Common Adrenal Disorders in Children

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Doctor note +435 note

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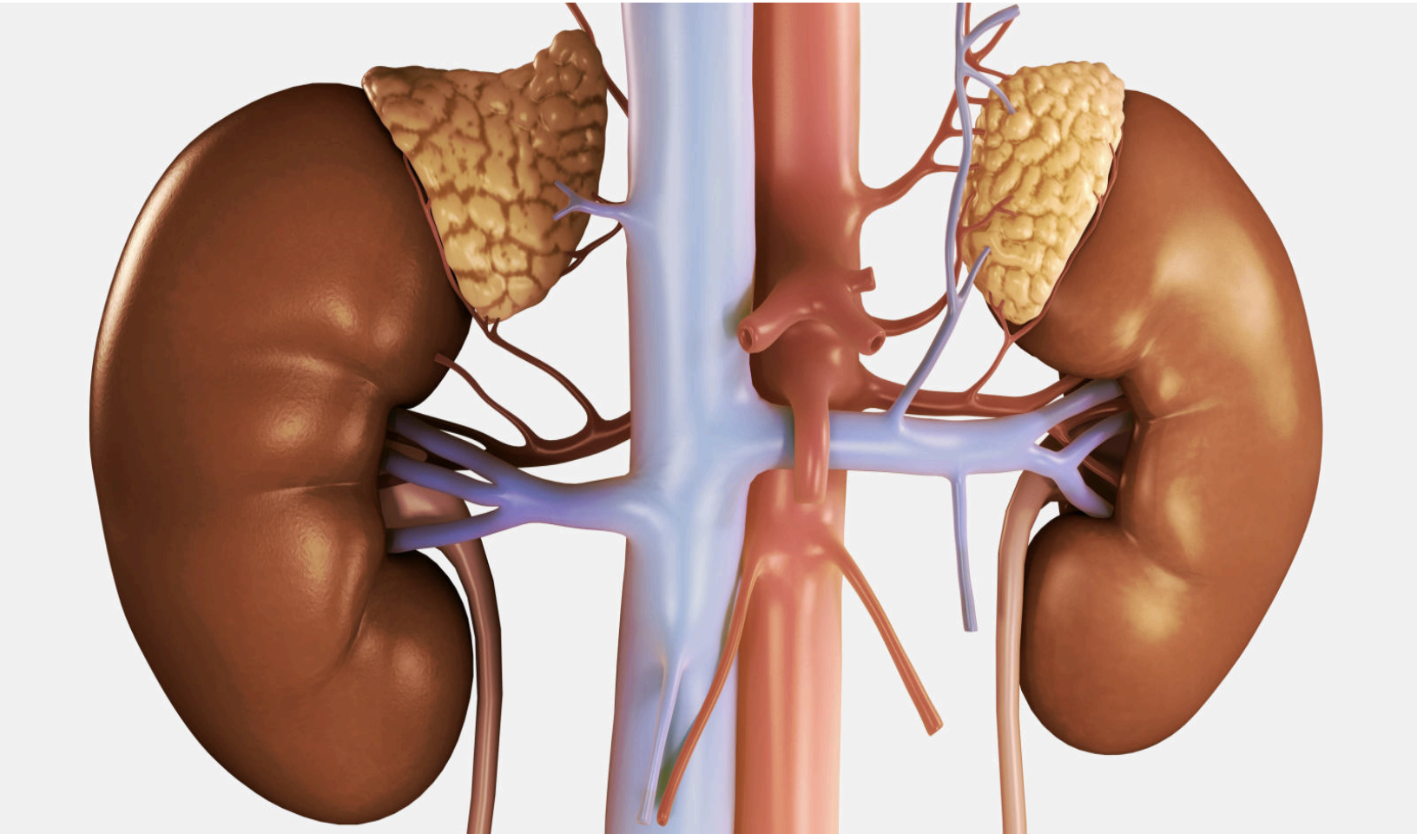
Objectives

- Understand physiology of adrenal
- Know Causes of adrenal insufficiency
- Cushing Syndrome



Adrenals are located north pole of the kidneys, shaped like a triangle, if you take a cut section, you'll find three major zones. GFR is an acronym to help you remember the zones.

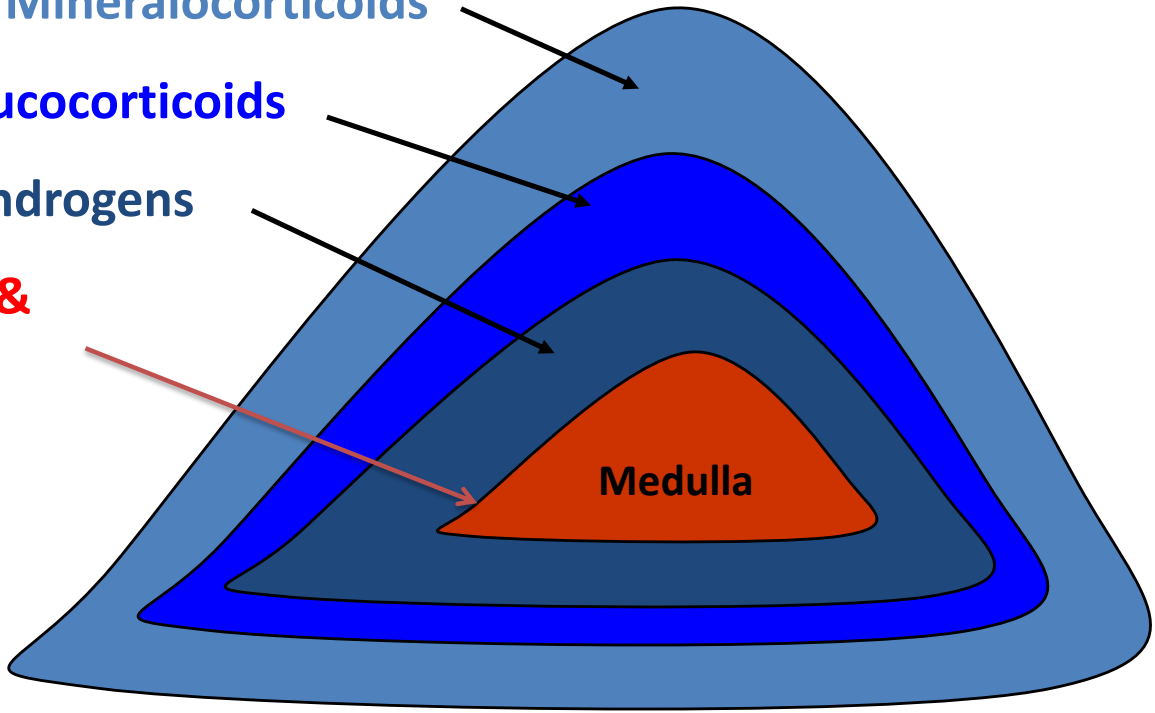
Adrenal Cortex

Zona Glomerulosa: Mineralocorticoids

Zona Fasiculata: Glucocorticoids

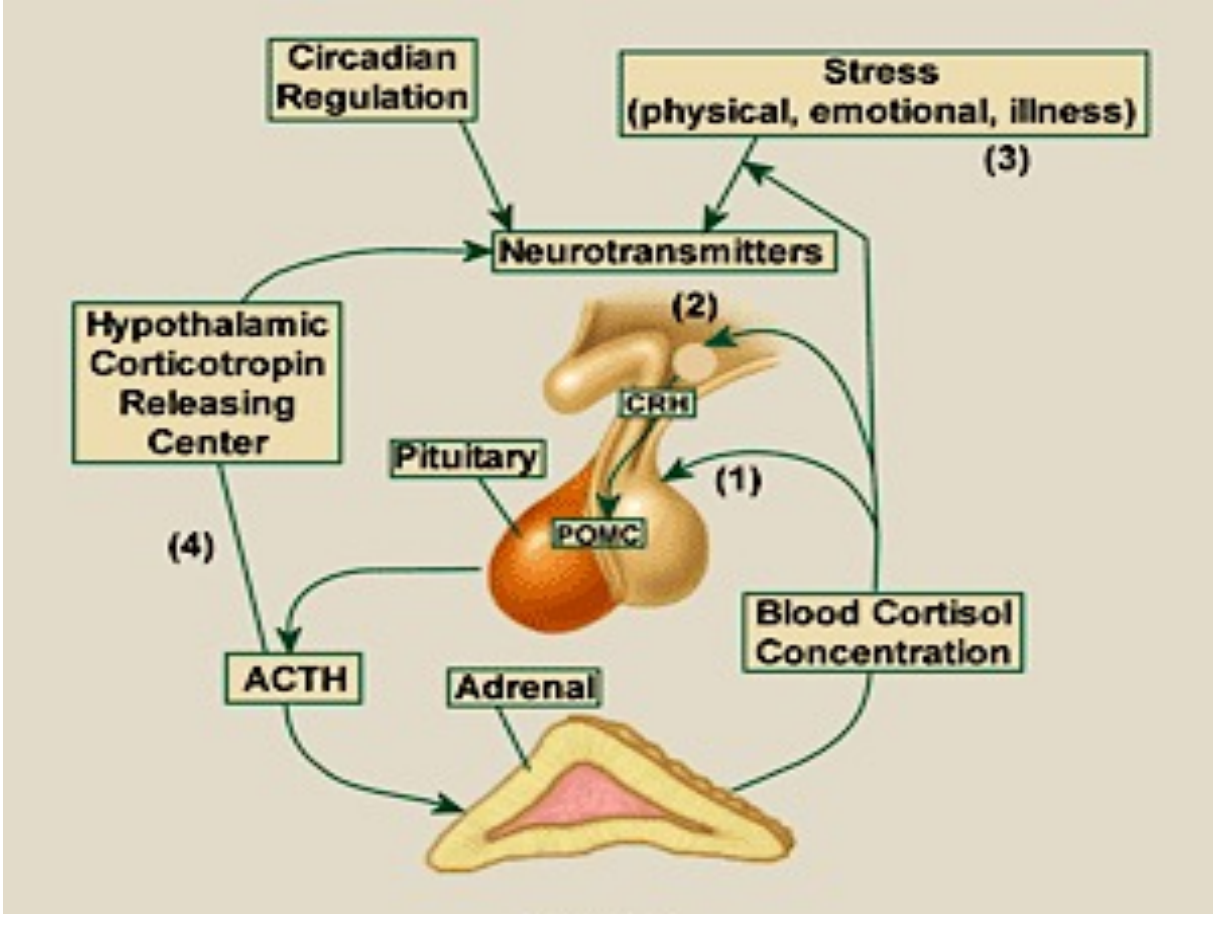
Zona Reticularis: Androgens

Medula: adrenalin & noradrenalin



Hypothalamus secretes CRH, which goes to the pituitary gland to secrete ACTH which goes to the adrenals(cortex) to secrete cortisol.

HPA axis



cortisol inhibits ACTH & CRH secretion (negative feedback).

What can controls of cortisol secretion?
- Circadian rhythm is one of the controls of cortisol secretion.
- We can increase the secretion by physical activity, stress or illness hypoglycemia

What could decrease the secretion of cortisol? Exogeneous steroids will activate feedback inhibition on the HPA axis

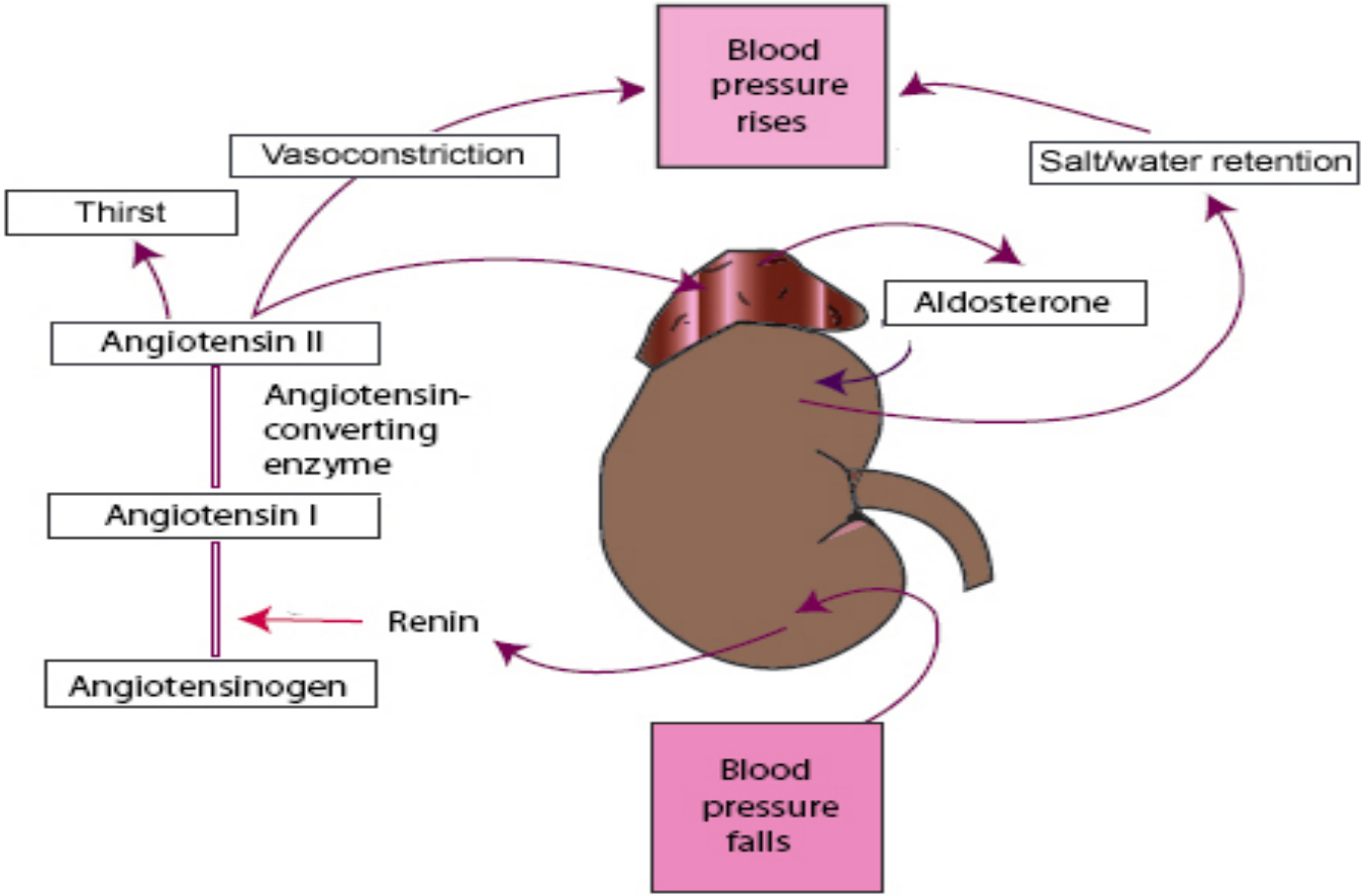
Renin Angiotensin System

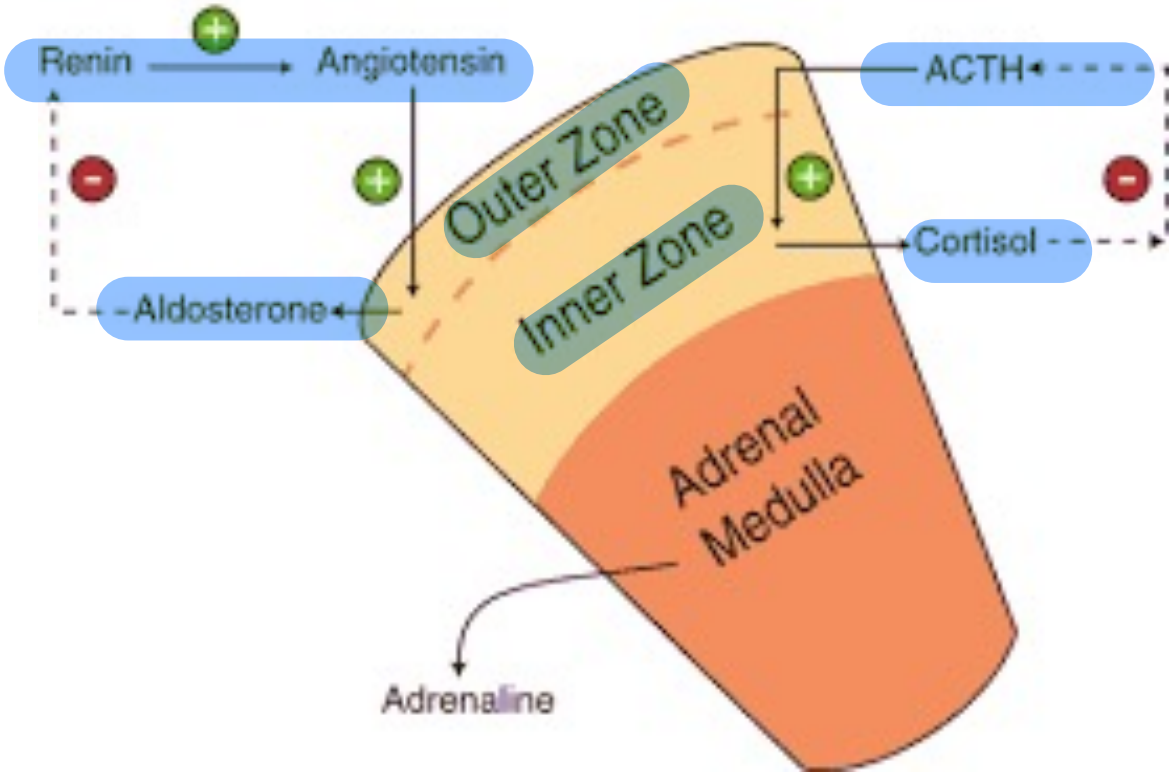
This is how the aldosterone is controlled, so when the blood pressure falls, renin will increase converting angiotensinogen into angiotensin I which will be then converted into angiotensin II.

Angiotensin II leads to **vasoconstriction and increases aldosterone** secretion leading to salt and water retention. Both will lead to blood pressure increase.

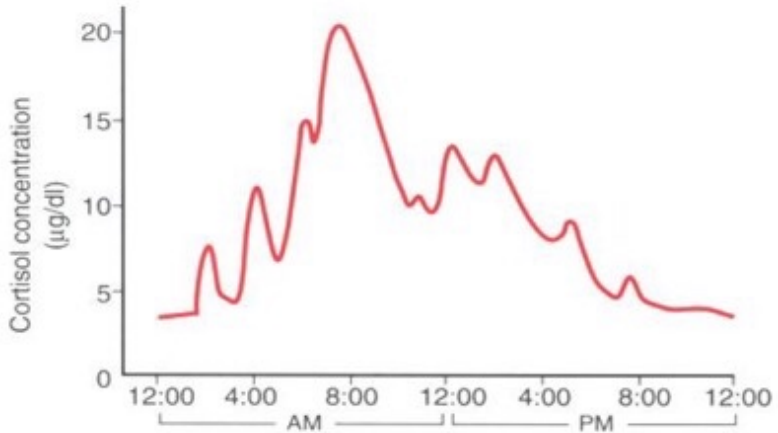
Renin-angiotensin system

The secretion of renin control by BP. If you have hypotension it is lead to positive feedback that stimulation renin release that is controlling the outer zone of the adrenal gland





To summarize, adrenal cortex is controlled by HPA axis and the RAS.

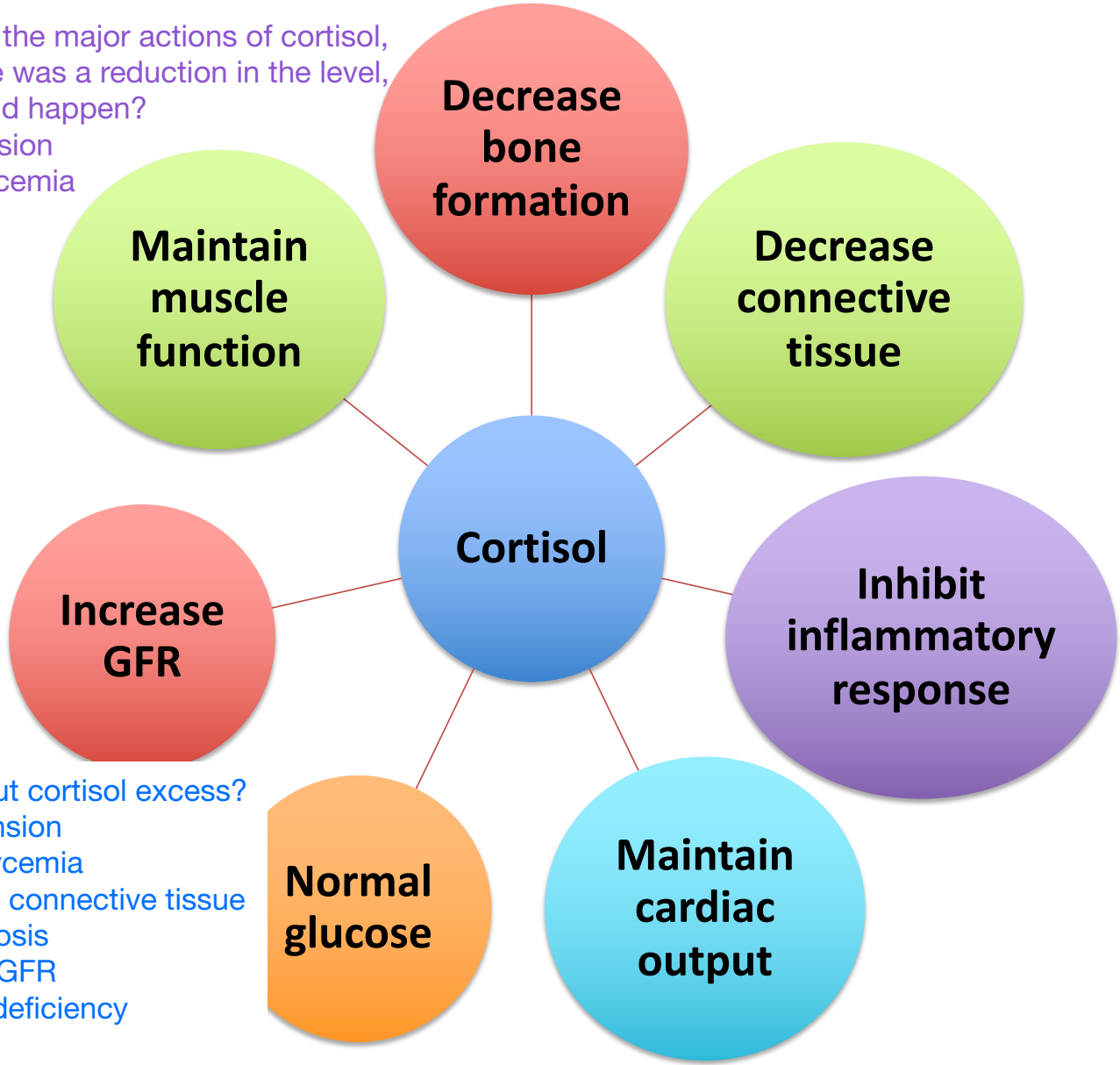


Cortisol is secreted in pulsatile ; however, it does have a peak around 8 am in the morning, then it drops until it is at its lowest around midnight.

This is very important, why? Because in adrenal insufficiency we measure cortisol, therefore, we wouldn't measure at the lower levels.

Can we do a similar test on a baby at 6 months old? They don't have a circadian rhythm; therefore, you can't
do AM cortisol. They start to develop circadian rhythm at around 1 year.

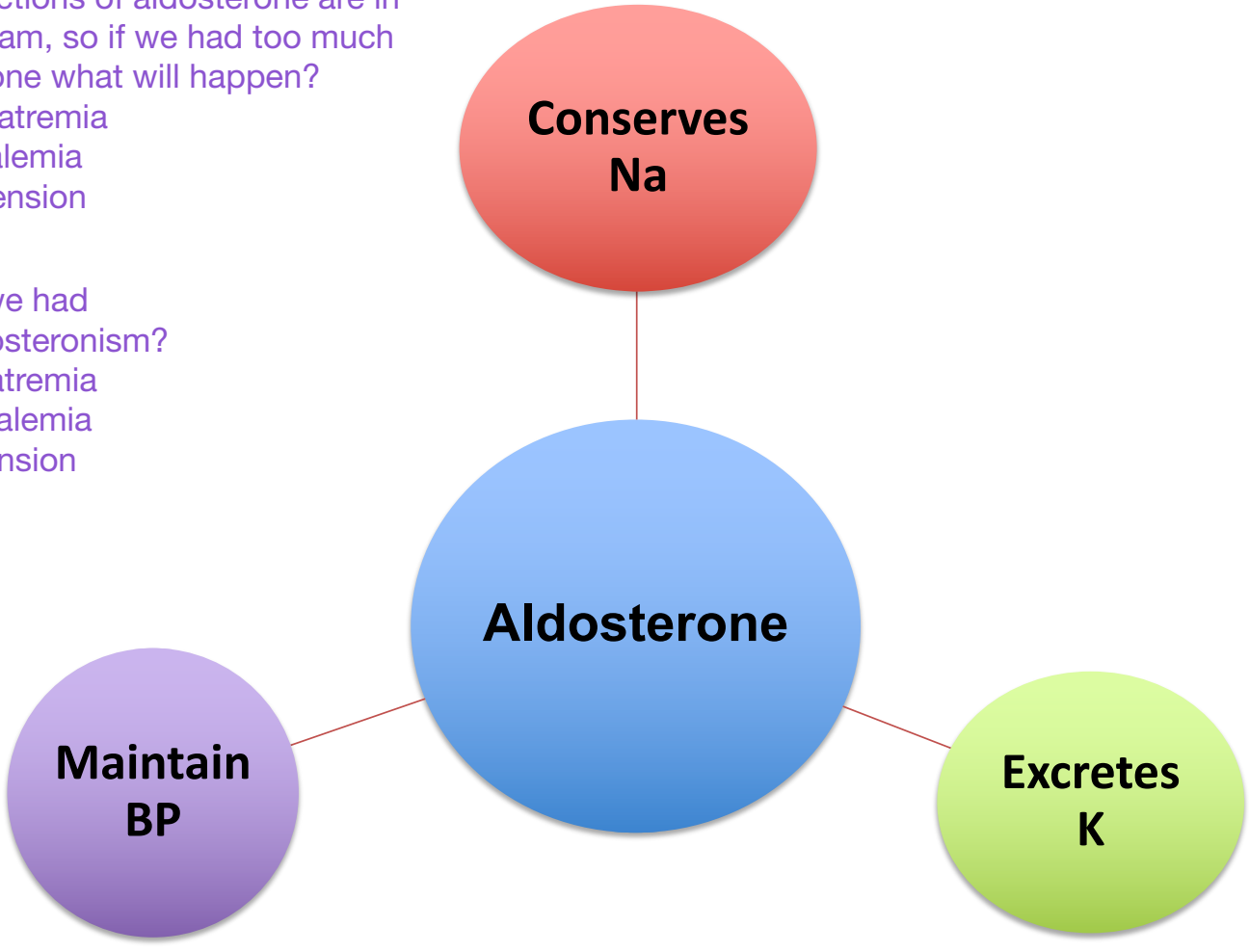
These are the major actions of cortisol, so if there was a reduction in the level, what could happen?
- Hypotension
- Hypoglycemia



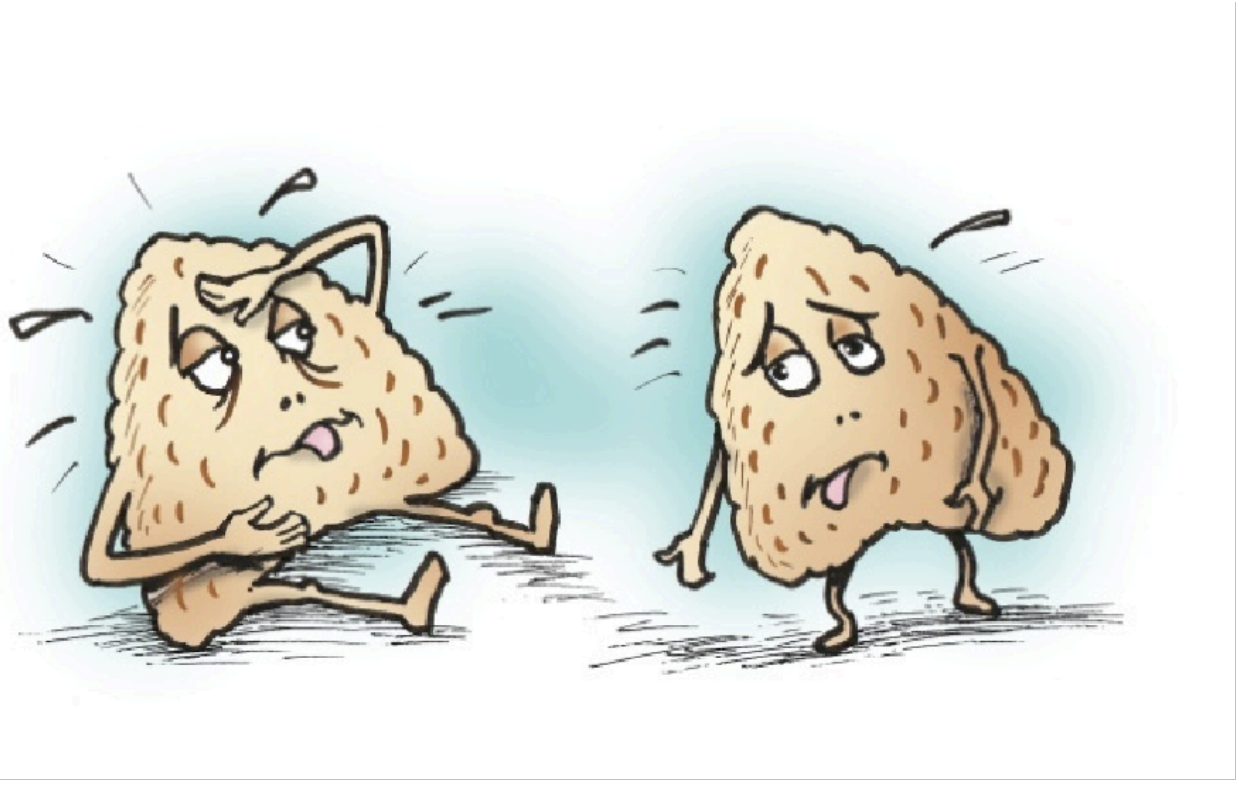
What about cortisol excess?
- Hypertension
- Hyperglycemia
- Issues in connective tissue
-osteoporosis
-increase GFR
-immune deficiency

Main functions of aldosterone are in the diagram, so if we had too much aldosterone what will happen?
- Hypernatremia
- Hypokalemia
- Hypertension

What if we had hypoaldosteronism?
- Hyponatremia
- Hyperkalemia
- Hypotension



Adrenal Dysfunction



Adrenal insufficiency

Primary

- **Acquired:**
  - Addison disease (autoimmune)
  - Infection (TB, sepsis)
  - Hemorrhage
- **Congenital:**
  - Congenital adrenal hyperplasia
- **Metabolic:**
  - Adrenoleukodystrophy

Infiltration from an infection

mostly with babies born with a traumatic delivery (forceps)

Secondary

- HPA suppression

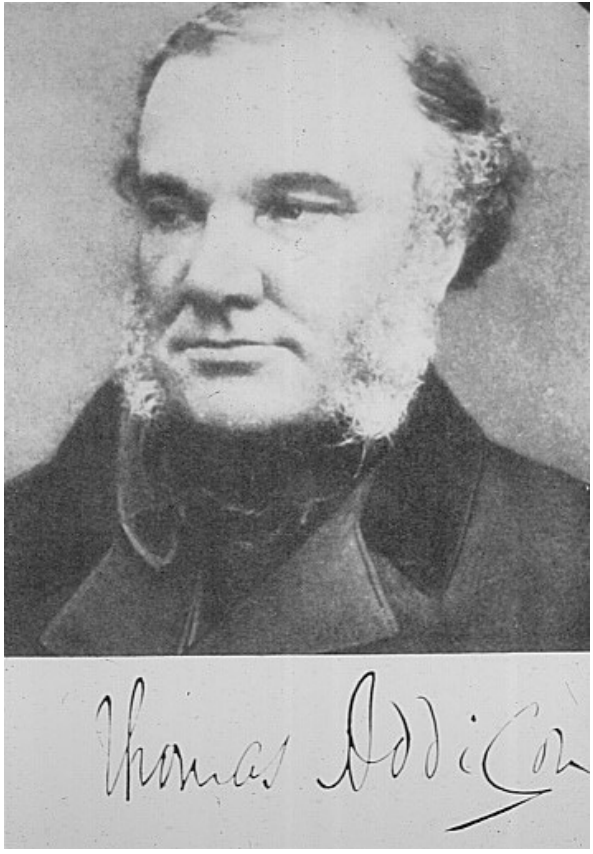
Any reason that leads to HPA axis suppression like exogenous steroids

- Pituitary:
  - Congenital
  - Tumor
  - Trauma
  - Infection

Primary Adrenal Insufficiency

- 1st described in 1855 by Dr. Thomas Addison
- Refers to acquired primary adrenal insufficiency
  - Usually autoimmune (~80%)

It is not that common in pediatrics. Congenital adrenal hyperplasia is the most common in pediatrics



Symptoms

- Fatigue
- Weakness
- Skin & mucous membrane hyperpigmentation
- Weight loss
- Poor appetite
- Nausea, vomiting
- Abdominal pain
- Salt craving

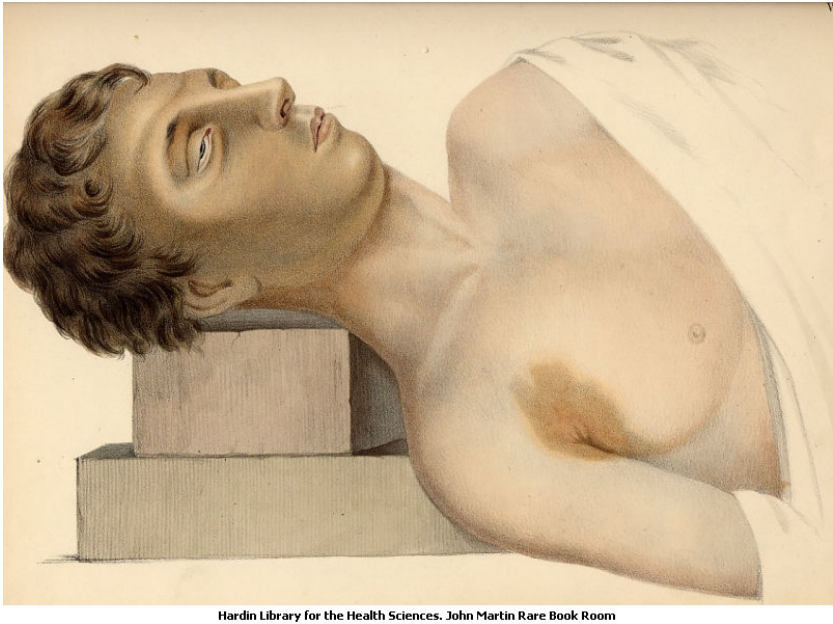
Unique sing for primary adrenal insufficient.

All primary adrenal insufficiency have similar symptoms. And they are similar between adults and pediatrics, what can be different in pediatrics?
Effect on growth! Growth could be impacted if it is not treated.
Also, ambiguous genitalia in adrenal congenital hyperplasia

Physical findings

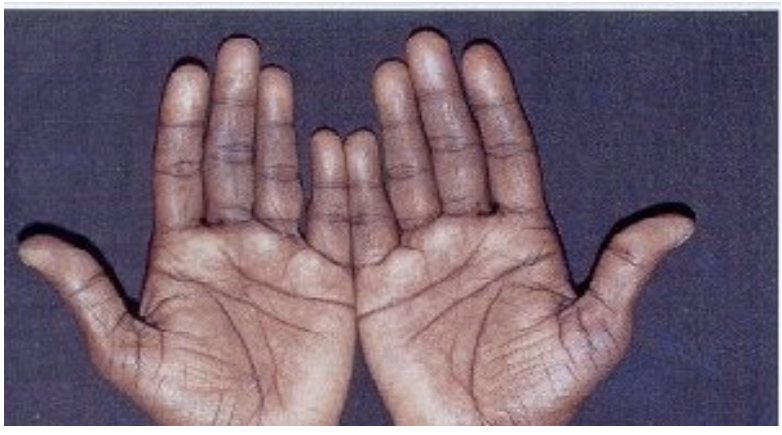
- Hyperpigmentation *
- Hypotension
- Dehydration
- Orthostatic changes
- Weak pulses
- Shock
- Loss of axillary/pubic hair (women)

to the extent of collapse and they present with shock

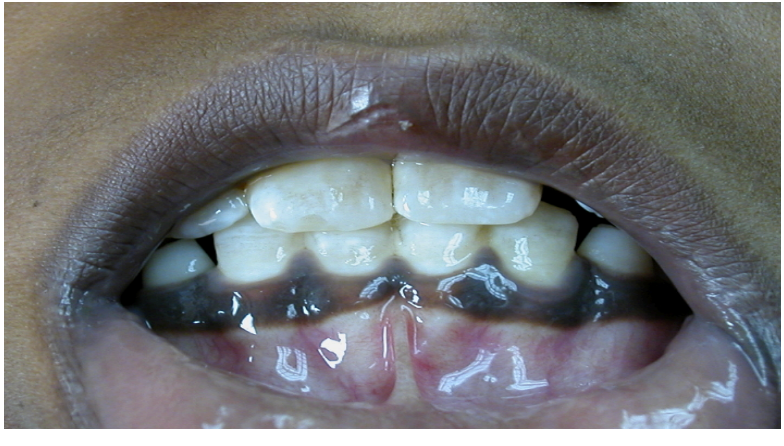


Hardin Library for the Health Sciences. John Martin Rare Book Room

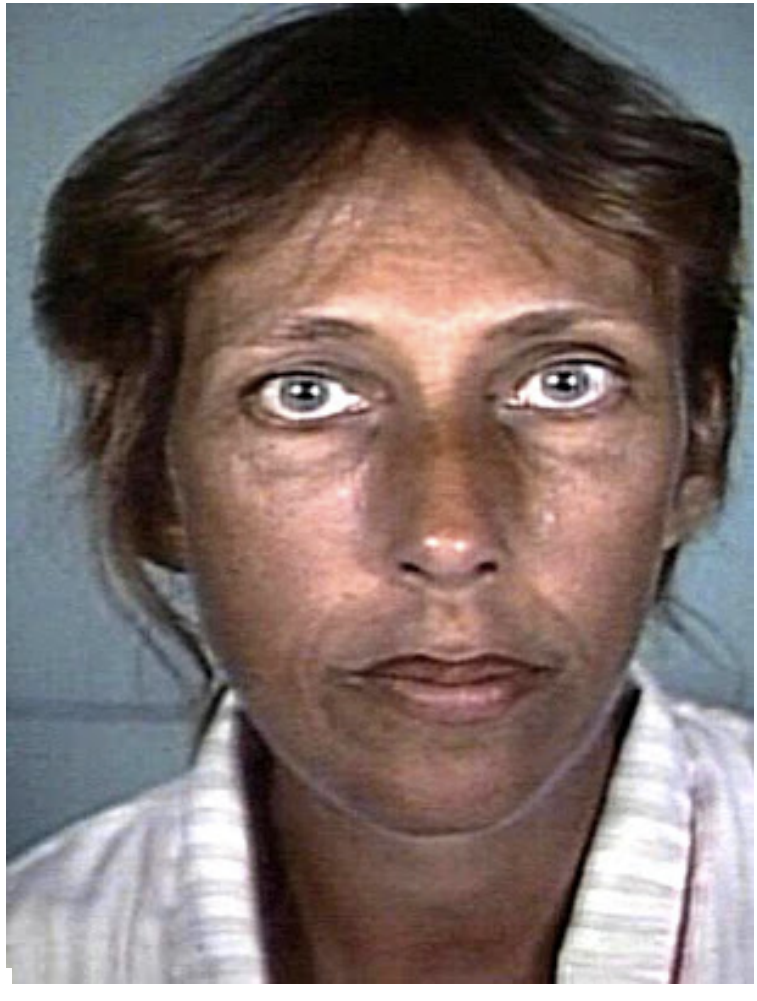
* Hyperpigmentation in palmar creases and axilla “sun unexposed area “, you only see it in primary, not secondary why? Because excess ACTH secretion has an effect on the melanin cells causing hyperpigmentation. In the secondary there is no excess ACTH secretion.



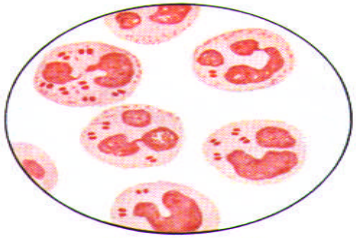
Hyperpigmentation in palmar
Skin creases very deep and Hyperpigmentation



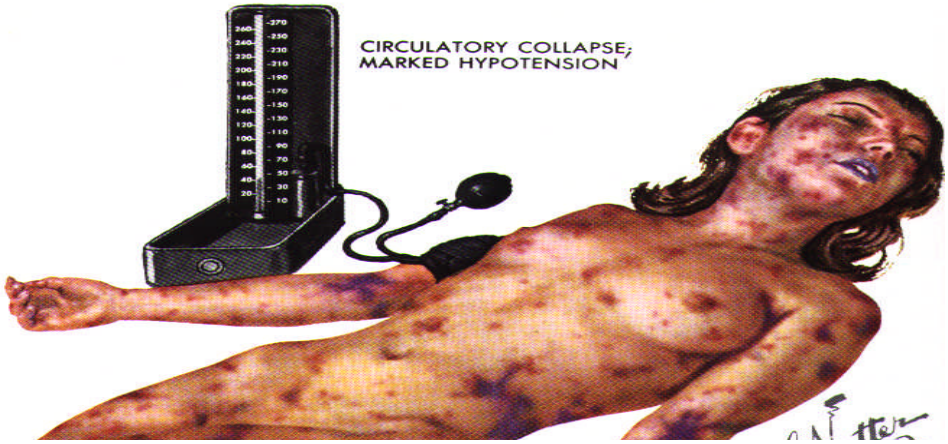
Not specific because if someone has poor dental health and hygiene, the gingiva could be infected so not everyone with gingiva discoloration would be labeled as primary adrenal insufficiency.



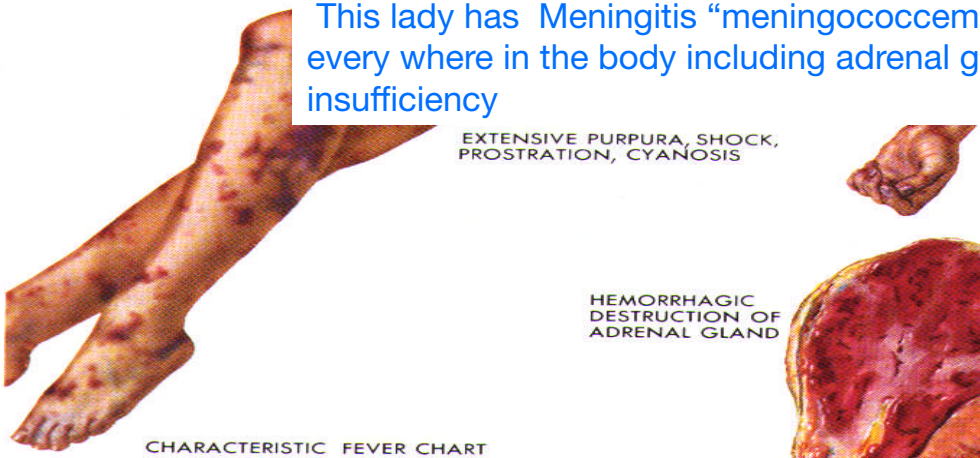
It is not the darkening skin that would you get when you expose to the sun. The color is dusky and slavery color.

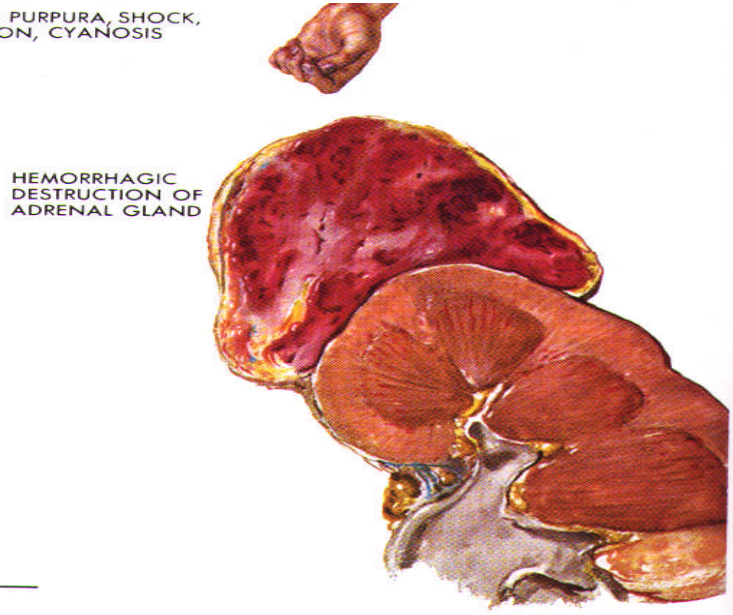


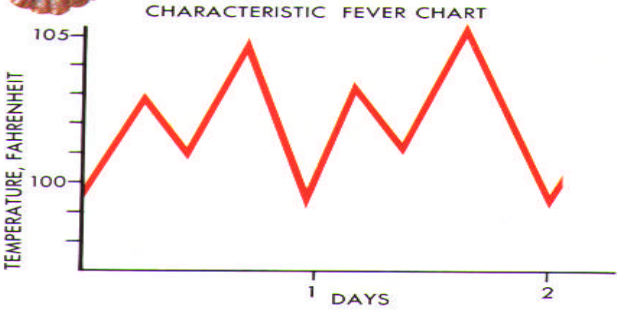
MENINGOCOCCI FROM BLOOD, SPINAL FLUID AND/OR THROAT



This lady has Meningitis “meningococcemia” that lead to hemorrhage every where in the body including adrenal gland hemorrhage and insufficiency







Laboratory findings

- Na ↓
- **K ↑**
- **Glucose ↓**
- **Cortisol ↓**
- **ACTH ↑**
- **Renin↑**
- **Aldosterone ↓**

Diagnosis

- Am cortisol, ACTH
- ACTH stimulation test
- Adrenal antibodies

if we suspect autoimmune “Addison disease”

high ACTH and low cortisol = primary adrenal insufficiency.What is the expected normal range for before 9AM cortisol? 200- 250

And if you usually not sleep at night That will cause a distribution your circadian rhythm that leads to abnormal cortisol secretion (low AM cortisol)

ACTH stimulation test

Measure the cortisol baseline then Give the patient ACTH, after 1h measure the level of cortisol

if the adrenals are normal, they will secrete high levels of cortisol, more than 500 or doubling the baseline , if the level less than 500 then this is adrenal insufficiency

Treatment

- Hydrocortisone main medication
- +/- Fludrocortisone

For life

For life except if the patients have adrenal insufficiency that is secondary to hypothalamic-pituitary Axis suppressions.Like who has a severe episode of asthma and would be in cortisol for a period,2 or 3 weeks.

Typically the adrenal when we pass through stress or illness will secret more cortisol in our body to make handle the stress otherwise if not increase the cortisol secretion the person will go through an adrenal crisis and if you do not manage it the patient may be die

STRESS MANAGEMENT

If you have an infection your body will increase cortisol secretion, that is the normal response, if you have someone with adrenal insufficiency, this feedback mechanism doesn't work, so during sick days this is what we have to do:

Sick day management

fever of 38.5 C - 39.4 C or moderate illness/stress, give a **double** dose

if the baseline in 2mg they have to take 4mg

fever > 39.5 C or severe illness, give a **triple** dose if the baseline in 2mg they have to take 6mg

Continue the double or triple doses during the duration of stress. Stop it after 24h of resolve the stress “e.g. fever”

Intubation & surgeries

just before the go to OR or if the patient comes to the ER with trauma

- Hydrocortisone 50mg/m^2 IV

this is extremely important for any patient with adrenal insufficiency. If you don't cover this they will collapse and die.

Adrenal crisis

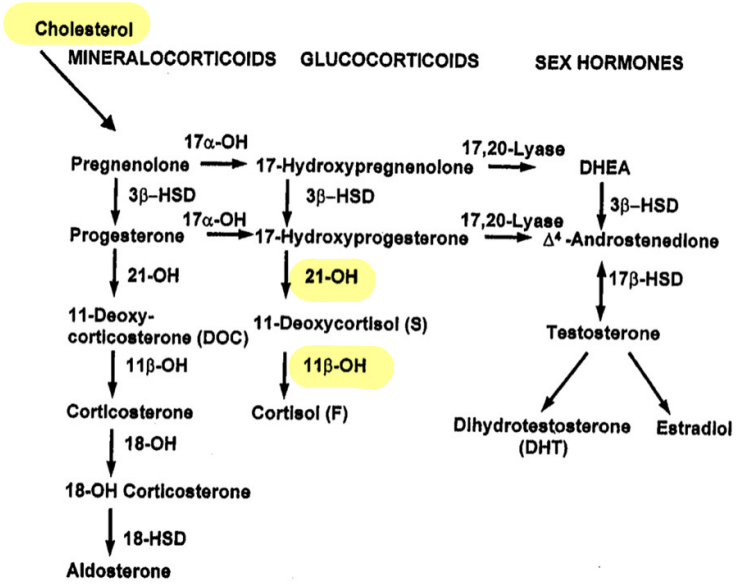
- Life threatening complication could happen upon diagnosis, they could present with it.
- Severe vomiting and diarrhoea followed by dehydration if you see these together always keep adrenal insufficiency in mind.
- Low BP & shock
- Hypoglycemia
- Loss of consciousness
- Treatment: IV fluids resuscitation +IV hydrocortisone (in a very high dose it can exert mineralocorticoid effect)

CONGENITAL ADRENAL HYPERPLASIA

CAH

- deficiency of one of several enzymes necessary for steroid synthesis
- Autosomal Recessive (M=F)
- 21-hydroxylase is the commonest form

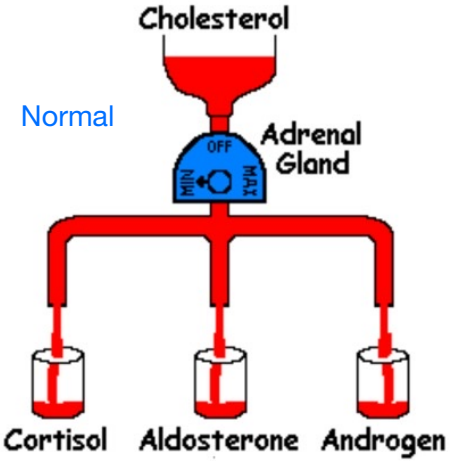
  this is highly prevalent in Saudi Arabia, 1:4000, due to high consanguinity

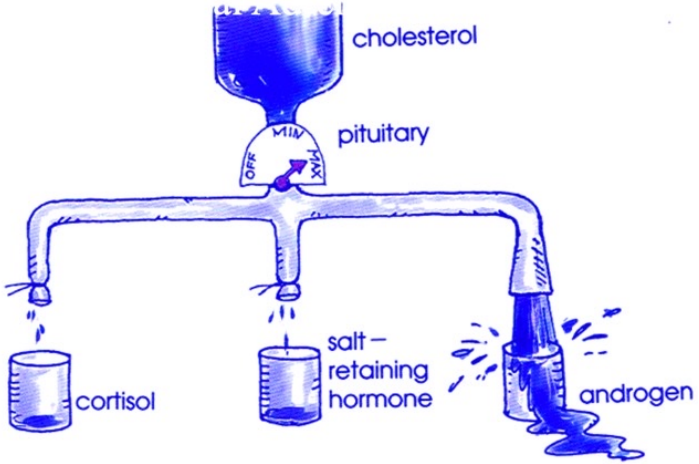


You have to talk about this pathway, the pathway starts with cholesterol, it enters the adrenal cortex and interact with multiple enzymes that will end up manufacturing cortisol, testosterone or aldosterone.
The first major is 21 OH and the second major is 11 ß OH

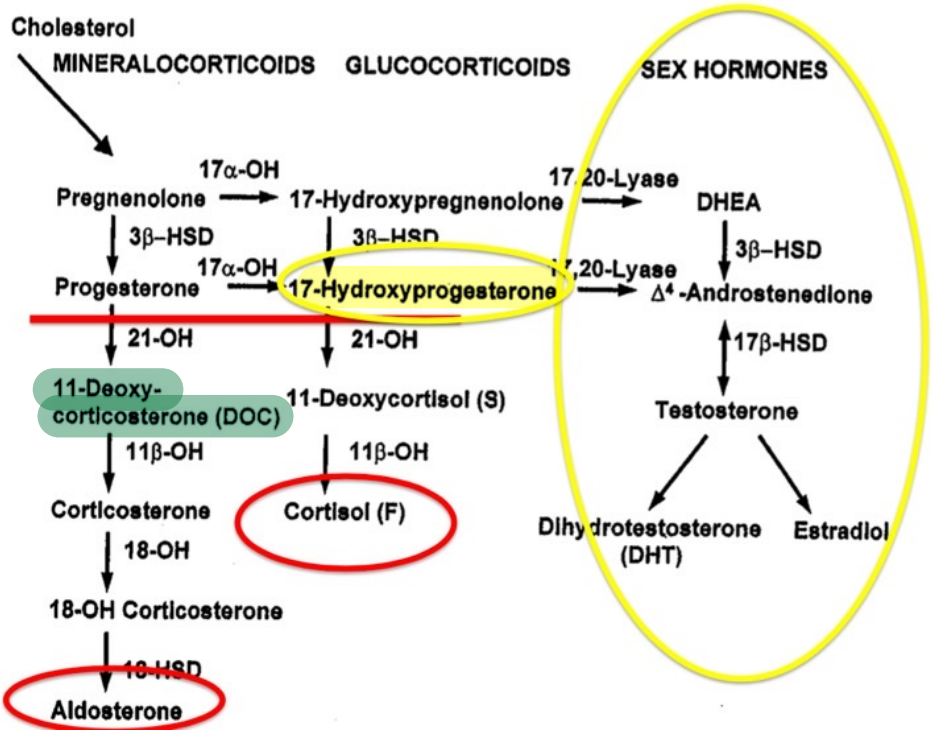
Any enzymes deficiency in these pathways will lead to lake of manufacture process of the end molecules that we interested in.

Congenital Adrenal Hyperplasia



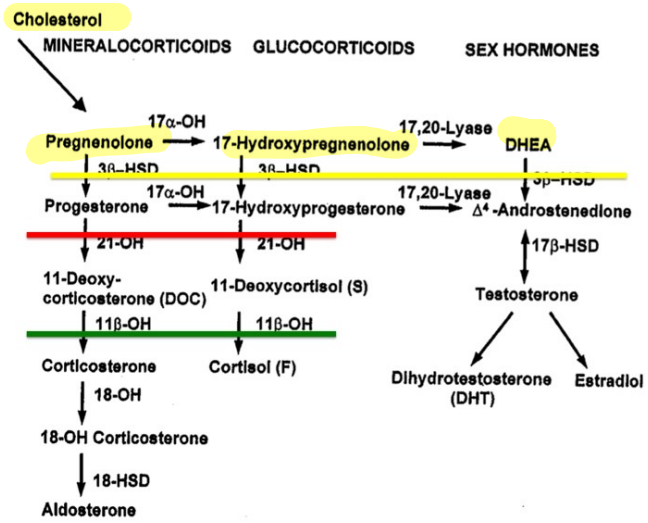


So how does CAH happen?
Cholesterol enters the adrenal gland and cortisol, aldosterone and androgens will be manufactured, if we block one of the pathways we'll have an excess product caused by the functional pathway and lake of one or more products .



If we block the 21-OH pathway, we cannot manufacture cortisol or aldosterone and at the end of result we'll have excess sex steroids. also 17- hydroxyprogesterone will be high, so we use it as a marker, this is what we can measure for CAH.

If we block the 11 ß OH, cortisol and aldosterone will be low but testosterone will be high.



If we block 3 ß HSD, we can't manufacture anything,So here
17- hydroxyprogesterone Will not be a good markers (it will deficiency.)
The pregnenolone,
17-hydroxypregnenolone, and DHEA will be high so we use them as diagnostic markers.
Mostly we use
17-hydroxypregnenolone

Other blocks are rare.

How we will differentiate between 21- Hydroxylase deficiency And 3 ß HSD?

21- Hydroxylase deficiency lead to excessive testosterone so the girls will have Ambiguous genitalia and the boys will have normal genitalia.

3 ß HSD The testosterone will be deficit so the boys will have Ambiguous genitalia and girls will have normal have genitalia

Presentations of 21-Hydroxylase CAH

Early	• **Complete enzyme defect**
Late	• **Partial enzyme defect**

Early Presentations of 21-Hydroxylase CAH

At what age? In the neonatal period, if it is partial, they'll present later (adolescence).

Boys	• **Normal genitalia**
Girls	• **Ambiguous genitalia**

Why? Because of the increase in androgens, the block that caused deficiency of estradiol and more testosterone to be manufactured which led to virilization.

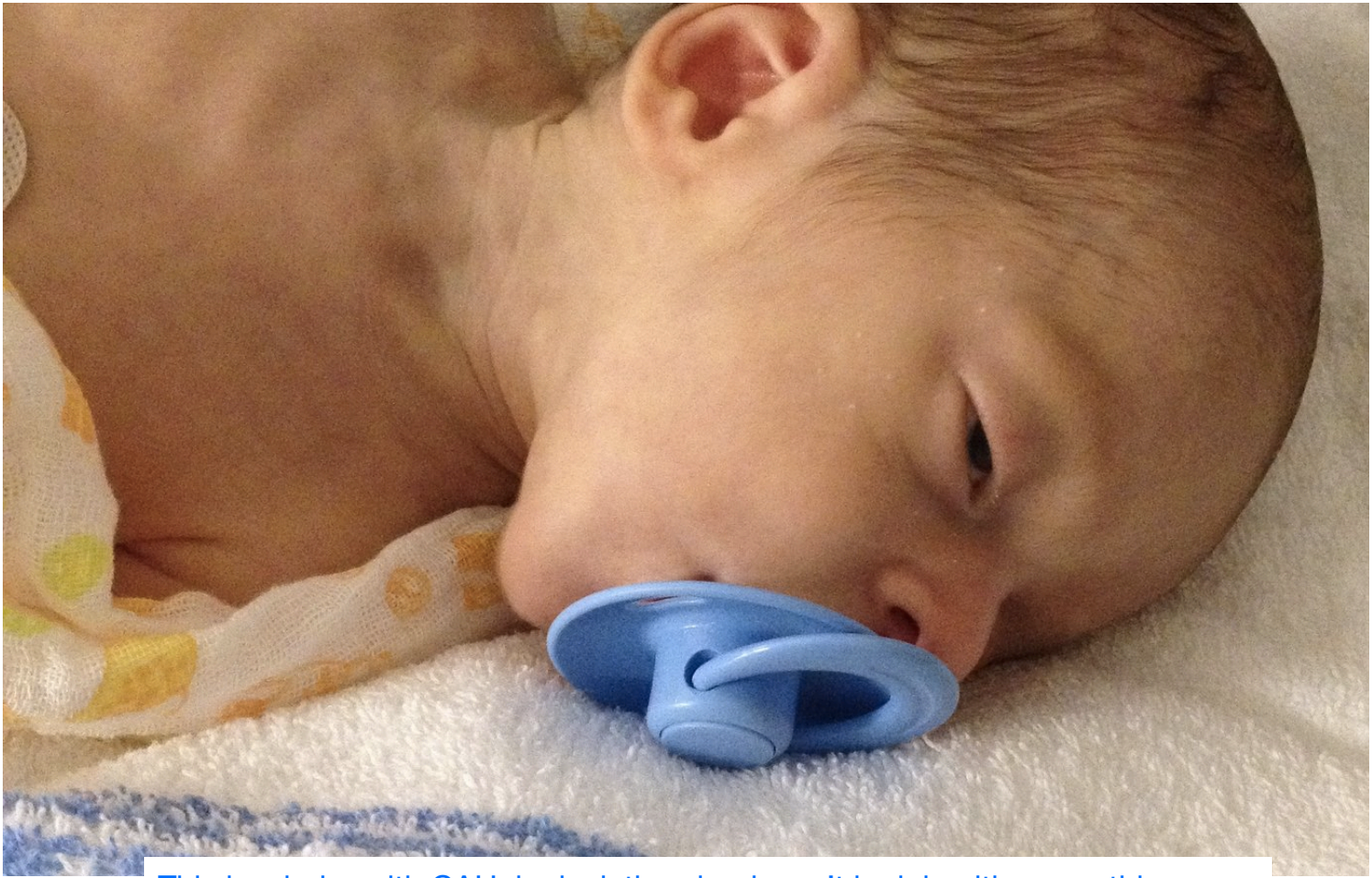
2nd week of life if genitalia looks normal or if not recognized:

let's assume this is a boy, he started having a salt loosing crisis, they'll present with:

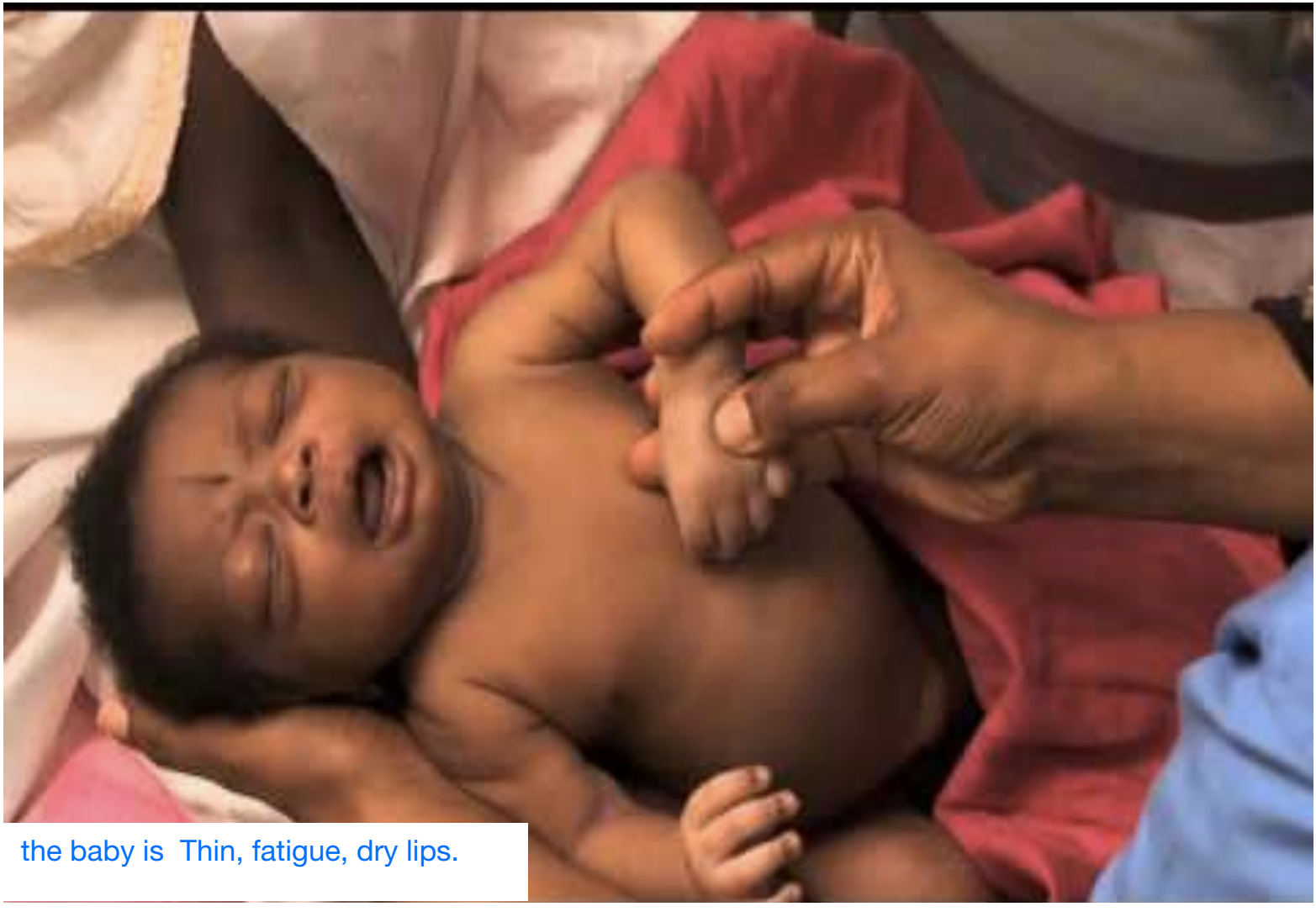
- Dehydration
- Shock
- Salt-loss presentations with electrolytes imbalance
  - Hypernatremia
  - Hyperkalaemia
  - Hypoglycaemia
- Hyper-pigementations

Salt loosing crisis

21- Hydroxylase have the same picture of adrenal insufficiency but without hypotension why? Because they have excessive 11-deoxy-corticosterone that leads to hypertension.



This is a baby with CAH, looks lethargic, doesn’t look healthy, very thin you can count the ribs



the baby is Thin, fatigue, dry lips.

The **most common** cause of **ambiguous genitalia** is Congenital adrenal hyperplasia

How we defined ambiguous genitalia?

You need two Abnormalities funding to call it ambiguous genitalia

Or undescended both gonads (testicle)

The ***abnormalities are***

1-one undescended gonad (testicle).

2-abnormal urethral opening not in the tip of tubercle .

3-cordi (The genital tubercle is curved not street because there is tissue pulling it.)

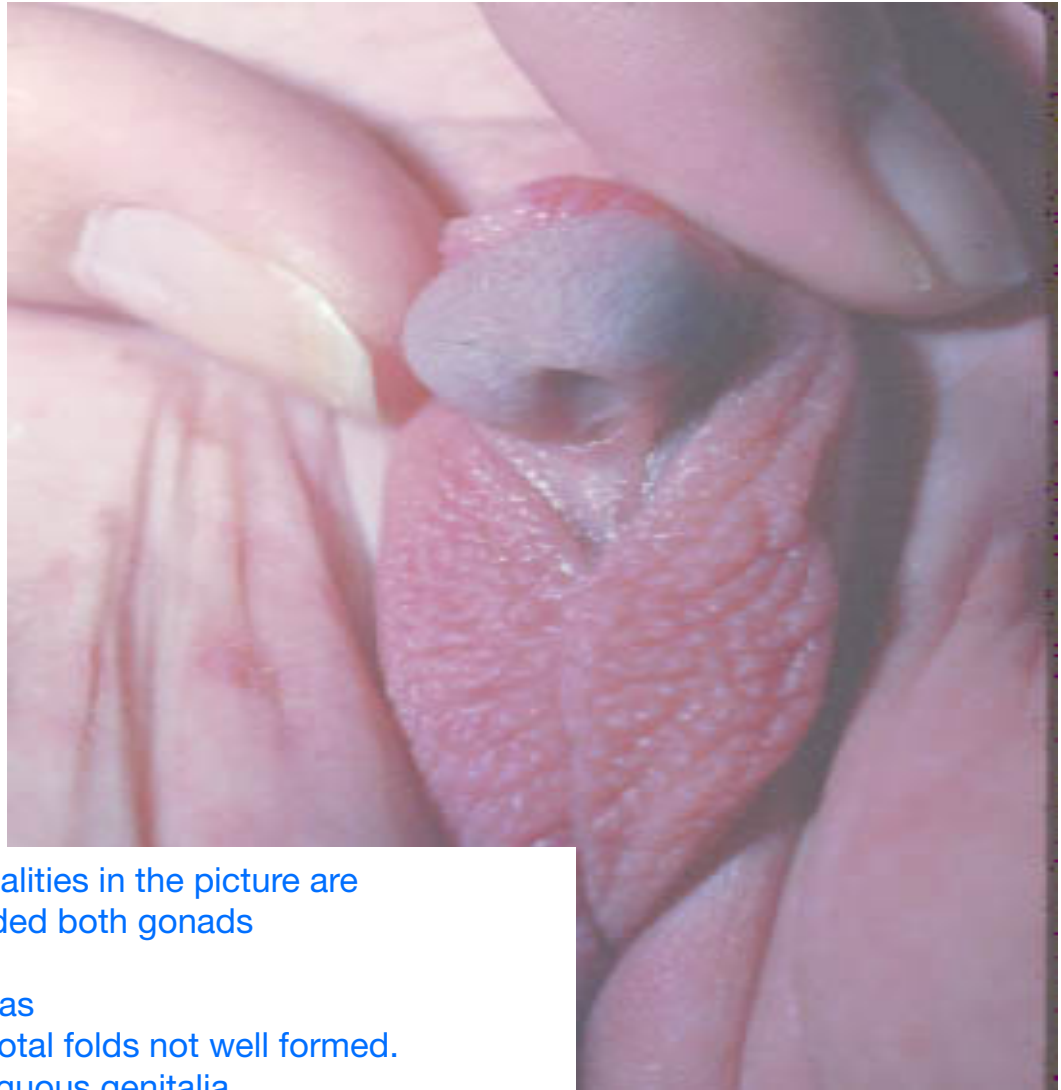
4-Abnormal length of genital tubercle. The genital tubercle length in boys need to be more than 2.5 cm and the normal length for girls need to be less than 1cm

When we deal with ambiguous genitalia, we avoid the gender-specific term , we use the gender-neutral term like

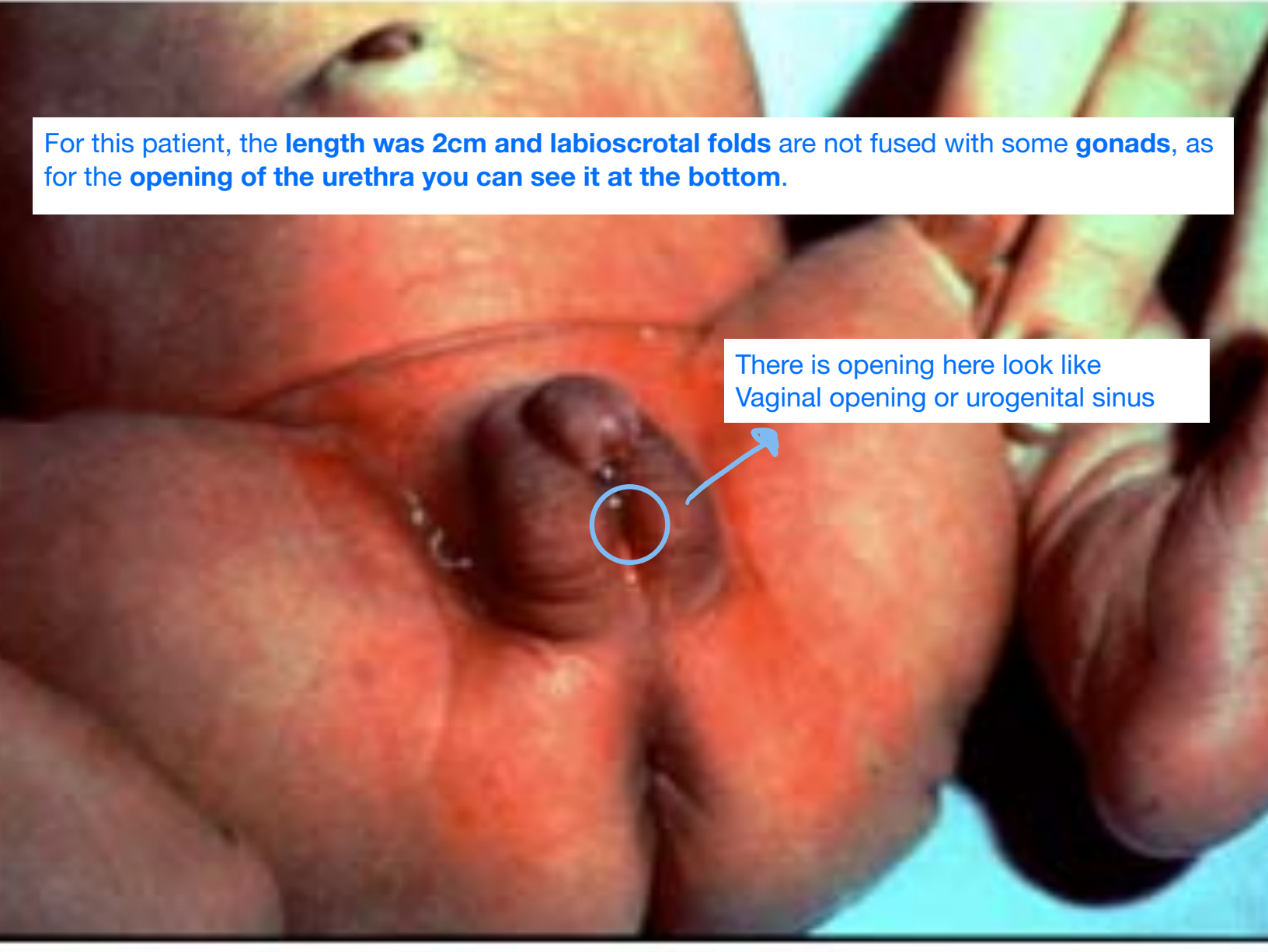
1-gonad instead to testicle and ovaries

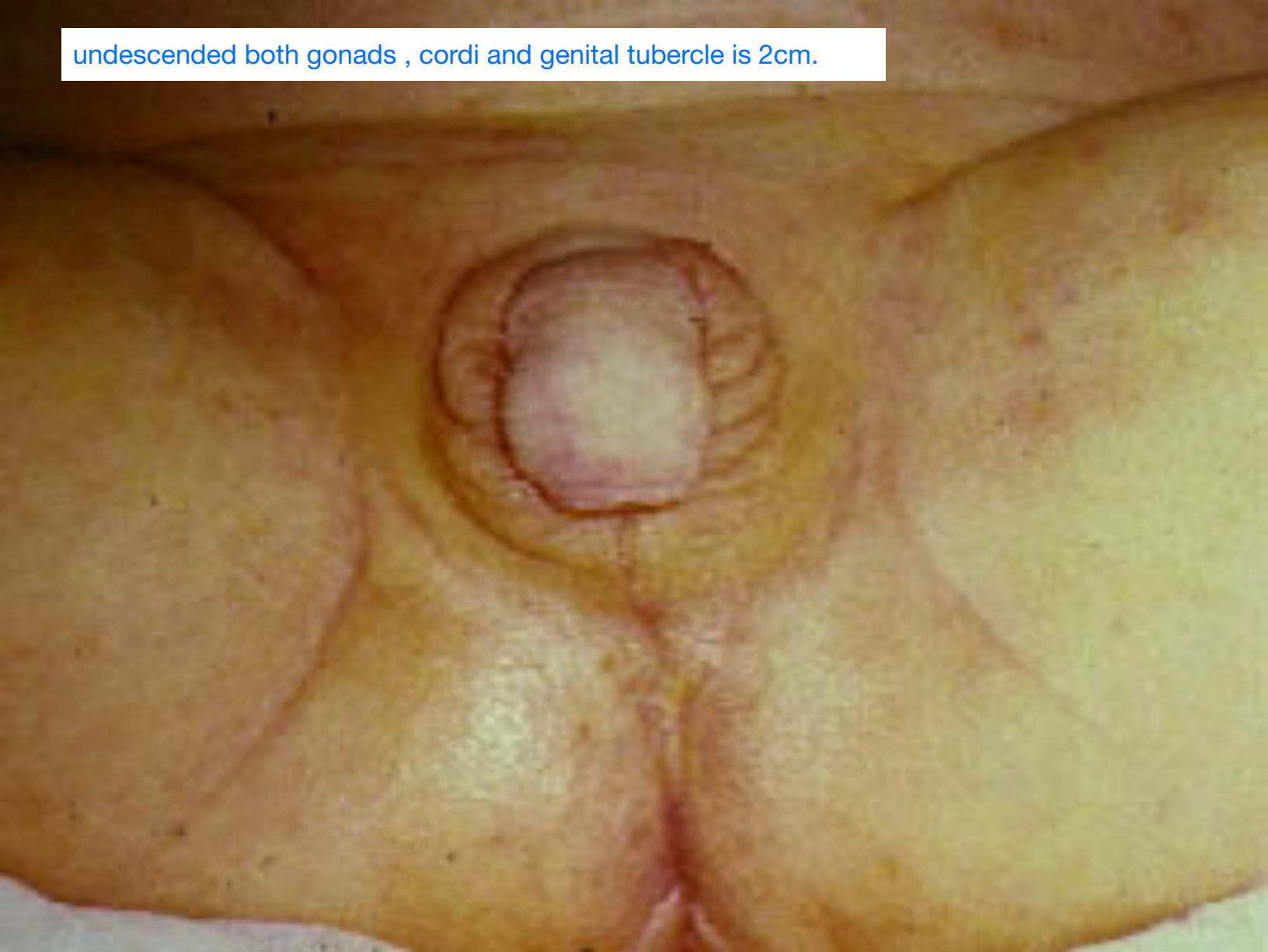
2-genital tubercle

3-labioscrotal folds



The abnormalities in the picture are
1-undescended both gonads
2-cordi
3-hypospadias
And labioscrotal folds not well formed.
So it is ambiguous genitalia.


For this patient, the **length was 2cm and labioscrotal folds** are not fused with some **gonads**, as for the **opening of the urethra you can see it at the bottom**.
There is opening here look like
Vaginal opening or urogenital sinus


undescended both gonads , cordi and genital tubercle is 2cm.

either the patient came early with ambiguous genitalia at birth, or a boy presenting in the 2nd week of birth with salt loosing crisis

Diagnosis

will be very very high if we have 21-OH or11B-OH deficiency

- Serum electrolytes & glucose
  - Low Na & high K
  - Fasting hypoglycemia
- Elevated plasma Renin & ACTH levels
- Low Cortisol
- Low Aldosterone

- High 17 OHP
- High androgens especially testosterone level
- Chromosomes
- Pelvic US

analysis will reflect either a boy or a girl

We ask the US technician to look at Mesonephric (Wolffian) ducts of girls And Paramesonephric (Mullerian) ducts of Boys which are embryological genital.

Management

The way we treat them is similar to Addison disease, take care when they undergo surgeries. The main difference between them is corrective surgeries for the ambiguous genitalia.

- Life-long Hydrocortisone
- Fludrocortisone 0.05 - 0.2 mg/day
- Triple hydrocortisone during stress
- During adrenal crisis intravenous hydrocortisone and IV fliud
- Corrective Surgery for female external genitalia
- Monitor growth

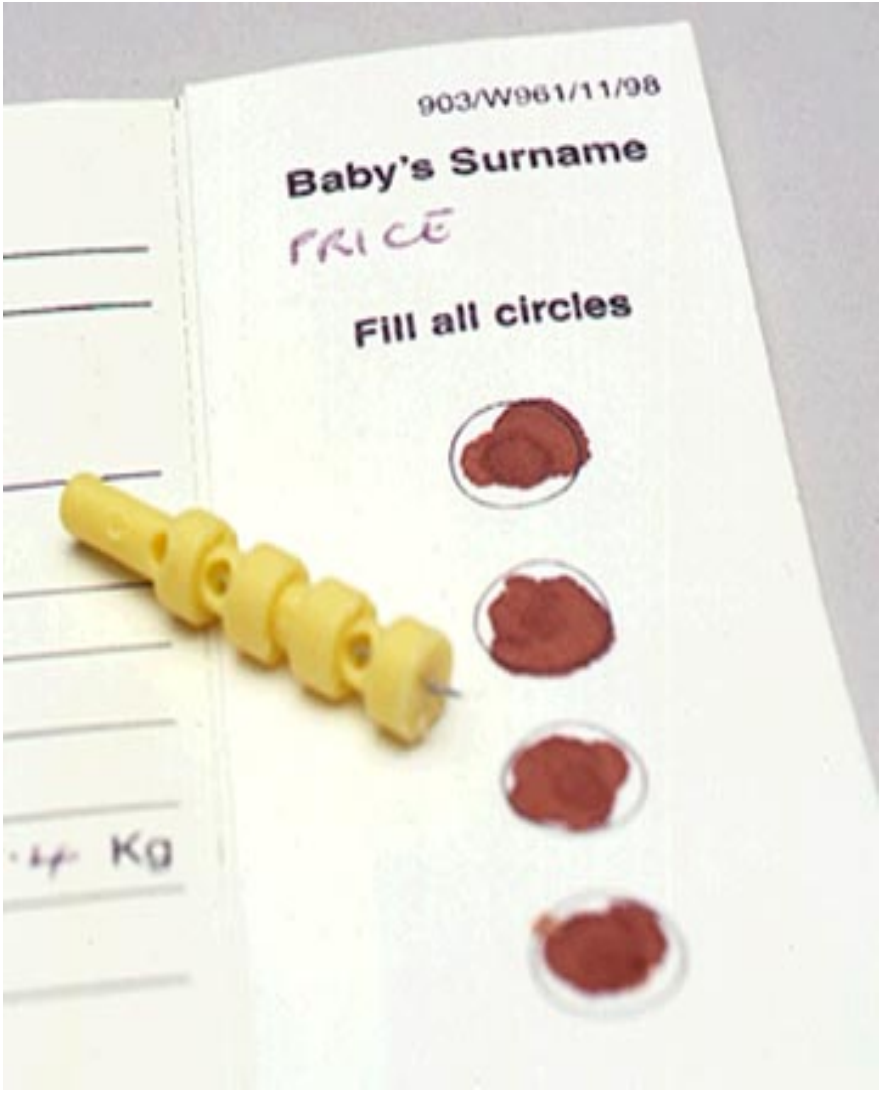
For girl Especially in the case of 21-Hydroxylase or 11B-Hydroxylase deficiency most likely need to female corrective external gentialia surgery. Boys with 17 B-Hydroxylase deficiency the need corrective surgery.

Newborn screening for CAH

very important, if you miss it the baby will die. Females are luckier because of the ambiguous genitalia, while boys are sometimes **missed so they present with adrenal crisis.**

- Neonatal screening by filter paper on 2nd day of life
- 17 Hydroxyprogestrone blood level

  (17 OHP) The will missed 3 ß HSD deficiency


903/W961/11/98
Baby's Surname
PRICE
Fill all circles
Kg

Late Presentations of 21-Hydroxylase

Non-classical CAH

No ambiguous genitalia

- Residual enzyme activity
- Non salt losing CAH

later in childhood

If girls she'll have acne, hair …etc.

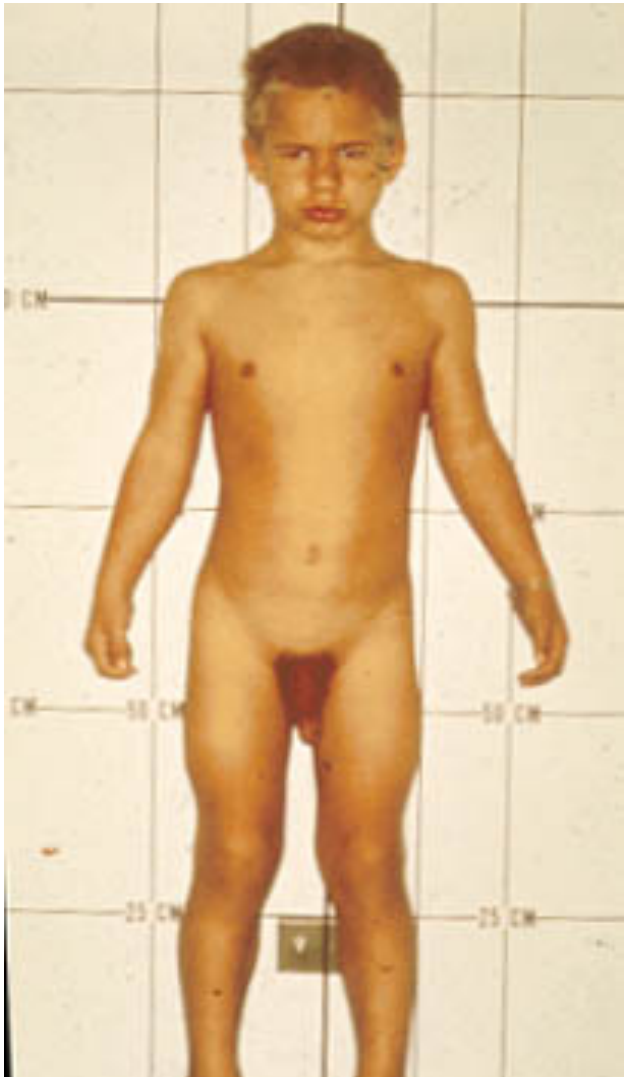
- **early pubic hair**
- **precocious puberty**
- **accelerated growth**

No crisis but they have excess testosterone

adolescence or adulthood

- **Virilization**
- **oligomenorrhea**
- **infertility**

Most misdiagnosed as PCOS



This is a boy presenting with (Non-classical CAH) precocious puberty, you can see the hair, he looks muscular and he is very tall even though he's only 5 years old, but he looks like he's 8.

Questions