hyperprolactine

Women	Men
Galactorrhea 30–80%	Galactorrhea <30%
Menstrual irregularity	Impotence
Infertility	Visual field abnormalities
	Headache
	Extraocular muscle weakness



Diagnostic paraclinic

Cea mai frecventa cauza de amenoree secundara = sarcina → test de sarcina/dozare β-HCG

PRL > 200ng/ml = macroprolactinom

100 – 200ng/ml = microprolactinom

< 100ng/ml = alte cauze de hiperprolactinemie (posibila asociere de microadenom nesecretant cu hiperprolactinemie de alta cauza)

RMN/CT hipofizar

Consult oftalmologic: CV, AV, FO

Alte cauze de hiperprolactinemie – Dg diferential

Leziuni ale hipotalamusului sau ale tijei (RMN/CT)

Medicamente (anamneza):

neuroleptice, antidepresive
antiemetice: metoclopramid, domperidon
estrogeni, CO, spironolactona
rezerpina, verapamil
metildopa, cimetidina
morfina, heroina, metadona

Boli endocrine:

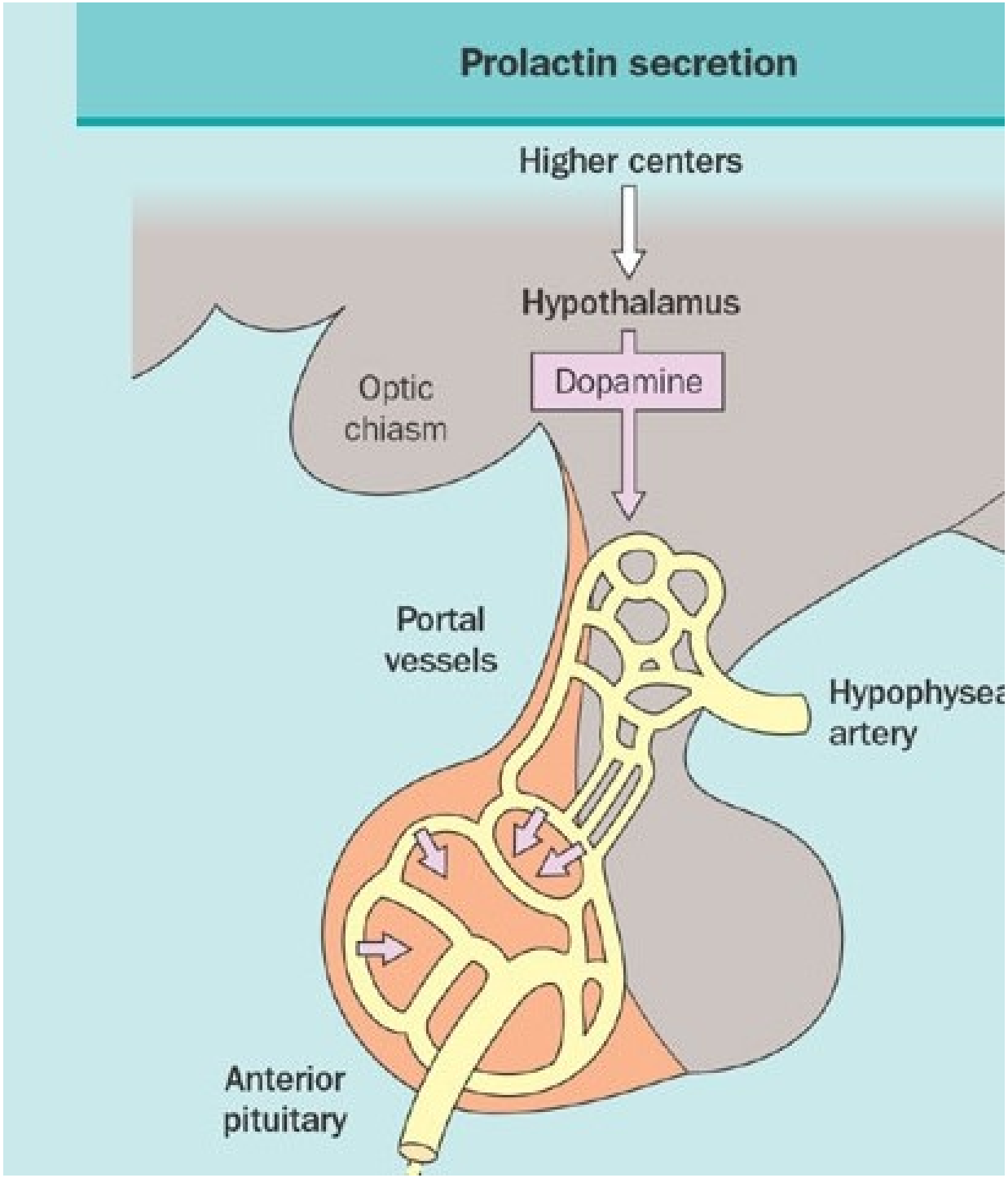
- mixedem (TSH, fT4)
- sindromul ovarelor polichistice (testosteron liber, eco utero-ovariana)\

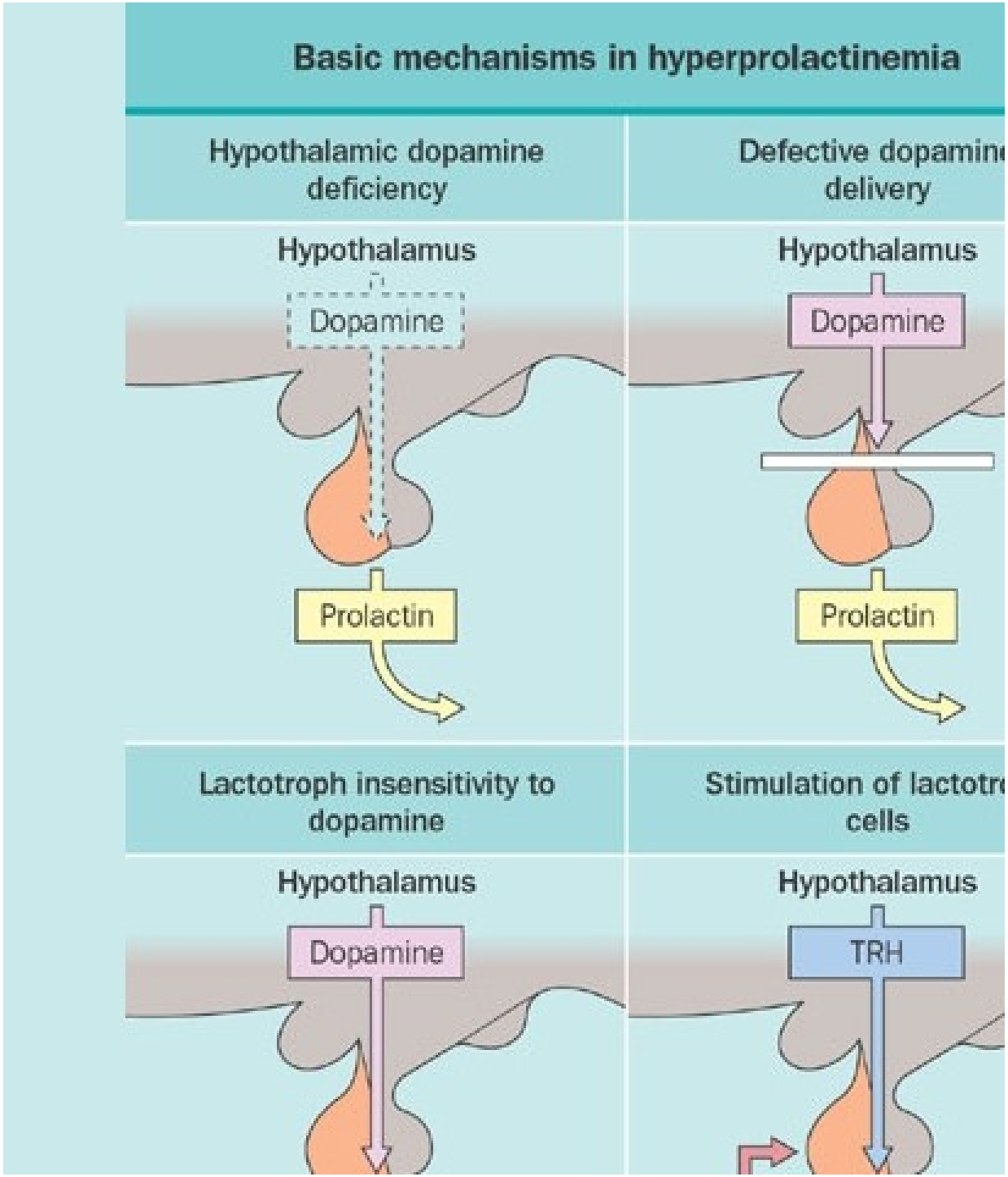
Boli cronice: IRC, ciroza hepatica

Mecanism neurogen reflex:

stimulare mamelonara, supt
traumatisme/arsuri perete toracic
leziuni medulare
herpes zoster
anexite, cicatrici uterine
papilom intraductal
- ecografie mamara
- examen citologic al secretiei mamare

Macroprolactinemia


Prolactin secretion
Higher centers
Hypothalamus
Dopamine
Optic chiasm
Portal vessels
Hypophysea artery
Anterior pituitary


Basic mechanisms in hyperprolactinemia
Hypothalamic dopamine deficiency
Hypothalamus
Dopamine
Prolactin
Defective dopamine delivery
Hypothalamus
Dopamine
Prolactin
Lactotroph insensitivity to dopamine
Hypothalamus
Dopamine
Stimulation of lactotr cells
Hypothalamus
TRH

Tratamentul prolactinoamelor

Obiective: - reducerea volumului tumoral
- refacerea functiei gonadale
- normalizarea hiperprolactinemiei

De electie: agonisti dopaminergici
- **Bromocriptina**
- **Cabergolina**

Tratament chirurgical:
- In formele rezistente la agonisti dopaminergici
- Macroprolactinoame cu compresie optochiasmatica

Agonistii dopaminergici

BROMOCRIPTINA

- alcaloid de secara cornuta
- 1 cp = 2,5 mg → 7,5 mg – 15 mg/zi
- efect citonecrotic > 10 mg/zi
- reactii adverse: greata si hTA ortostatica → cresterea gradata a dozelor
- se poate administra si pe perioada sarcinii

CABERGOLINA (Dostinex)

- 1 cp = 0,5mg → 0,5 – 4 mg/saptamana (administrare bisaptamanala)
- efect citonecrotic > 2 mg/saptamana

PROLACTINOAMELE SI SARCINA

Menstre ovulatorii dupa 1-3 luni de tratament la 57-100%

! Ovulatia precede menstruatia!

Rata de sarcina la pacientele tratate: 37-81%

In sarcina riscul cresterii tumorale:

5% in microprolactinoame

15-25% in macroprolactinoame

(*e preferabila reducerea volumului tumoral inaintea obtinerii sarcinii*)

Atitudinea terapeutica in sarcina: **oprirea administrarii** de agonisti dopaminergici cu **monitorizarea clinica** (incusiv ex. CV),
mai ales in macroprolactinoame si reintroducerea tratamentului in contextul semnelor de compresie optochiasmatica sau altor complicatii neurologice

ADENOAME HIPOFIZARE CLINIC NESECRETANTE

Clinic: - sdr. mecanic tumoral: cefalee, defecte CV, oftalmoplegie, etc.
- hipopituitarism: cel mai adesea hipogonadism
- asimptomatice, descoperite intamplator

Dg: - RMN hipofizar
- PRL pentru excluderea unui prolactinom
(*terapie esential diferita!!)*
- nivelul hipopituitarismului.
- *imunohistochimic:*
negativ (adenoame nule)
ACTH (adenoame corticotrope silentioase)
hormoni gonadotropi sau subunitati alfa

TRATAMENTUL ADENOAMELOR HIPOFIZARE CLINIC NESECRETANTE

1. Chirurgical
2. Radioterapie - radiorezistente
3. Medical: substitutiv al insuficientei hipofizare

CRANIOFARINGIOMUL

Tumoră disembrioplazică derivată din resturi ale pungii Rathke

Localizare: supraselară/intraselară sau mixtă

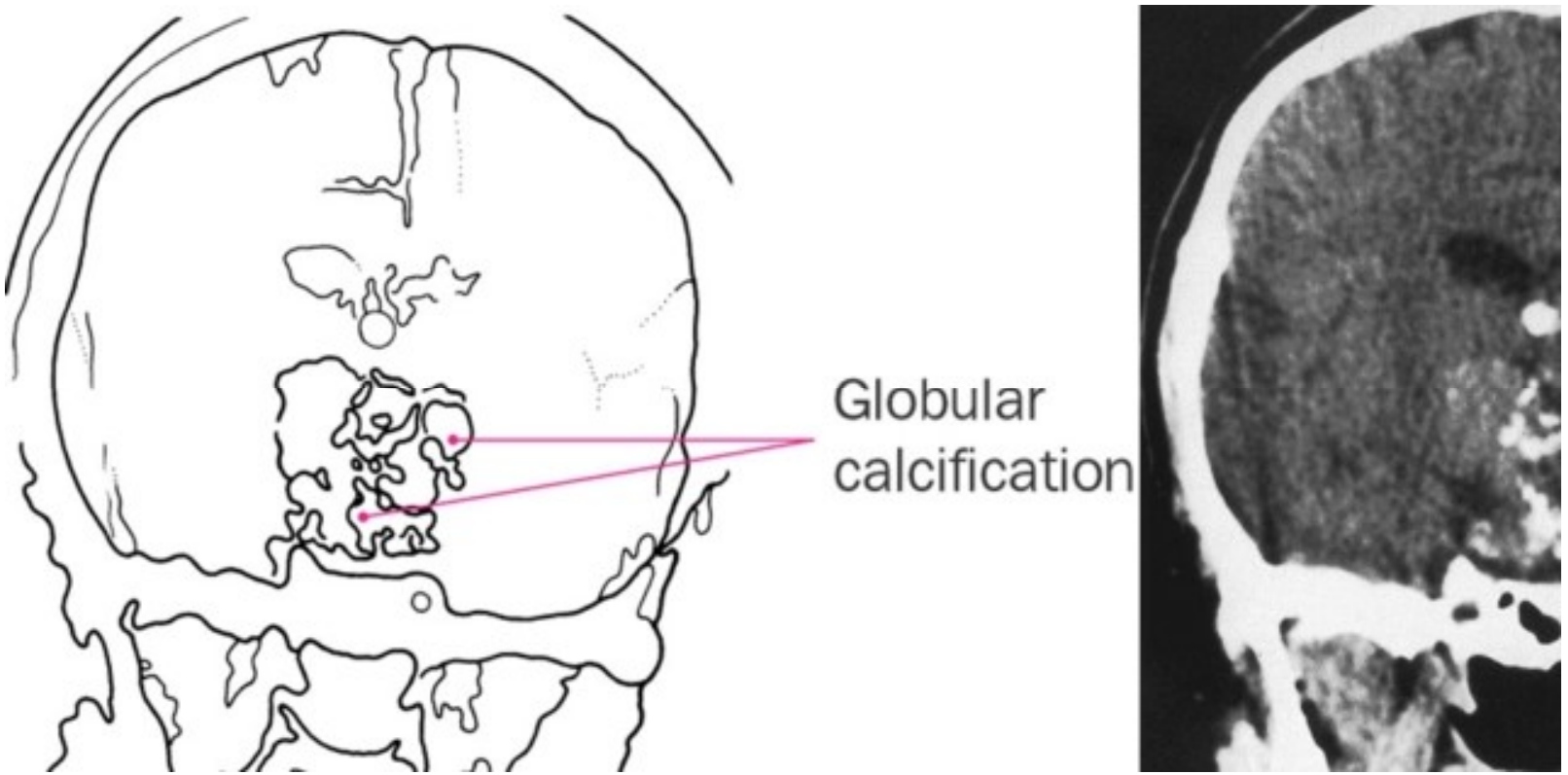
Cea mai frecventă tumoră intracraniană la copii.

Clinic: sdr. hipertensiune intracraniană la copii

- modificări de câmp vizual
- diabet insipid
- hipopituitarism (nanism, pubertate intarziată)
- obezitate

Imagistic: masă tumorală cu zone chistice şi calcificări

Tratament: chirurgical asociat cu radioterapie


Globular
calcification