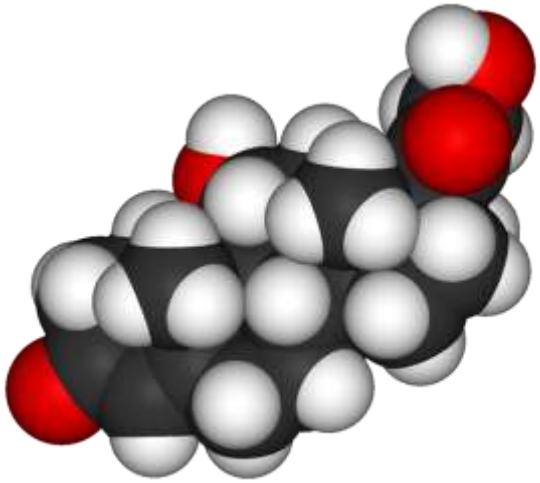

Cortisol, électrolytes et laboratoire

Cours Labmed 3ème partie, CPLN Neuchâtel 22 mars 2010

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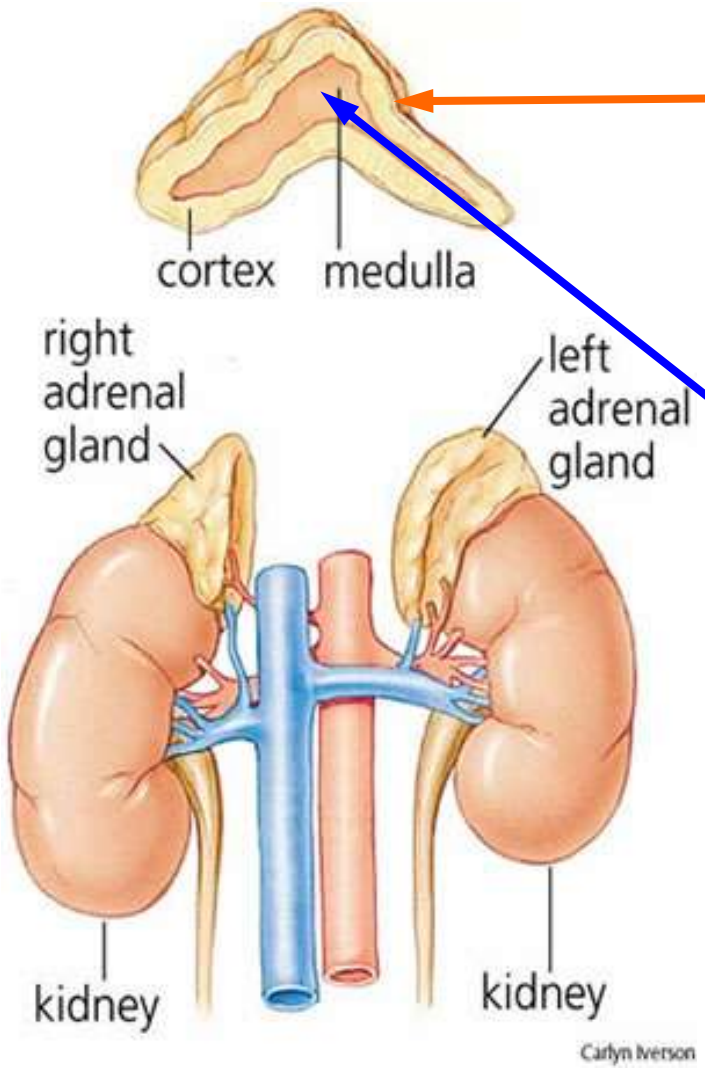
Section romande

Ecole Supérieure du canton de Neuchâtel

Cortisol, électrolytes et laboratoire

- Cortisol
  - Excès: syndrome de Cushing
  - Manque: insuffisance surrénalienne
- Electrolytes:
  - Sodium
    - Hyponatrémie
    - Hypernatrémie
  - Potassium
    - Hypokaliémie
    - Hyperkaliémie

Hormones et surrénale



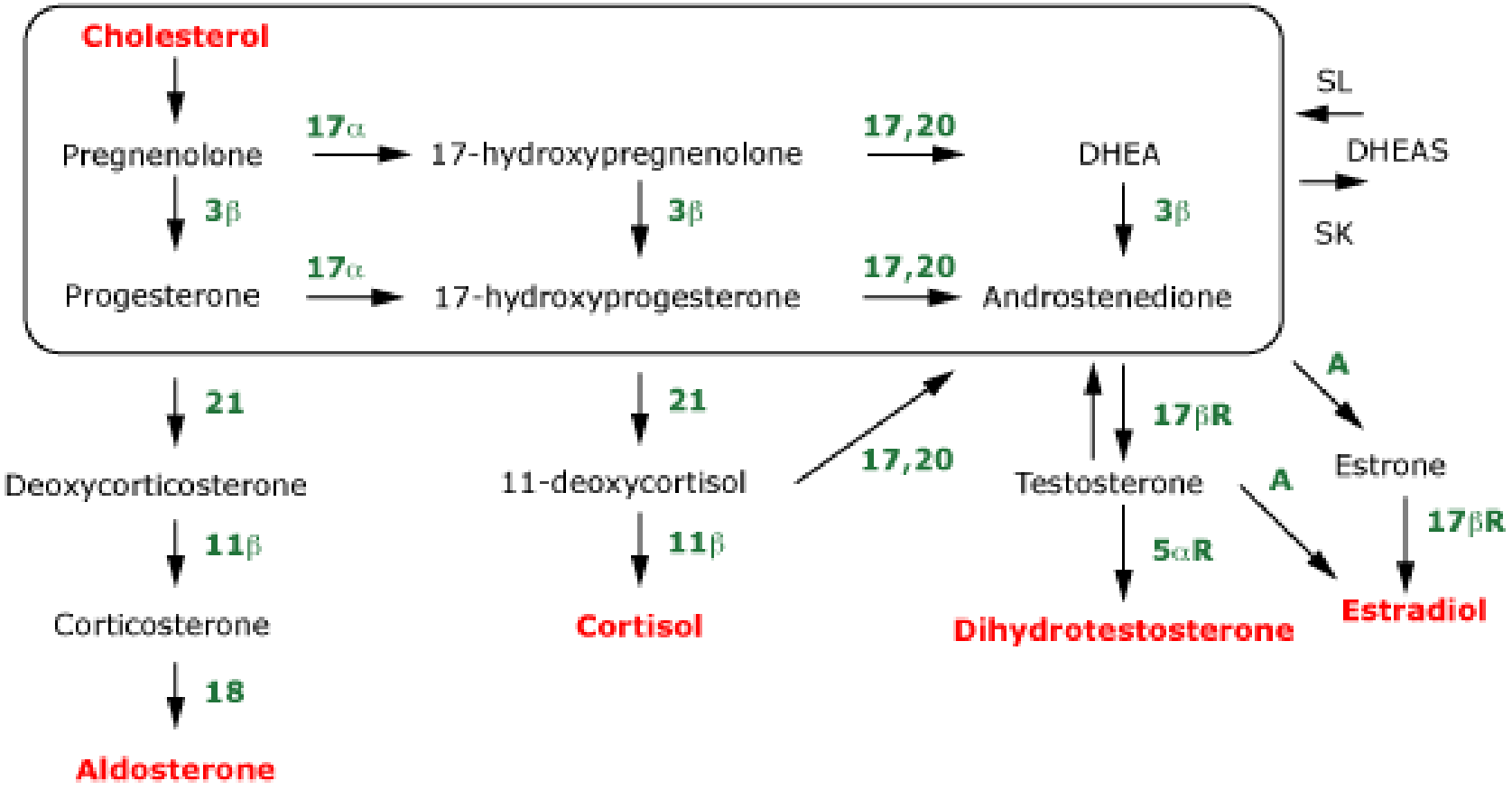
Cortex:

- **Cortisol**
- Aldostérone
- Androgènes

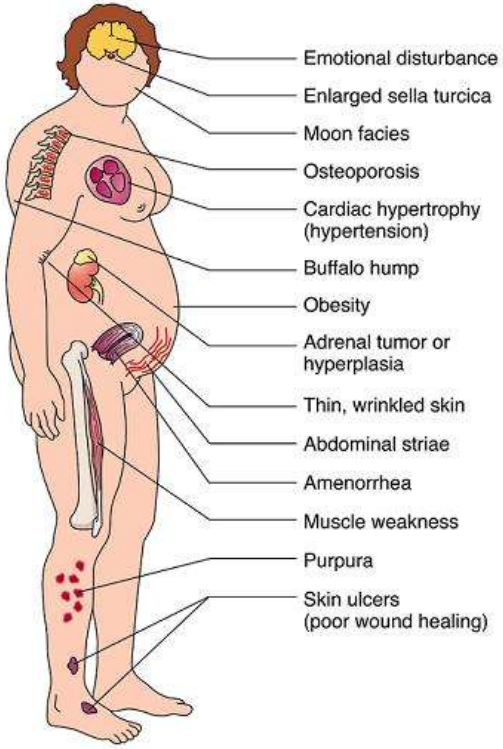
Medulla:

- Catécholamines
  - Noradrénaline
  - Adrénaline
  - (dopamine)

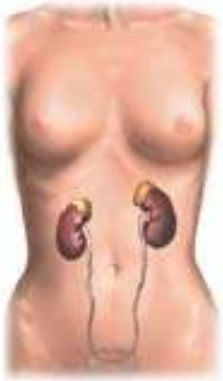
Synthèse des stéroïdes surrénaliens

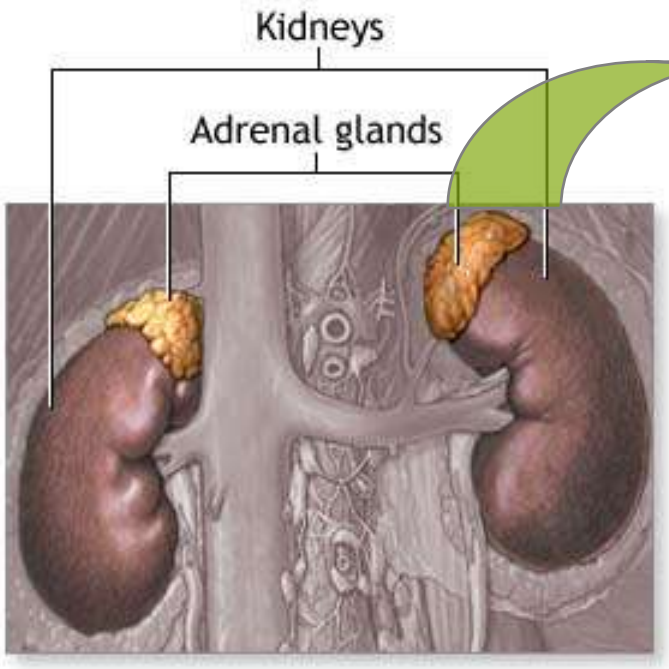


Syndrome de Cushing (Excès de glucocorticoïdes = cortisol, hypercorticisme)



Syndrome de Cushing: production par la surrénale d'un excès de cortisol (ACTH dép ou ACTH indép)

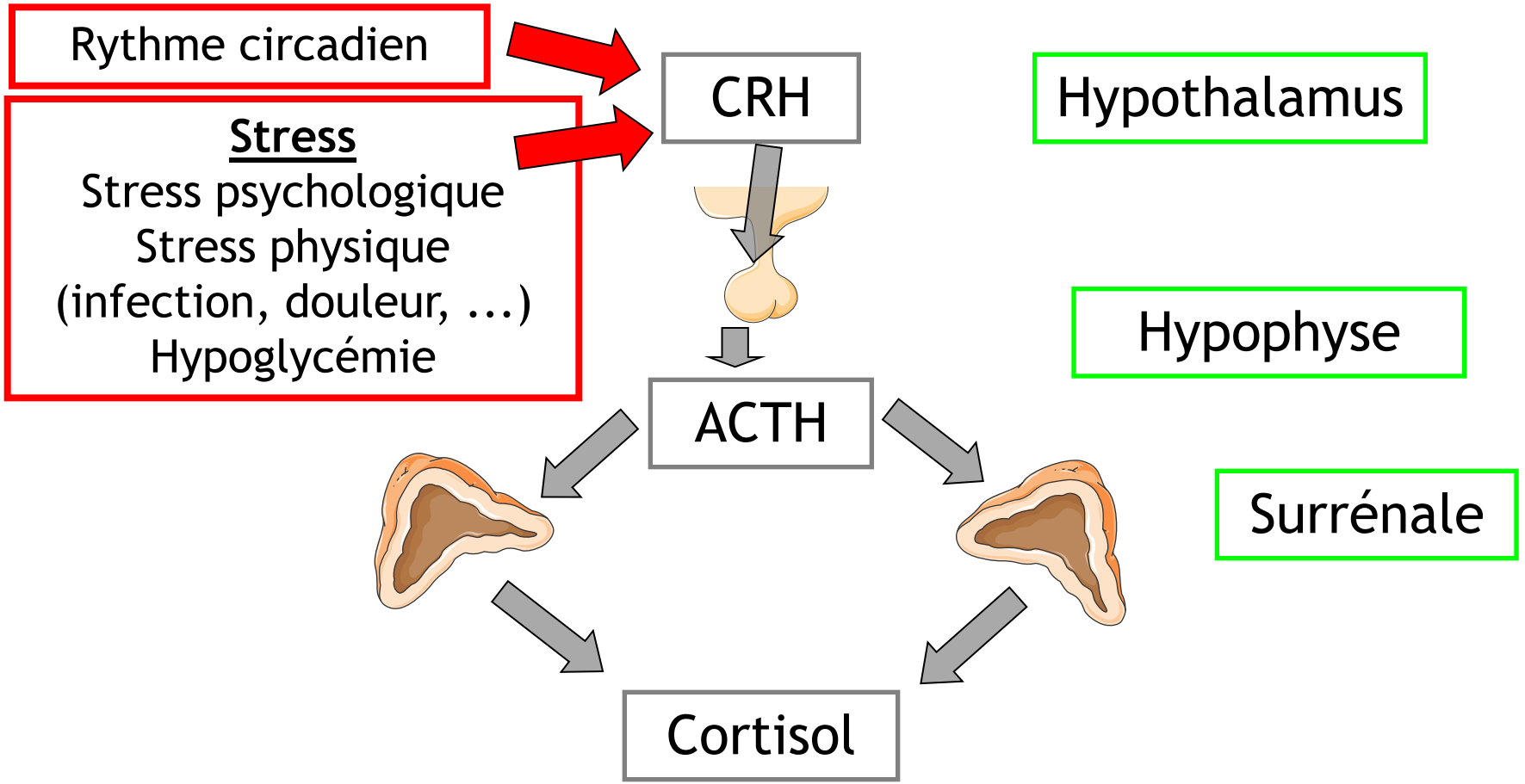




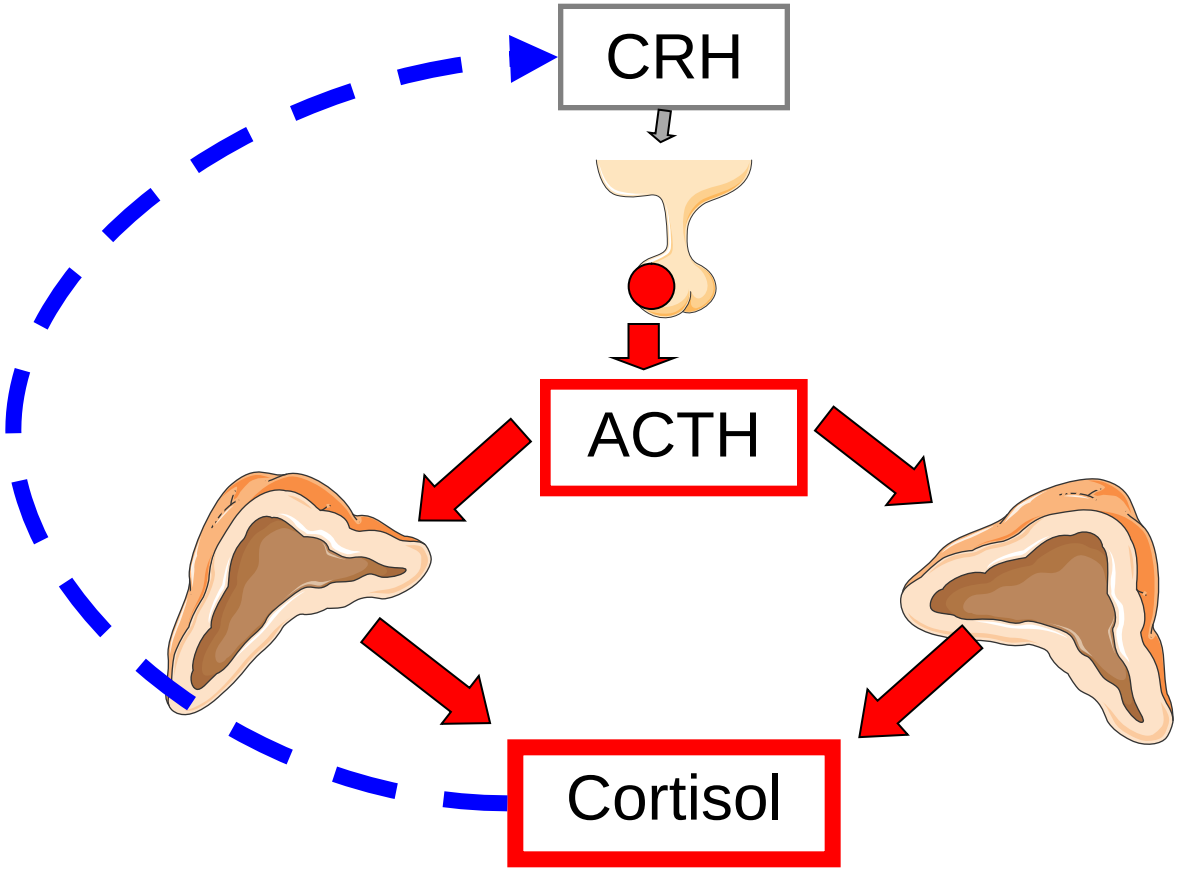
Cortisol

Antiinflammatoire, stress, immunité

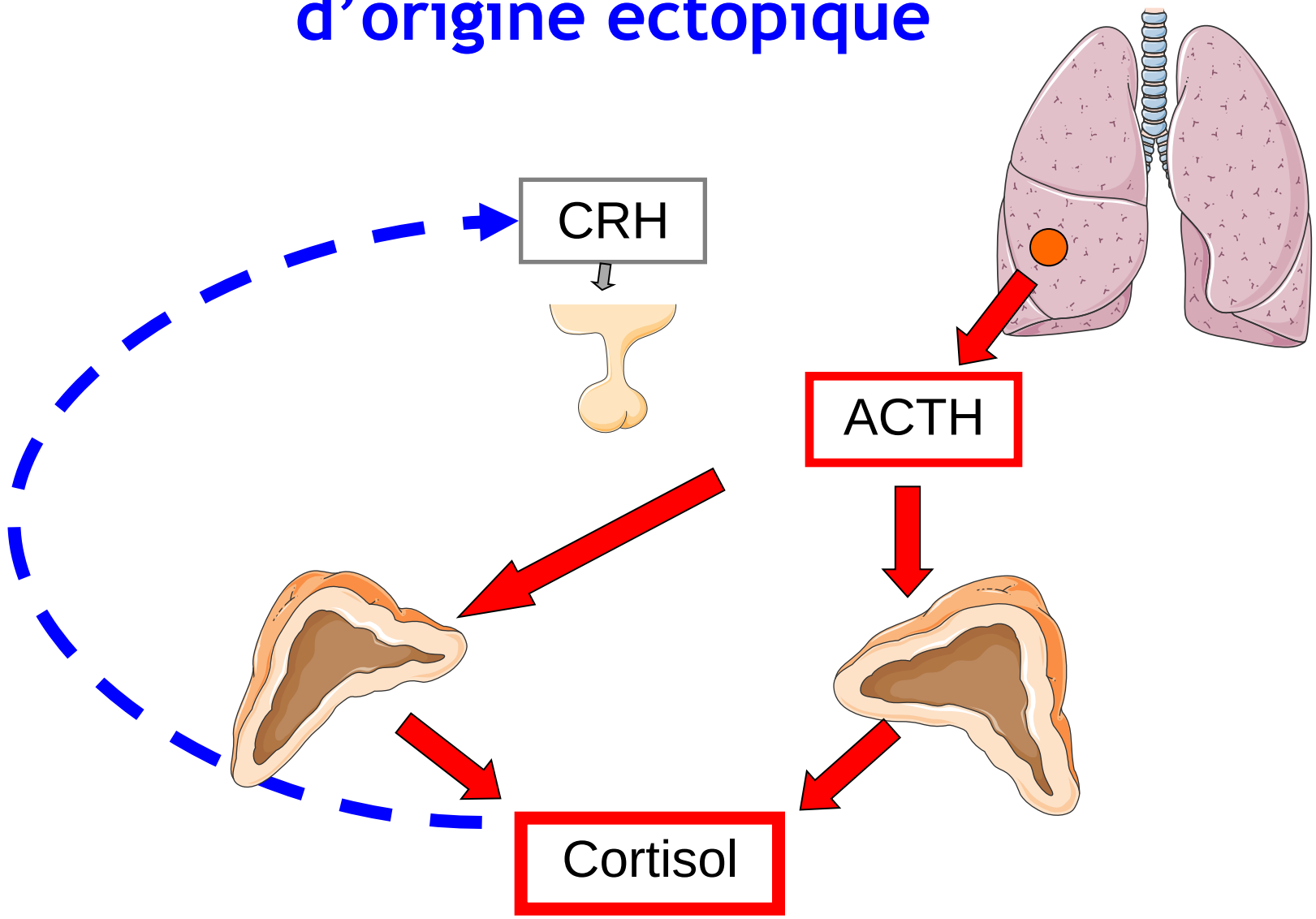
Physiologie normale de l'axe hypothalamo-hypophysaire-surrénalien (HHS)



Maladie de Cushing
(Adénome hypophysaire à ACTH)

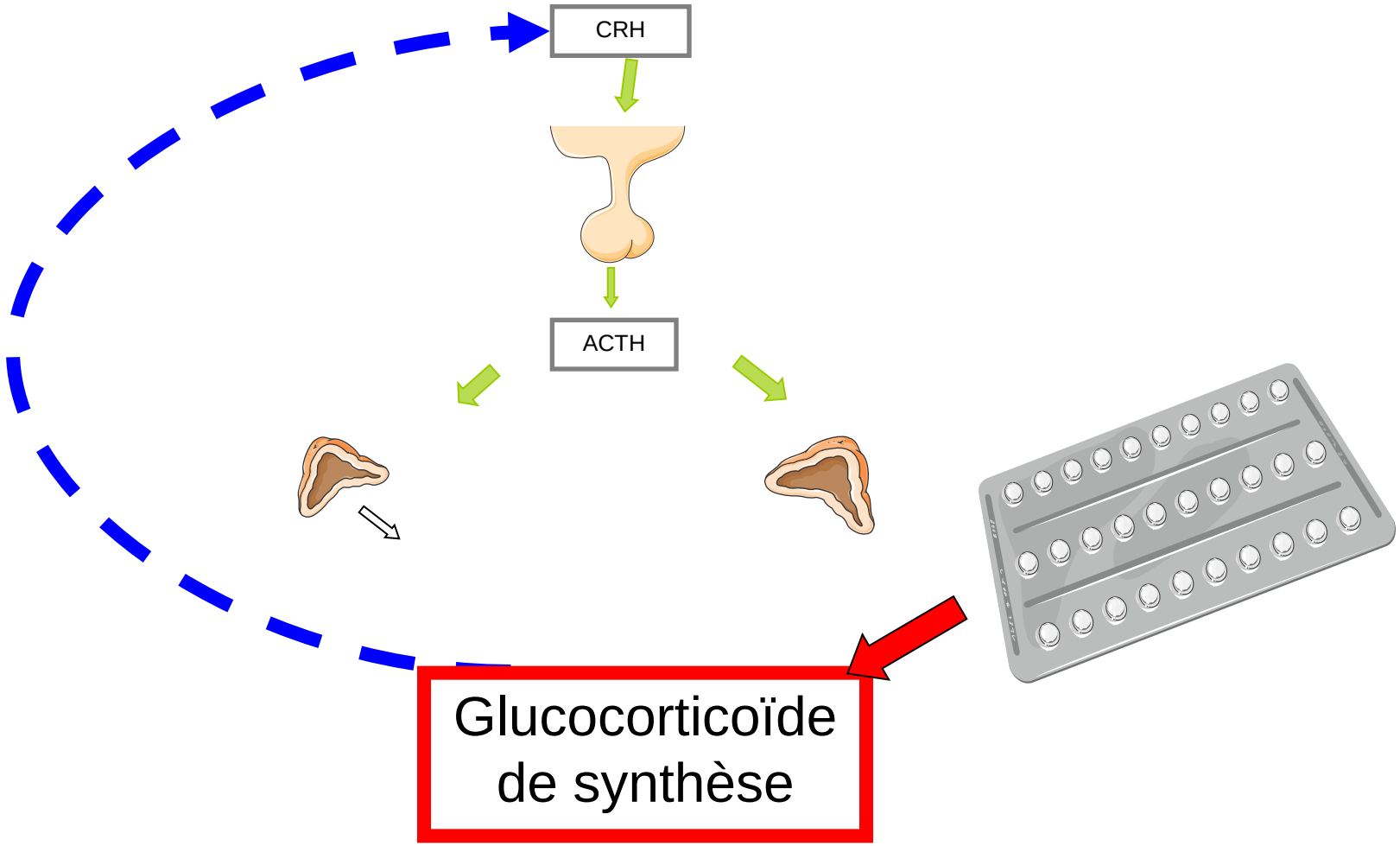


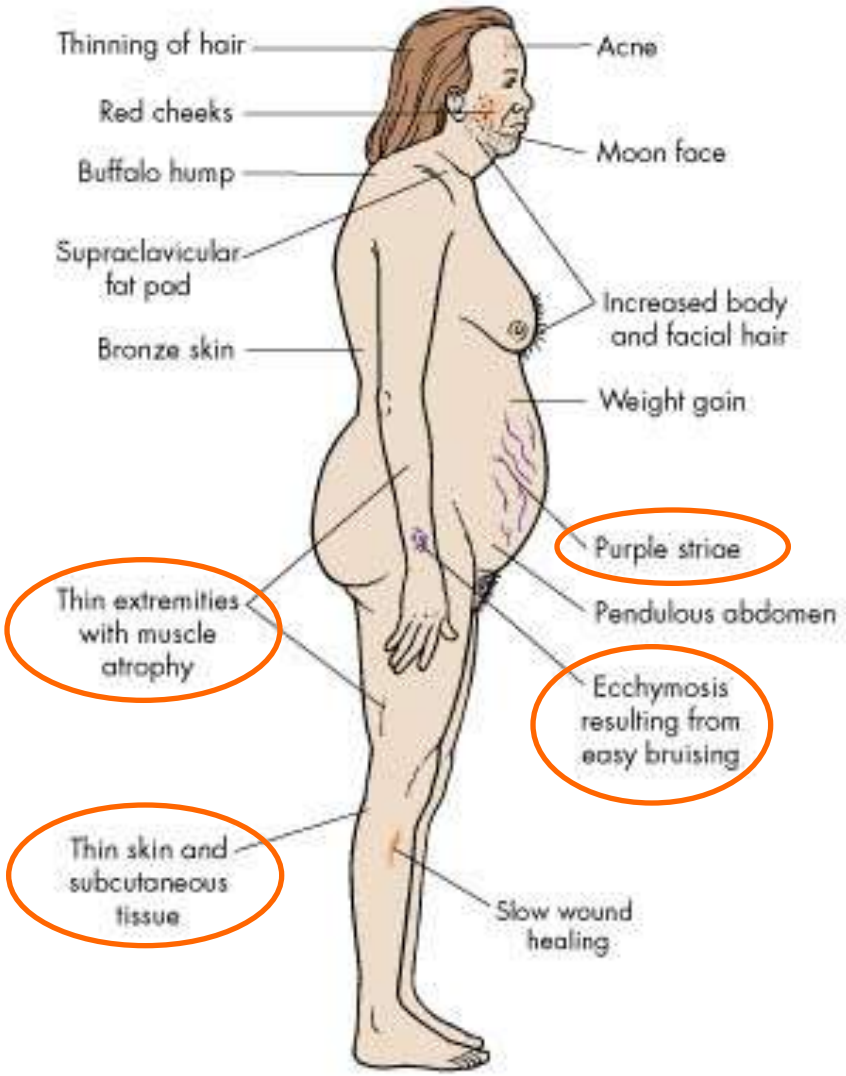
Syndrome de Cushing d'origine ectopique



“Cushing” iatrogène

(traitement par glucocorticoïdes: prednisone, dexamethasone, …)





Dynamique
(voir anciennes photos!)

Troubles psy

Ostéoporose

HTA

DM

Infections

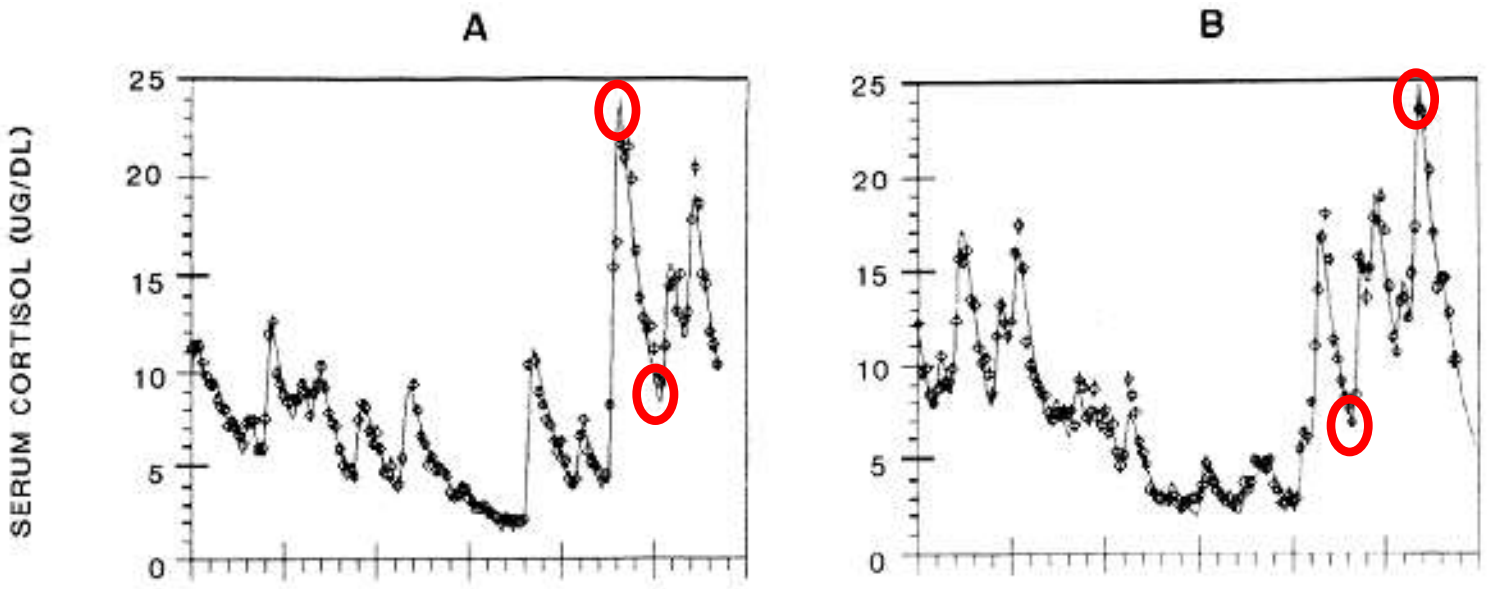
Comment le rechercher?

1. **Estimer probabilité clinique**
2. **Etablir l'hypersécrétion autonome de cortisol**
   - Test de suppression court 1mg Dex (overnight)
     - 23h00 1mg Dexa
     - 8h00 Cortisol plasmatique (<50 nmol/l = freination adéquate)
   - Cortisolurie de 24h (2x) (avec la créat)
   - Cortisol salivaire 23h00
     - Choix du laboratoire (HUG)
3. **ACTH dépendant/indépendant**
4. **Recherche cause:**
   1. IRM hypophysaire / CT thoracoabdominal (ectopique?)
   2. CT surrénales

Caractéristiques de la production physiologique de cortisol

- Quantité normale totale sur la journée
  - Cortisolurie libre 24h: < 300 nmol/l/24h
- Rythme circadien:
  - Pic matinal
  - Nadir la nuit (23h00-minuit):
    - Cortisol plasma < 50 nmol/l
    - Cortisol salivaire < 6 nmol/l
- Suppression par la Dexaméthasone:
  - Test 1 mg dex: cortisol plasma < 50 nmol/l

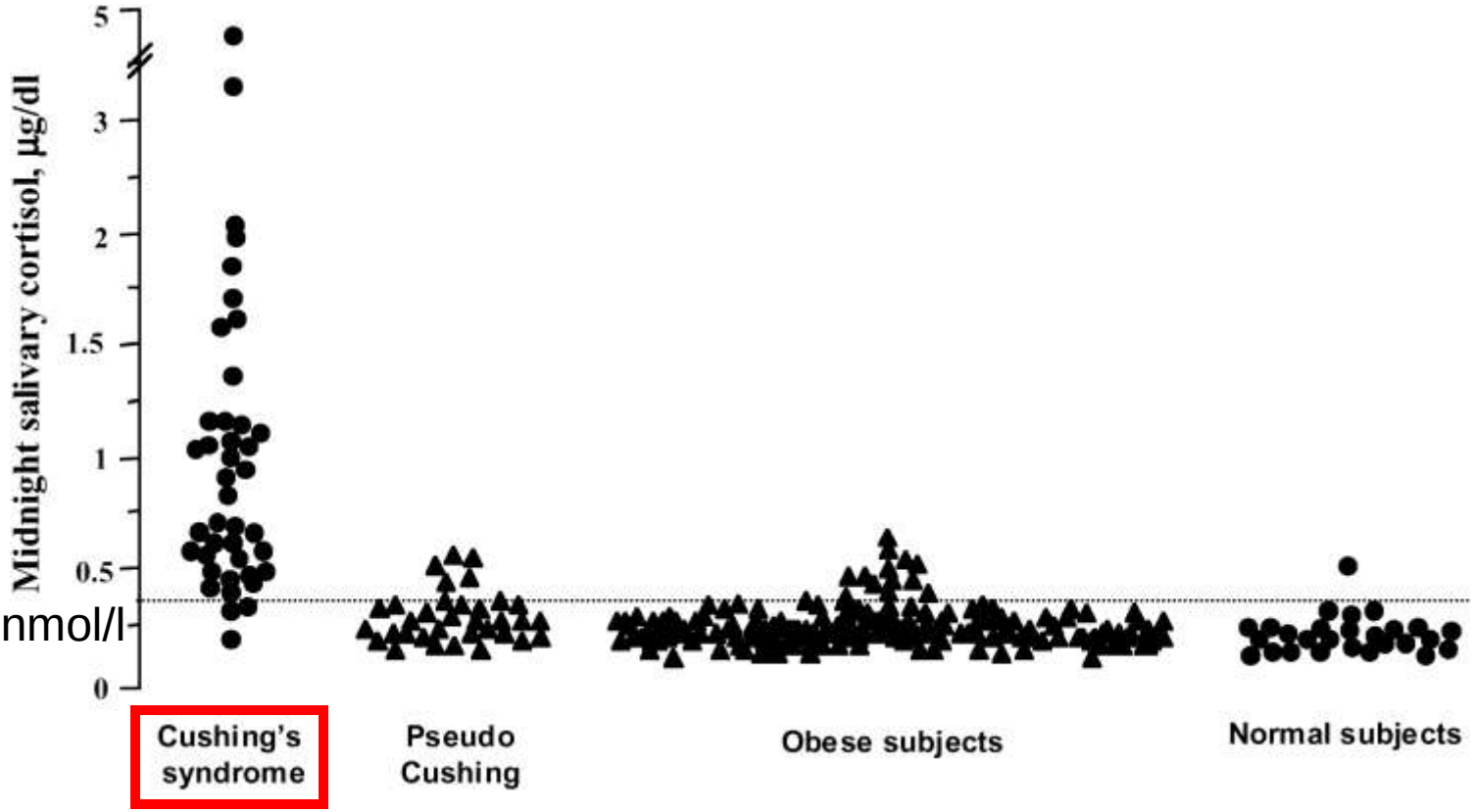
Pulsatilité de la production de cortisol



- Prise de sang « random » pour cortisol: inutile dans le diagnostic du Cushing

- **Tests pour diagnostic de Cushing**:
  - récolte urinaire de 24h (cortisol libre)
  - prélèvements à minuit (sang: cortisol total / **salive**: cortisol libre)
  - test de suppression à la dexaméthasone

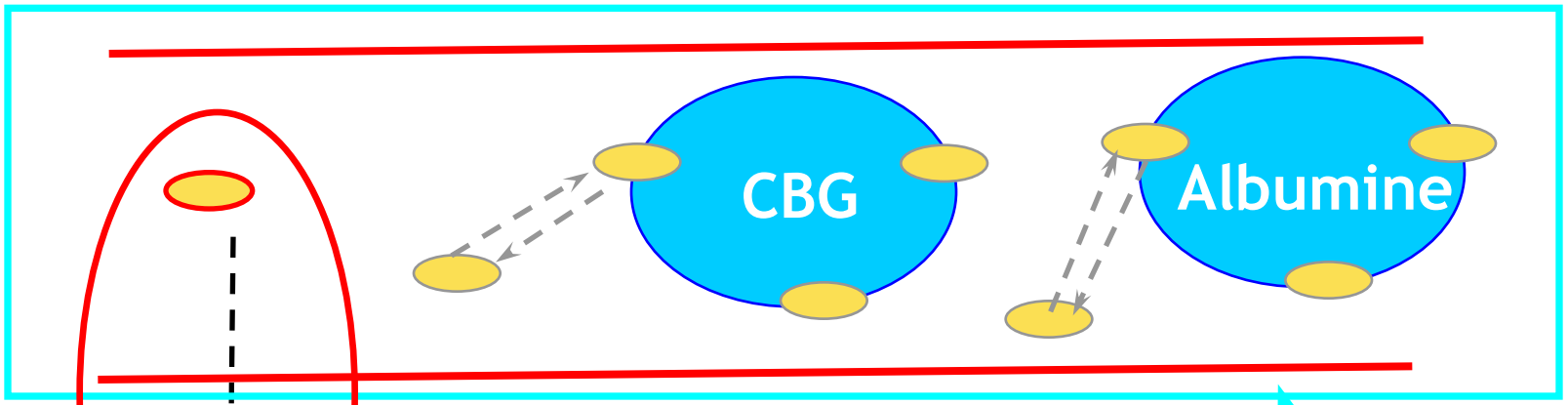
Cortisol salivaire



0.35 = 9.7 nmol/l

Putignano, P. et al. J Clin Endocrinol Metab 2003;88:4153-4157

Cortisol plasmatique = total



CBG = Cortisol
Binding Globulin

Cortisol **libre**

Salive/urines 24h

Actions cellulaires

Cortisol <u>total</u>:
libre + **lié**

Plasmatique

Augmentation CBG

- Contraception orale (E2)
- Grossesse

Insuffisance surrénalienne (Déficit en glucocorticoïdes+/- déficit en minéralocorticoïdes)

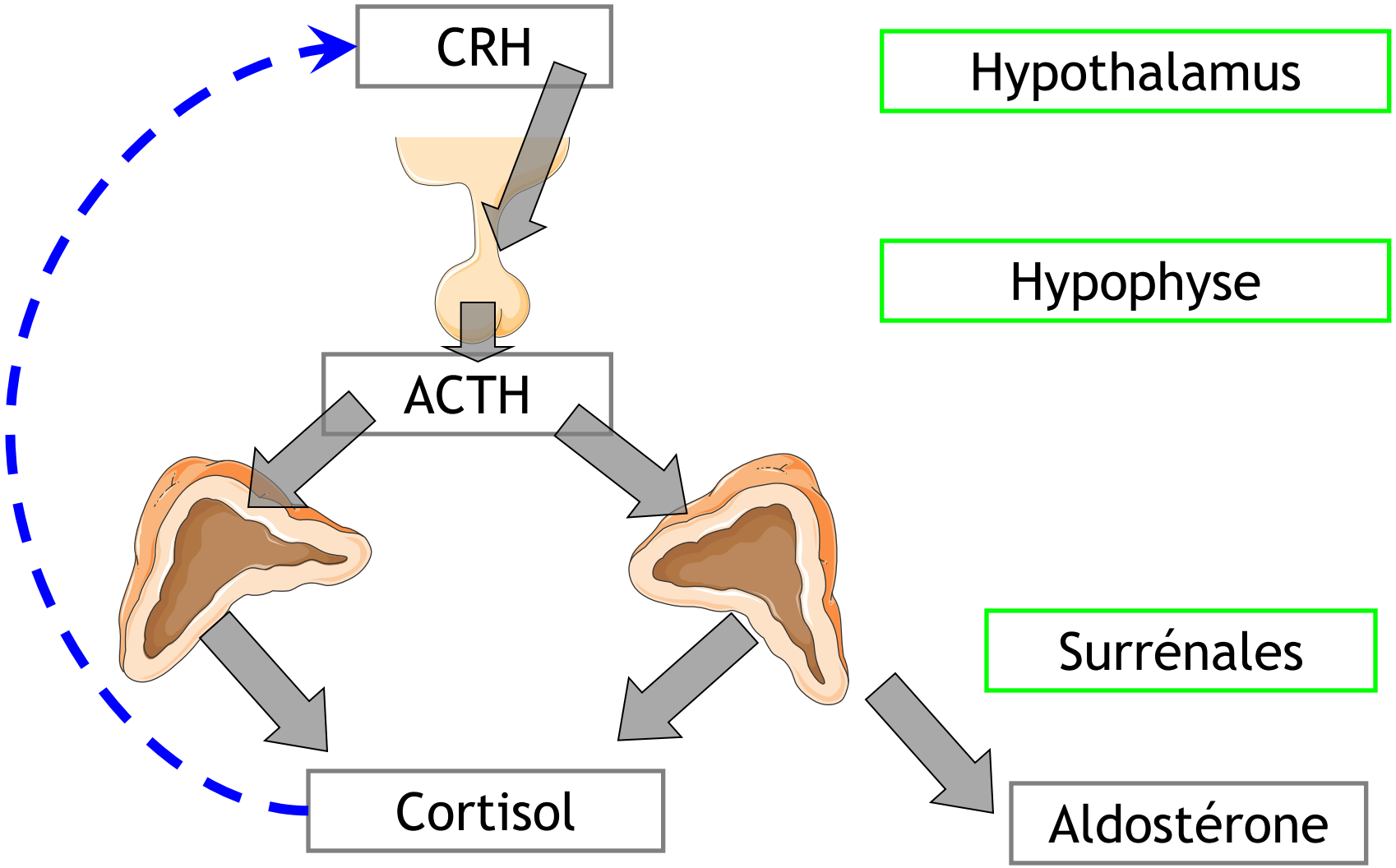
Presentation

Although very non-specific, hypoadrenocorticism is usually presented as the owners complaining of anorexia, vomiting, diarrhea, weight loss, lethargy and weakness. Physical examination by the veterinarian.may show mental depression, dehydration, bradycardia and slow capillary refill time.

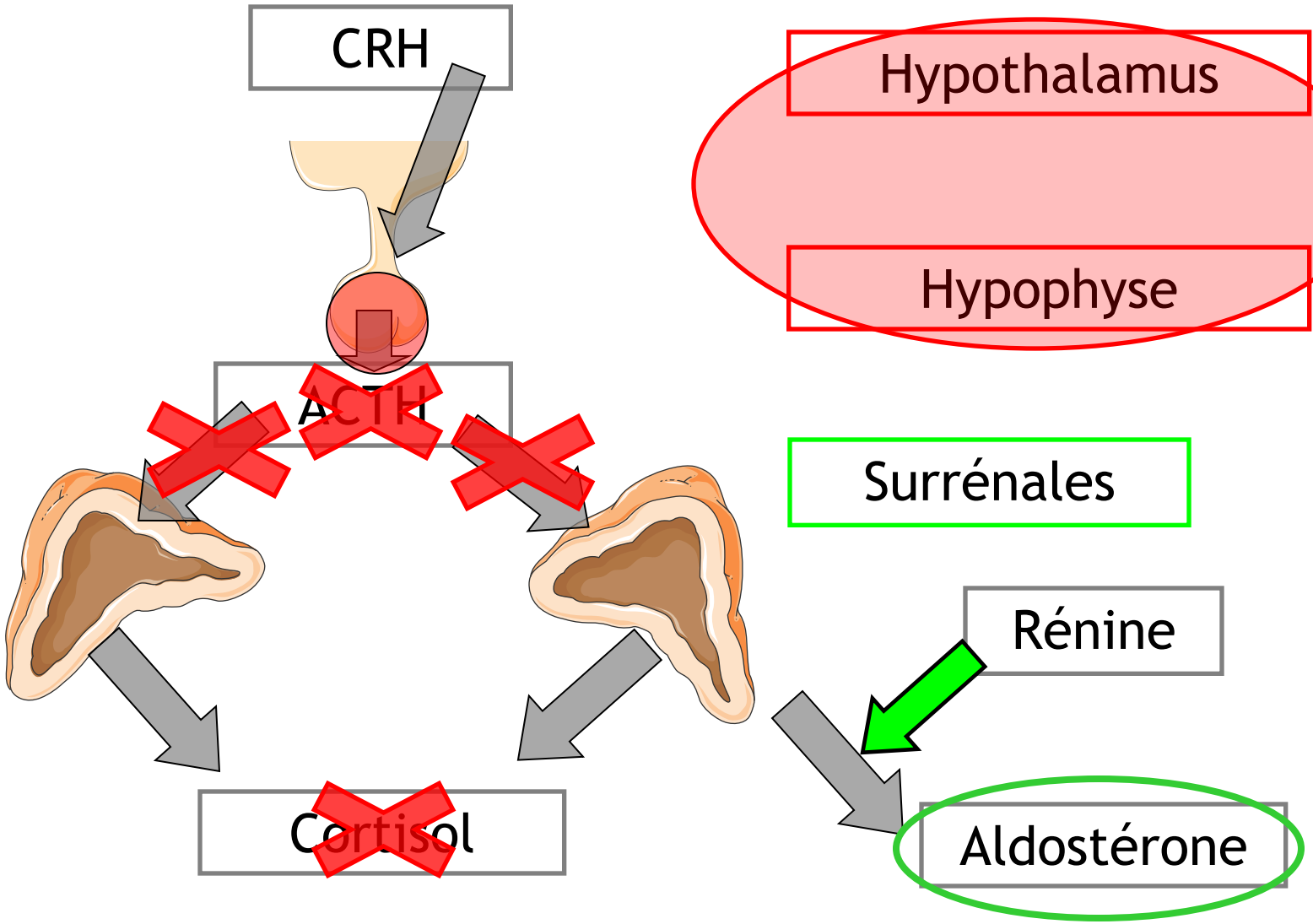
Diagnosis

The current definitive diagnostic tool for the diagnosis of hypoadrenocorticism is a blood profile followed by an ACTH stimulation test. The blood profile may show reduced sodium and chlorine, with increased potassium and calcium.

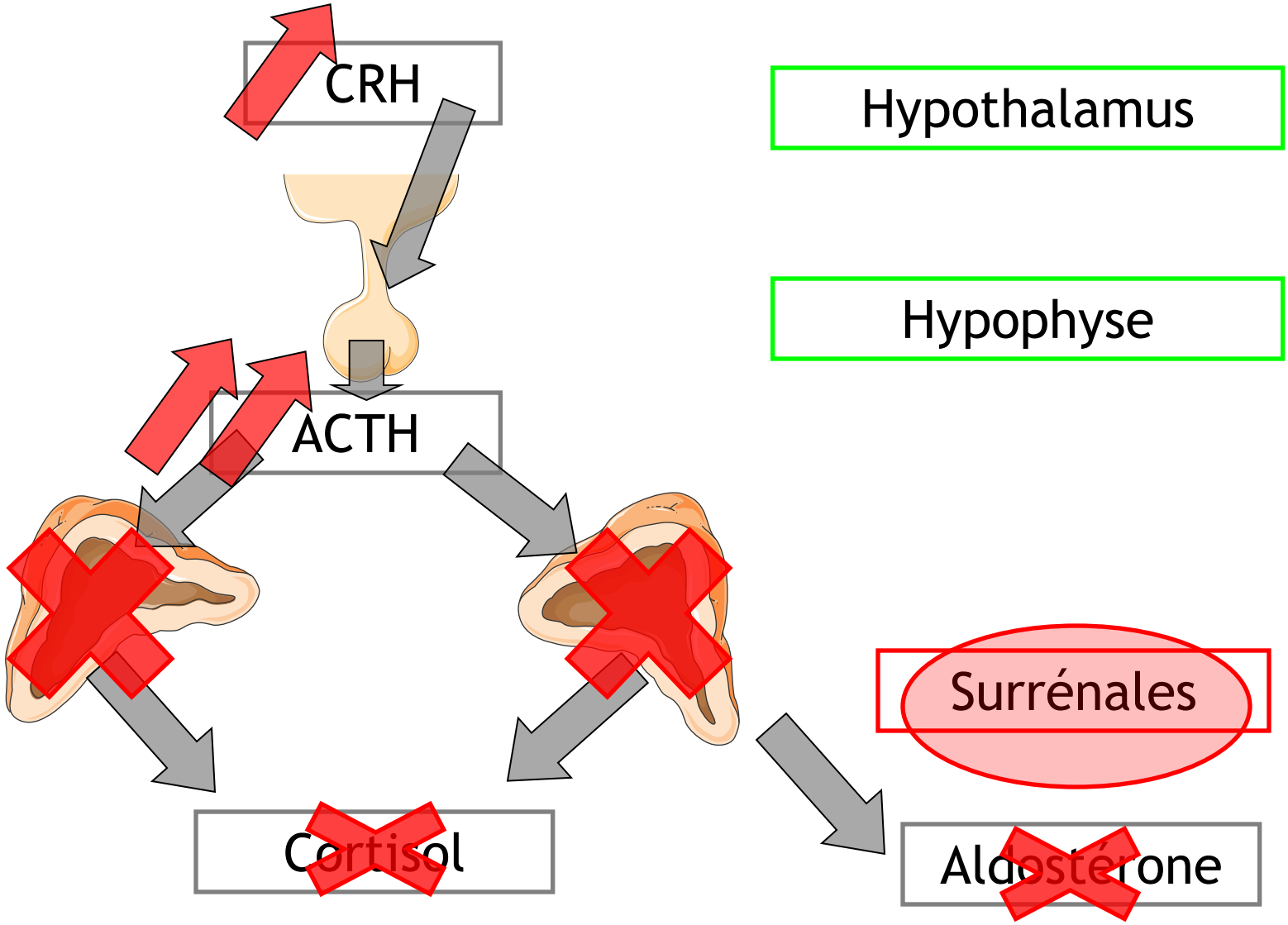
Régulation axe HHS



Insuffisance secondaire (centrale)



Insuffisance primaire (Addison)

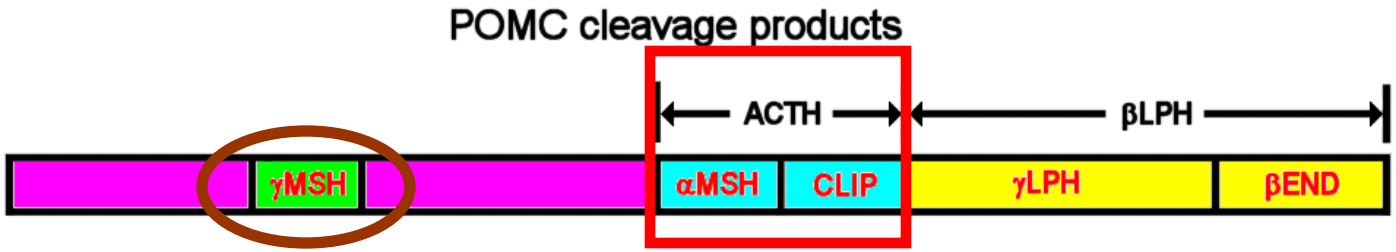


Manifestations de l'insuffisance

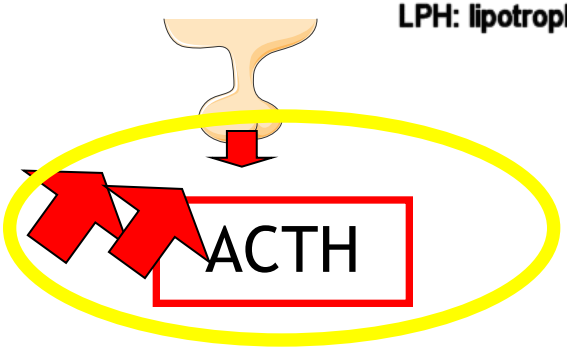
- **Primaire ou secondaire:**
  - **Asthénie, faiblesse, dépression**
  - Anorexie, perte pondérale
  - Nausées, vomissements, douleurs abdominales
  - Hyponatrémie, hypoglycémie
  - anémie, éosinophilie
- **Primaire:**
  - Hyperpigmentation
  - Orthostatisme, hypotension, choc, **« crise addisonnienne »**
  - Hyperkaliémie, acidose métabolique

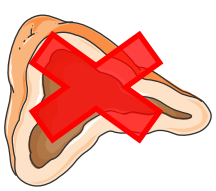
Déficit en minéralo-corticoïdes!

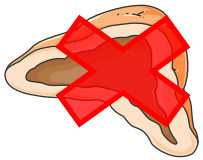
Insuffisance primaire (Addison)



MSH: melanocyte stimulating hormone, CLIP: corticotropin-like intermediate lobe peptide, END: endorphin, LPH: lipotrophin, ACTH: adrenocorticotropic hormone

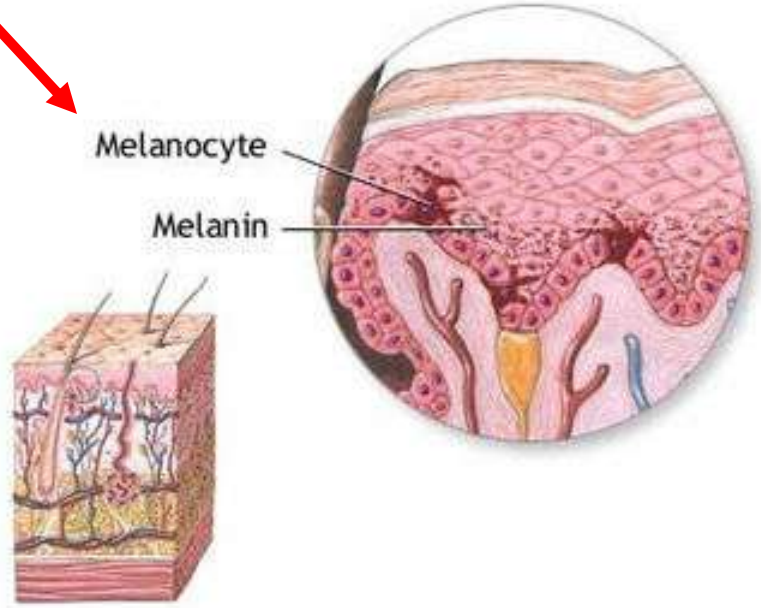






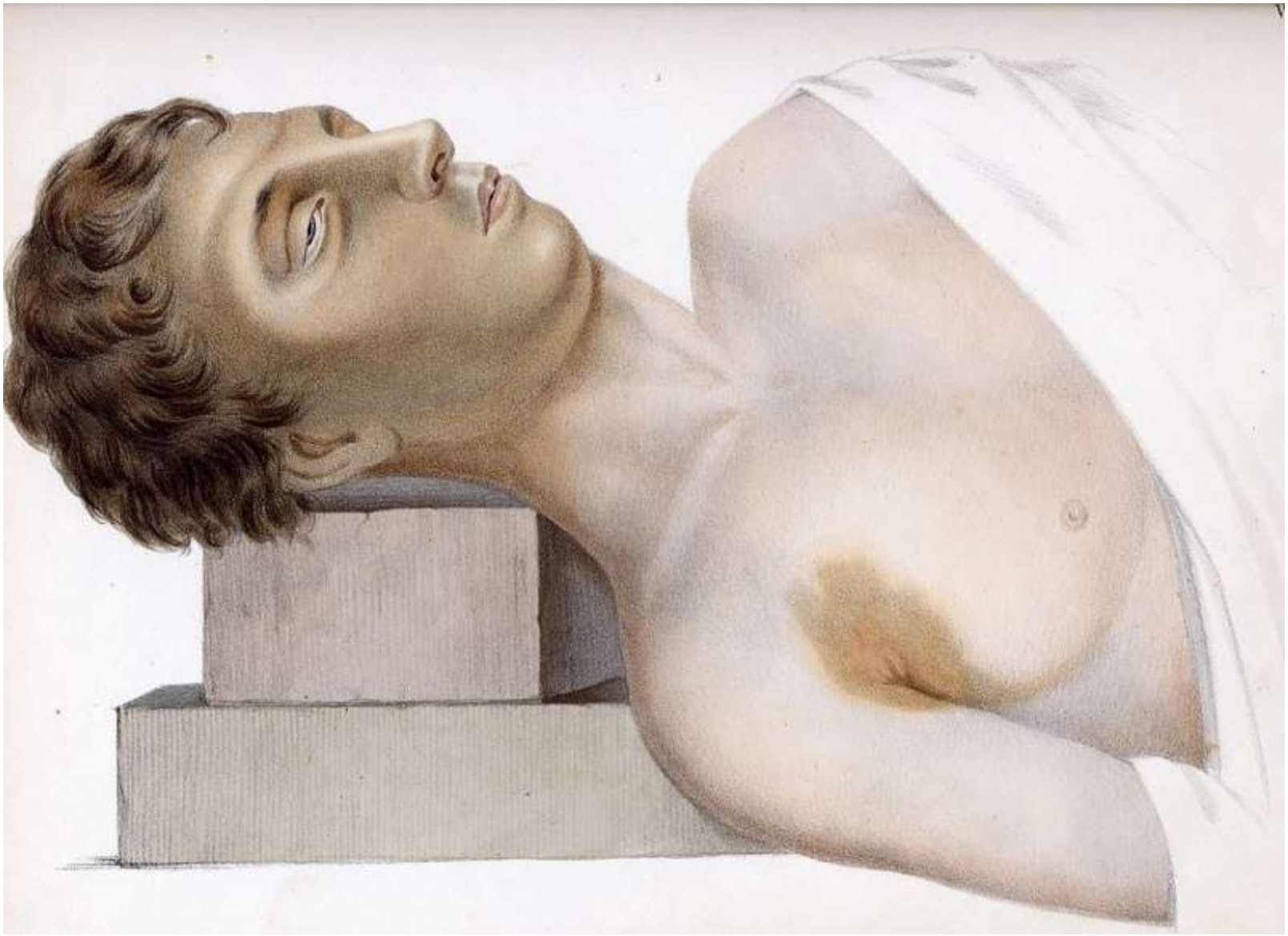
Cortisol

Aldostérone

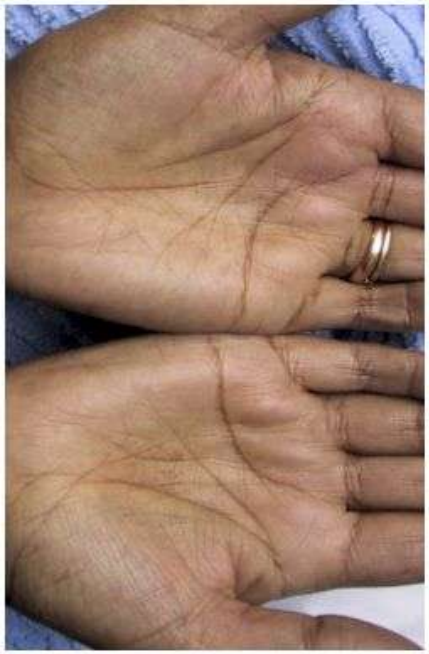


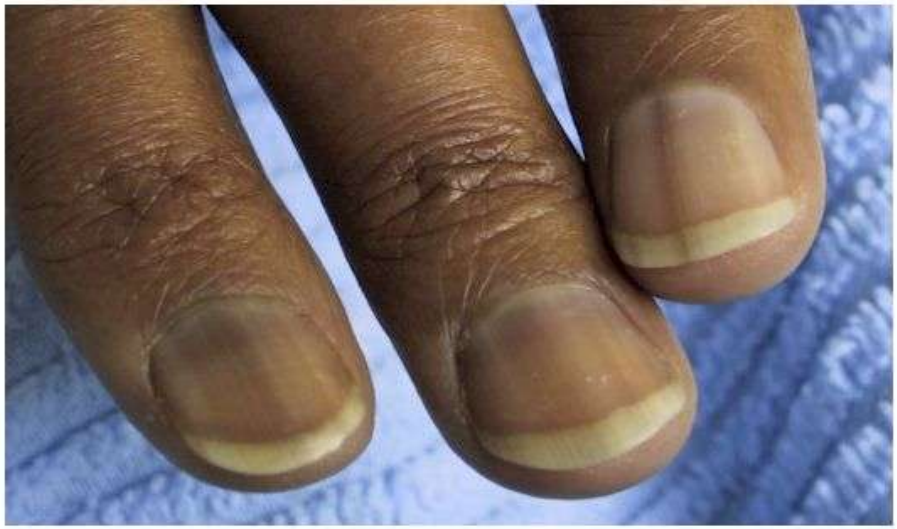
Manifestations de l'insuffisance

- **Si primaire auto-immune et APS2:**
  - Hypothyroïdie (hyperthyroïdie)
  - Biermer
  - Vitiligo, DM1, coeliaquie, …
- **Secondaire (centrale):**
  - Si masse hypophysaire:
    - Panhypopituitarisme
      - Hypogonadisme central
      - Hypothyroïdie centrale, …
    - Hémianopsie bitemporale
    - Pas d'hyperkaliémie, en principe pas d'hypotension

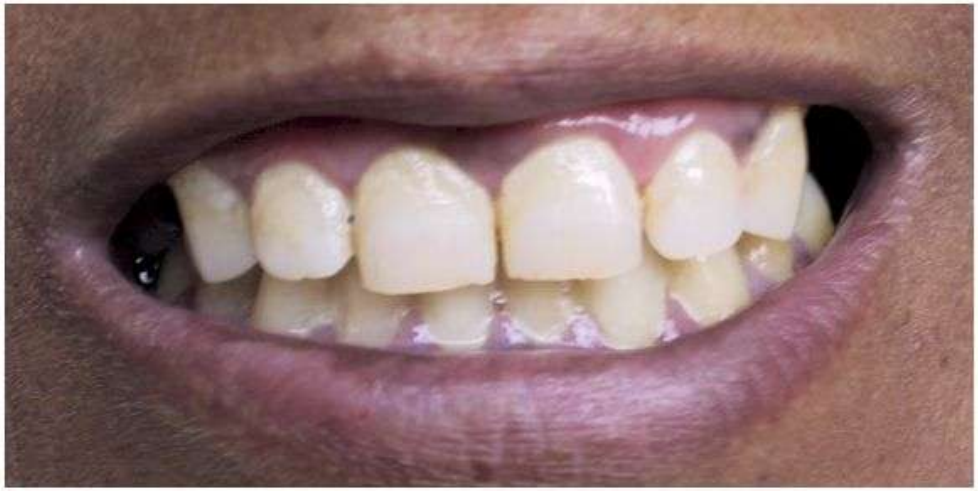


http://www.lib.uiowa.edu/hARDIN/MD/ui/addisons/index.html

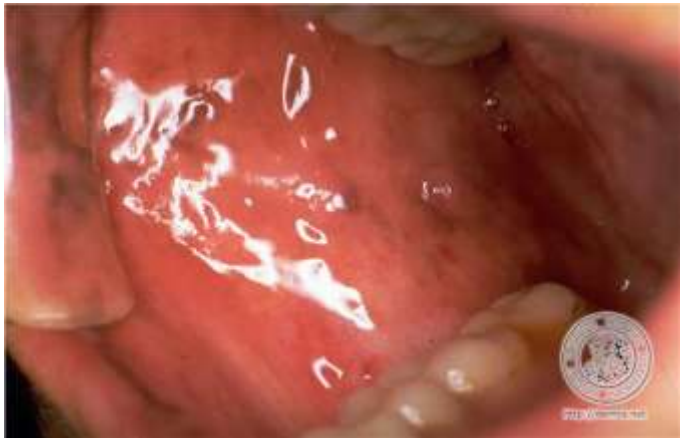




Addison's disease:



- Note the generalised skin pigmentation (in a Caucasion patient) but especially the deposition in the palmer skin creases, nails and gums.



ON THE

CONSTITUTIONAL AND LOCAL EFFECTS

OF

DISEASE

OF THE

SUPRA-RENAL CAPSULES.

BY

THOMAS ADDISON, M.D.,

SENIOR PHYSICIAN TO GUY'S HOSPITAL

LONDON:

SAMUEL HIGHLEY, 32 FLEET STREET.

1855.

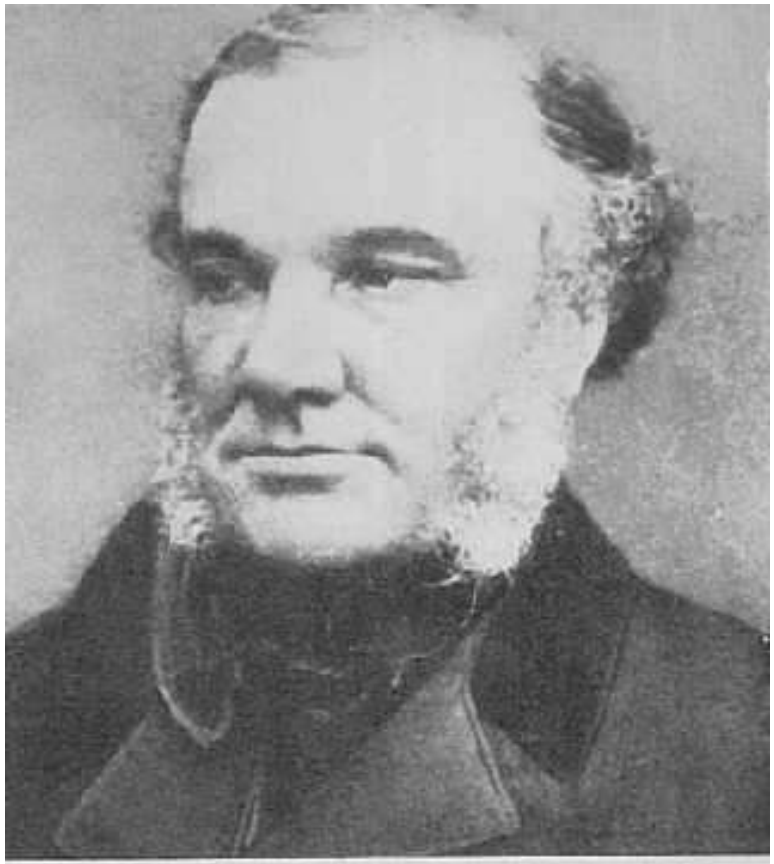
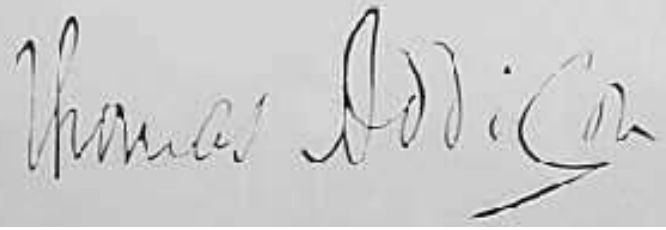
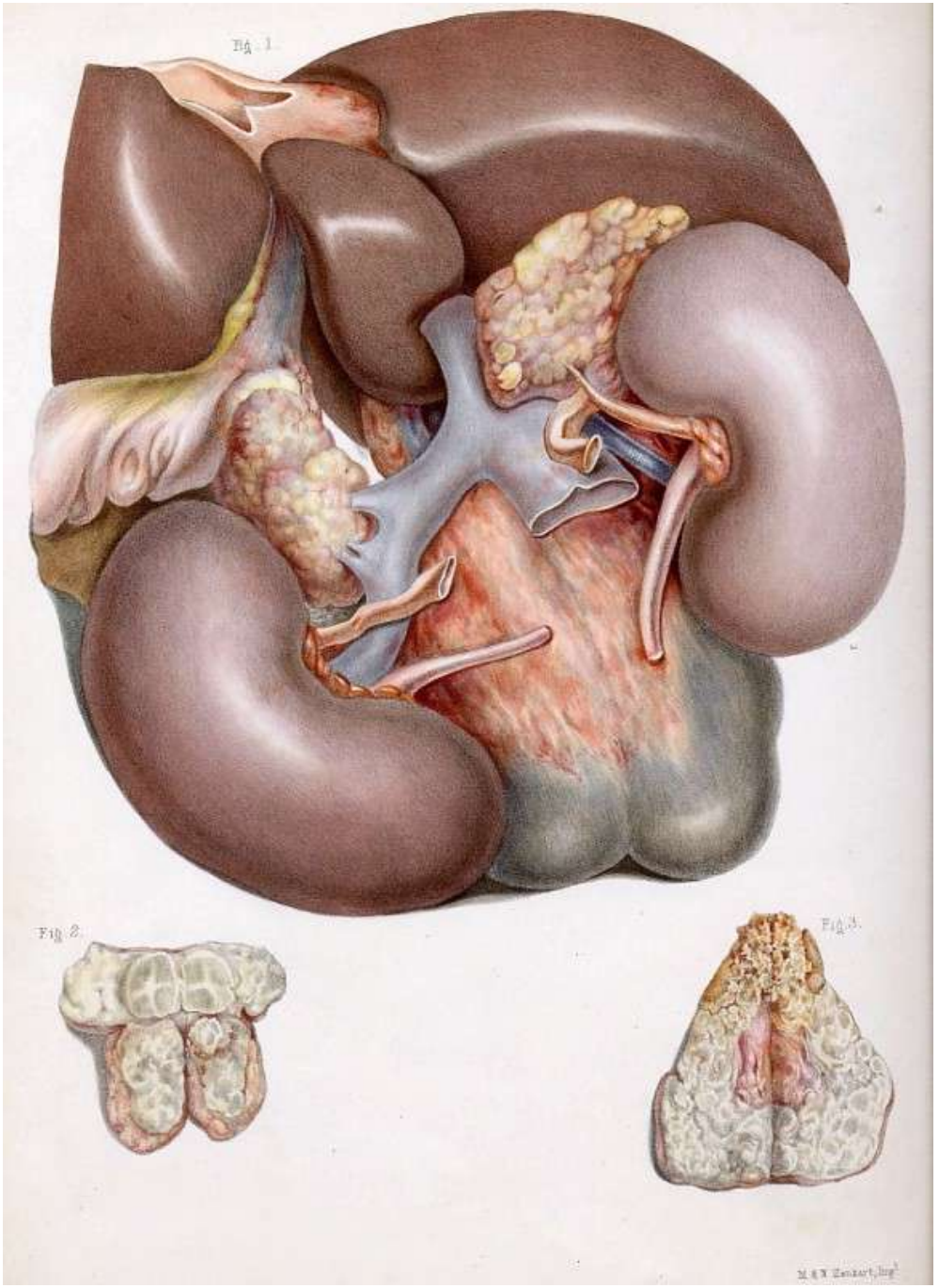


Image in Gordon Museum, Guy`s Hospital





Dr Procopiou

http://www.lib.uiowa.edu/hARDIN/MD/ui/addisons/index.html

http://www.lib.uiowa.edu/hARDIN/MD/ui/addisons/index.html

President John F. Kennedy is now known to have had **adrenal insufficiency**. At the post mortem, his adrenals were found to be greatly reduced in size, the result of disease and suppression following replacement therapy. Yet Kennedy, his doctors and his family consistently presented an image of him as being fully fit, apart from a wartime back injury, both prior to and after his election. His brother, Bobby Kennedy, went as far as to deny he had 'classical Addison's disease' using the word classical as a cover in that he did not have TB-induced disease, then the most prevalent cause. There were rumours that Kennedy was on heavy doses of steroids, particularly on occasions when his face showed a degree of puffiness, but they were never followed through by the press. Most political commentators agree that if it had been known that Kennedy was suffering from Addison's and was on steroids he would not have beaten Vice-President Richard Nixon in the very close Presidential election of 1960. **Ironically, the American Medical Association's Archives of Surgery in an article published in 1955 entitled 'Management of Adreno-cortical Insufficiency During Surgery' explained how a 37-year-old man had been operated on for serious back pain, and was the first Addisonian to survive such traumatic surgery. Only one small newspaper chain published the story in 1961 that this man was President Kennedy.**

Causes insuffisance primaire

- **90% Autoimmune:**
  - 40 % Isolée
  - 60 % Syndrome auto-immun poly glandulaire
    - (APS 1 = APECED)
      - Hypoparathyroïdie
      - Candidose mucocutanée (dès l'enfance)
    - APS 2
      - Hypothyroïdie / hyperthyroïdie
      - DM1
      - Vitiligo
      - Biermer (=gastrite atrophique autoimmune+déficit B12)
      - Maladie cœliaque, …

Arlt, Lancet 2003

Causes insuffisance primaire (rares)

- Métastases
  - Ca pulm (sein)
  - lymphome
- Infiltratives bénignes
  - Src
  - Amyloïdose,
  - hémochromatose
- Infectieuses
  - Tbc
  - Mycoses profondes
- Hémorragie bilatérale surrénalienne
- Iatrogènes
- Congénitales (CAH, X-linked adrenoleucodystrophy, …)

Arlt, Lancet 2003

Causes insuffisance centrale

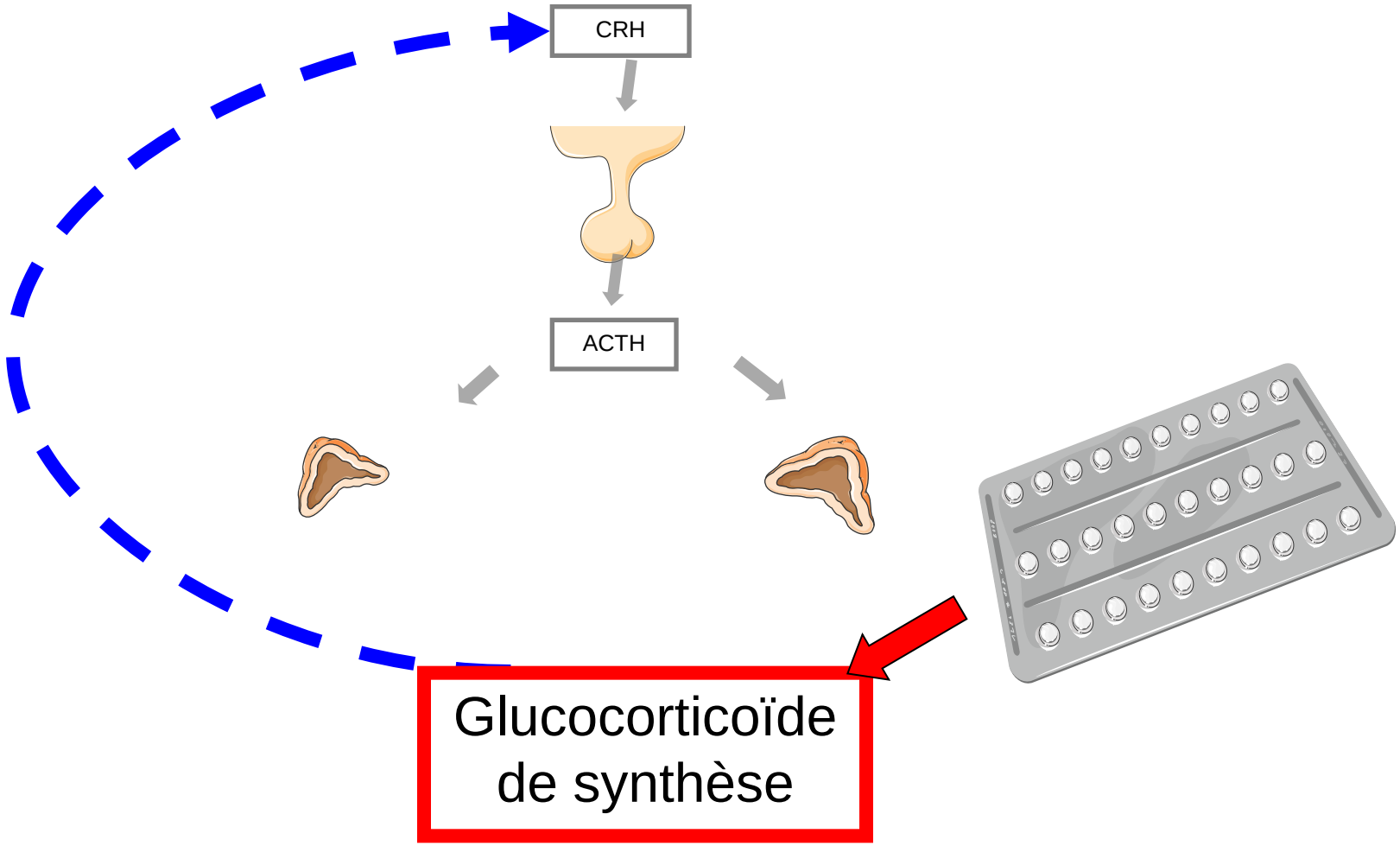
- **Inhibition axe corticotrope après corticothérapie (> 4 semaines)**
- **Tumeur hypophysaire (adénome)**
  - Macroadénome ➔ panhypopituitarisme
  - Iatrogène (chir hypophyse, irradiation)

- <u>Autres causes</u>:
  - Autres tumeurs (craniopharyngiome)
  - Hypophysite autoimmune
  - Apoplexie hypophysaire
  - Infiltratives (src, histiocytose X, tbc, …)
  - Traumatisme cranien sévère ? (TBI)
  - Déficit isolé en ACTH / CRH (sans anomalie à l'IRM)

Arlt, Lancet 2003

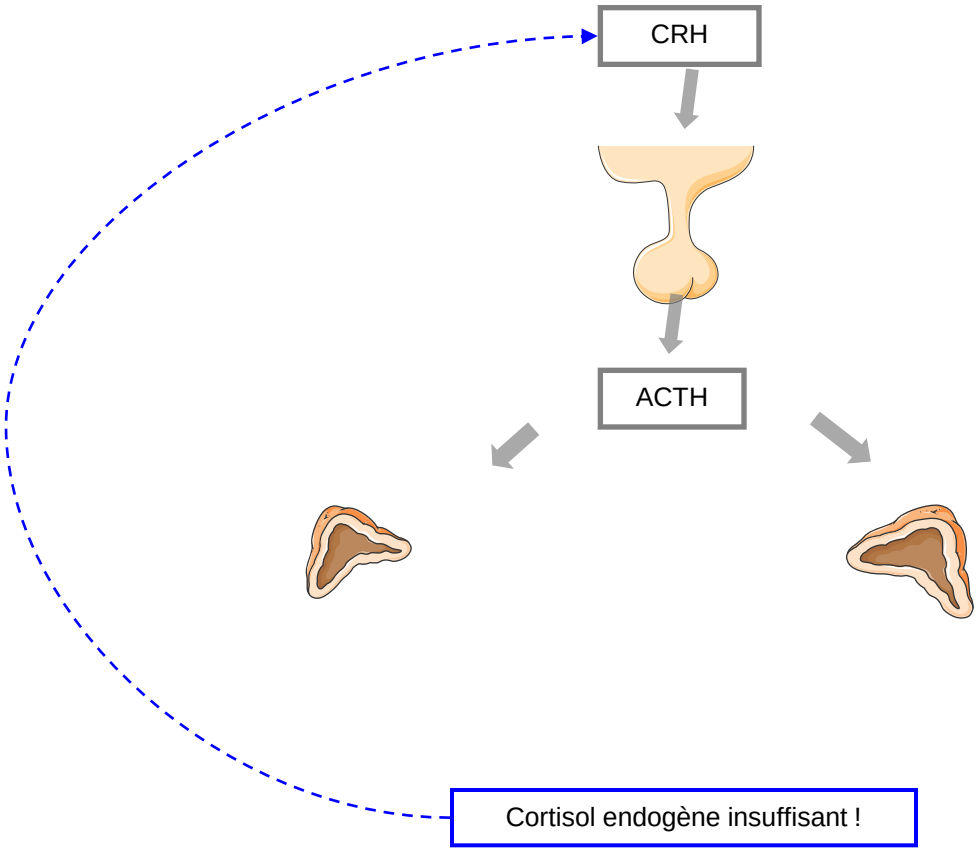
Insuffisance centrale iatrogène

(suppression de l'axe HHS post corticothérapie)
(traitement prolongé par glucocorticoïdes: prednisone, dexamethasone, ...)



Insuffisance centrale iatrogène

(suppression de l'axe HHS post corticothérapie)
(traitement prolongé par glucocorticoïdes: prednisone, dexamethasone, ...)



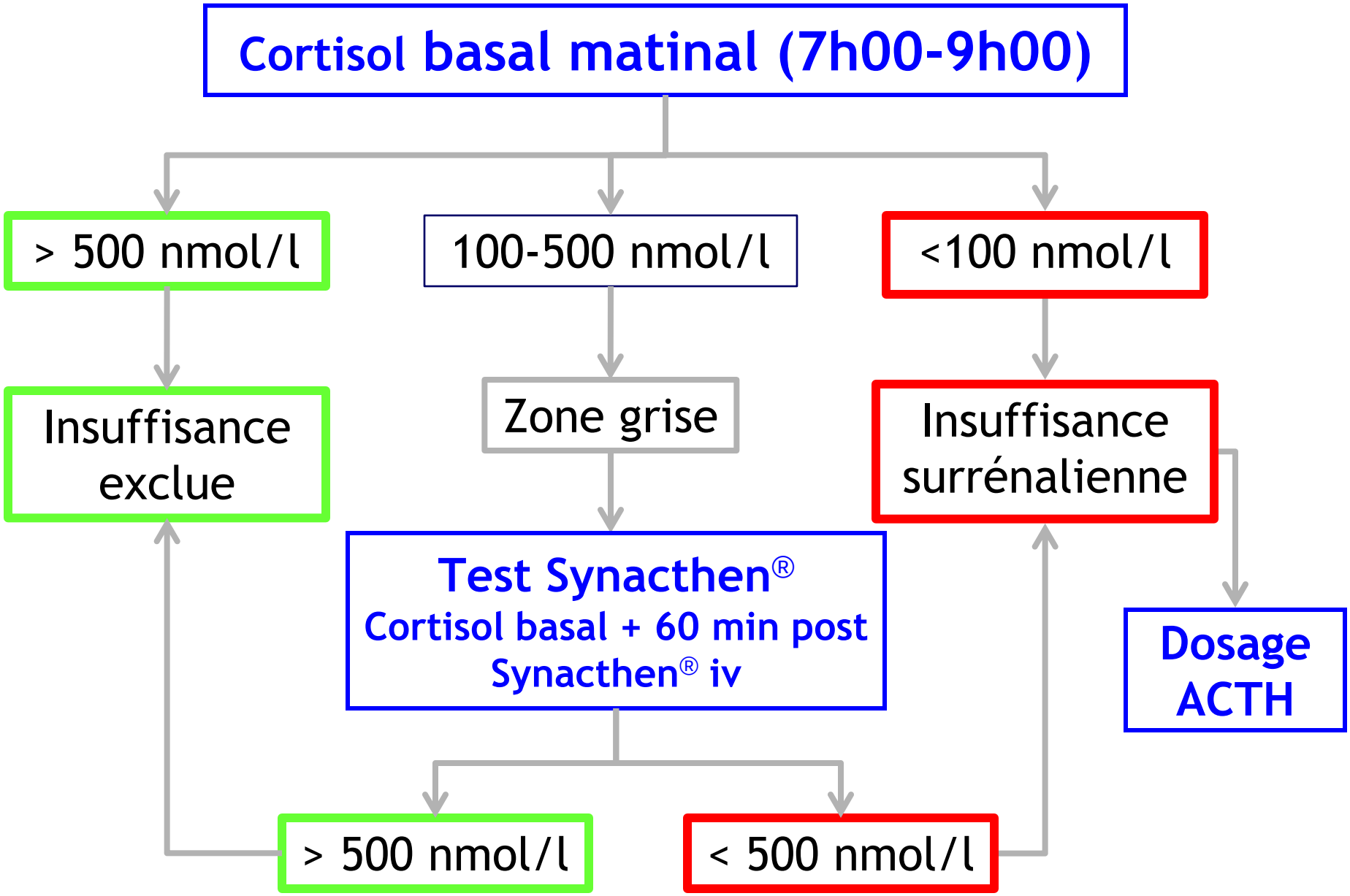
Diagnostic

1. S'agit-il d'une insuffisance surrénalienne?

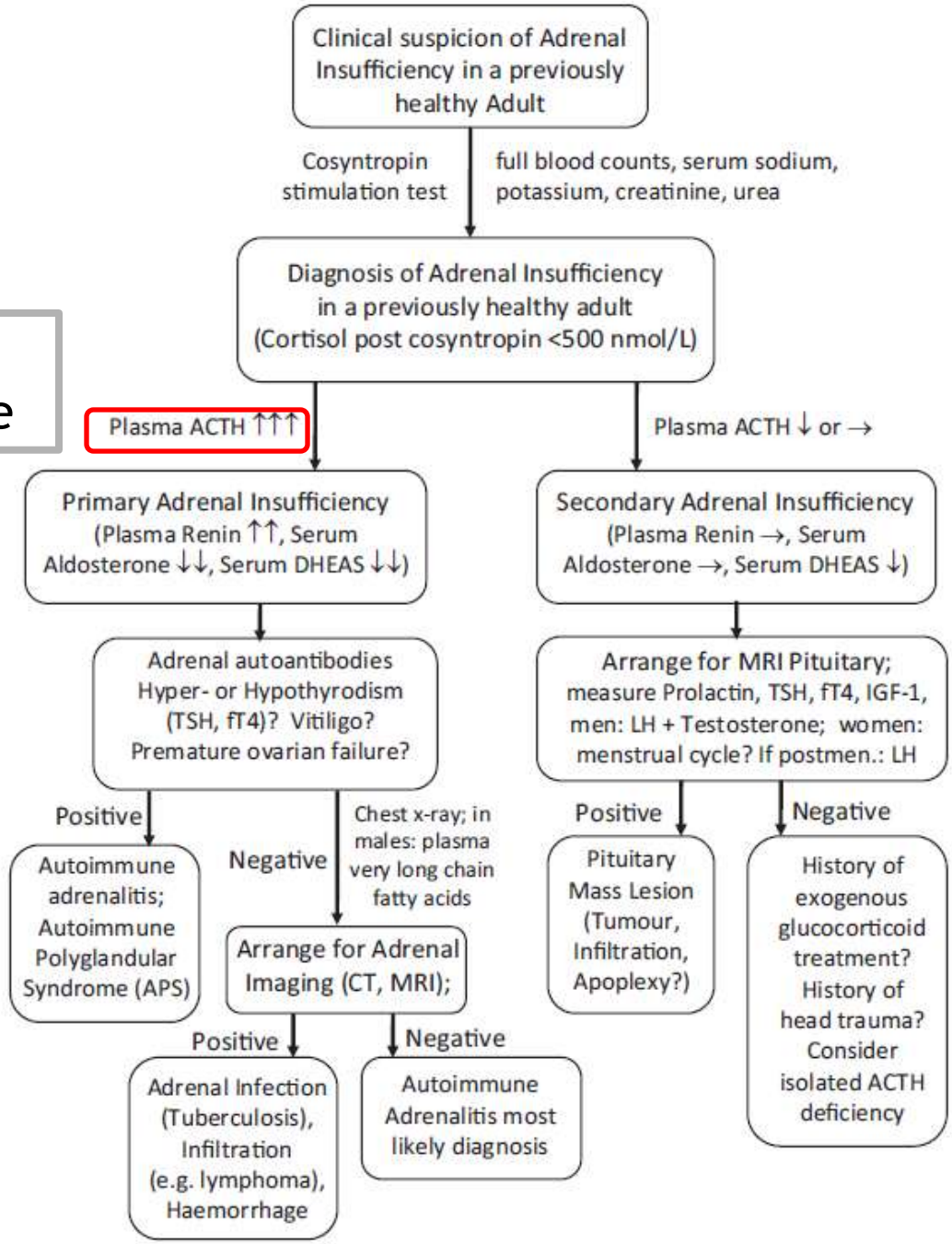
- **Urgence**:
  - **cortisol basal**, Na, K, créat, glycémie, TSH
  - **Solucortef 100 mg iv/im, volume**
- **Hors urgence**:
  - Na, K, créat, glycémie, FSC, TSH (T4l)
  - **Cortisol basal matinal** (7h00-9h00)
  - +/- **Test Synacthen®**

2. Primaire ou secondaire/ étiologie

- **ACTH**
- Anamnèse: ttt par stéroïdes récent??


Cortisol basal matinal (7h00-9h00)
> 500 nmol/l
100-500 nmol/l
<100 nmol/l
Insuffisance exclue
Zone grise
Insuffisance surrénalienne
Test Synacthen®
Cortisol basal + 60 min post Synacthen® iv
Dosage ACTH
> 500 nmol/l
< 500 nmol/l

Avis endocrinologue



Dr Procopiou

Arlt, JCEM 2009

Caveats

- Augmentation de la CBG ➔ augmentation du cortisol plasmatique total (libre inchangé!):
  - Pillule !!
  - Grossesse
- **Insuffisance médicamenteuse !!**
  - Iatrogène:
    - Glucocorticoïdes p os
    - Injection im formes dépôt (Kenacort®, Diprophos®)
  - Automédication: blanchiment de la peau !
- Insuffisance centrale < 4 semaines (réponse encore possible des surrénales à l'ACTH injecté!)

Traitement

- Dose substitutive glucocorticoïdes **15-25 mg/j d'hydocortisone** (Hydrocortisone Galepharm cp 10 mg secables) en 2 à 3 doses: 10-5-0 mg/j
  15-5-5 mg/j

20 mg HC = 5 mg Prednisone = 0.5 mg de dexamethasone = dose substitutive

- Minéralocorticoïdes: fludrocortisone cp 100 µg (Florinef®) 50-250 µg 1x/j
  - Note: 20 mg HC = « MCU » = 20 µg fludro
- Androgènes: DHEA ?? (25-50 mg 1x/j)

www.addisons.org.uk

www.medicalert.org.uk

Enseignement +++

ttt VITAL à VIE

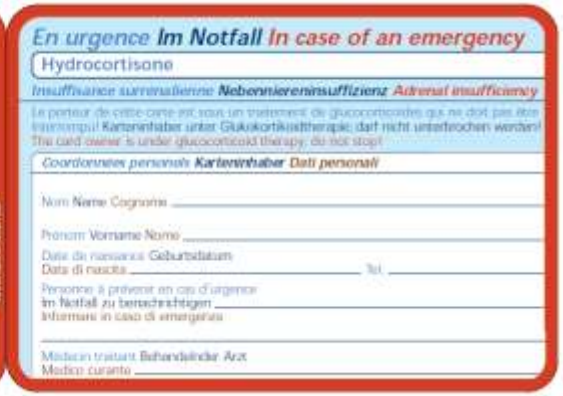
- Maladie intercurrente
- EF > 38°

➔Doubler dose + consulter

- Vomissements / diarrhées

➔Injection Solucortef im + consulter

- Carte (bracelet)
- Suivi 1 à 2x/an



Cas clinique (n°1)

- Labo sang:
  - Na=**113** mmol/l, K=4.7 mmol/l
- Spot urinaire:
  - Na=117 mmol/l, K=76 mmol/l, osm 808 mosmol/kg

➔ SIADH : cause ??

- Cortisol basal= **21 nmol/l** (aucune stimulation 60 min post Synacthen)
  = **insuffisance surrénalienne**
- ACTH ↗↗↗ = 651 ng/l (10-60) = **primaire**
- Auto AC antisurrénaliens: +++ = **autoimmune**

Cas clinique (n°2): panhypopituitarisme

- TSH = 0.3 mU/l (0.3-4.0) avec T4l = **8.1** pmol/l (13-22)
- LH et FSH: 0.5 U/l (1.5-10) avec testo <**0.1** nmol/l
- PRL = 20 μg/l (4-18)
- IGF1 = basse
- Cortisol = **2 nmol/l**
- Diabète insipide

- Atteinte ++ au champ visuel formel

Cas clinique (n°3)

- Cortisol = **27 nmol/l !!**
- Hydrocortisone : 30-10-10 mg/j
- Aucune amélioration ???

- **Injection de Diprophos im 10 jours auparavant!**
- = 7 mg de bétaméthasone (= 60 mg prednisone) sous forme **dépôt** (après **10 jours, seul 50%** de la dose éliminée!)
- Suppression vraie ? Couvert par béta?
- Hydrocortisone 10-5-0 mg/j
- 1 mois plus tard: cortisol basal = **543 nmol/l**

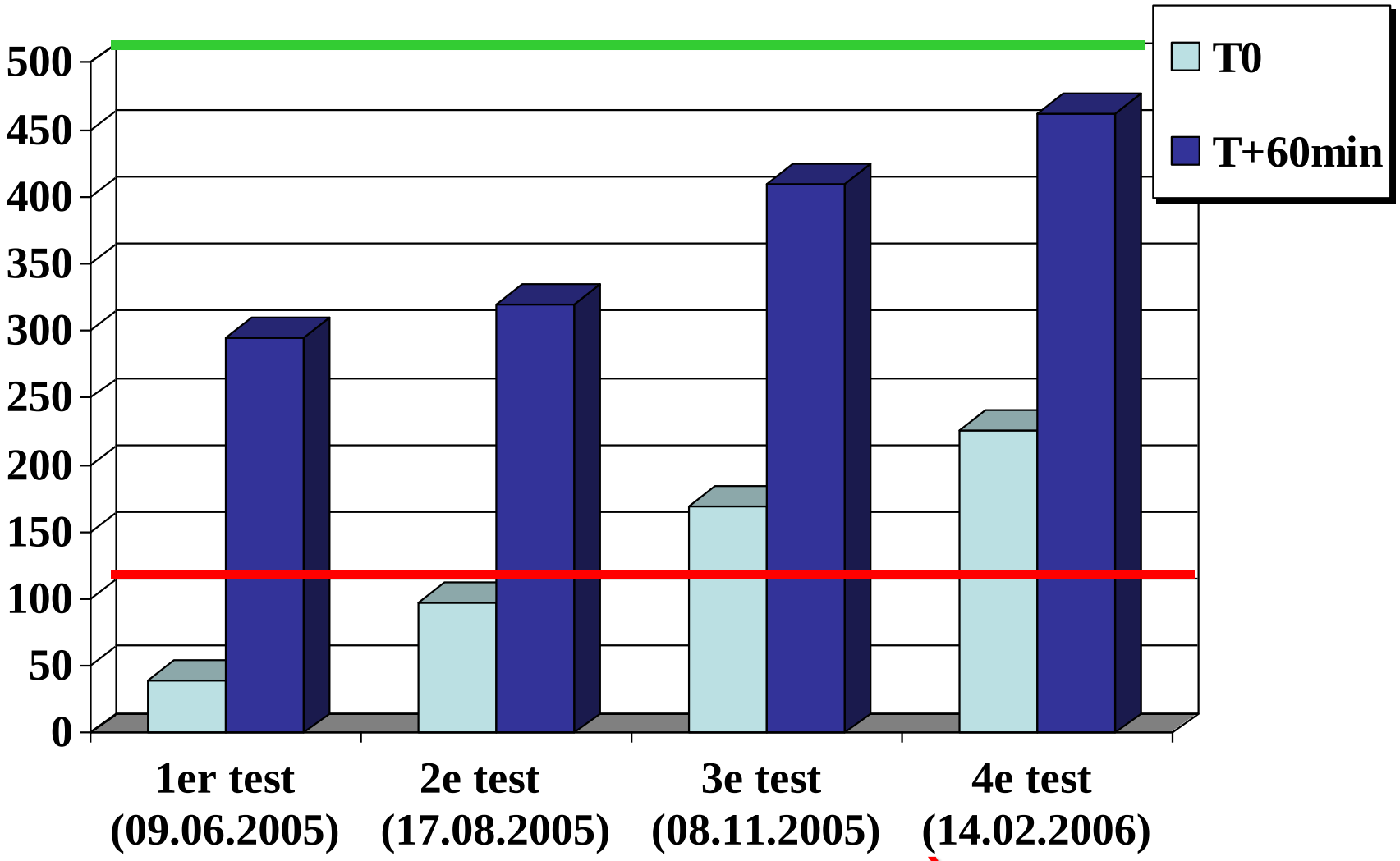
Cas clinique n°4

- Transplantation hépatique
- 2 ans sous Prednisone (>10 mg/j)

- Sevrage sur 6 semaines

- Douleurs articulaires +++
- Consultation rhumato: cortisol basal **28 nmol/l**

Mme A. Tests au Synacthen
Suppression axe post corticothérapie prolongée



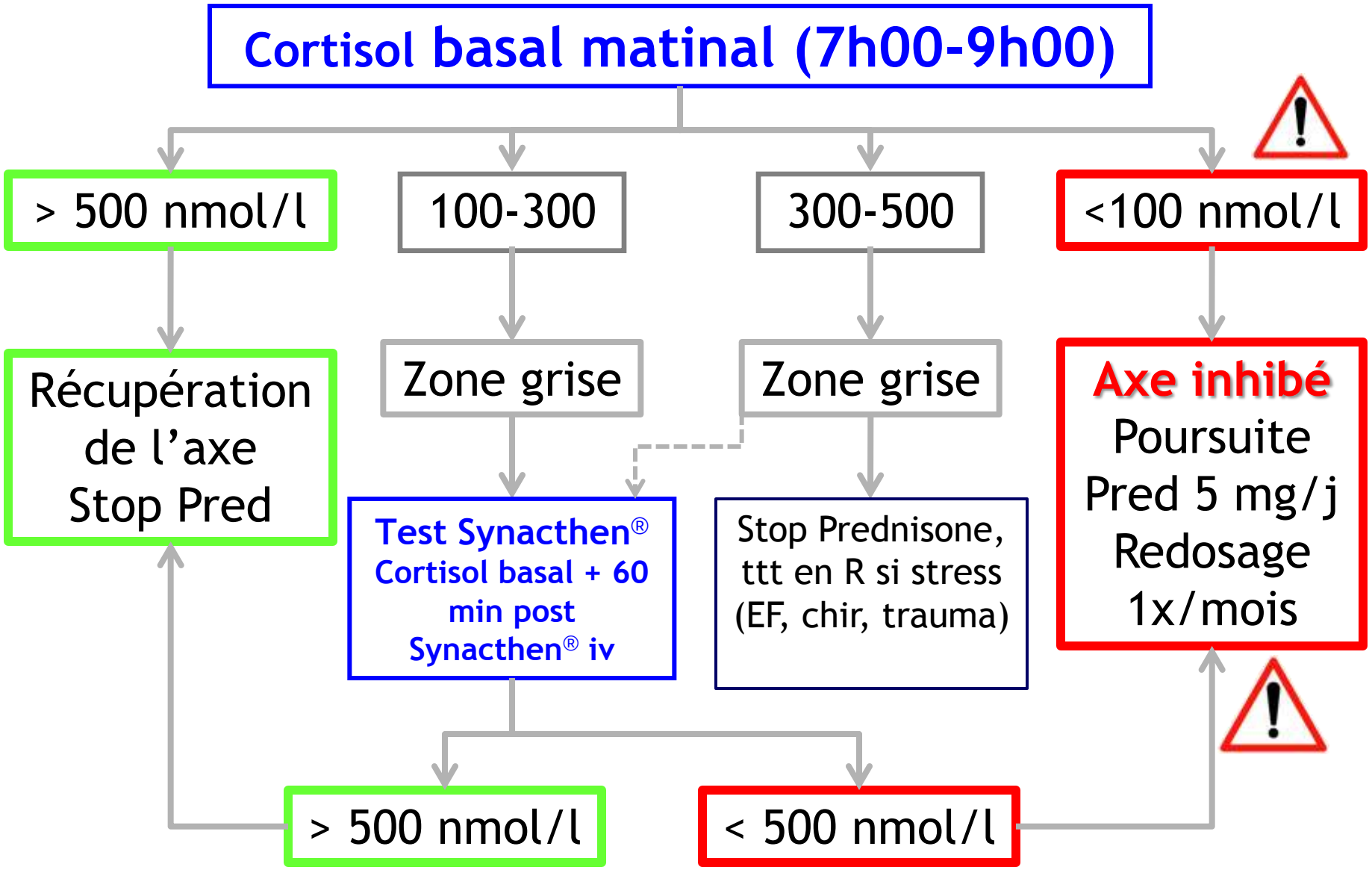
À 8 mois !

Comment sevrer les stéroïdes: 2 aspects

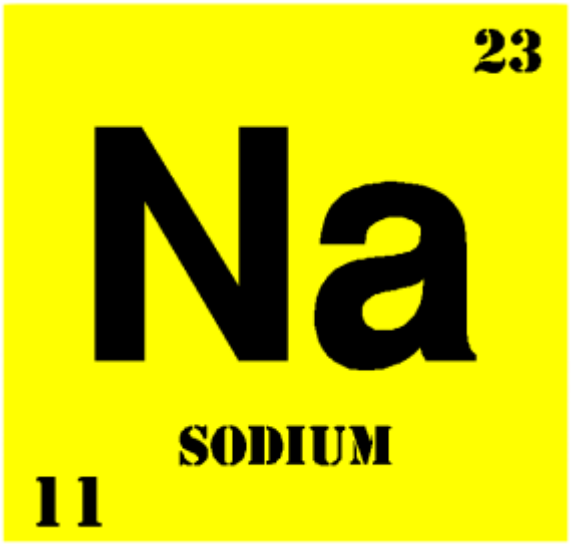
1. Fonction de la **maladie de base**

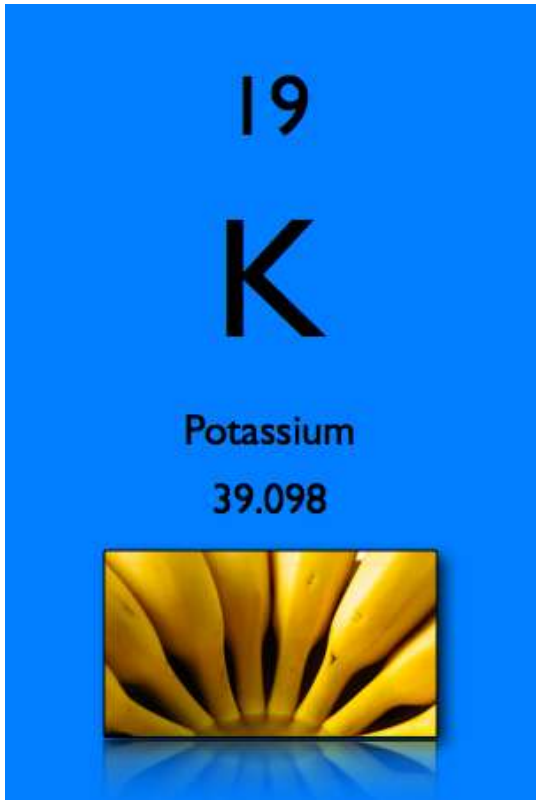
2. Sur le plan **endocrinien**
    - En se basant sur la clinique
    - En se basant sur les dosages

Sevrage basé sur les dosages



Électrolytes





Anomalies plasmatiques
Na+ ou K+

Analyse urine (« spot »): Na+, K+, osm

23

Na

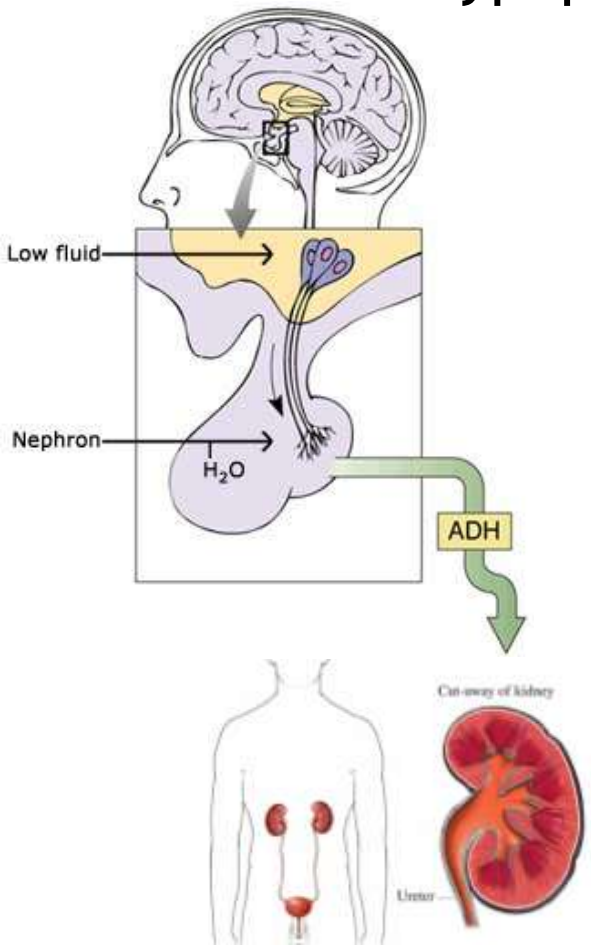
SODIUM

11

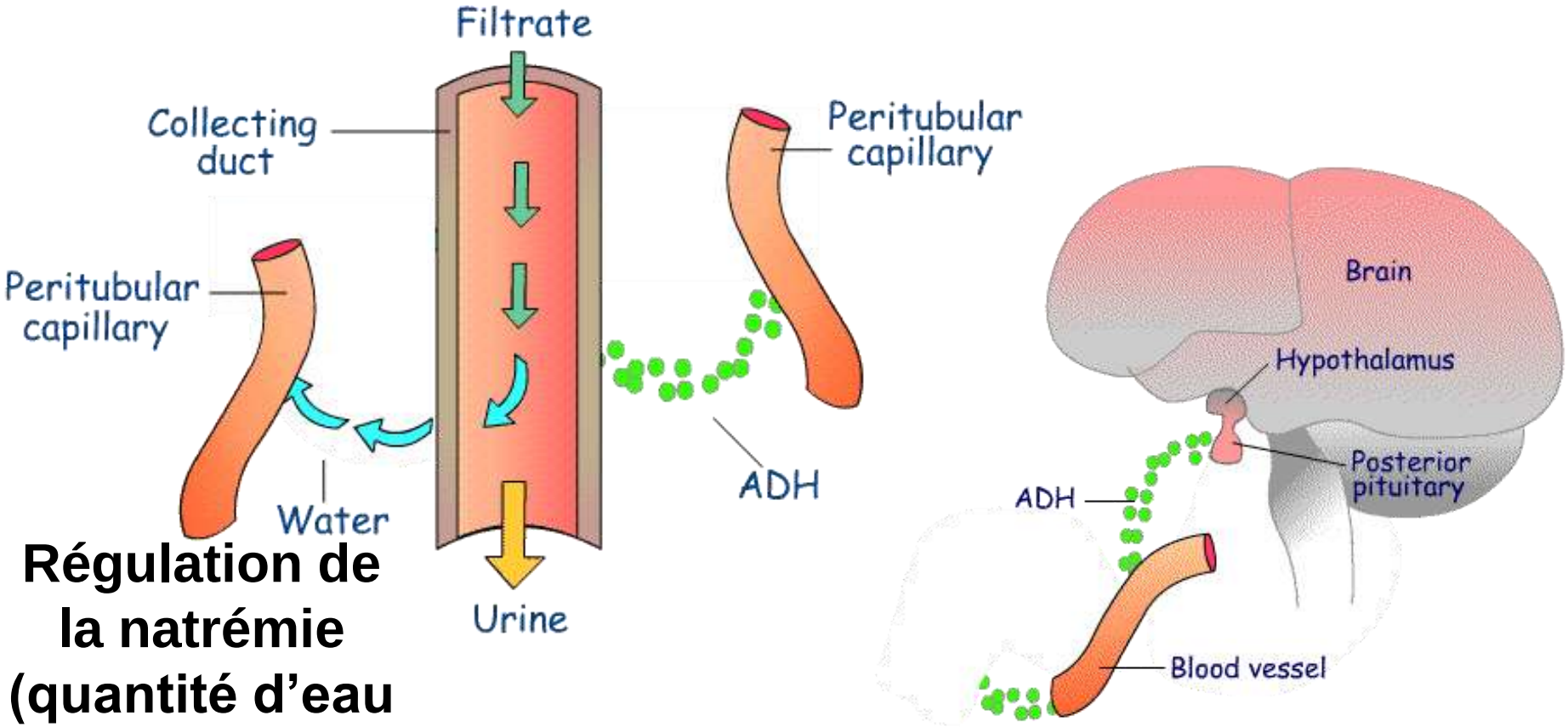
Sodium (natrium)

ADH (Hormone Anti Diurétique): régulateur de l'osmo plasmatique (et donc de la natrémie!)

Hypophyse postérieure

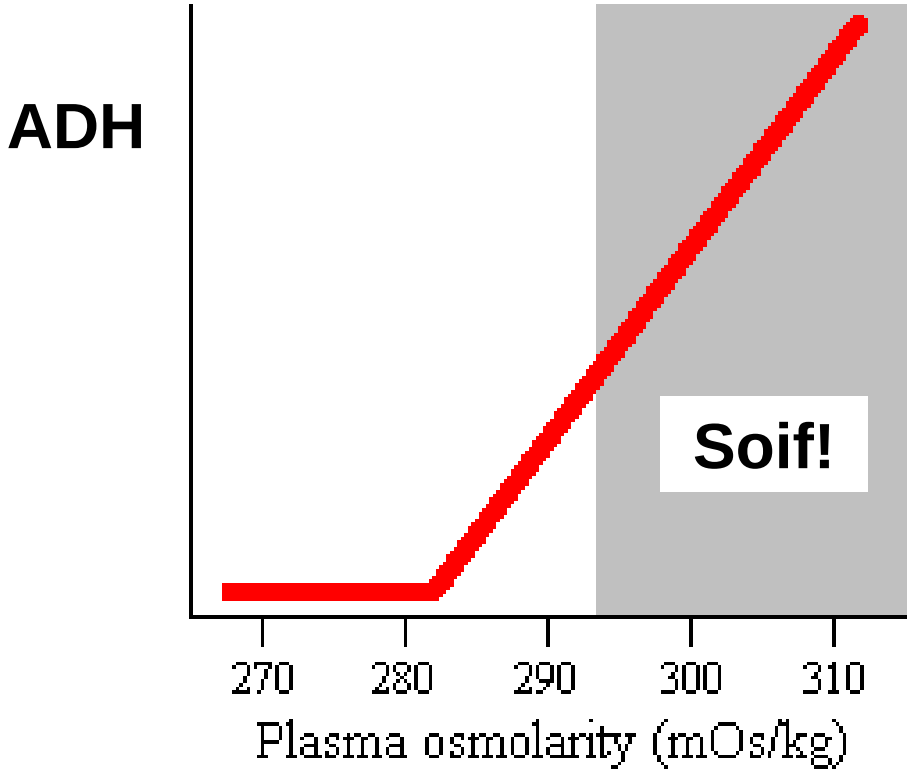


ADH (Hormone Anti Diurétique): régulateur de l'osmo plasmatique (et donc de la natrémie!)



Régulation de la natrémie (quantité d'eau à bord)

ADH (Hormone Anti Diurétique): régulateur de l'osmo plasmatique (et donc de la natrémie!)



Hypernatrémie (=déshydratation)

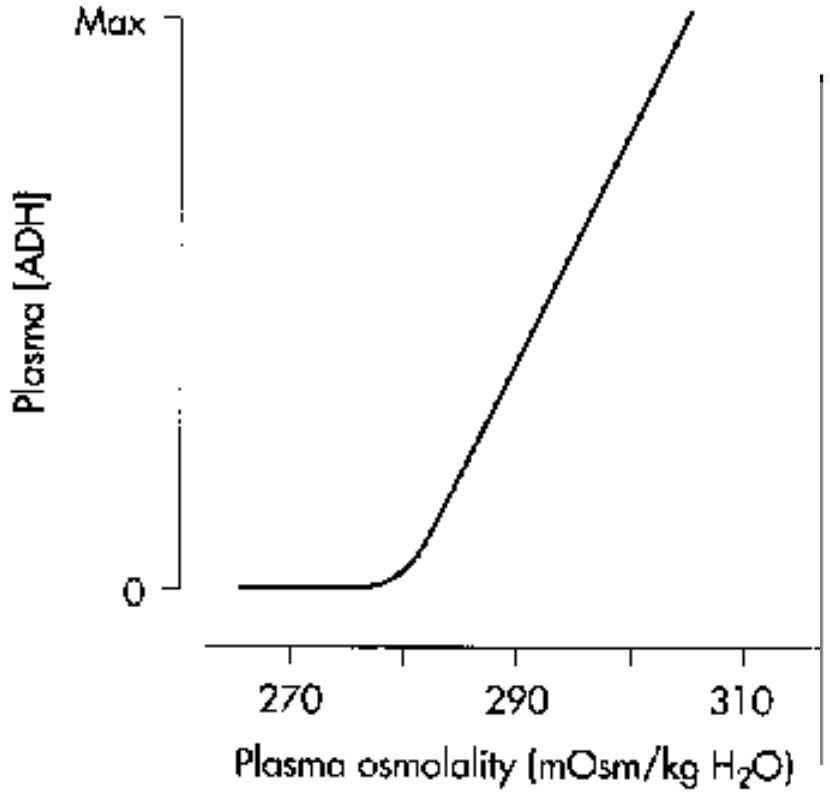
- Déshydratation
  - Désert: mort de soif…
    - ↗↗ ADH → ↗↗ osm urinaire (urines concentrées) **> 800 mOsm**

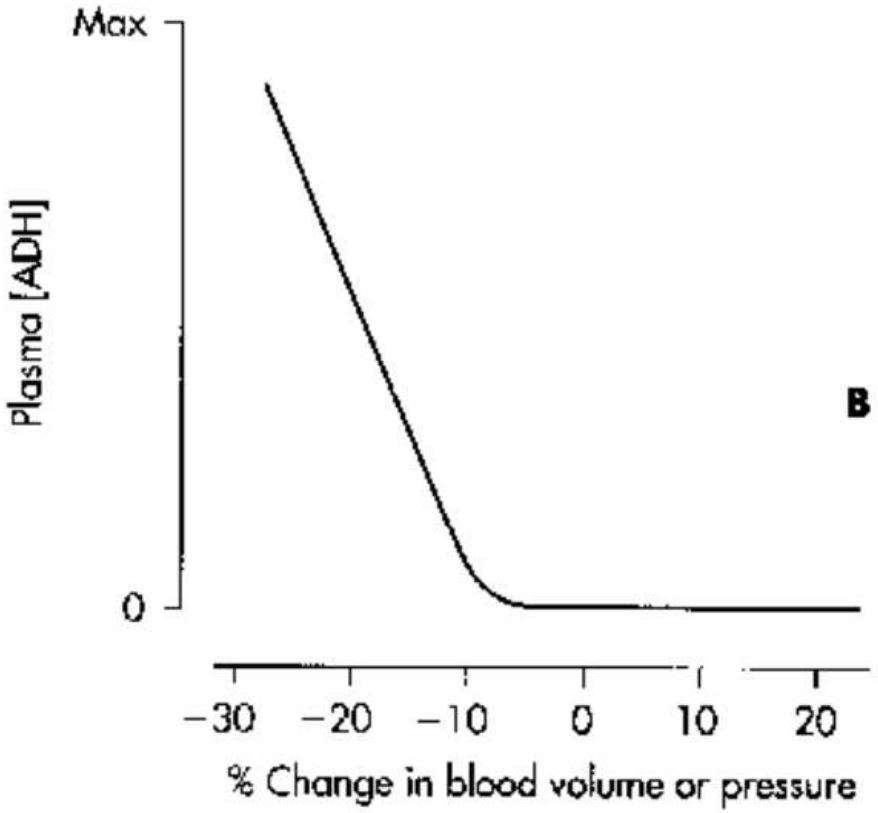
- Diabète insipide (polyurie!): hypernatrémie
  - Central (manque d'ADH)
    - **Ø ADH** → osm urinaire basse (urine diluée!) → **<300mOsm**
  - Néphrogène (résistance à l'ADH)
    - ↗↗ ADH → **mais pas de réponse du rein!** → osm urinaire basse (urine diluée!) → **< 300 Osm**
  - Diabète insipide partiel: 300-800 mOsm

Hyponatrémie

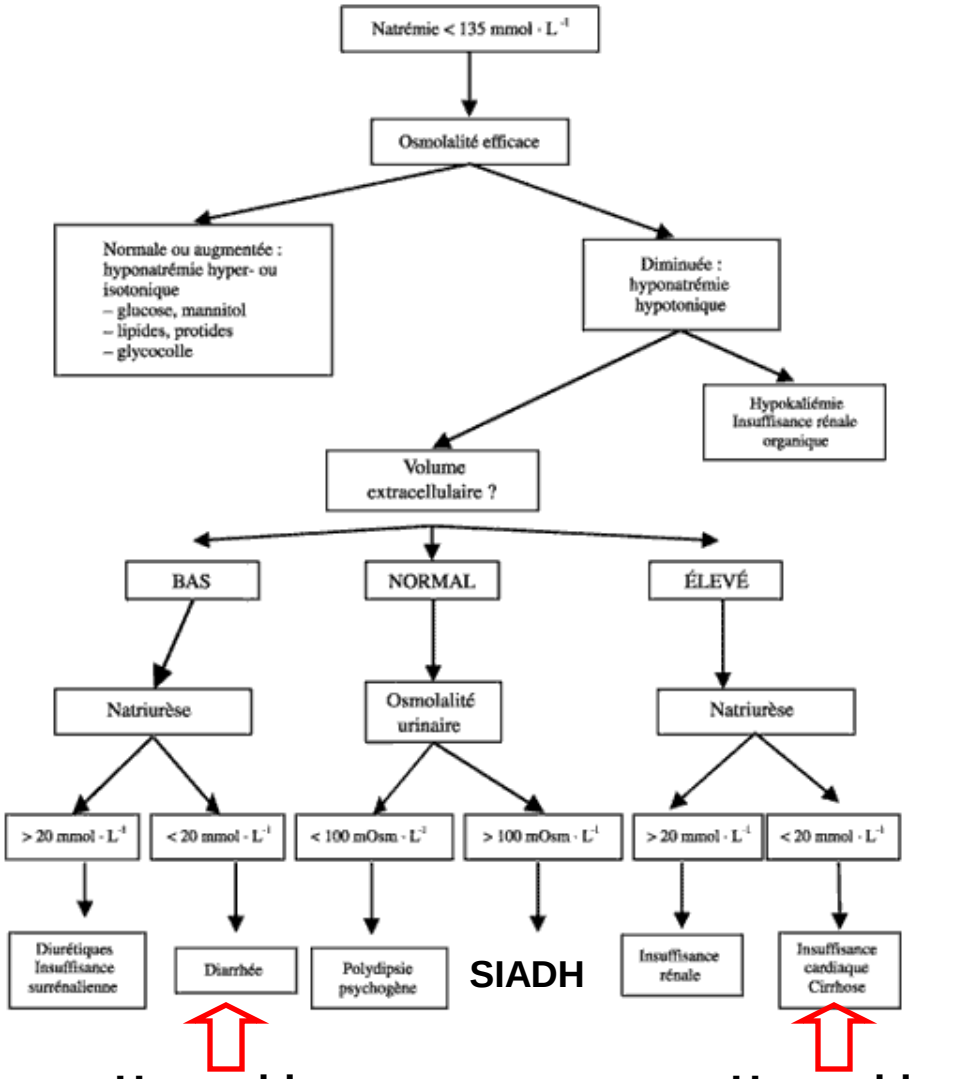
- Régulation de la natrémie: ADH
  - Excès d'ADH ➔ hyponatrémie
  - « SIADH » sécrétion inappropriée d'ADH
- Régulation du volume (pression):
  - rénine ➔ angiotensine ➔ aldostérone
  - Aldostérone:
    - ↗ réabsorption du Na+
    - ↘ réabsorption du K+ ➔ ↗ élimination du K+
    - Urine: K+ > Na+
  - Stimulation de l'ADH !! (ADH appropriée au volume mais sacrifice de l'osmolarité!)

L'autre stimulus de l'ADH: hypovolémie/hypotension





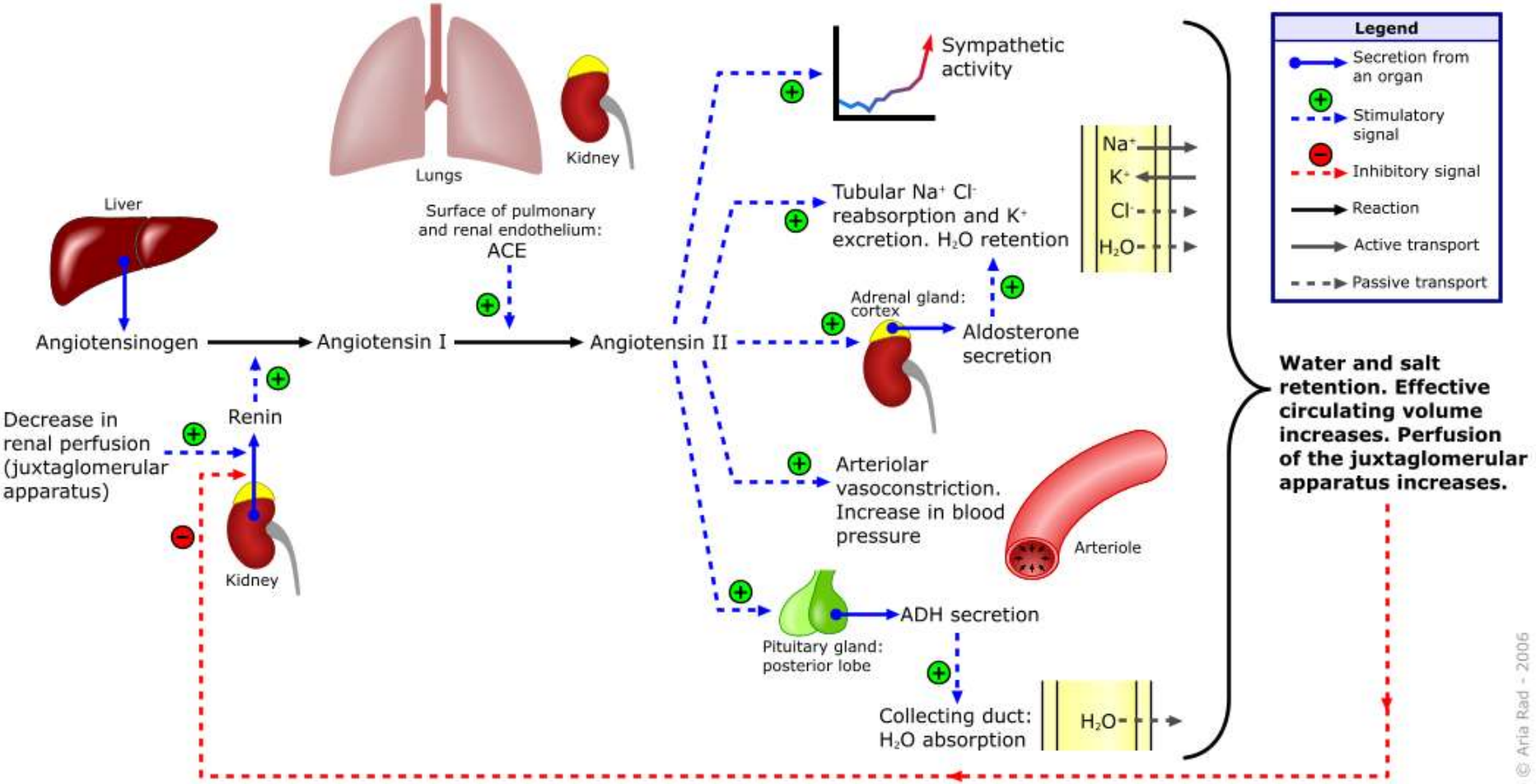
Hyponatrémie



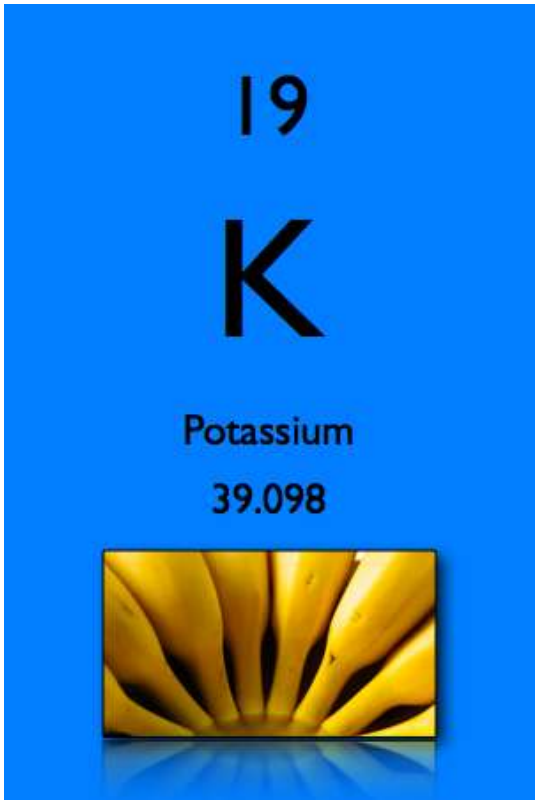
Hyperaldo secondaire à l'hypovolémie

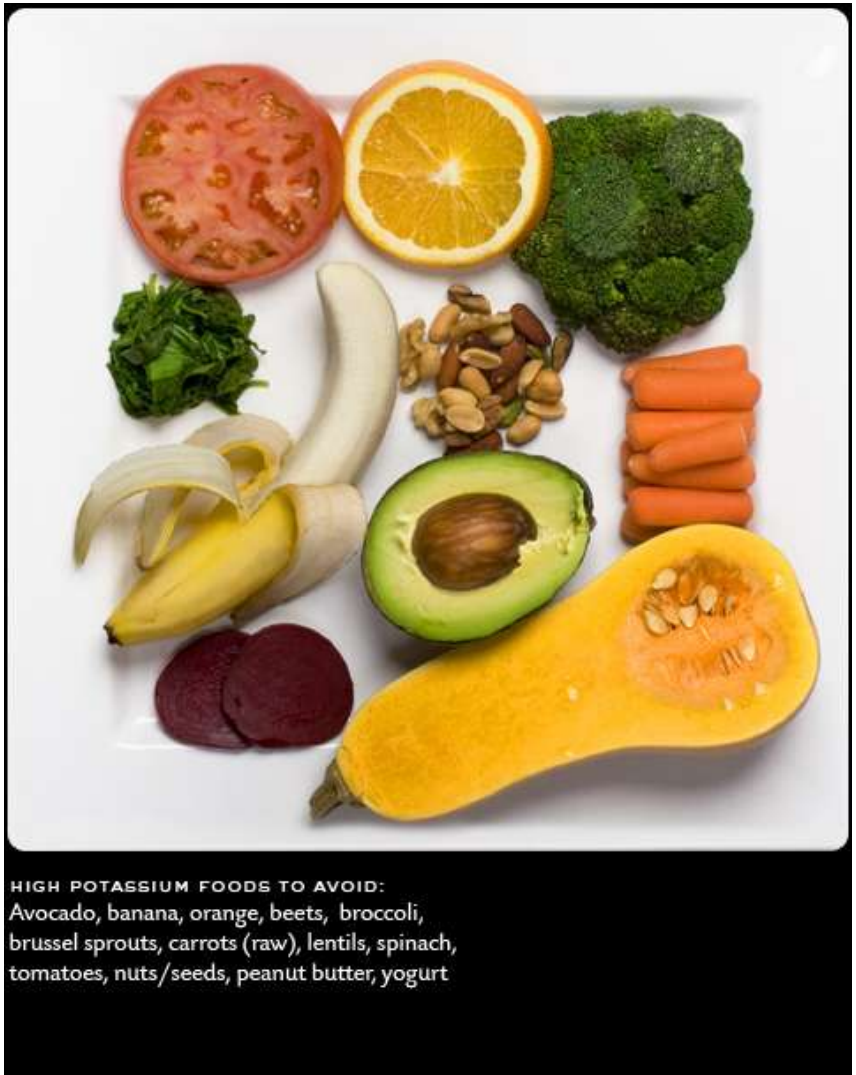
Hyperaldo secondaire (hypovolémie relative)

Renin-angiotensin-aldosterone system

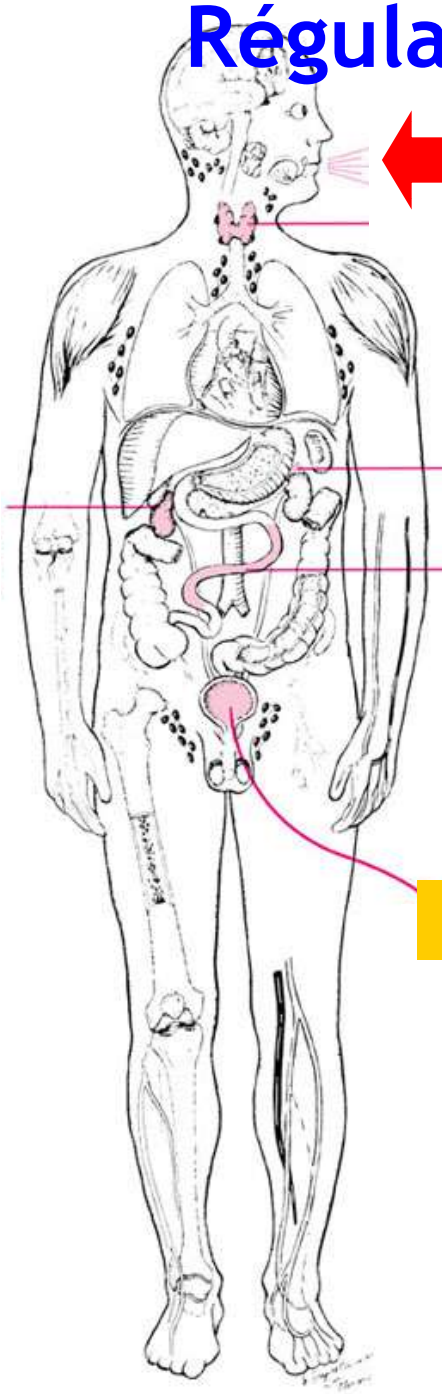


Potassium (kalium)





Régulation potassium



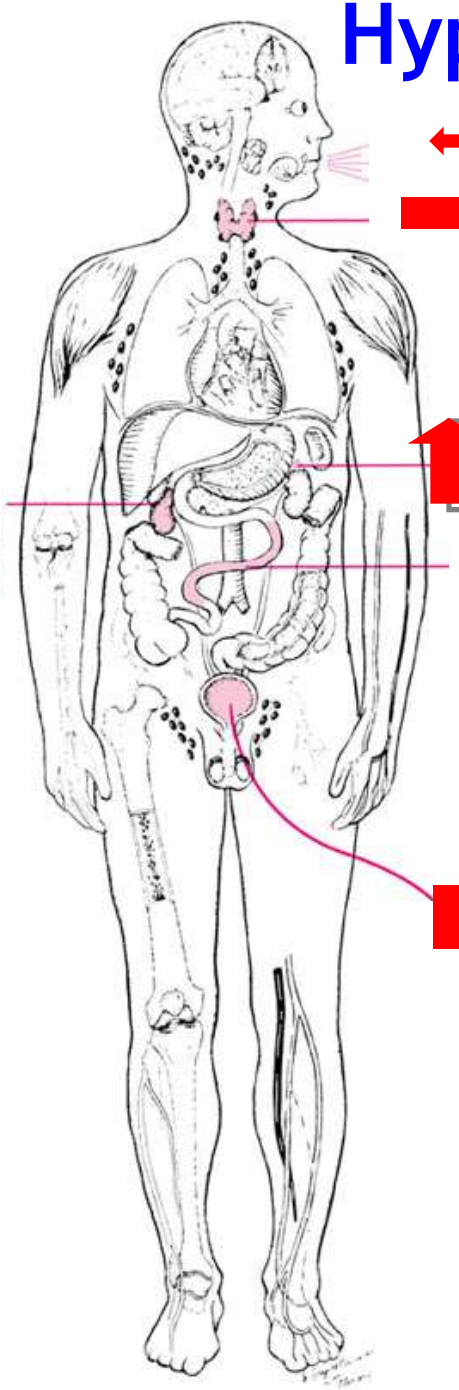
Apports alimentaires de K+

Aldostérone: ↗ excrétion urinaire de K+

<10%: élimination digestives (selles)

>90%: excrétion rénale

Hypokaliémie



Apports insuffisants de K+

Vomissements ! (pertes digestives)

Aldostérone: ↑ excrétion urinaire de K+

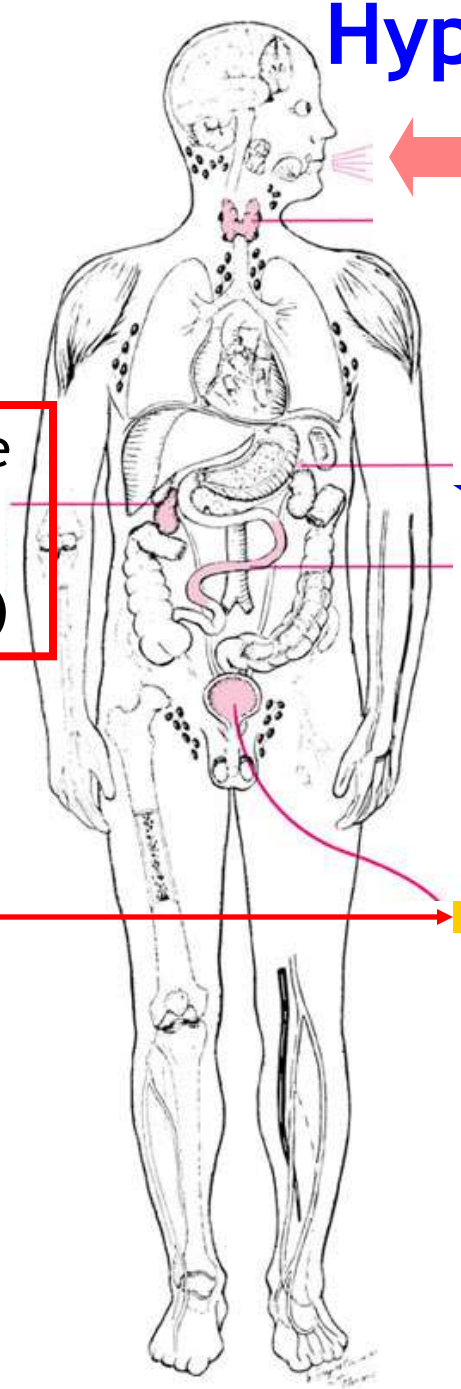
Diarrhées +++ (pertes digestives)

Pertes rénales: diurétiques, hyperaldostéronisme

Hypokaliémie ➔ spot urinaire

- K+ urinaire:
  - **< 20 mmol/l**
    - Pertes extrarénales (digestives)
    - Manque d'apports ?
  - **>20 mmol/l**
    - Pertes rénales
      - Diurétiques ?
      - Hyperaldostéronisme ?

Hyperkaliémie



Apports alimentaires excessifs de K+
(seulement en cas d'insuffisance rénale)

Insuffisance rénale

(IRA ou IRC)

↓ Aldostérone: ↓ excrétion urinaire de K+

↓ Diminution de l'élimination rénale du K+

Médicaments:
- IEC/sartans
- Diurétiques d'épargne potassique: spironolactone, amiloride


Kea, Cycladic Islands, 2006