Congenital Adrenal Hyperplasia, case presentation

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- 10 – day- old Saudi baby, presented to Emergency room with vomiting & decreased activity for the last 12 hours
- Home delivery
- Product of FT ,SVD ,unknown birth weight
- Mother is not DM or HTN and she doesn't have antenatal care
- The baby didn't cried immediately after birth for 5 min and then after tapping on his back he cried
- Named by his parents as " Ali"

- Vomiting about 7 times /day ,first notice at 4th day of age
- Vomits what ate,not projectile
- Associated with diarrhea with mucus or blood
- No jaundice
- No history of seizure
- No cough /runny nose / sore throat / fever /no hemoptysis
- No change in urine color no loin pain

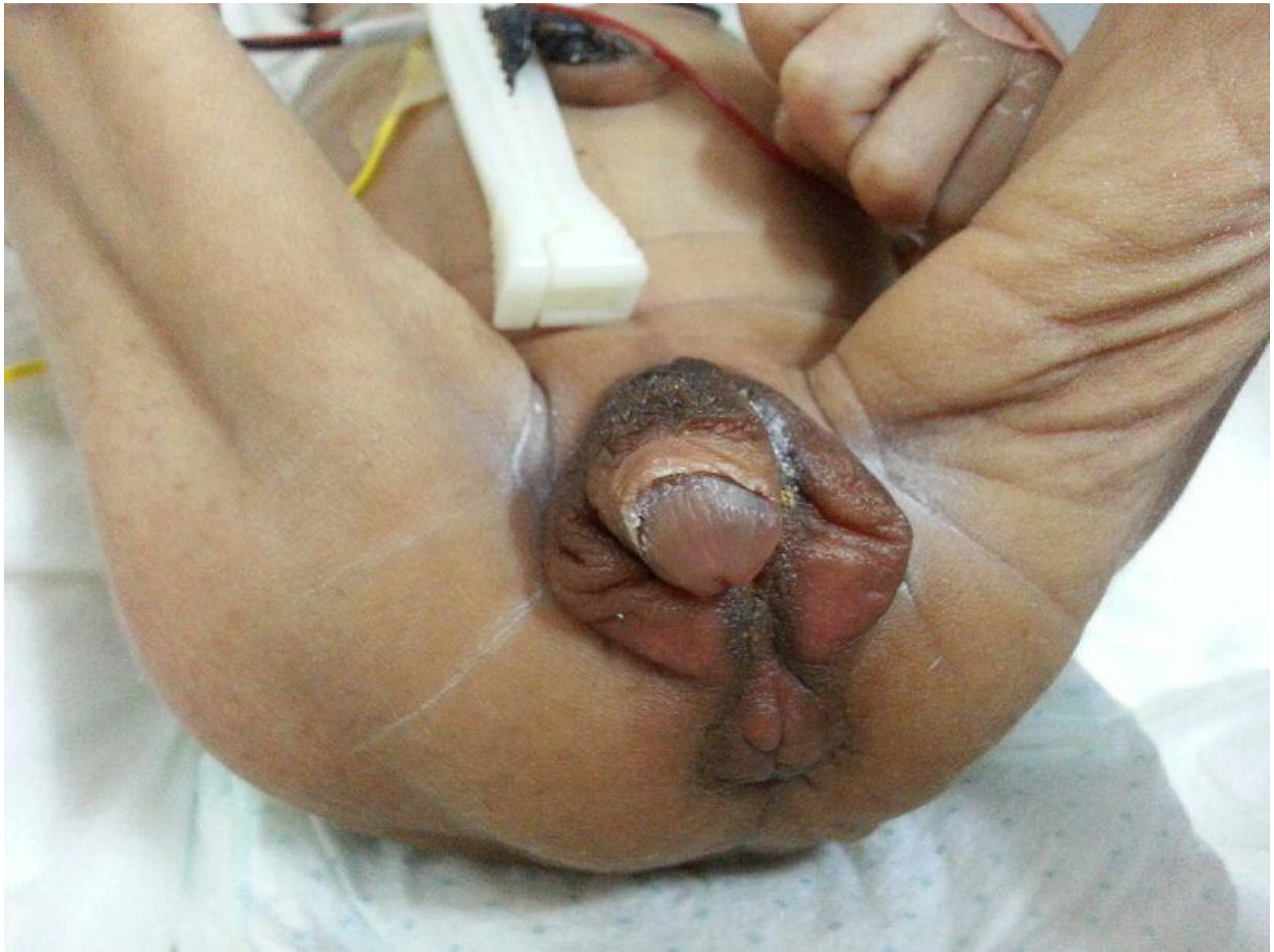
- Family history :Mother and father are 2nd cousins
- Both are medically free
- Two other siblings both of them are
  - healthy
- Social hx: father is smoker ,they live in far town from Jeddah
  - Feeding hx :mother didn‘t breast fed her
  - baby ,was on formula since birth
- Vaccination :up to age (birth vaccines)

- In ER: vitals were
  Hr 144
  - RR 44
  - Temp
  36.4 Bp
  42/26 O2
  95%
- Baby was normal looking, not dysmorphic, conscious, but not active , not alert not on distress
- Systemic Examinations, all were normal

What else you need to look in examination of this baby ???

What is your possible differential diagnoses?

What do you think ??



Investigations

WHAT DO YOU WANT TO DO ?

- **Na 125 mmol/l (135-145)**
  K 5.8 mmol/l (3.5-5)
  Cl 93 mmol/l (95-105)
  Urea 11.4 mmol/ l(1.2-6)
  Creatinine 58 micromol/l (60-120)
  HCO3 11 (22-26)
- **Cortical 8 am 79 nmol /l (125-550)**
- **ACTH 1250 pg /ml (20-35)**
- **Rennin high 1245.9 ng/l**
- **Aldosteron Low 15 ng/l**
- **DHEA high**

17 HYDROXYPROGESTRONE WAS 390 NG/DL (neonate up to 30)

Karyotype !!!!

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Abdominal and pelvic ultrasound

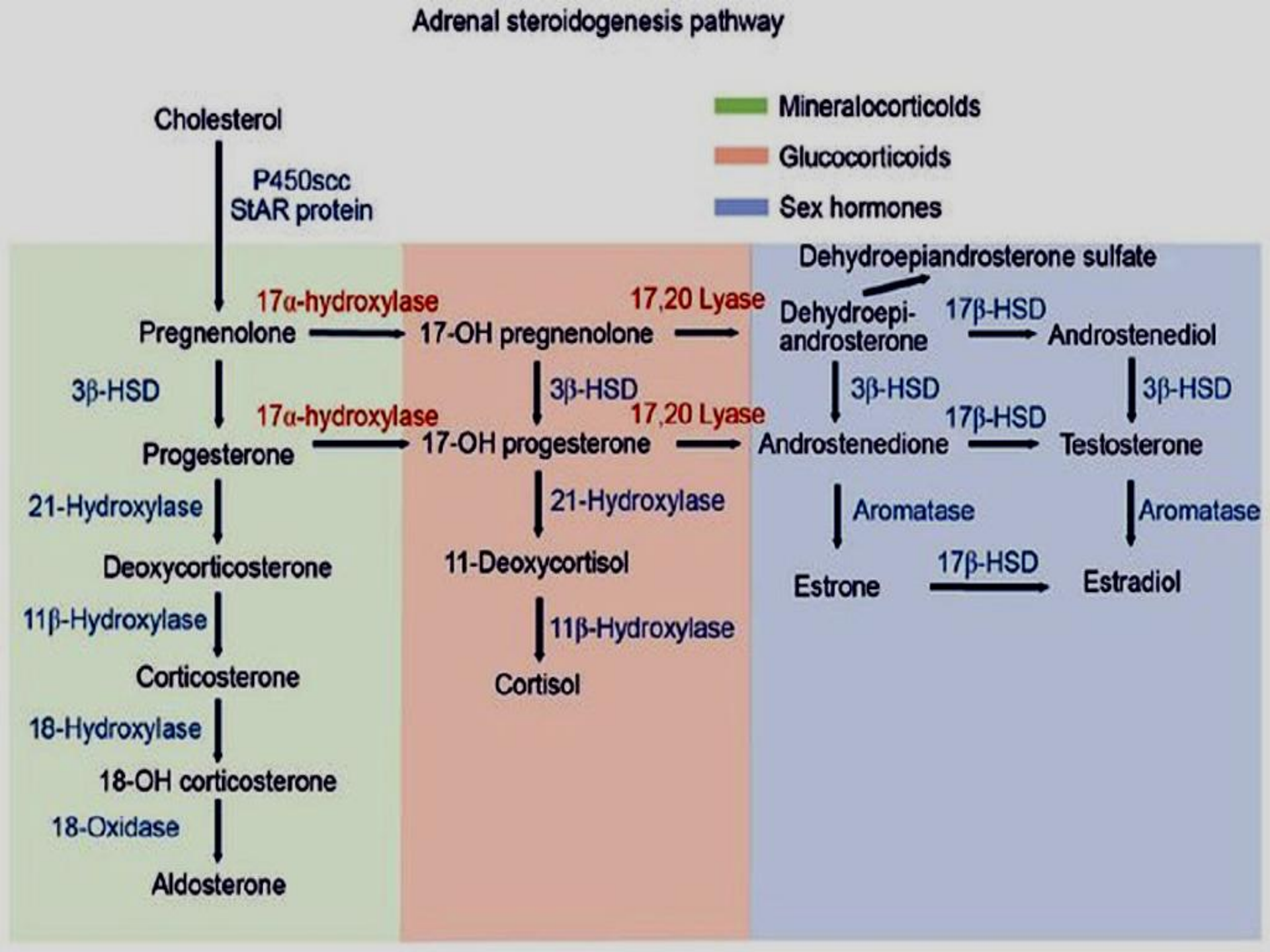
NORMAL FEMALE INTERNAL STRUCTURES

WHAT IS YOUR FINAL DIAGNOSIS?

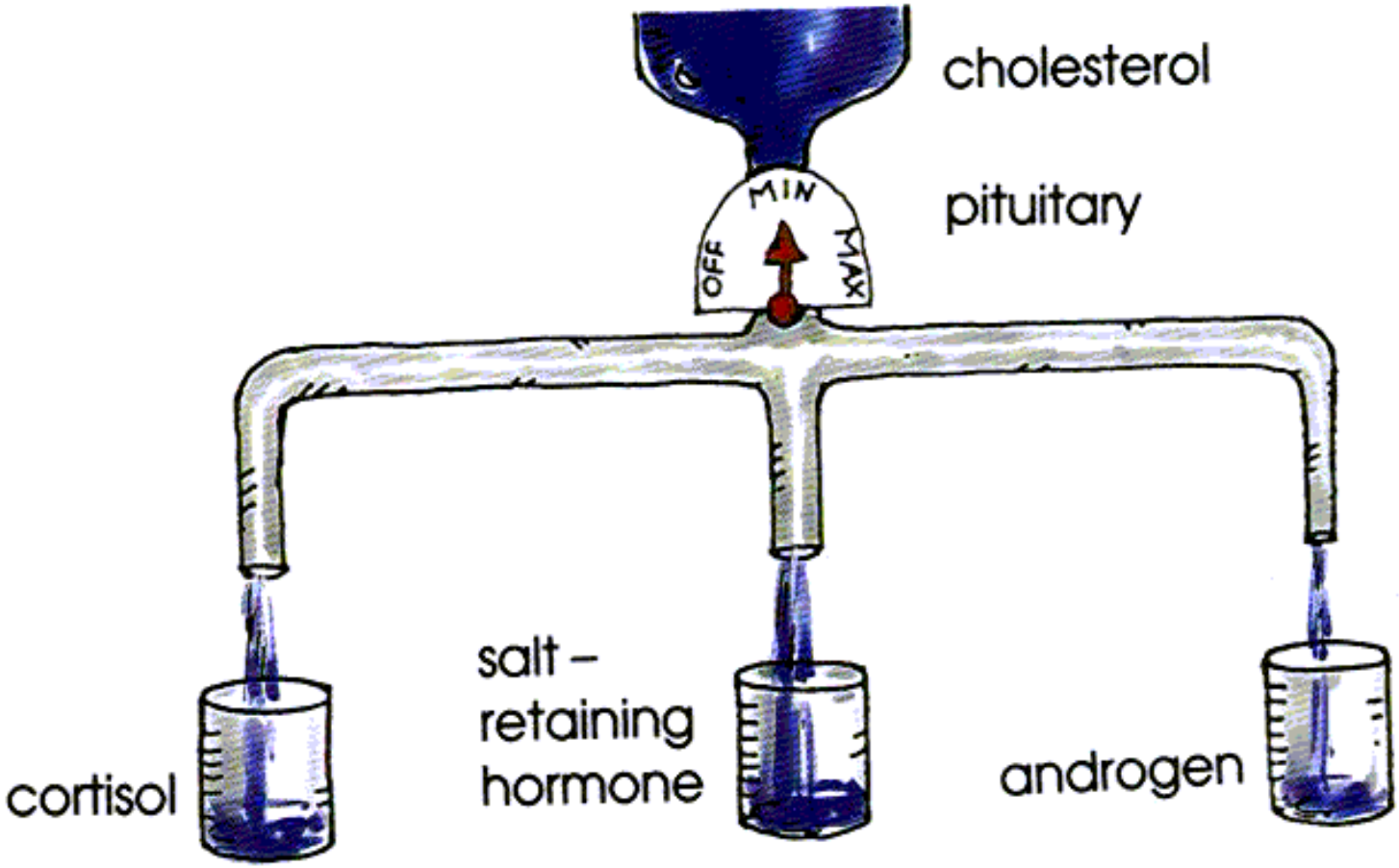
CAH management

Multidisciplinary approach

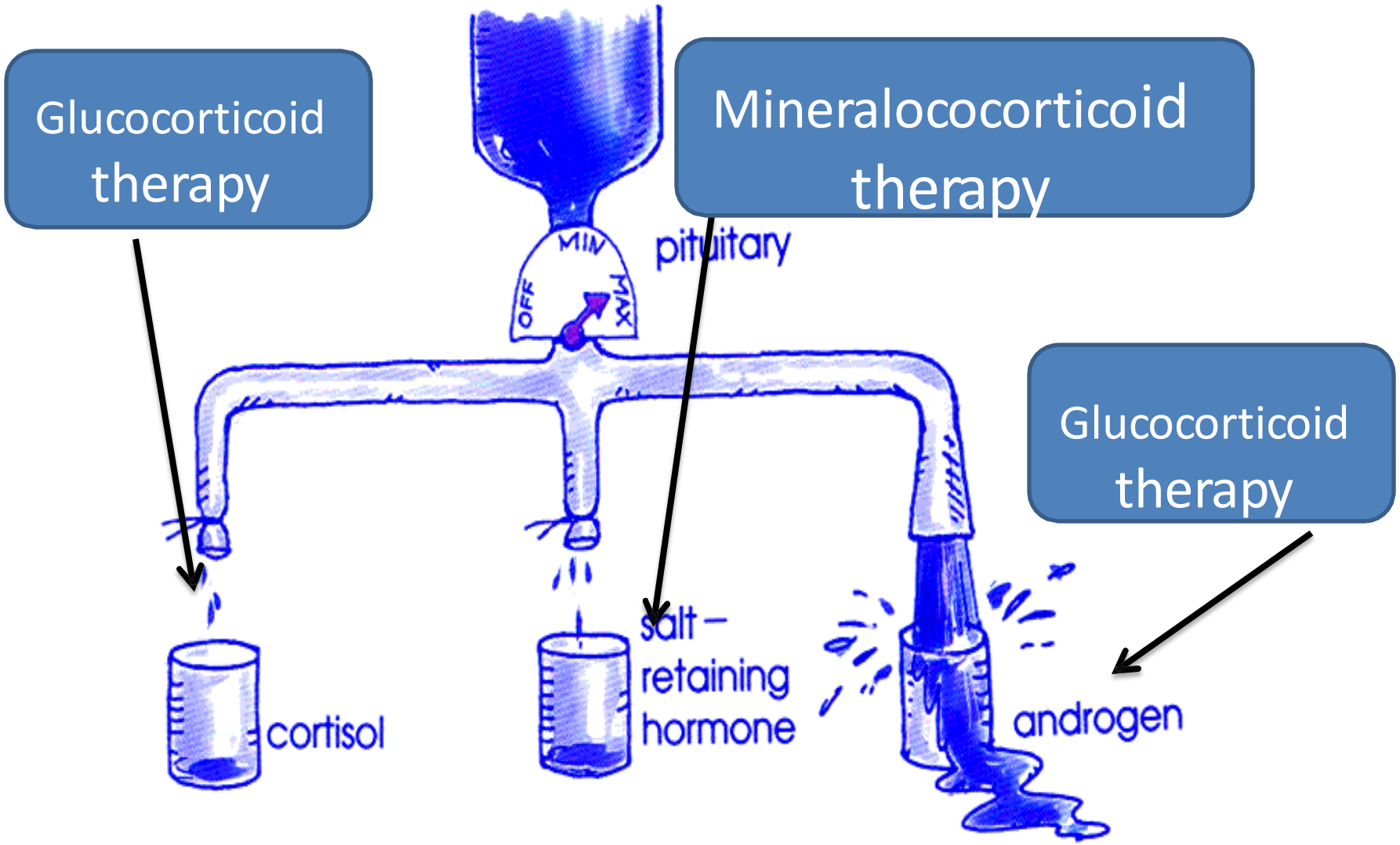
- Medical
- Surgical
- Psychological


Adrenal steroidogenesis pathway
Mineralocorticoids
Glucocorticoids
Sex hormones
Cholesterol
P450scc
StAR protein
Pregnenolone
17α-hydroxylase
17-OH pregnenolone
17,20 Lyase
Dehydroepiandrosterone sulfate
Dehydroepi-androsterone
17β-HSD
Androstenediol
3β-HSD
3β-HSD
3β-HSD
3β-HSD
Progesterone
17α-hydroxylase
17-OH progesterone
17,20 Lyase
Androstenedione
17β-HSD
Testosterone
21-Hydroxylase
21-Hydroxylase
Aromatase
Aromatase
Deoxycorticosterone
11-Deoxycortisol
Estrone
17β-HSD
Estradiol
11β-Hydroxylase
11β-Hydroxylase
Corticosterone
Cortisol
18-Hydroxylase
18-OH corticosterone
18-Oxidase
Aldosterone

Normal Adrenal Cortex Production



Goals of CAH Therapies



Adrenal crisis

- The initial treatment of hypotension and dehydration by intravenous bolus of 10 to 20 ml/kg of normal saline or ringer's lacate should be administered once or repeatedly depending on dehydration status
- An intravenous bolus of 2 to 4 ml/kg of 10 % dextrose should be considered if there is significant hypoglycemia after fluid resuscitation, the preferred type of fluid is 5 % dextrose in normal saline
- Reversal of electrolyte abnormalities
  - Hyponatraemia, hypochloremia and hyperkalemia

- Hypotonic saline should not be used because it can worsen the hyponatraemia; the same is true of 5 % dextrose without the addition of normal saline
- Hyperkalemia should be corrected with the administration of sodium Resonium, bicarbonate infusion, salbutamol and glucose and insulin if necessary
- Metabolic acidosis should be corrected with sodium bicarbonate slow infusions
- Doses of 50-100 mg per square meter per day are given during adrenal crises and life-threatening situations

Goals of glucocorticoid therapy

- Replace the deficient cortisol while minimizing adrenal sex hormone excess
- Preventing virilization
- Optimizing growth
- Protecting potential adulthood fertility

- Despite expert efforts, Outcome sometimes "not always" ideal !!

Consensus Statement from The Lawson Wilkins Pediatric Endocrine Society and The European Society for Pediatric Endocrinology , 2010

- Consensus is based on clinical experience.
- During infancy, initial reduction of markedly elevated adrenal sex hormones may require up to 20 mg hydrocortisone (HC)/m^2·d, but typical dosing is 10–15 mg/m^2·d divided three times daily
- HC oral suspension is not recommended
- Divided or crushed tablets of HC should be used in growing children

- HC is considered the drug of first choice
- Excessive doses, especially during infancy, may cause persistent growth suppression, obesity, and other Cushingoid features
- Complete adrenal suppression should be avoided
- Insufficient data exist to recommend higher morning or evening dosages !!

There are four types of cortisol replacement:

- Hydrocortisone, Cortisone acetate (now rarely available in some countries), Prednisolone and Dexamethasone
- They vary in their dose and duration of action
- Prednisolone is 5 times more potent, and dexamethasone is 40 times more potent than cortisol
- Both prednisolone and dexamethasone are comparatively long acting, where as cortisone acetate and hydrocortisone are shorter acting, and need to be taken 3 times a day

Stress dosing of glucocorticoid

- During periods of stress (surgery, febrile illness, shock), all patients with classical CAH require increased amounts of glucocorticoid
- Typically, 2 to 3 times the normal dose is administered orally, or by intramuscular injection when oral intake is not tolerated or and if there is vomiting or diarrhea
- Up to 5 to 10 times the daily dosage may be required during surgical procedures
- The mineralocorticoid dose does not need to be increased during stress

Stressing dose

- Dose of intravenous bolus of 50-100 mg/m2 stat followed by 100 mg/m2/ day divided into 4 doses
- Guidelines for iv bolus and subsequent dosage are as follows:
  - children younger than 3 yr of age, 25 mg stat followed by 25–30 mg/day
  - children 3–12 yr of age, 50 mg followed by 50–60 mg/d
  - adolescents and adults, 100 mg followed by 100 mg/d

Monitoring

- Successful treatment of affected children hinges on the delicate balance of suppressing adrenal androgen secretion with glucocorticoid administration while maintaining normal growth
- Patients should be monitored carefully for signs of iatrogenic Cushing's syndrome, such as rapid weight gain, hypertension, pigmented striae, and osteopenia

Monitoring

- In growing children, follow-up is every 3 months
- In adolescents, follow-up can be spaced to every 6 to 12 months
- Growth data, pubertal assessment, and blood pressure measurements are necessary for each visit

Monitoring

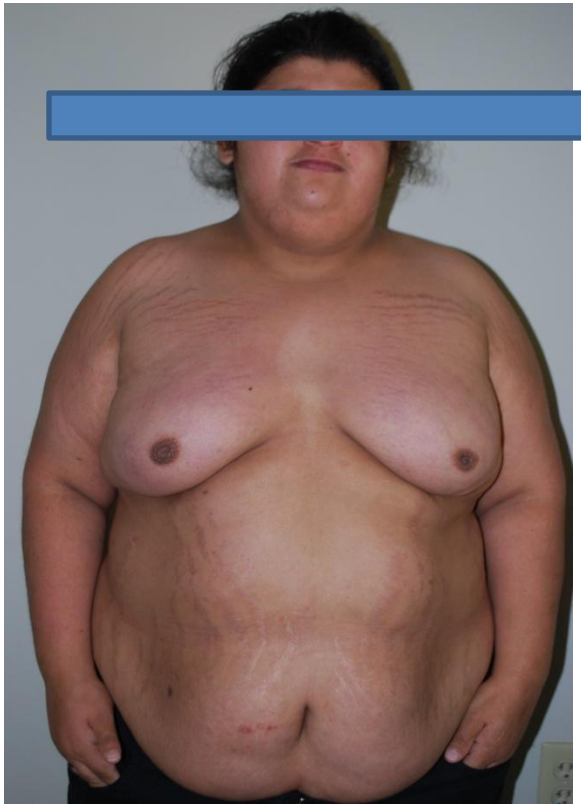
- Serum concentrations of 17-hydroxyprogesterone, delta-4-androstenedione, dehydroepiandrosterone, testosterone and renin are monitored every 6 months
- Bone maturation is assessed by bone age of the left hand, usually annually
- In adolescents, bone mineral density to assess bone strength and imaging of the gonads to assess adrenal rest tumors are performed periodically

- 17-OHP should not return to normal for age levels, but being kept in a reasonable range in the morning before the first therapeutic doses (30–100 nmol/l)
- Testosterone is also a very useful parameter in females at all ages, and in prepubertal boys, and contrary to 17-OHP should be maintained in the normal range for age
- In pubertal females, androstenedione and LH/FSH should be monitored because of the risk of developing polycystic ovaries

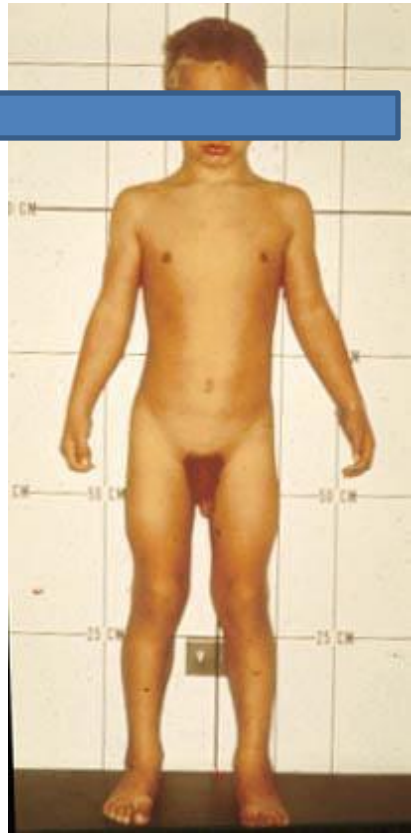
- CAH is associated with short stature in adults even when optimal adrenal hormonal control is maintained throughout childhood and puberty
- Short stature in adulthood due to excess androgens causing precocious puberty and advanced bone age
- optimum glucocorticoid replacement therapy and in some cases a combination treatment of growth hormone and GnRH analogues results in improved final height and reduction of the early onset of puberty, but it is considered experimental

Treatment Balance is Highly Important

Overtreatment



Under treatment



Mineralocorticoid replacement

- The usual pediatric dose of fludrocortisone is 0.05 to 0.2 mg / day
- Infants with the salt-losing may require higher doses of fludrocortisone (occasionally up to 0.3 mg per day)
- Also require sodium chloride supplementation of 1 to 3 g / day (equal to 17 to 51 meq / day) distributed over several feedings

Monitoring of Mineralocorticoid

- Plasma renin activity immunoassays is used to monitor the adequacy of mineralocorticoid
- Hypotension, hyperkalemia, and elevated renin levels suggest the need for an increase in the dose, whereas hypertension, edema, tachycardia, and suppressed plasma renin activity signify overtreatment with mineralocorticoids

This presentation is available at:
Website: http://aagha.kau.edu.sa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