PRL

CE - 198 AA

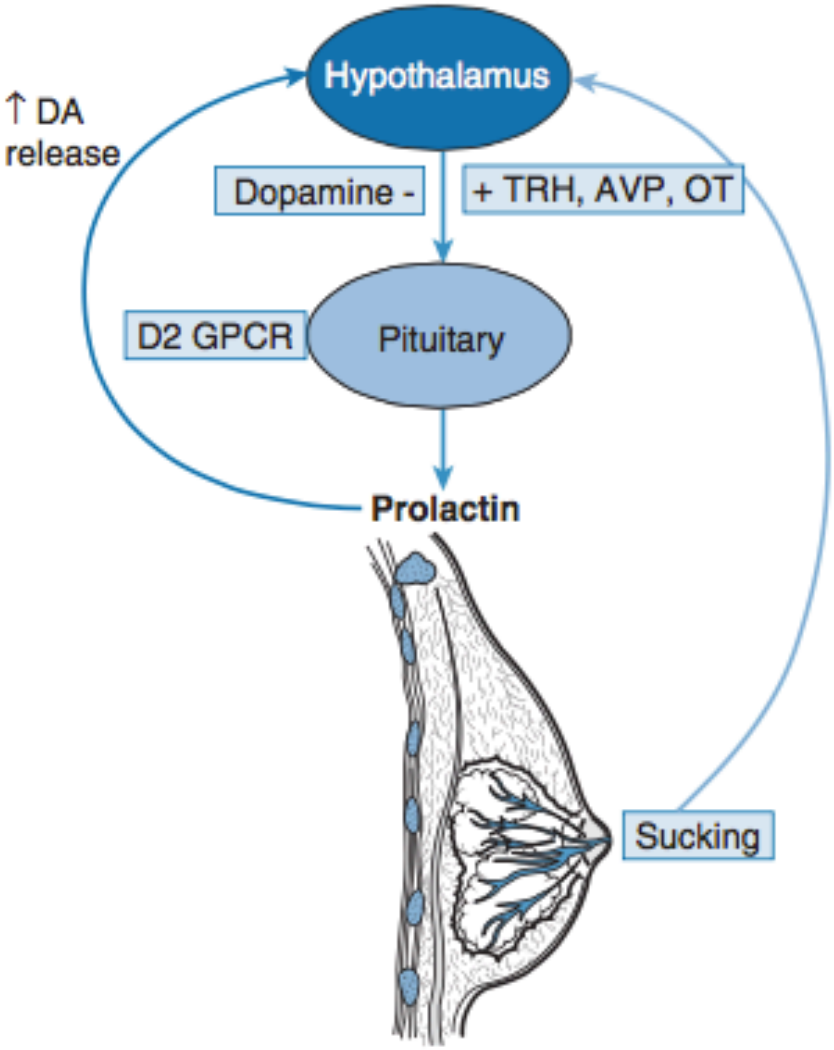
CINE = celulele lactotrope, acidofile, dispuse difuz

CUM =

? Dezvoltare glandulara mamara in sarcina

? Stimuleaza lactatia in postpartum

- Efect asupra gonadostatului DOAR IN HIPERSECRETIE PRL


Hypothalamus
↑ DA release
Dopamine -
+ TRH, AVP, OT
D2 GPCR
Pituitary
Prolactin
Sucking
Breast differentiation
Duct proliferation & branching
Glandular tissue development
Milk protein & lactogenic enzyme synthesis

Modificarea PRL INNAFARA patologiei

Cresterea PRL	Scaderea PRL
Sarcina, alaptare, neonatal Stimulare mamelonara Efort fizic Somn Hipoglicemie	
TRH Estradiol VIP Antagonisti Dopaminergici Haloperidol, Risperidona, Rezerpina, Methyl Dopa, opioide, Metoclopramid Inhibitori moaminoxidazei Cimetiidna Verapamil	Agonisti Dopaminergici Levodopa Apomorfina Bromocriptina Pergolid Cabergolid
Leziuni perete toracic	Pseudohipoparatiroidism
Leziuni medulare	
Hipotiroidism	
BCR stadiul IV, V	
Insuficienta hepatca	

Prolactinomul

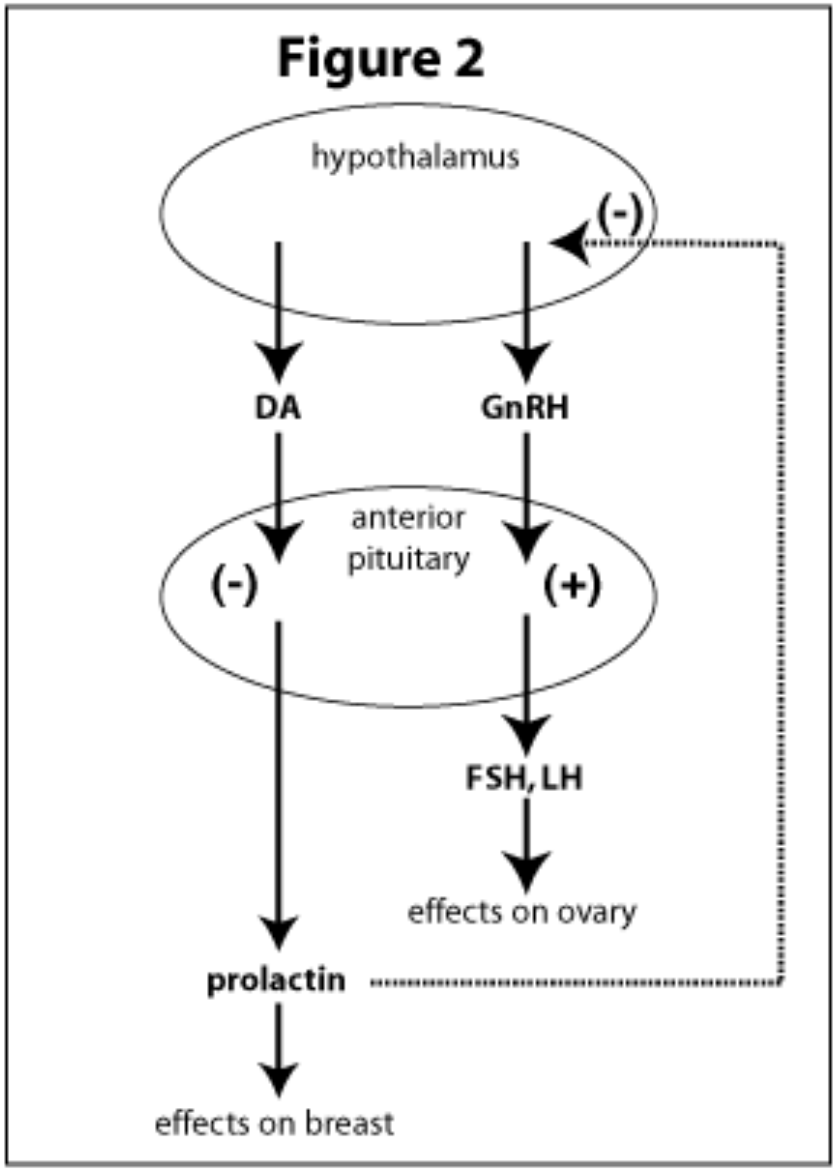
Cel mai frecvent adenom hipofizar secretant

? Screening activ

1. **Galactoree**
2. **Incidentalom hipofizar**
3. **Suspiciune tumora hipofizara**
4. **Amenoree/oligomenoree/scadere flux menstrual**
5. **Hipogonadism masculin**
6. **Infertilitate (feminina, masculina)**

Majoritatea microadenoame (> 90 %)

Figure 2


hypothalamus
(-)
DA
GnRH
anterior
pituitary
(-)
(+)
FSH, LH
effects on ovary
prolactin
effects on breast

SOMATIC galactoree (tardiv)

HORMONAL sd endocrin
RAPID Insuficienta FSH + LH
TARDIV insuficienta celorlalti tropi

?

TUMORAL sd functional
= sd tumoral hipofizar

Extrem de rar in copilarie

Frecvent adult: F:B = 10:1, tipic 20-50 de ani

Sd endocrin

FEMEI

- Anovulatie
  - hipo-, oligo
  - frecvent
  - Inhiba se
- Hipoestrog
  - Uscaciun
  - Crestere
  - Iritabilita
  - Retentie
- Galactoree
- Demineral

lism

libidou

ıte

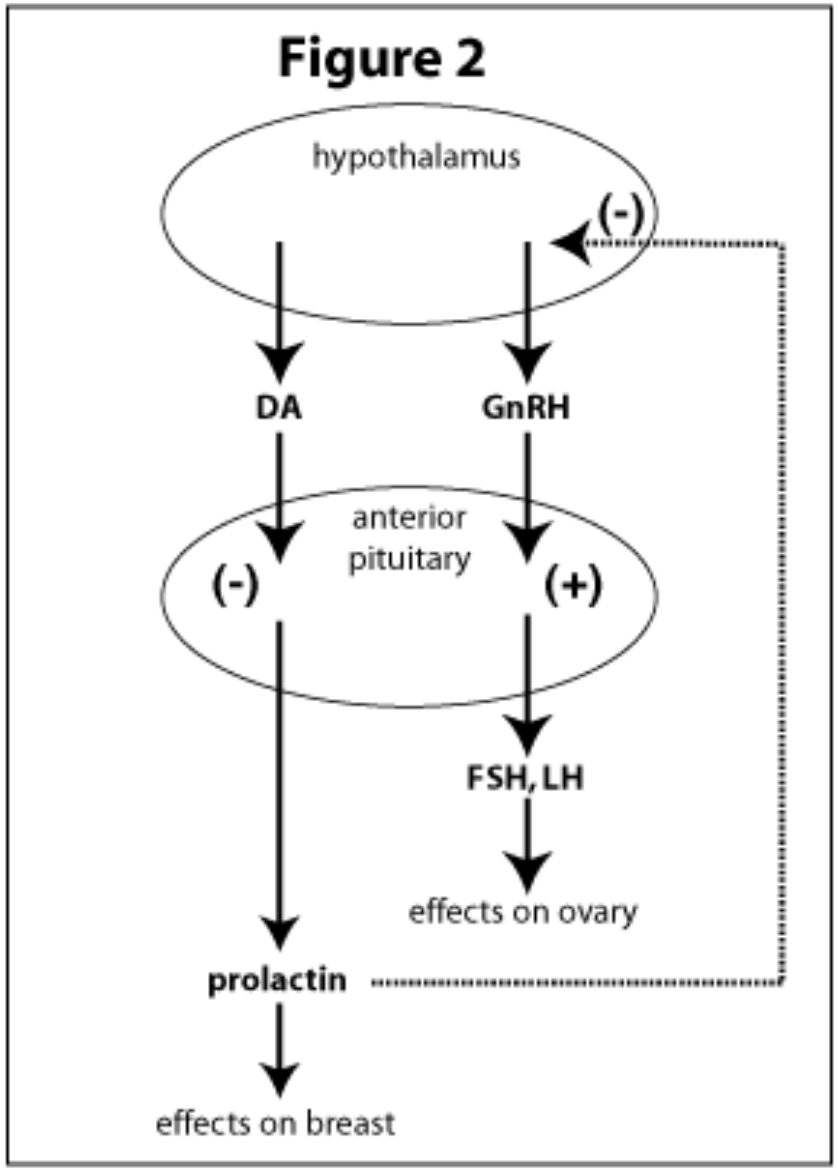
ziare osoasa

tardiv

d tumoral hipofizar

PRL ↑ + LH, F

+ LH, FSH ↓



Diagnostic ≠

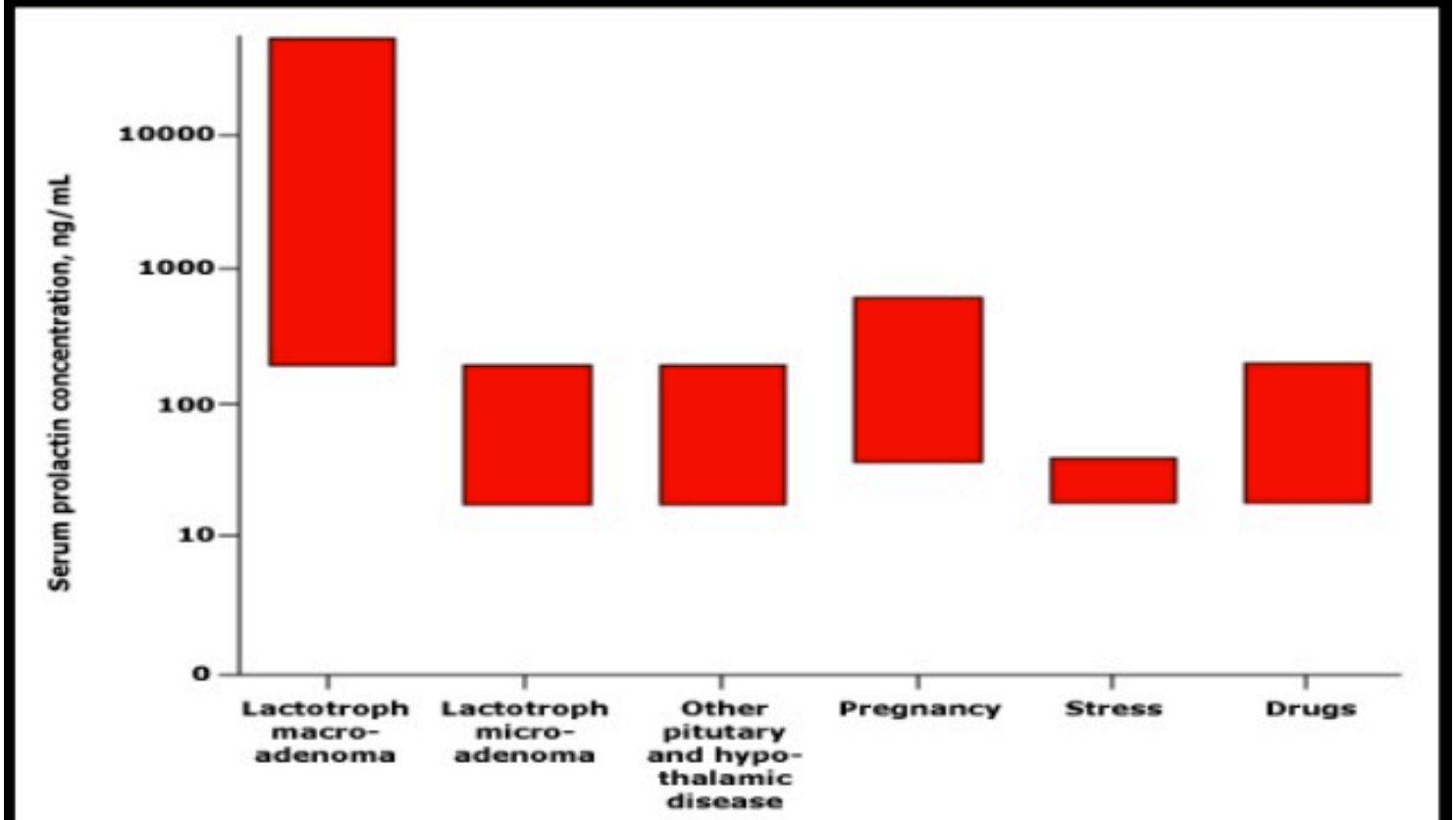
1. Tumora secretanta de PRL

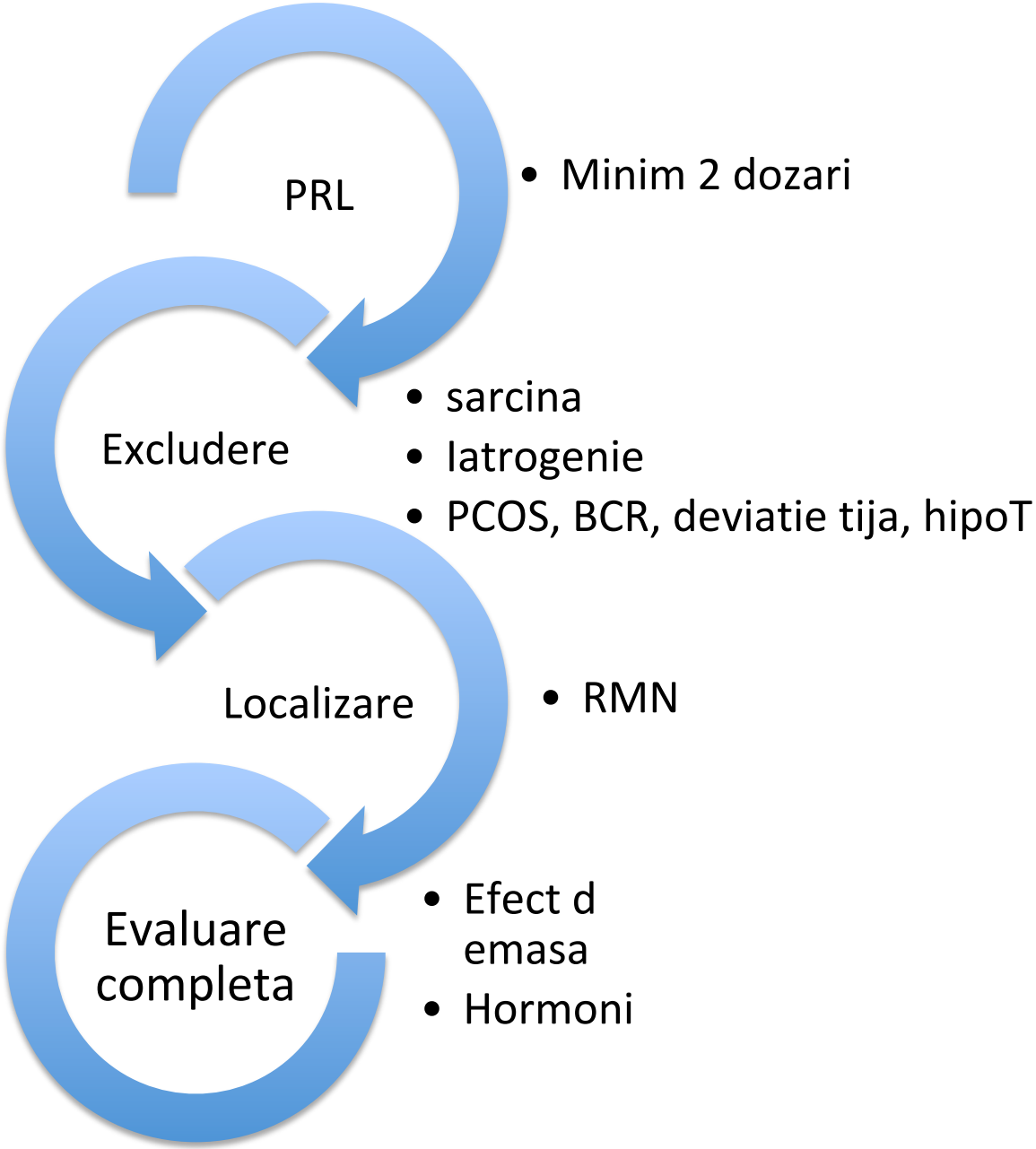
!!!! Proportionalitate nivel PRL – volum prolactinom

Tipic > 100 ng/mL

2. Tumora nesecretanta ce deplaseaza tija
3. Cauze functionale de crestere a PRL
4. Cauze fiziologice de cretsere ale PRL
   - = COC
   - = sarcina
   - = alaptare (3 – 4 luni)

Ranges of serum prolactin concentrations in several causes of hyperprolactinemia

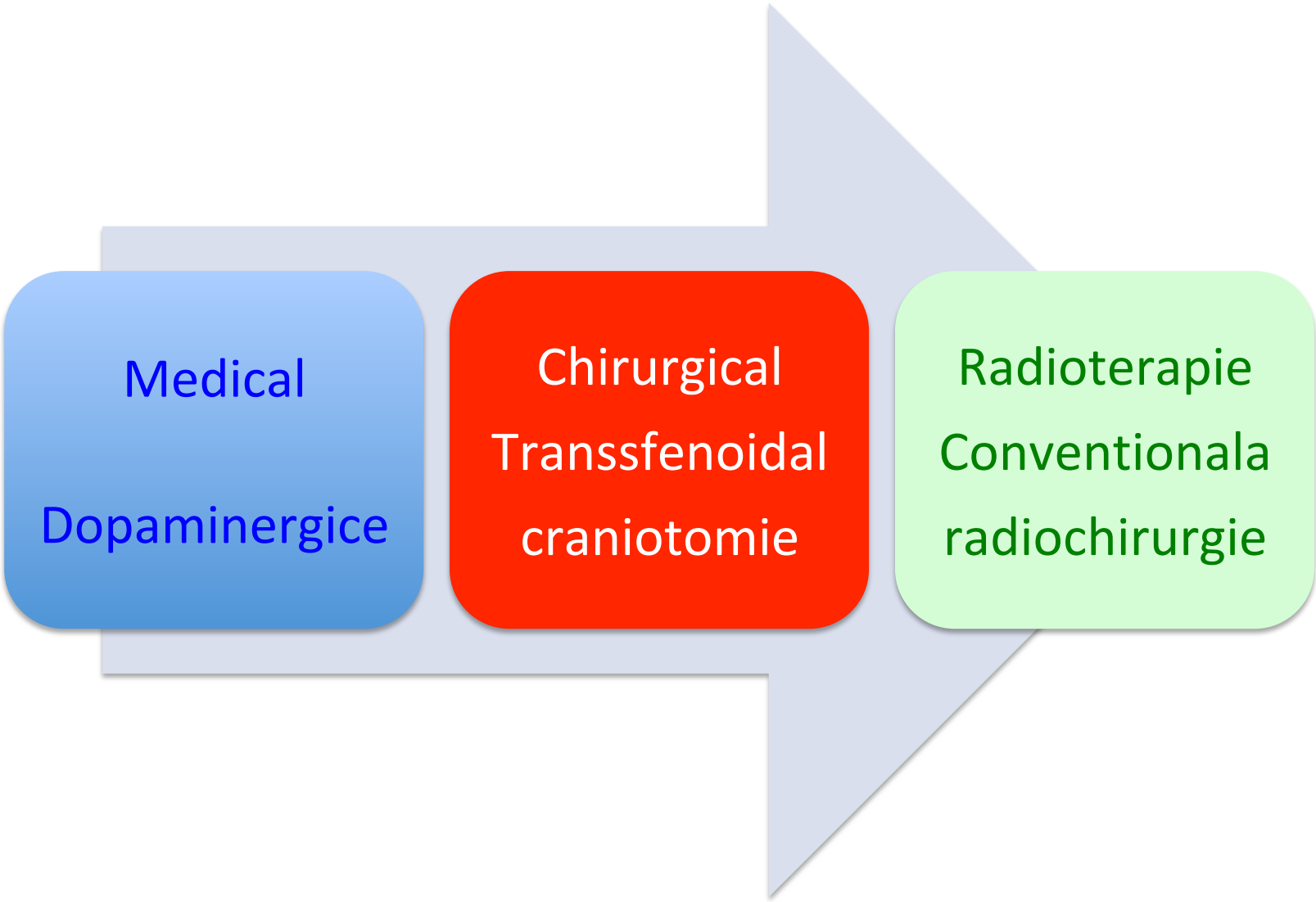



PRL
Minim 2 dozari
Excludere
sarcina
Iatrogenie
PCOS, BCR, deviatie tija, hipoT
Localizare
RMN
Evaluare completa
Efect d emasa
Hormoni

PRL

- Recoltare 08.00-11.00
  - TREAZA de 2 ore
  - FARA
    - SEX
    - Somn
    - Sport
    - Mancare
    - Administrare de alte medicamente

Tratament


Medical
Dopaminergice
Chirurgical
Transsfenoidal
craniotomie
Radioterapie
Conventionala
radiochirurgie

- Linia I = MEDICAMENTOS
  - ✓ Control hipersecretie
  - ✓ Scadere volum tumoral
  - ✓ Reluare ax HhG/fertilitate

BROMOCRIPTINA 1.25-2.5x2/zi

= stimuleaza receptorii DOPA din hipotalamus
= T1/2 scurt zilnic
= toleranta relativa

CABERGOLIN 0.5 x2/saptamana

= stimuleaza receptorii DOPA din hipotalamus
= T1/2 lung saptamanal
= toleranta excelenta
= ? Creste incidenta b.Parkinson (regimuri zilnice)
= leziuni valvulare cardiace ..... Monitorizare ecografica cardiaca periodica

	Cabergoline	Bromocriptin
Normal PRL	83%	59%
Pregnancies (Ovulation)	72%	52%
Stopped S/E	3%	12%

Tratament

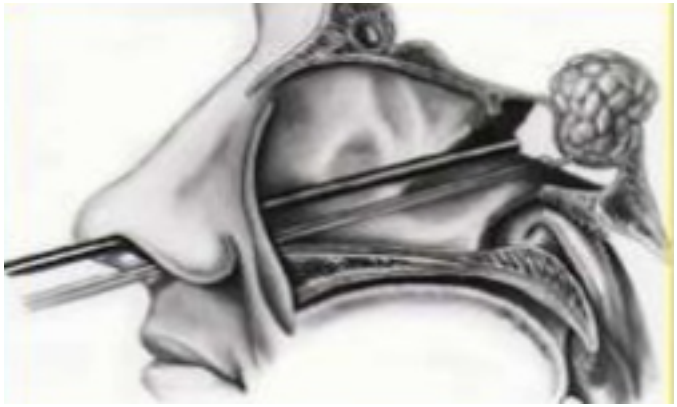
Linia II Chirurgie

Microprolactinoame

- PRL < 200 ng/mL
- Amenoree< 5 ani

Vincedare 85-90%

Recurenta 15%



Macroprolactinoame

- PRL < 200 ng/ml
- Tumora 1-2 cm

Vindecare 80%

- PRL > 200 ng/mL
- Extensie extraselara

Vindecare 25-50%

In forme avansate se prefera medicatia

Alegere terapie

Microadenoame

- Tratament universal

1. Dopaminergice
   - Cabergolin cp 0.5 mg
   - 0.2-1 mgx2/sapt
   - Raspuns bun: ↓PRL + tumora
   - 2-3 ani = renuntare
   - Verificare Prl + RMN

2. Transsfenoidal
   - Recurenta
   - Macroadenom (2 cm)
   - Remisiune pe termen lung
   - Risc minimal

3. Radioterapie
   - Nu este indicata

Macroadenoame

1. Dopaminergice - 1st line therapy

   PRL > 200 ng/dL

   tumora > 2 cm

2. Abord transfenoidal

   - tumori mari +resturi/HPRL

3. Radioterapie

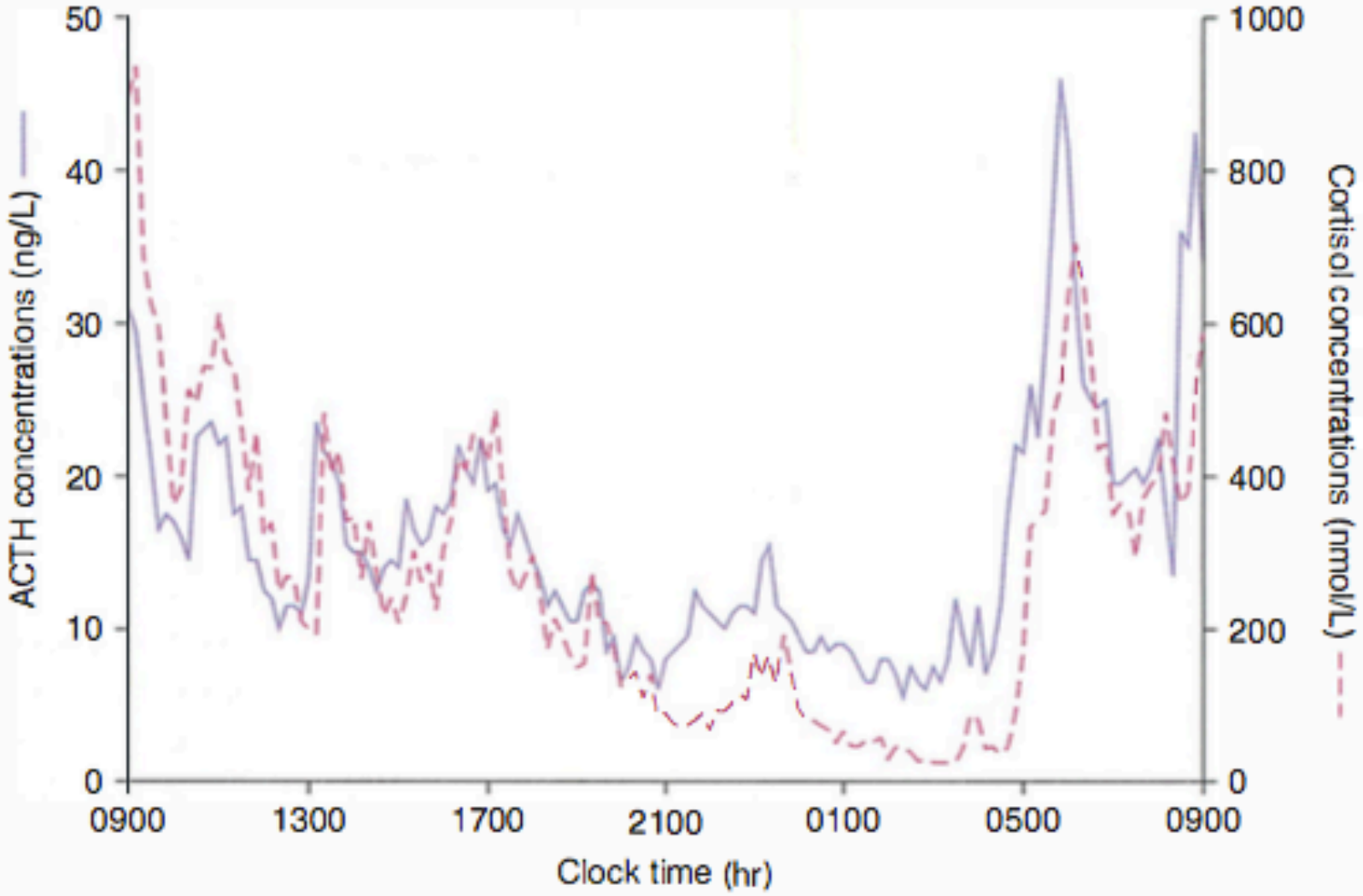
   - pacienti postchirurgical, cu reziduri adenomatoase+ control partial cu dopaminergice

POMC-ACTH

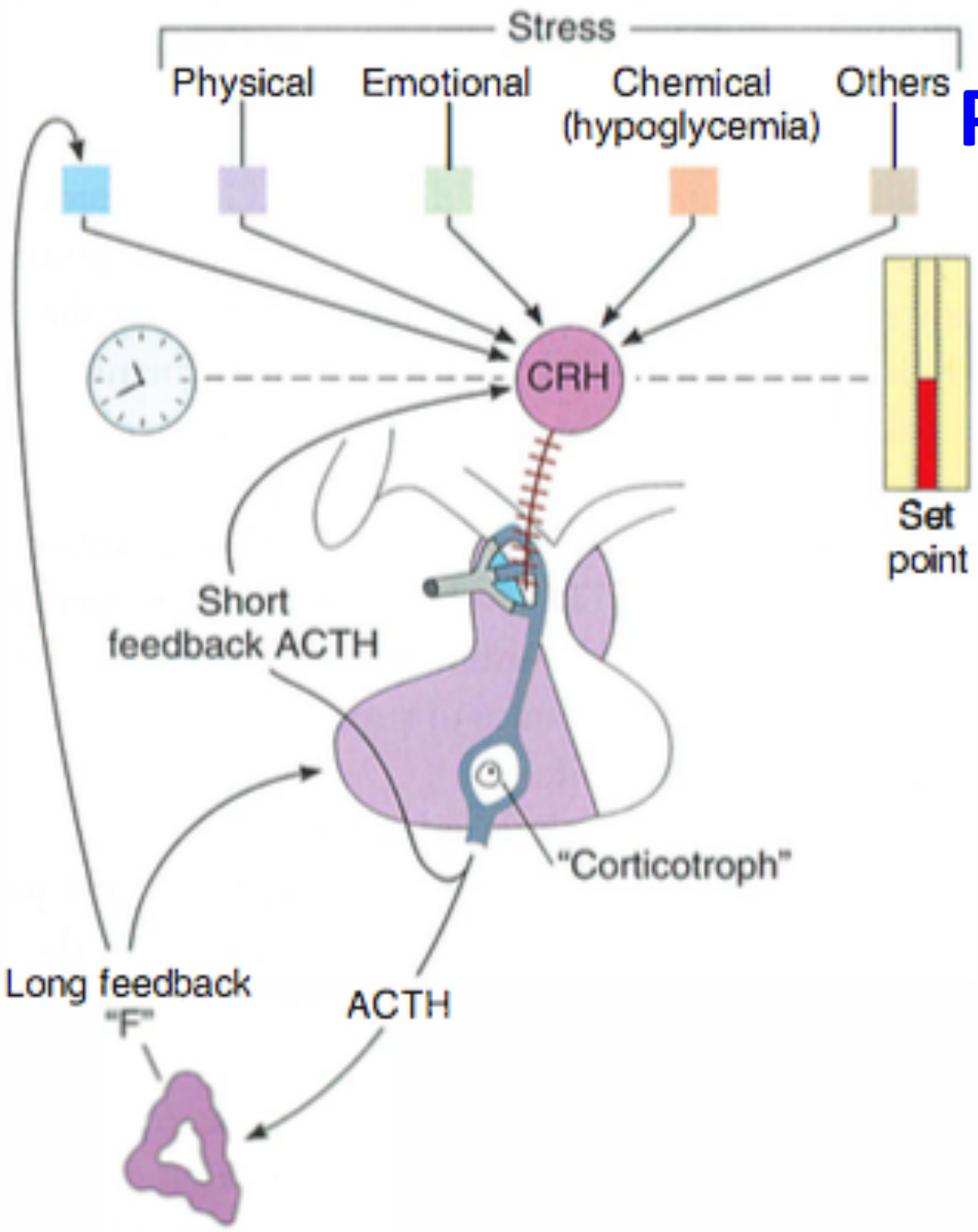
- Secretie episodica reactie la stres (+ CRH, + ADH)

  durere, traumatism, hipoxie, hipoglicemie, expunere la frig, chirurgie, depresie

- Fluctuatii mari


ACTH concentrations (ng/L)
Cortisol concentrations (nmol/L)
50
40
30
20
10
0
1000
800
600
400
200
0
0900
1300
1700
2100
0100
0500
0900
Clock time (hr)

POMC-ACTH


Stress
Physical
Emotional
Chemical
(hypoglycemia)
Others
CRH
Set
point
Short
feedback ACTH
"Corticotroph"
Long feedback
"F"
ACTH

- Virtual TOATE CELULELE au receptori de GCS

1. METABOLISM INTERMEDIAR
    1. ↑ProteolIZA
    2. ↑GluconeogeneZA.rezistenta la insulina
    3. ↓sinteza proteica musculara
    4. ↑mobilizare acizi grasi liberi
2. os , cartilaj: ↓ efectul IGF1
3. Afecteaza legarea h.tiroidieni de Rec, conversia T4→T3
4. Moduleaza raspunsul imun
5. Moduleaza reactivitatea vasculara la NAdr, Ang II
6. SNC: moduleaza perceptie,emotionalitatea

CUSHING

- Exces de glucocorticoizi
  - ENDOGENi HIPOFIZA
    SUPRARENALA
  - EXOGENI CORTICOTERAPIE
    ? >3 saptamani de 7.5 mg Prednison/zi

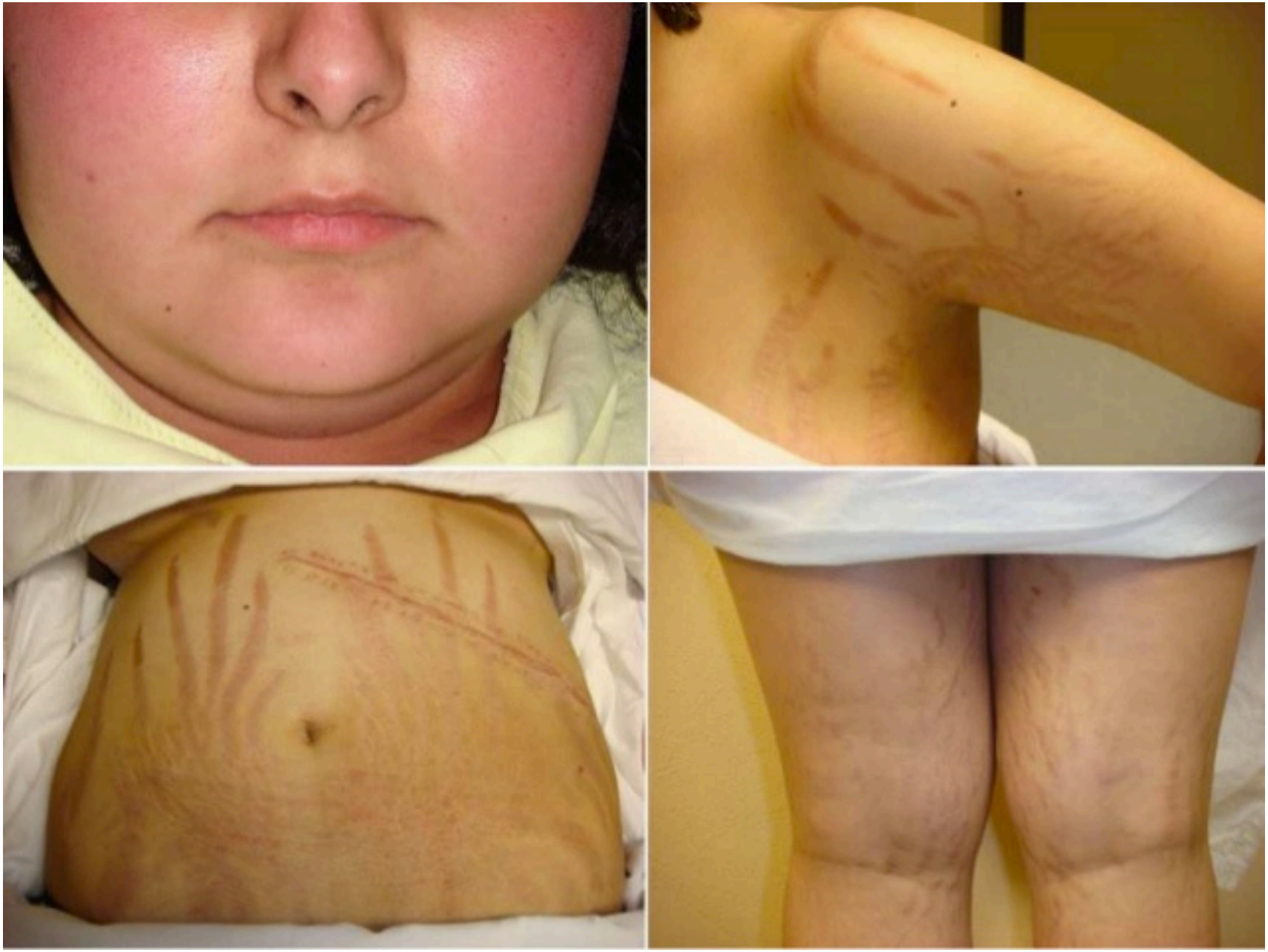
Semne clinice

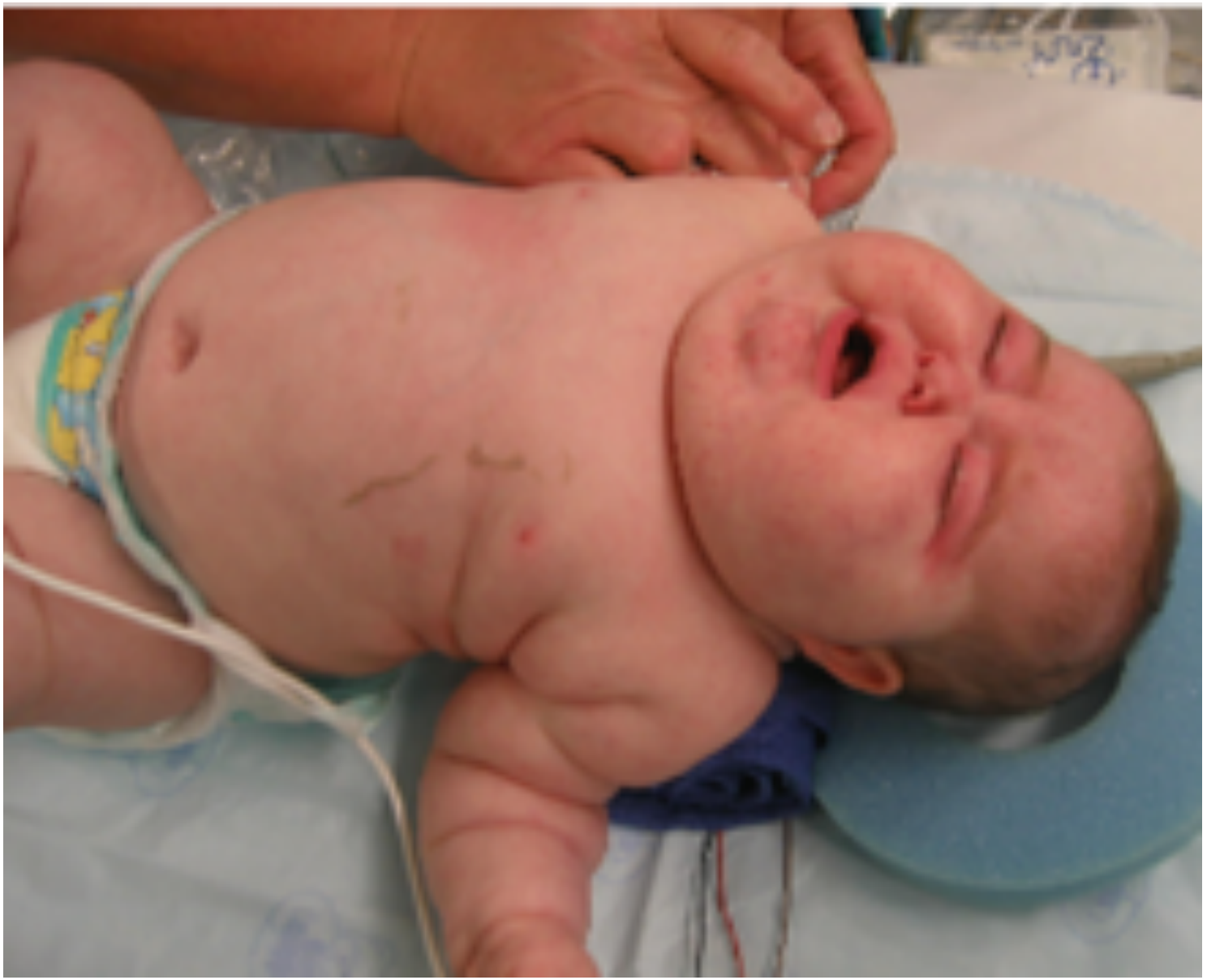
- Obezitate
  - Cel mai frecvent semn
  - Centrala: facies, gat, truchi, abdomen, cu crutarea membrelor
  - FATA DE LUNA PLINA= 75%
  - COCOASA DE BIZON = 65%
  - Alterarea distributiei tesutului adipos
  - Obezitate viscerala

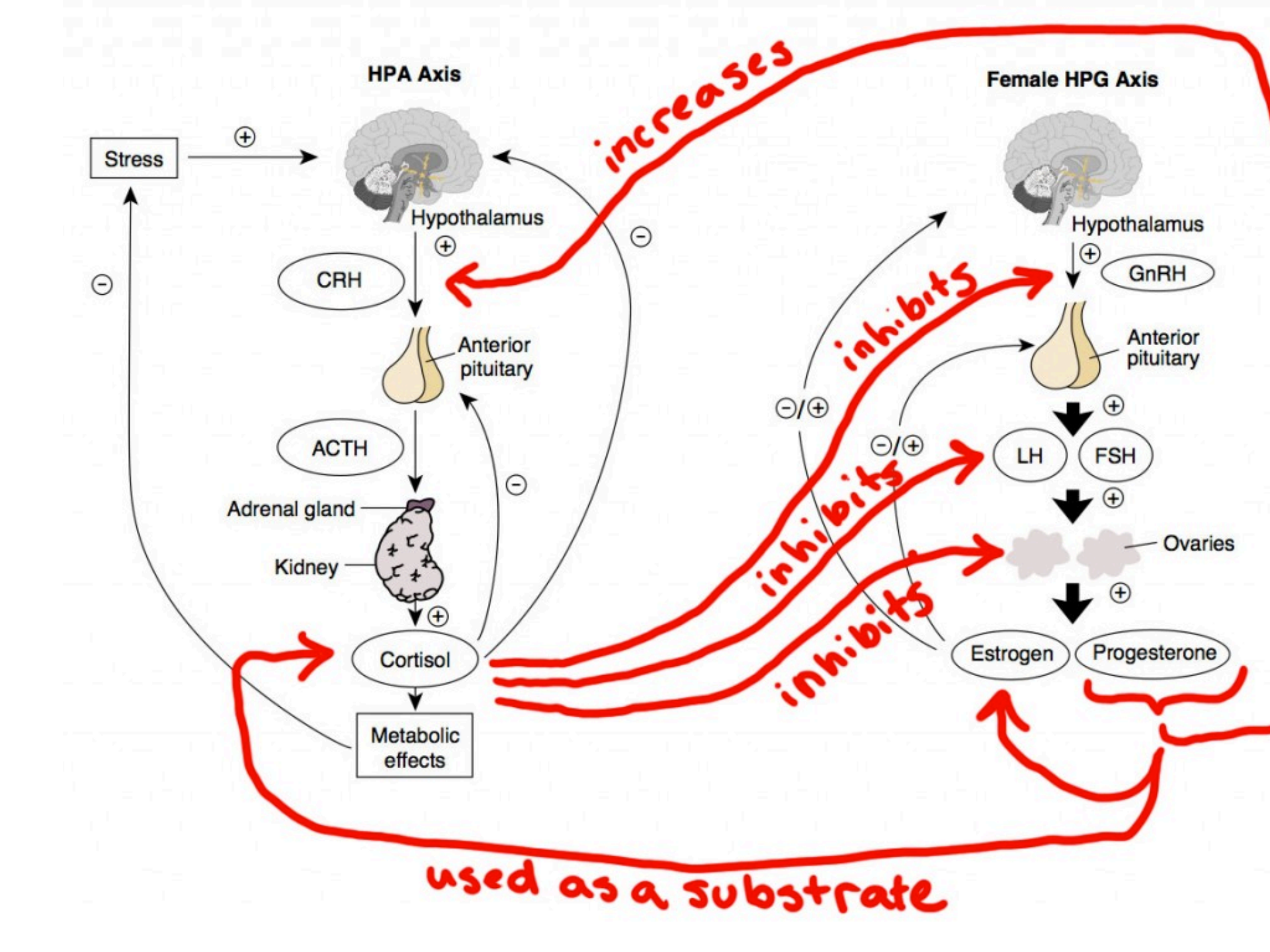
Semne clinice

- Modificari cutanate
  - Subtiere = aspect transpoaent
  - Pletorism facial
  - Sensibilitate = 40%
  - Vergeturi = 50% (atipic la pacientii tineri) = rosii, violete, adanci, depresibile (0.5-2 cm)
  - Vindecare dificila
  - Acnee (excesul de GC si de androgeni)
  - Infectii fungice: tinea versicoloc

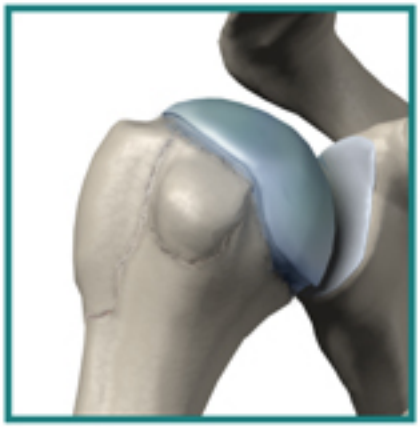
- Hirsutism = PILOZITATE
  - 80% femei = androgeni adrenali!!!
  - Facial
  - Abdomen, sani, torace, fata interna coapse
- Virilism exceptie !!! Carcinom



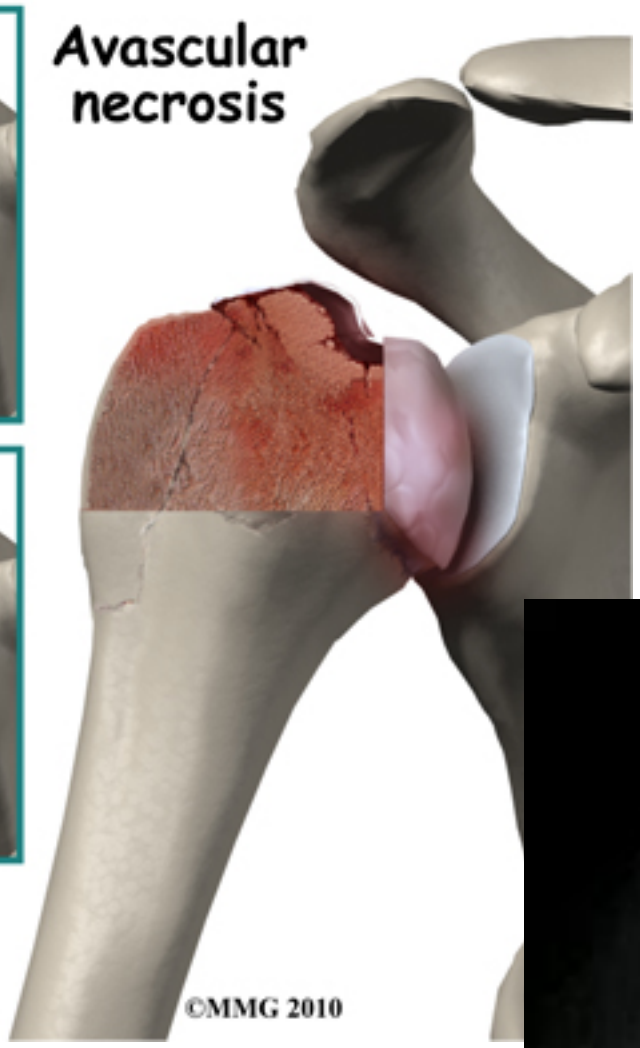


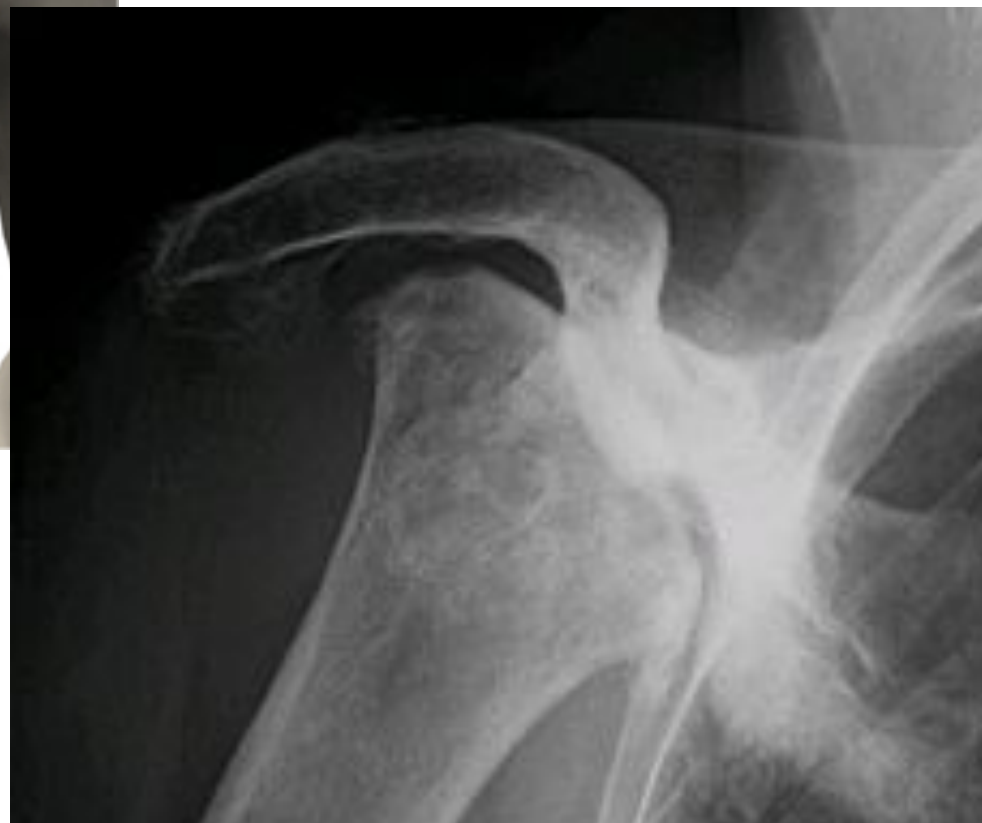

HPA Axis
Female HPG Axis
Stress
Hypothalamus
CRH
Anterior pituitary
ACTH
Adrenal gland
Kidney
Cortisol
Metabolic effects
Hypothalamus
GnRH
Anterior pituitary
LH
FSH
Ovaries
Estrogen
Progesterone
increases
inhibits
inhibits
inhibits
used as a substrate

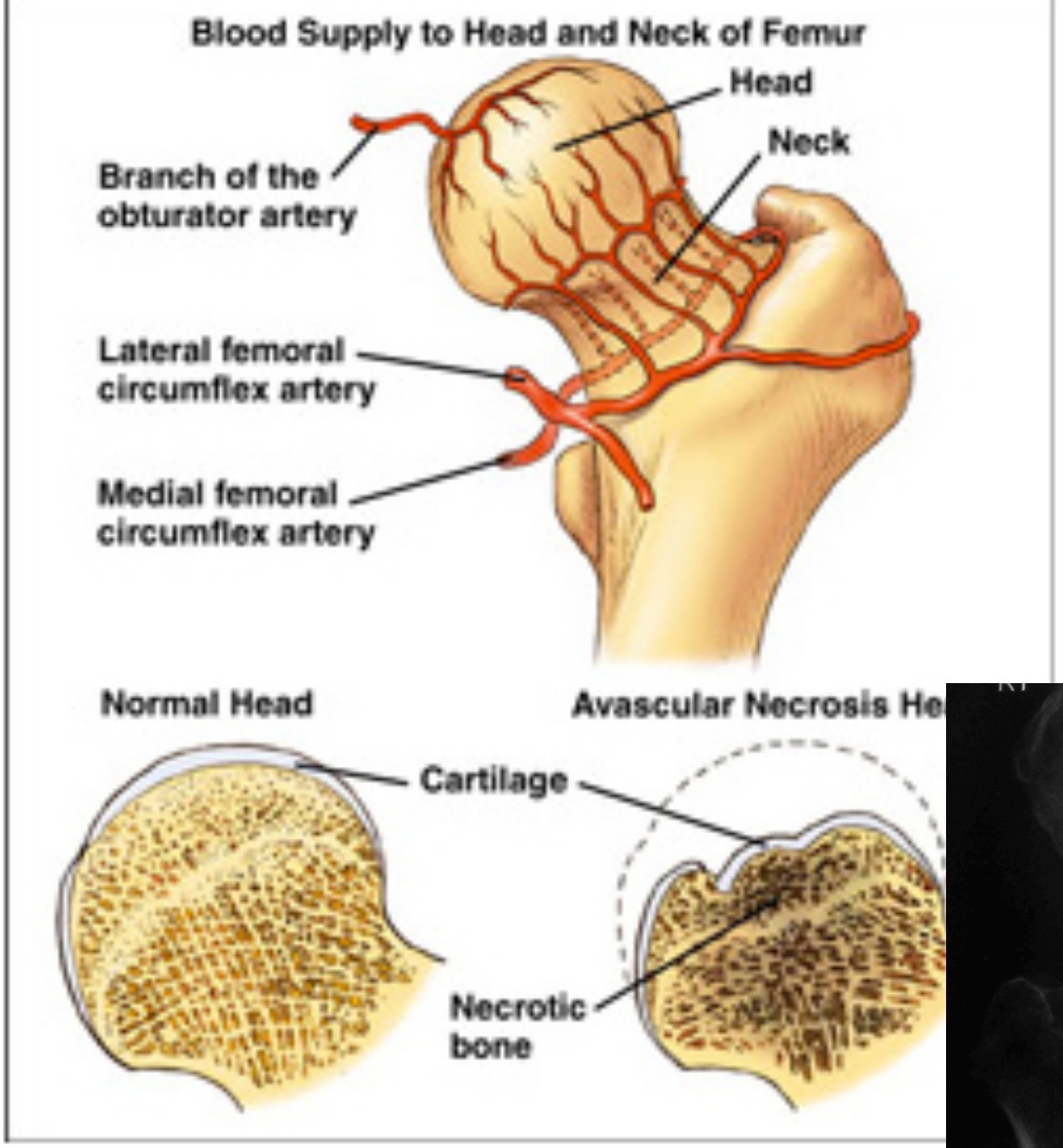
- Muscular = oboseala, pierdere musculara
  - Tipic proximal: centura scapulara/pelvina
- Os – demineralizare
  - Intarzierea cresterii... copii
  - Pierdere osoasa... Adulti
  - Fracturi de fragilitate
  - Fractur vertebrale compresive 20% din cazuri
  - Necroza avasculara de cap femural/humeral
- Calculi renali – hipercalciuria – 15%
- Sete + poliurie

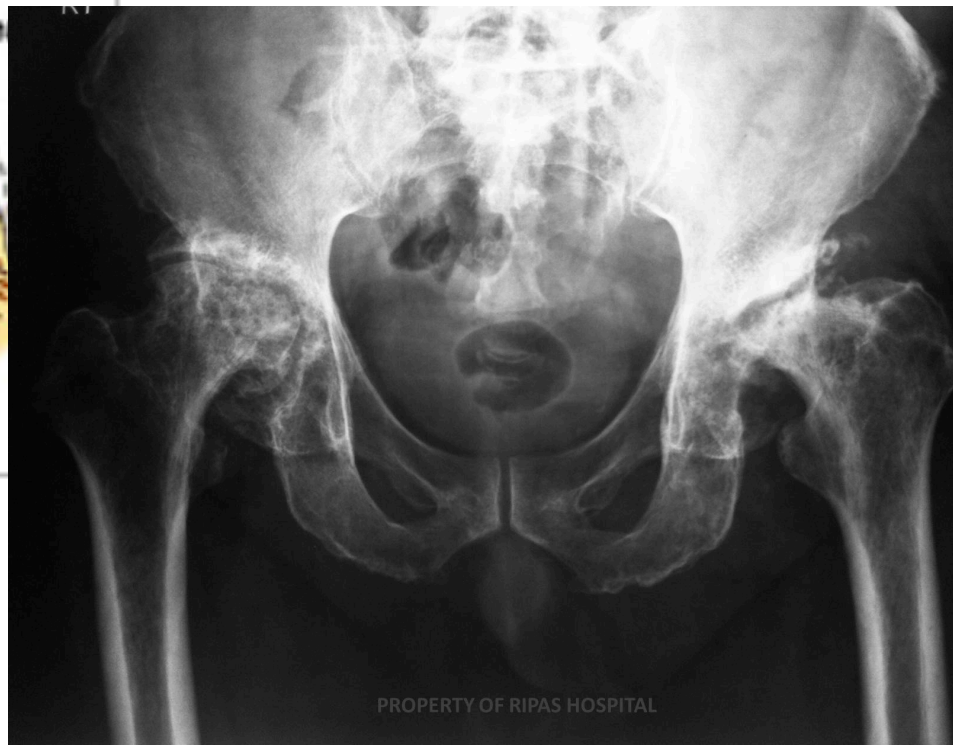


Blood supply to humeral head disrupted






Blood Supply to Head and Neck of Femur
Head
Neck
Branch of the obturator artery
Lateral femoral circumflex artery
Medial femoral circumflex artery
Normal Head
Avascular Necrosis He
Cartilage
Necrotic bone


PROPERTY OF RIPAS HOSPITAL

Dg +

- SECRETIE DISPROPORTIONATA ➢ **PREA MULT**
- ALTERARE RITM CIRCADIAN ➢ **NOAPTEA**
- ALTERARE MECANISM FEEDBACK ➢ **R - INHIBITIE**

Screening = HIPER+ RITM

- Cortizol Liber Urinar
  - urina de 24 de ore
  - innafara menstruatiei
  - prima urina se arunca
  - se colecteaza intregaa urina + I de a2a zi la trezire
  - se pasteraza la rece
  - se noteaza volumul

- Cortizol salvar nocturn
  - Neinfluentat de variatiile CBG
  - Demonsteraza ALTERAREA RITMULUI DIURN
- FARA MANCAre dupa orele 20.00
- FARA LICHIDE dupa orele 23.00
- RECOLATRE SALIVA orele 24.00


1
2
3
4
5
6
7
8

TEST DE INHIBITIE

- Nocturn
  - Ziua 1 – recoltare cortizol ora 08.00
  - Orele 23.00 – administrare DEXAMETHASON
  - Ziua 2 – recoltare cortizol ora 0.88

!!!!!

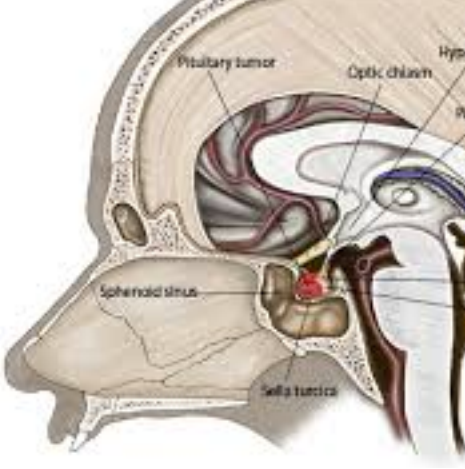
- Toate adenoamele hipofizare
  - Secretante
  - Nesecretante

POT RECIDIVA

- Tratamentul **nu este intotdeauna CURATIV**

- Pacient in urmarire medicala **PE VIATA**!!!!!

Boala Cushing

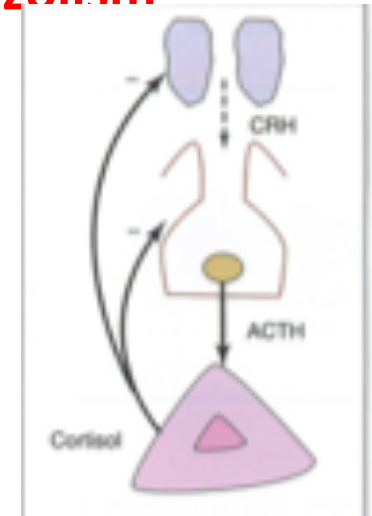


- Cea mai frecventa cauza 80%
- F:M = 8:1
- Max 20-40 ani, distributie de la copil – 70 ani
- Adenoame hipofizare: 90% microadenoma (50%<5 mm)
- Rar: hiperplazie hipofizara a celulelor corticotrope

= hipersecretie de GCS + hipersecretie de androgeni = hiperplazia adrenala bilaterala zona reticulara si fasciculata = exces de cortizol + androgeni

Mecanism:

1. **Hipersecretie de ACTH + hiperplazie adrenala + hipercortizolism**
2. **Absenta ritmului circadian a ACTH si cortizolului**
3. **Absenta raspunsului la stres**
4. **Abnormal feedbackului la glucocorticoizi**
5. **Raspuns anormal al GH,TSH, LH+FSH la stimulare**
6. **Exces de androgeni**



1. Sd morfologic = aspecte Cushing
2. Sd tumoral hipofizar = compresiune
3. Sd. hormonal =alterarea altor linii
4. SD metabolic = Hiperglicemie + HTA

Diagnosis ≠

- Formele de CGS
- Pseudo Cushing
  - Depresie
  - Obesitate cu crestere ponderala rapida
  - Alcoolism cronic
  - Bulimia nervosa
- Sd adregogemital (CAH)
- Sd adipozogenital = Obezitate + hipogonadism
- Tumori gonadice producatoare de androgeni

DIABET INSIPID

- = alterarea productiei de ADH = h.antidiuretic

- Idiopatic
- Postruatmatic
- Postchirurgical

1. Trigger = modificare a Osm cu 1%

↓

2. Osmoreceptori = neuroni osmoreceptori hipotalamus + lamina terminalis

↓

3. Pierderea apei celulare= deshidratare↓ = micsorare celulara = semnal pentru neuronii magnocelulari producatori de AVP

↓

4. Eliberare de AVP **inainte de aparitia senzatiei de sete**

↓

5. Reabsorptie crescuta de H2O: AQP2

Tablou clinic

ACUT = central

LENT = nefrogen

- Poliuria
  - Permanenta
  - Urina decolorata/diluata
  - volum crescut

usor	4-5 l/zi
mediu	6-10 l/zi
sever	> 10 l/zi

- Polidipsia
  - Consum de lichide, preferential reci
  - Compensatoriu pentru pierderile urinare

- Semne etiopatogenetice
  - Istoric de traumatism/chirurgie
  - Visual fiedl defects/panhipopituitarism
  - Acute headache
  - Anorexia/bulimia

DIAGNOSTIC

1. Documentarea poliuriei
2. Osm plasmatica n, ↑
3. Osm urinara ↓ < 200 mOsm/kgH_2o
4. Densitate urinara ↓ < 1005
5. Clearance apa libera = POZITIV

$C_{H2O} = V - OSM_u/OSM_p \times V = V (1- OSM_u/OSM_p)$

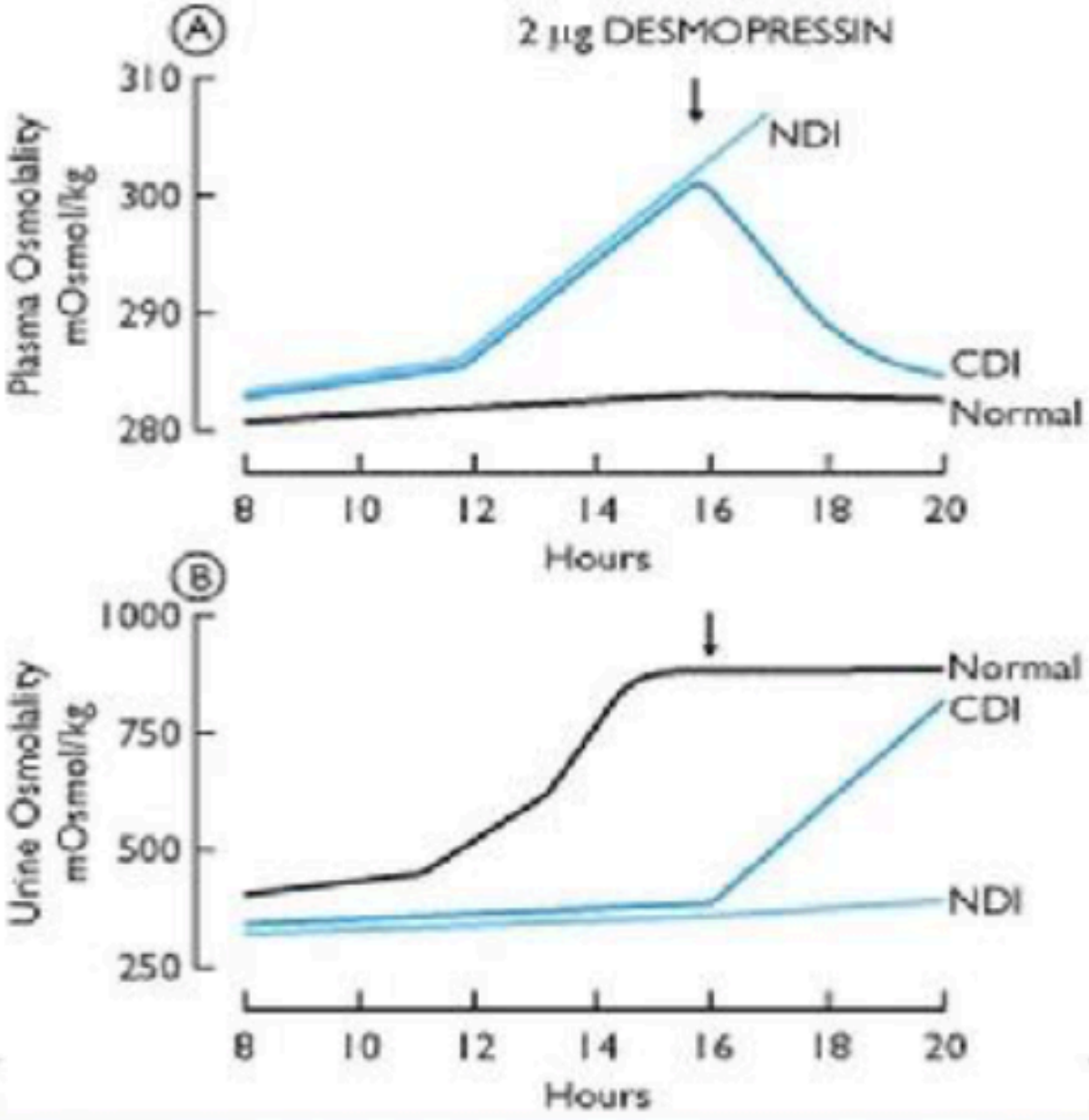
Normal $OSM_u >>>> OSM_p$ C_{H2O} = negativ

DI $OSM_u <<< OSM_p$ C_{H2O} = pozitiv

PROBA SETEI

- Dimineata, fara aport de apa
- Masurare
  - Greutate
  - TA
  - Natrenie, Osmolaritate plasmatica si urinara
- DEPRIVARE DE APA … minim 4 ore

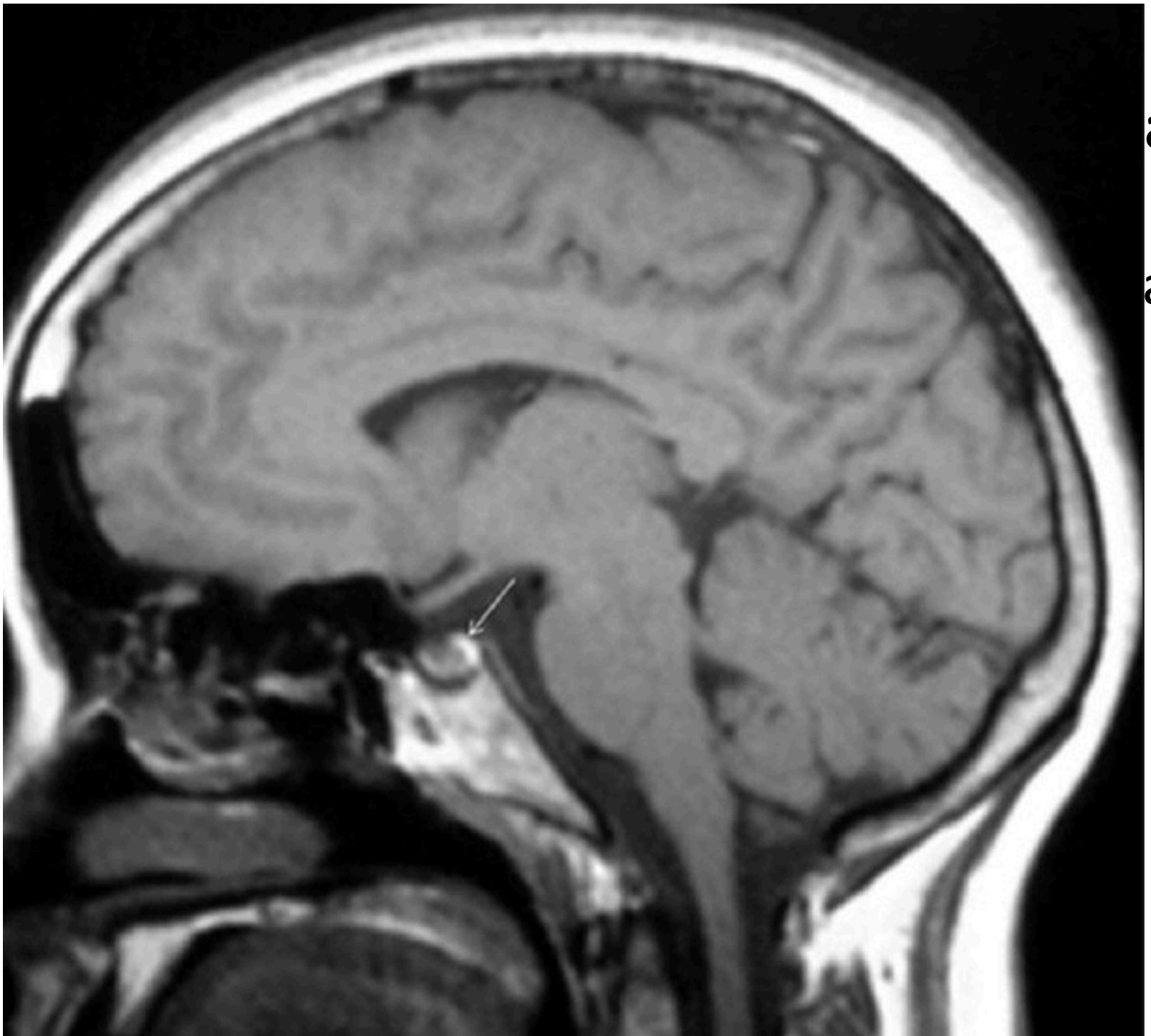
- MASURARE La fiecare ora a
  - Greutate
  - TA
  - Natrenie, Osmolaritate plasmatica si urinara

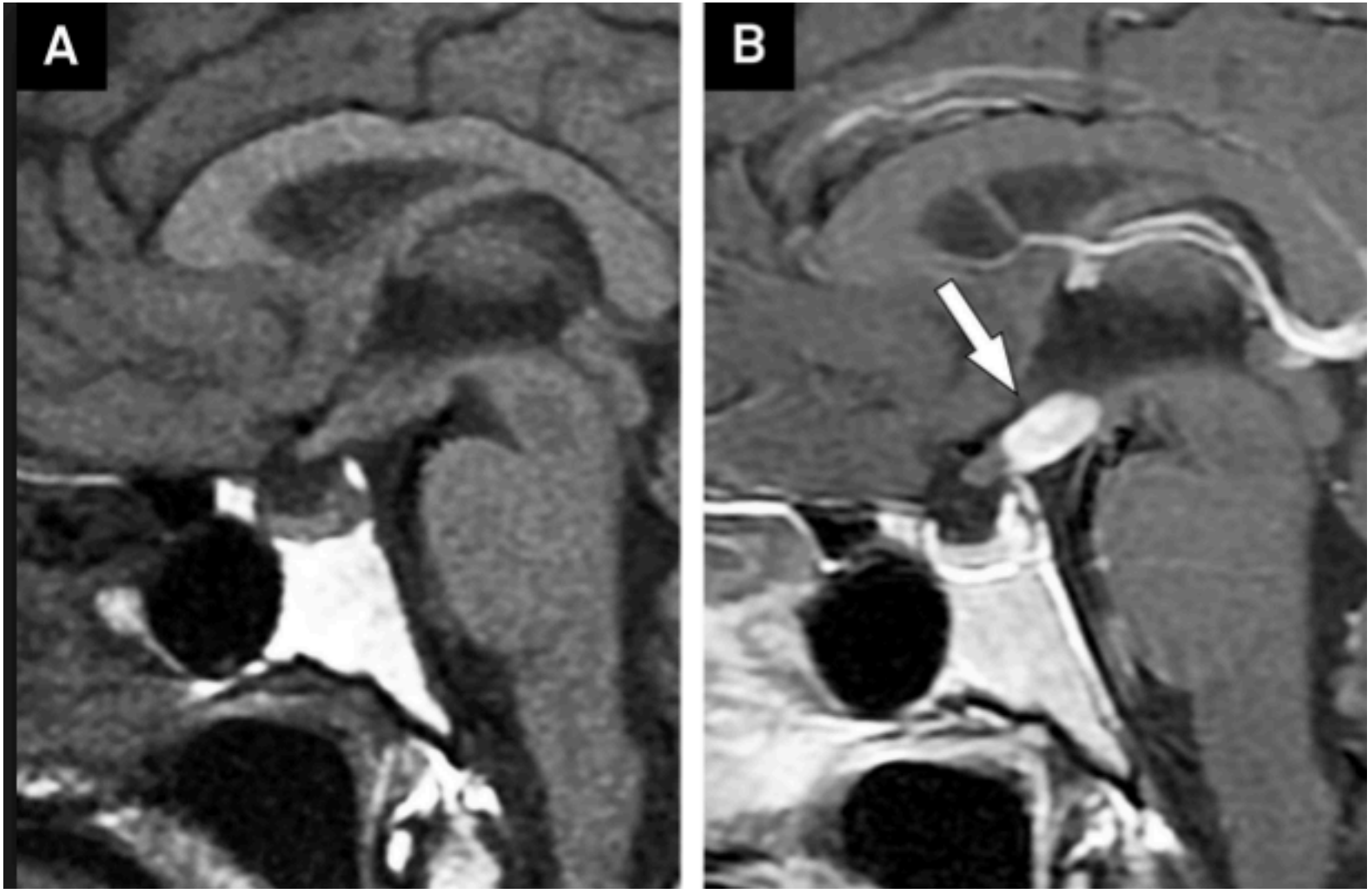

A
2 μg DESMOPRESSIN
Plasma Osmolality
mOsmol/kg
310
300
290
280
NDI
CDI
Normal
8
10
12
14
16
18
20
Hours
B
Urine Osmolality
mOsmol/kg
1000
750
500
250
Normal
CDI
NDI
8
10
12
14
16
18
20
Hours

- ! Dupa 4 ore/ la peirdere a 5% din greutate
- Administrare de desmopresina

- Masurarea dinnou a
  - Greutatii
  - TA
    osmolaritate plasmatica si urinara

- **a**
- a
-




A
B

? urmarire

Normalizarea PRL = micsorarea adenemului

2. Efecte secundare restul hipofizei

3. Efecte adverse medicatie eco cardiac