METABOLIC ALKALOSIS

CASE SCENARIOS

Initiating Process

Gain of HCO_3^- — endogenous: metabolism of ketoacids — exogenous: citrate, NaHCO3, lactate, antacid

Loss of H^+ — Renal: diuretics ; GI: vomiting, nasogastric losses

Maintenance Process

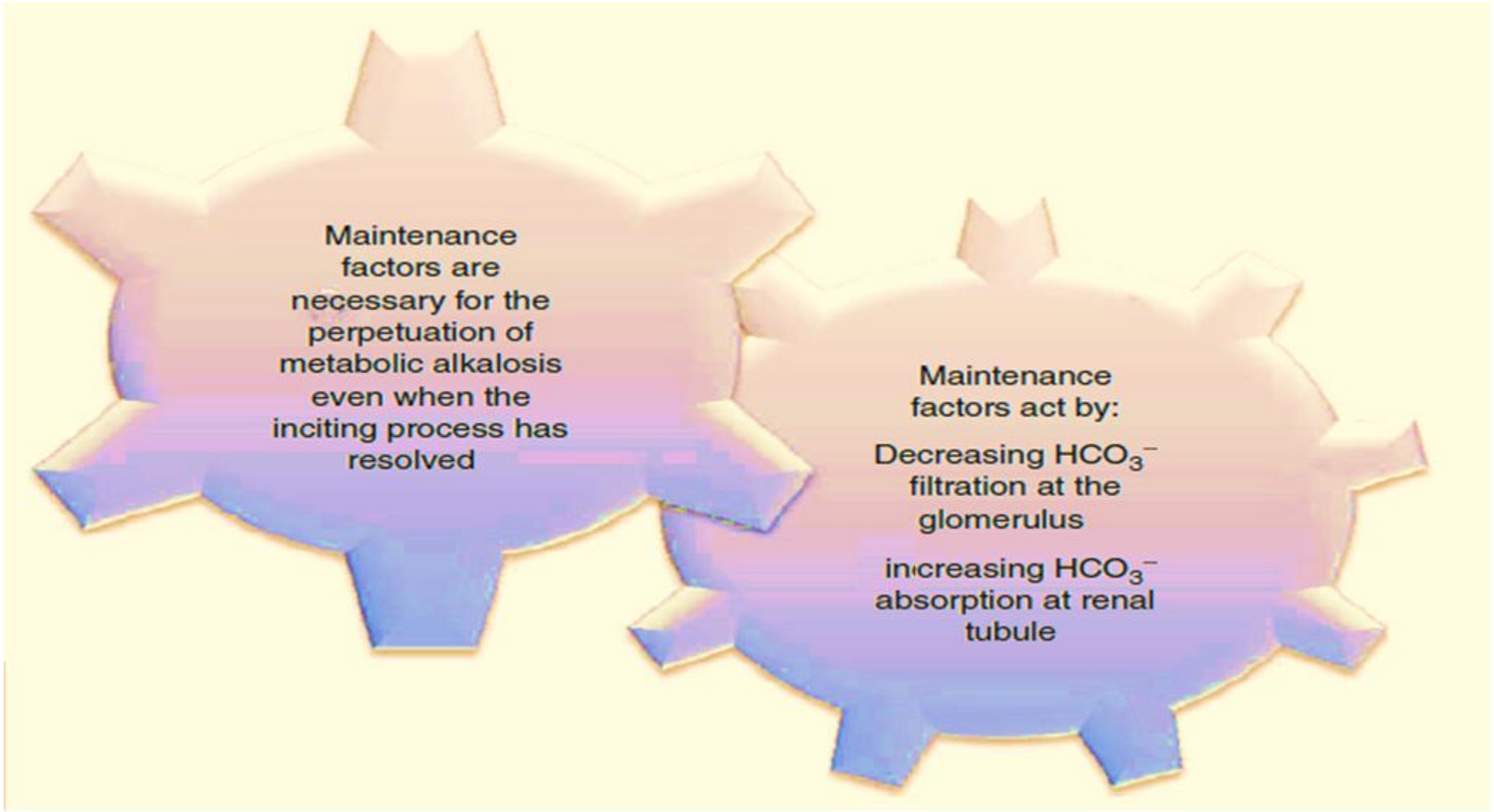
Volume contraction

Hypochloraemia

Hypokalaemia

Hypomagnesaemia

Increased adrenocorticoids (endogenous or exogenous)


Maintenance factors are necessary for the perpetuation of metabolic alkalosis even when the inciting process has resolved
Maintenance factors act by:
Decreasing HCO_3^- filtration at the glomerulus
increasing HCO_3^- absorption at renal tubule

Signs and symptoms

Related to etiology (history of GI/Skin/Renal fluid losses)

Related to complications (hypokalemia- muscle weakness/hypocalcemia-tetany/hypertension-headache,seizures)

Metabolic alkalosis

Chloride responsive	Chloride resistant	
	High Blood Pressure	Normal Blood Pressure
Gastric losses Emesis Nasogastric suction Diuretics (loop or thiazide) Cystic fibrosis Chloride-losing diarrhea Low chloride formula Post hypercapnia	Cushing syndrome Adrenal adenoma/ hyperplasia Glucocorticoid-remediable aldosteronism Renovascular disease Renin-secreting tumor 17α-Hydroxylase deficiency 11β-Hydroxylase deficiency 11β-Hydroxysteroid dehydrogenase deficiency Licorice ingestion Liddle syndrome	Bartter syndrome Gitelman syndrome Autosomal dominant hypoparathyroidism EAST syndrome Base administration

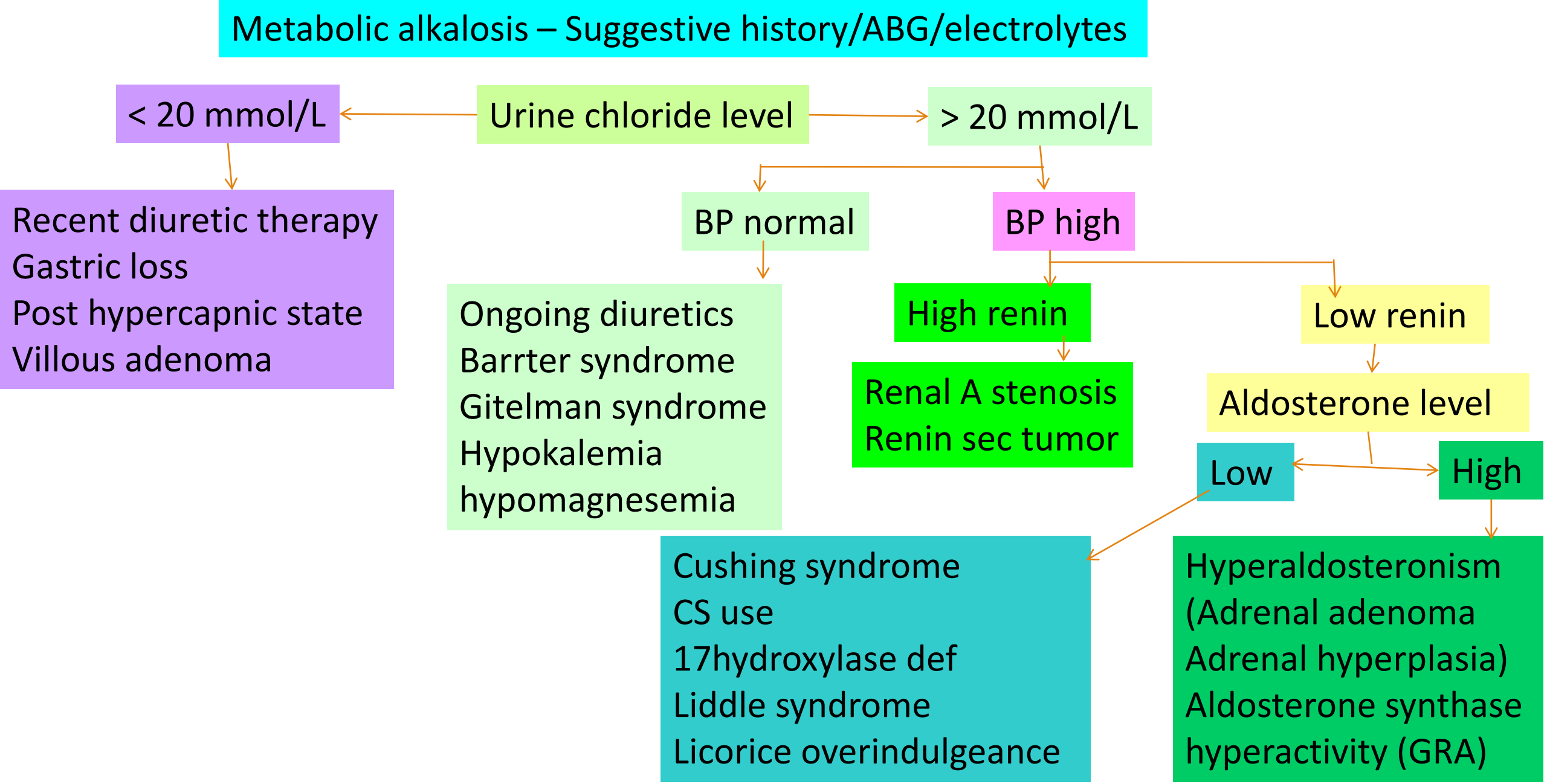
Chloride resistant alkalosis

Urine chloride >20

Hypertension +/-

Renin levels

Aldosterone levels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Urine chloride level
< 20 mmol/L
> 20 mmol/L
Recent diuretic therapy
Gastric loss
Post hypercapnic state
Villous adenoma
BP normal
BP high
Ongoing diuretics
Barrter syndrome
Gitelman syndrome
Hypokalemia
hypomagnesemia
High renin
Renal A stenosis
Renin sec tumor
Low renin
Aldosterone level
Low
High
Cushing syndrome
CS use
17hydroxylase def
Liddle syndrome
Licorice overindulgeance
Hyperaldosteronism
(Adrenal adenoma
Adrenal hyperplasia)
Aldosterone synthase
hyperactivity (GRA)

Case Scenarios

1. Normotensive Chloride resistant metabolic alkalosis

Next 4 children Hypertensive chloride resistant metabolic alkalosis

2. High renin and high aldosterone levels

3. Low renin and low aldosterone levels

4. Low renin and low aldosterone levels

5. Low renin and low aldosterone levels

Case Scenario -1

A 2yr female child is brought with failure to thrive (6 kg , 62 cm), recurrent vomiting since 6 months of age. Was being treated like GER.

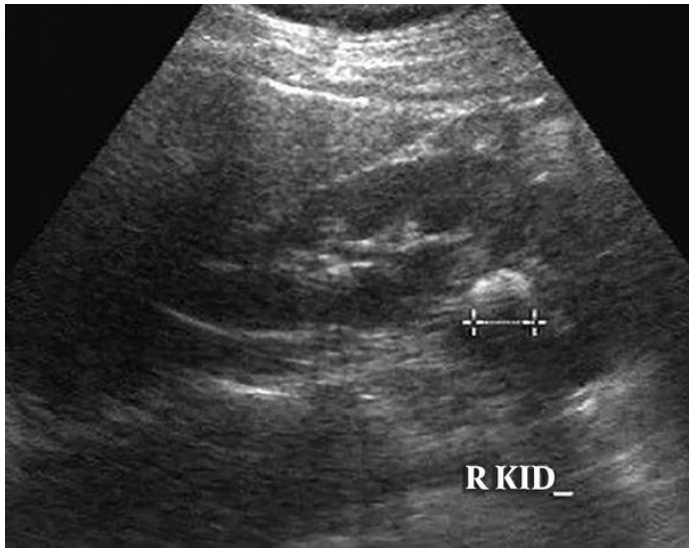
Child had signs of dehydration – despite which had good urine output and with BP 80/50 without features of shock.

Blood Urea, S. creatinine – Normal. Hypokalemia -2 mEq/l, hyponatremia-125 mEq/L, and hypochloremia -63 mEq/l, metabolic alkalosis (pH 7.67, bicarbonate level 38.7, $PaCO_2$ - 33.6) S. Mg 2.0 mg/dl

Given intravenous normal saline along with potassium, antiemetics, and H2-blockers but alkalosis and vomiting persisted

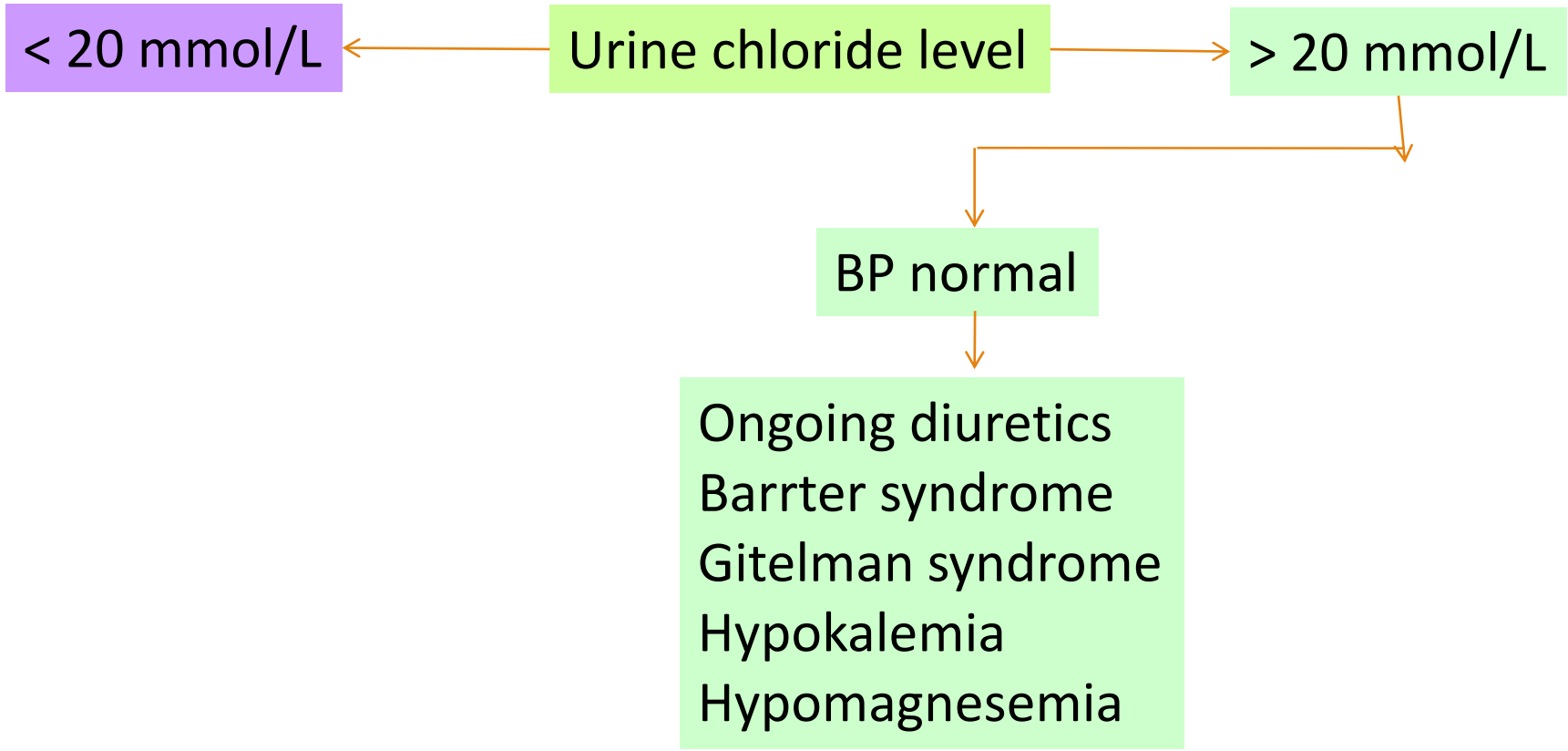
Urine biochemical analysis (sent priorly) showed high sodium (87 mmEq/L), high potassium (38 mEq/L), and high chloride (90 mEq/l) level. Urinary calcium to creatinine ratio was 0.6 and specifific gravity was 1.005.

USG abdomen - Renal ultrasound revealed a renal calculus (measuring 5 x 3.9 mm in size) in the lower calyx of the right kidney with hydronephrosis



Child with FTT- hyponatremic hypochloremic hypokalemic metabolic alkalosis- polyuria-hypercalciuria- renal stone- BARTTER SYNDROME

Metabolic alkalosis – Suggestive history/ABG/electrolytes



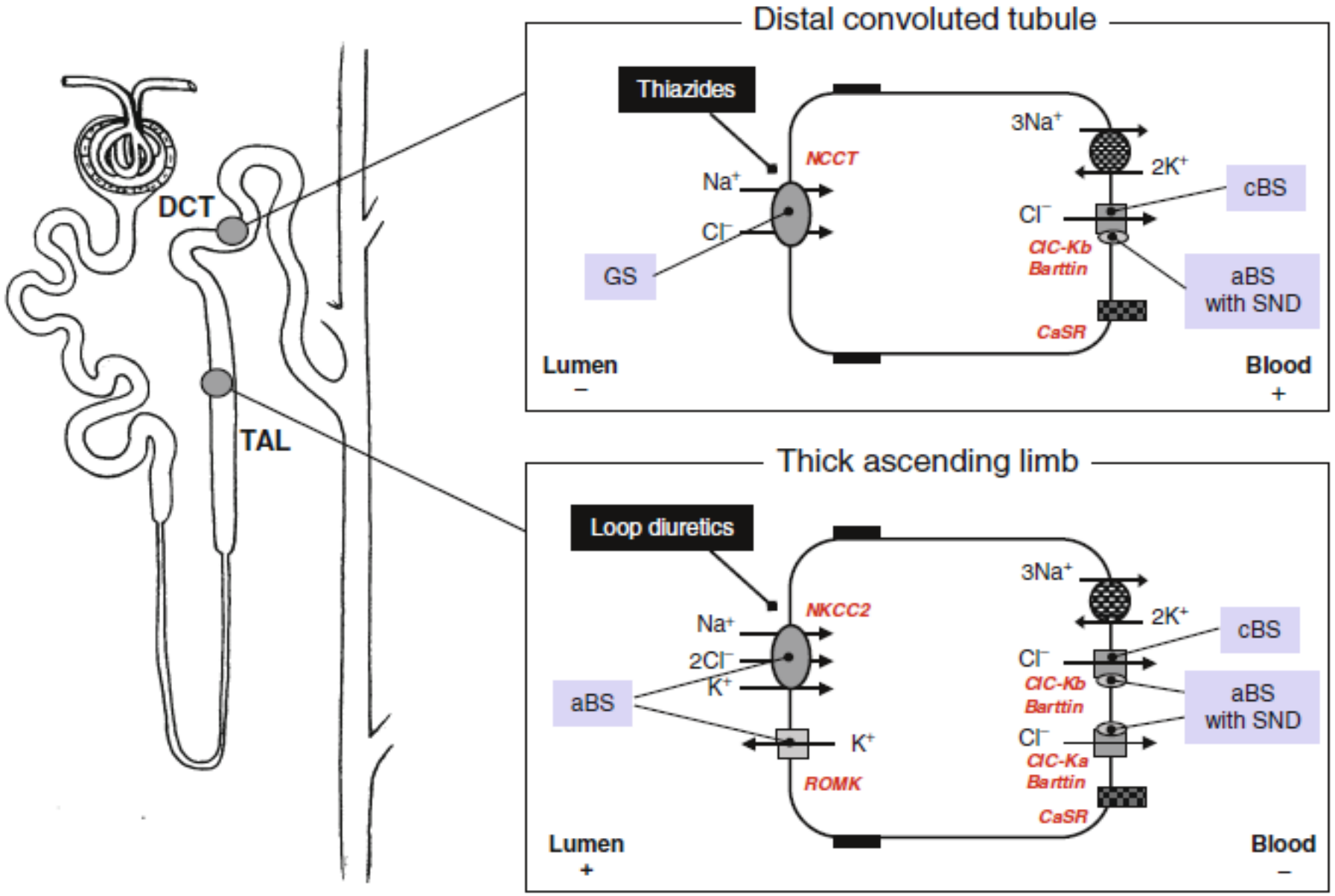
How will be renin, aldosterone levels in them??

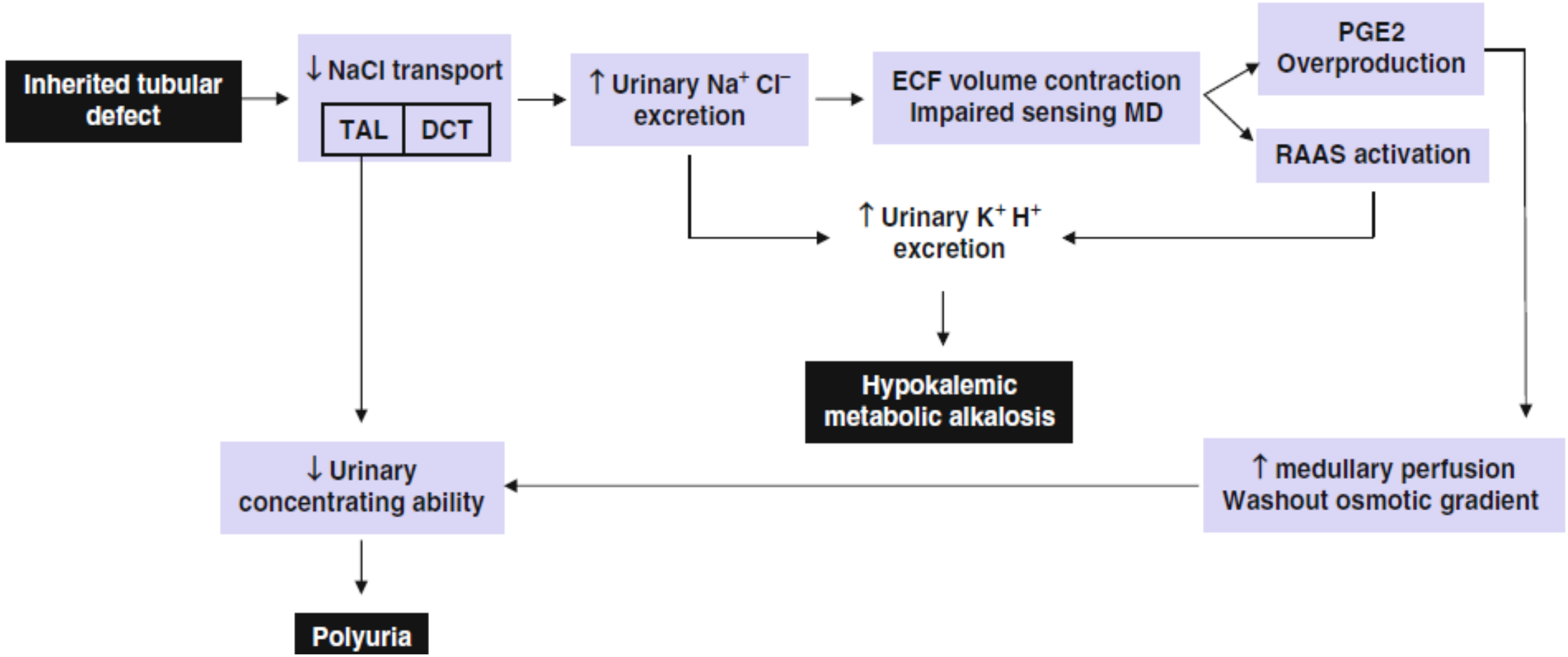
Why are they not hypertensive then?

Why hypercalciuria occur in Bartter syndrome?

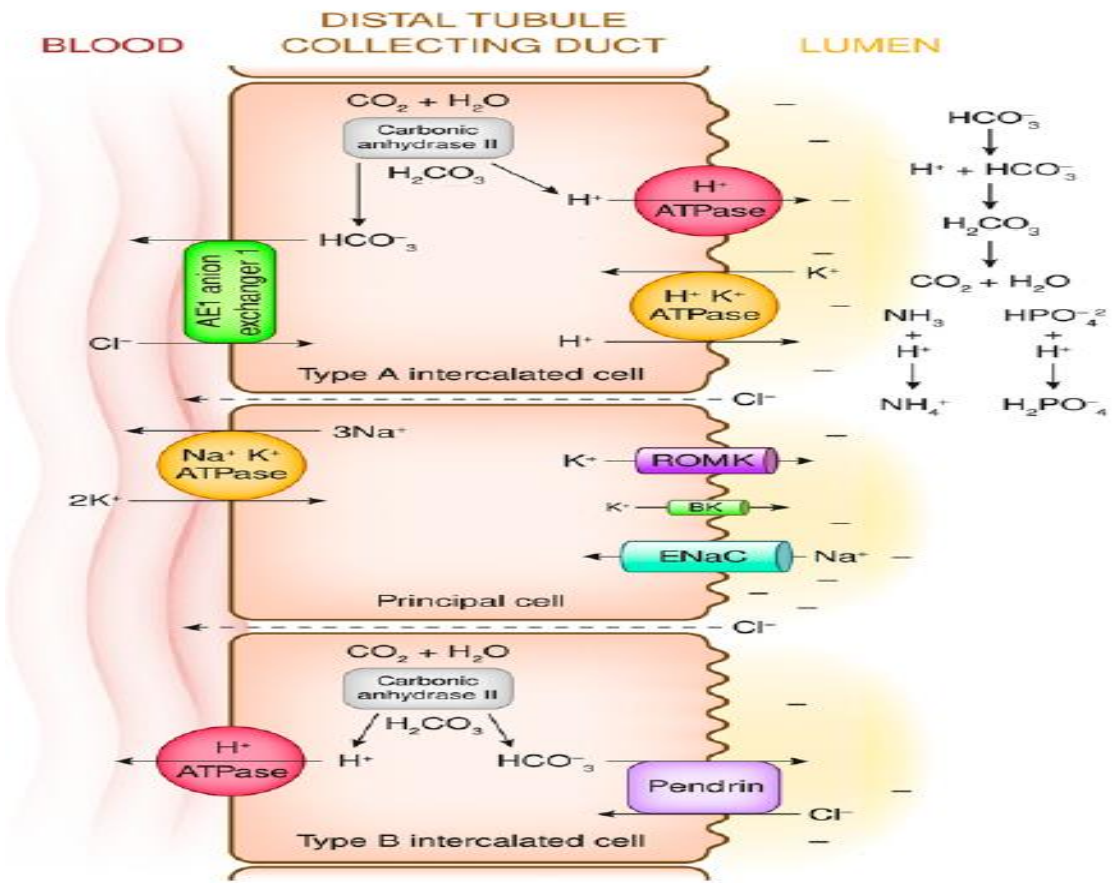
What is the relation between Potassium and Hco3?

What is the relation between chloride and Hco3?


DCT
TAL
Distal convoluted tubule
Thiazides
NCCT
Na+
Cl−
GS
3Na+
2K+
cBS
Cl−
ClC-Kb
Barttin
aBS
with SND
CaSR
Lumen
−
Blood
+
Thick ascending limb
Loop diuretics
NKCC2
Na+
2Cl−
K+
aBS
K+
ROMK
3Na+
2K+
cBS
Cl−
ClC-Kb
Barttin
aBS
with SND
Cl−
ClC-Ka
Barttin
CaSR
Lumen
+
Blood
−


Inherited tubular defect
↓ NaCl transport
TAL
DCT
↑ Urinary Na^+ Cl^- excretion
ECF volume contraction
Impaired sensing MD
PGE2 Overproduction
RAAS activation
↑ Urinary K^+ H^+ excretion
Hypokalemic metabolic alkalosis
↓ Urinary concentrating ability
↑ medullary perfusion
Washout osmotic gradient
Polyuria

Potassium and alkalosis



Hypokalemia

K^+ migrates out of the intracellular compartment. H^+ migrates into the intracellular compartment to maintain electro-neutrality. Intracellular acidosis results.

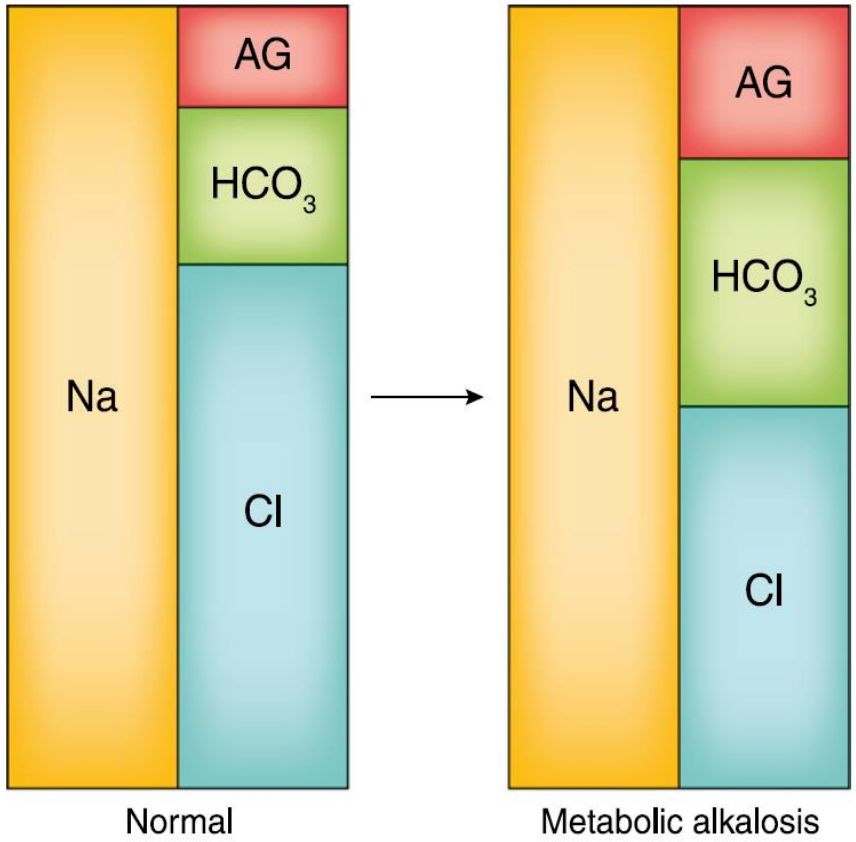
Increased activity of H^+K^+ATP-ase pump

H^+ secretion and HCO_3^- absorption

Increased H^+ secretion

metabolic alkalosis

Chloride and alkalosis

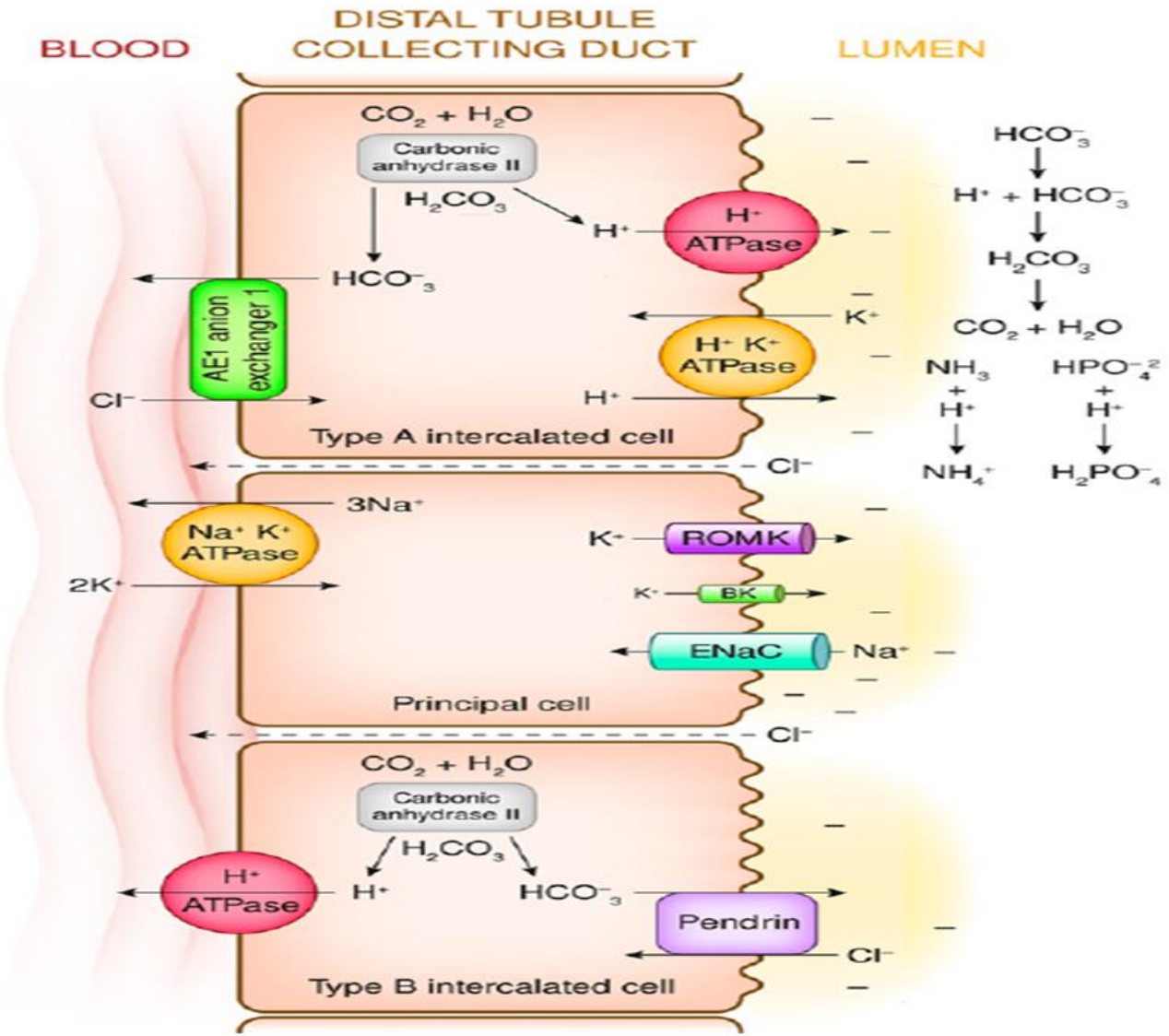


Hypochloremia

Hypochloremia usually occurs secondary to chloride depletion. Chloride depletion has a powerful effect in maintaining metabolic alkalosis.

Type A intercalated cells of the collecting tubule: Increased bicarbonate reabsorption.

Type B intercalated cells of the collecting tubule: Decreased bicarbonate secretion.



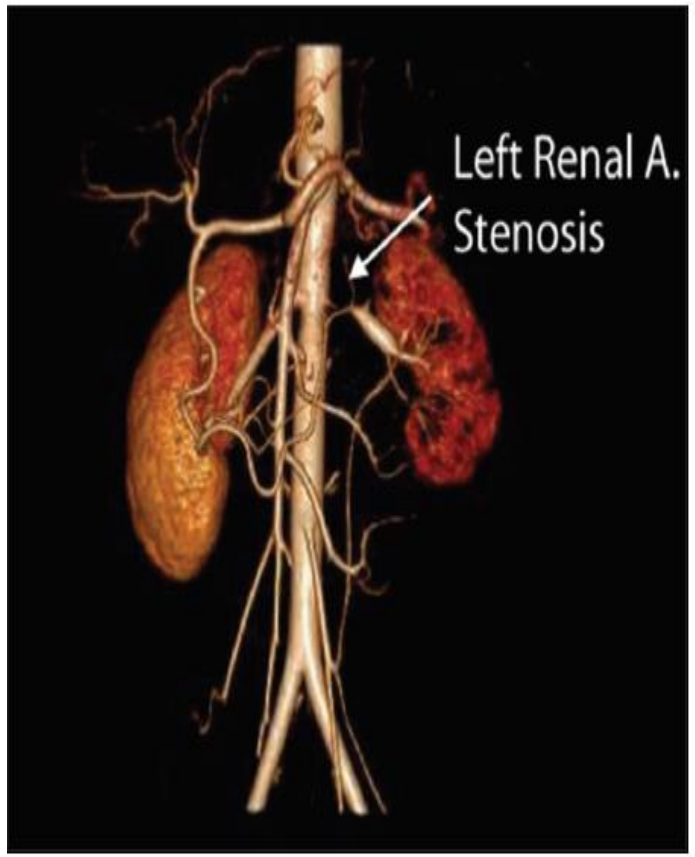
Case Scenario -2

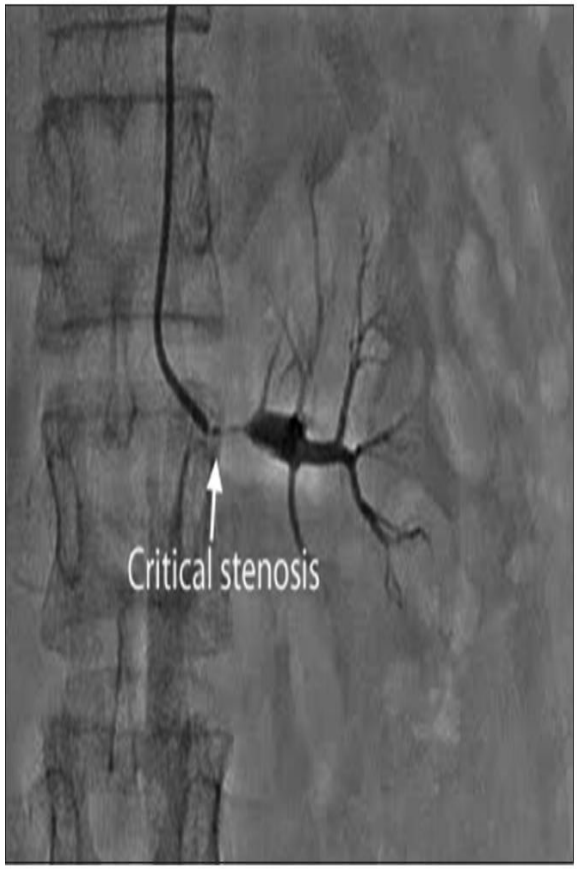
14 year old girl with headache

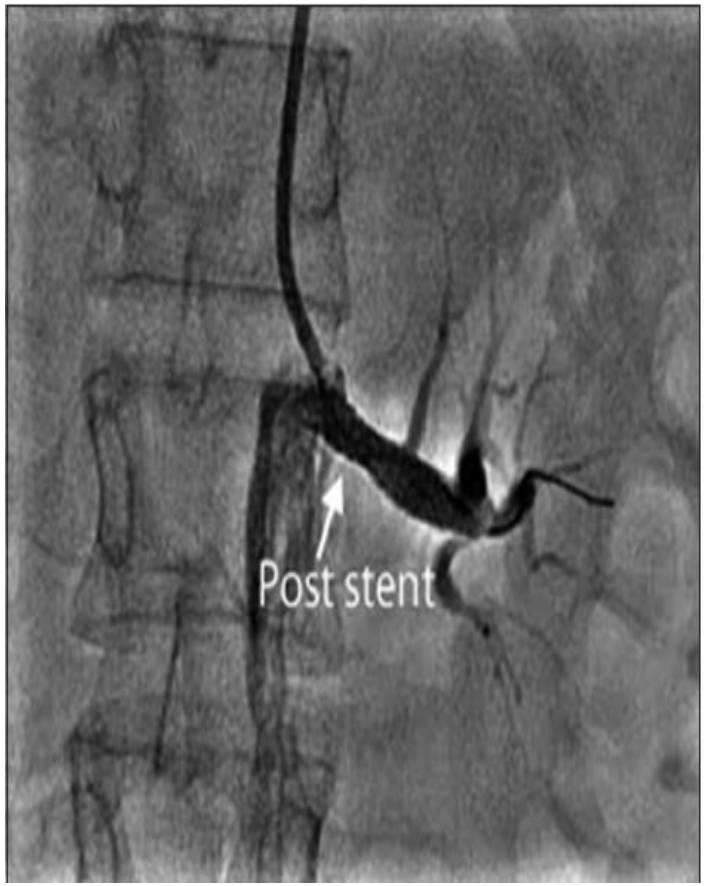
Found to have stage 2 hypertension with LVH. Had abdominal bruit in Left loin without any abdominal mass. Blood tests reveal – Na -140, K -3.2, Cl- 90, Hco3- 30 (Hypokalemia with metabolic alkalosis). Serum renin levels are high.

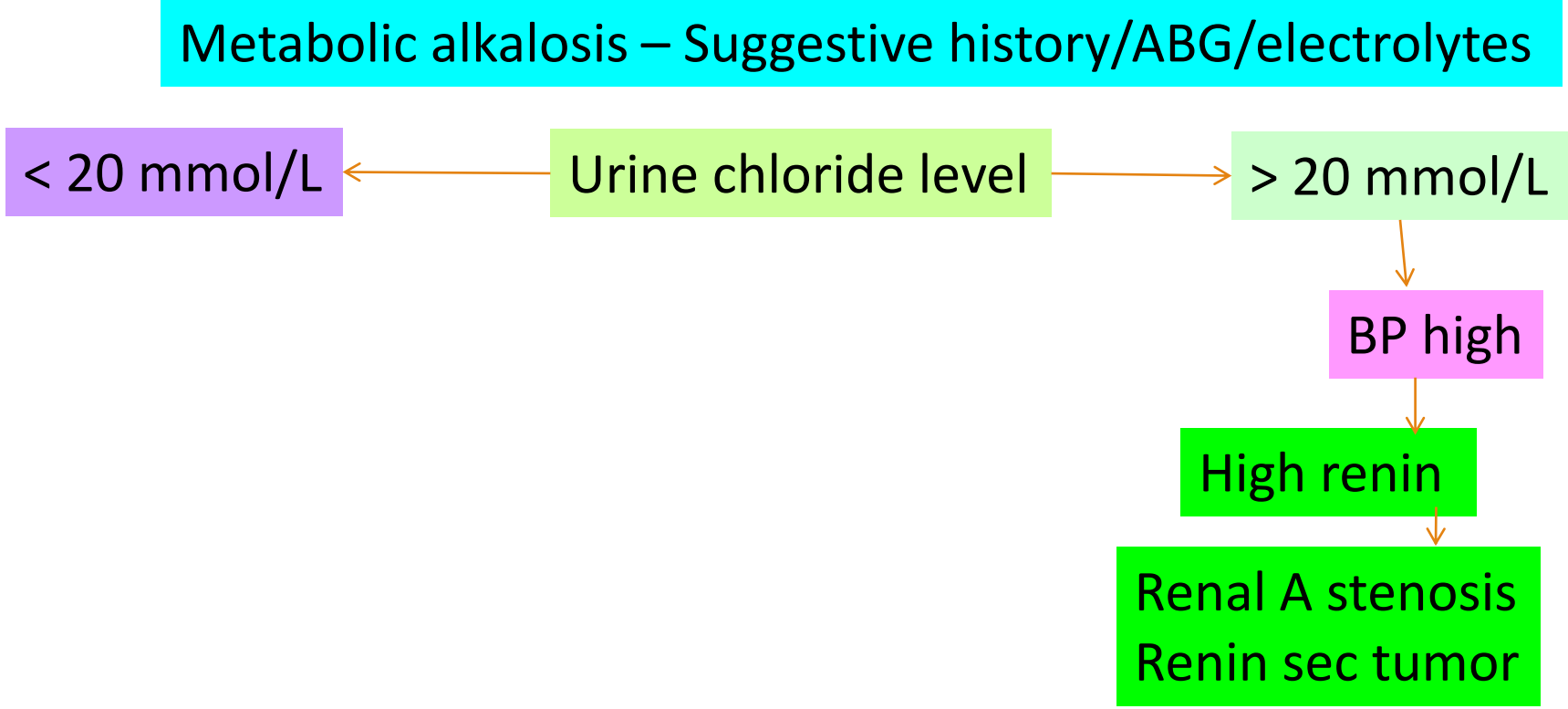
Child with hypertension-hypokalemic metabolic alkalosis- renal artery bruit – high renin levels – RENAL ARTERY STENOSIS

USG KUB with Doppler done – asymmetric kidney with restricted blood flow in left kidney- confirmed with CT Angiogram . Both renin and aldosterone levels are high
Post stenting-Hypertension and electrolyte abnormalities improved.








Metabolic alkalosis – Suggestive history/ABG/electrolytes
< 20 mmol/L
Urine chloride level
> 20 mmol/L
BP high
High renin
Renal A stenosis
Renin sec tumor

Case Scenarios -3

14-year-old girl born out of consanguineous marriage presented with acute onset quadriparesis. Her BP 160/100. She had delayed puberty with stage 1 breast development with normal stature

Investigations revealed hypokalemia (1.9 meq/L), metabolic alkalosis (pH, 7.6, HCO_3, 30 mmol/L, $PaCO_2$ 40 mmHg).

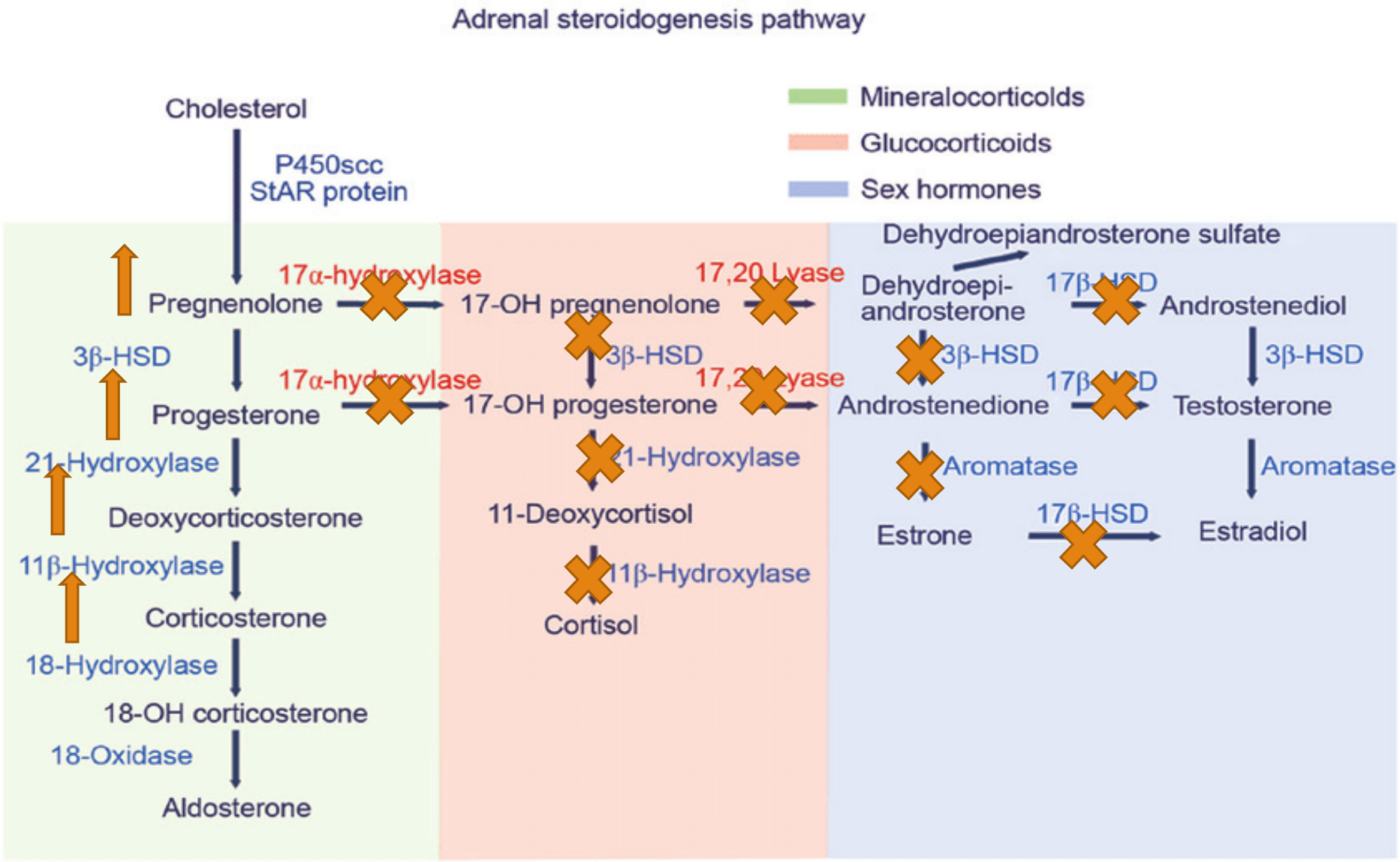
Other investigations were low serum cortisol (1.5 mcg/dL), high ACTH (513 pg/mL), and high FSH (45 mIU/L). Her karyotype was 46XX and serum progesterone was elevated (8.5 ng/mL, normal < 1.5 ng/mL).

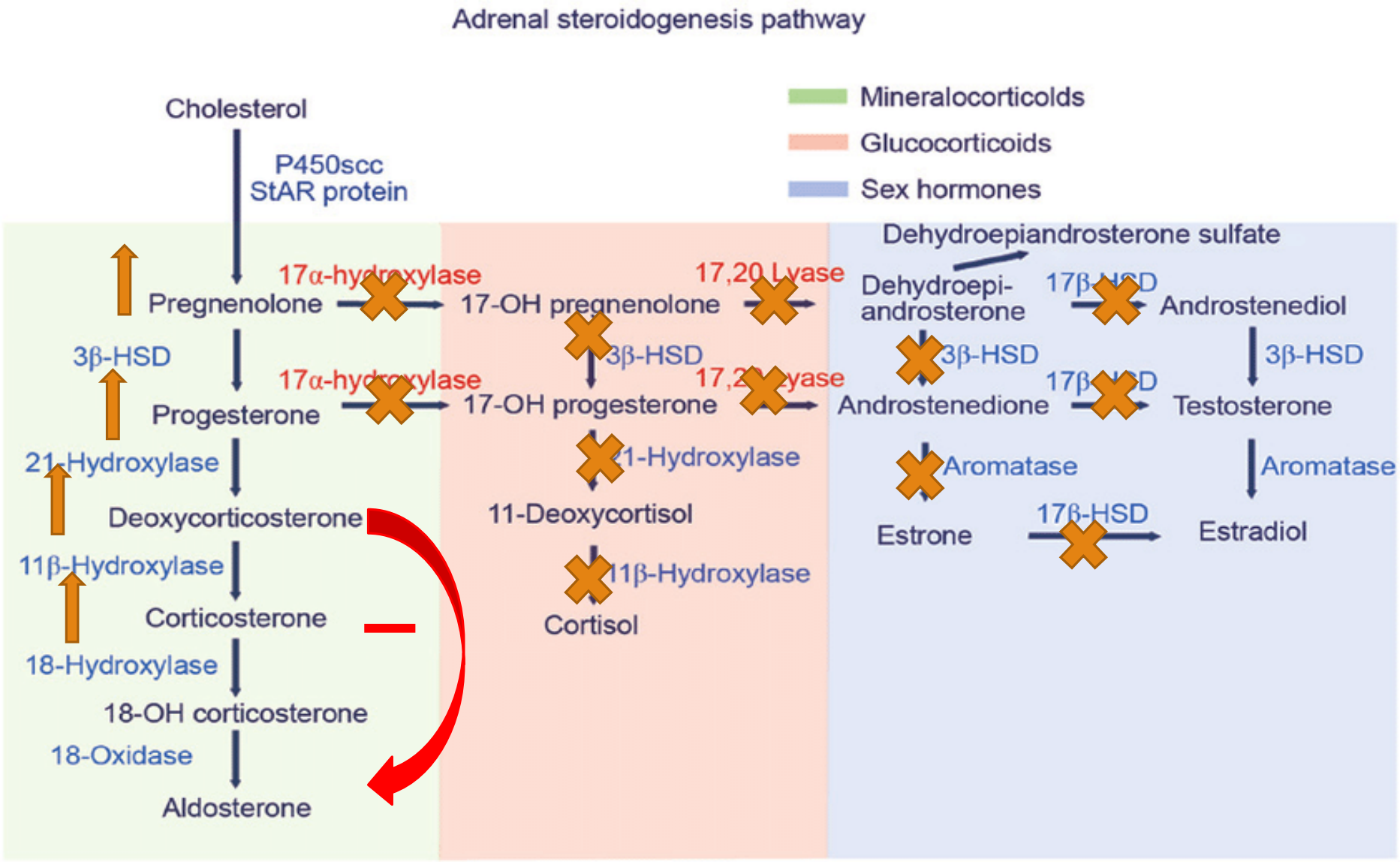
Hypergonadotropic hypogonadism (primary amenorrhea, breast B1 stage with high FSH)

Adrenal insufficiency (low cortisol with high ACTH) and

Hypertension with metabolic alkalosis (signifying mineralocorticoid excess) in a girl of pubertal age suggest 17-α-hydroxylase deficiency

Potassium supplementation, prednisolone, ethinyl estradiol, and amlodipine (during acute phase)


Adrenal steroidogenesis pathway
Mineralocorticolds
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
Progesterone
17α-hydroxylase
17-OH progesterone
17,20 Lyase
Androstenedione
17β-HSD
Testosterone
21-Hydroxylase
21-Hydroxylase
Deoxycorticosterone
11-Deoxycortisol
Aromatase
Aromatase
11β-Hydroxylase
Corticosterone
11β-Hydroxylase
Cortisol
Estrone
17β-HSD
Estradiol
18-Hydroxylase
18-OH corticosterone
18-Oxidase
Aldosterone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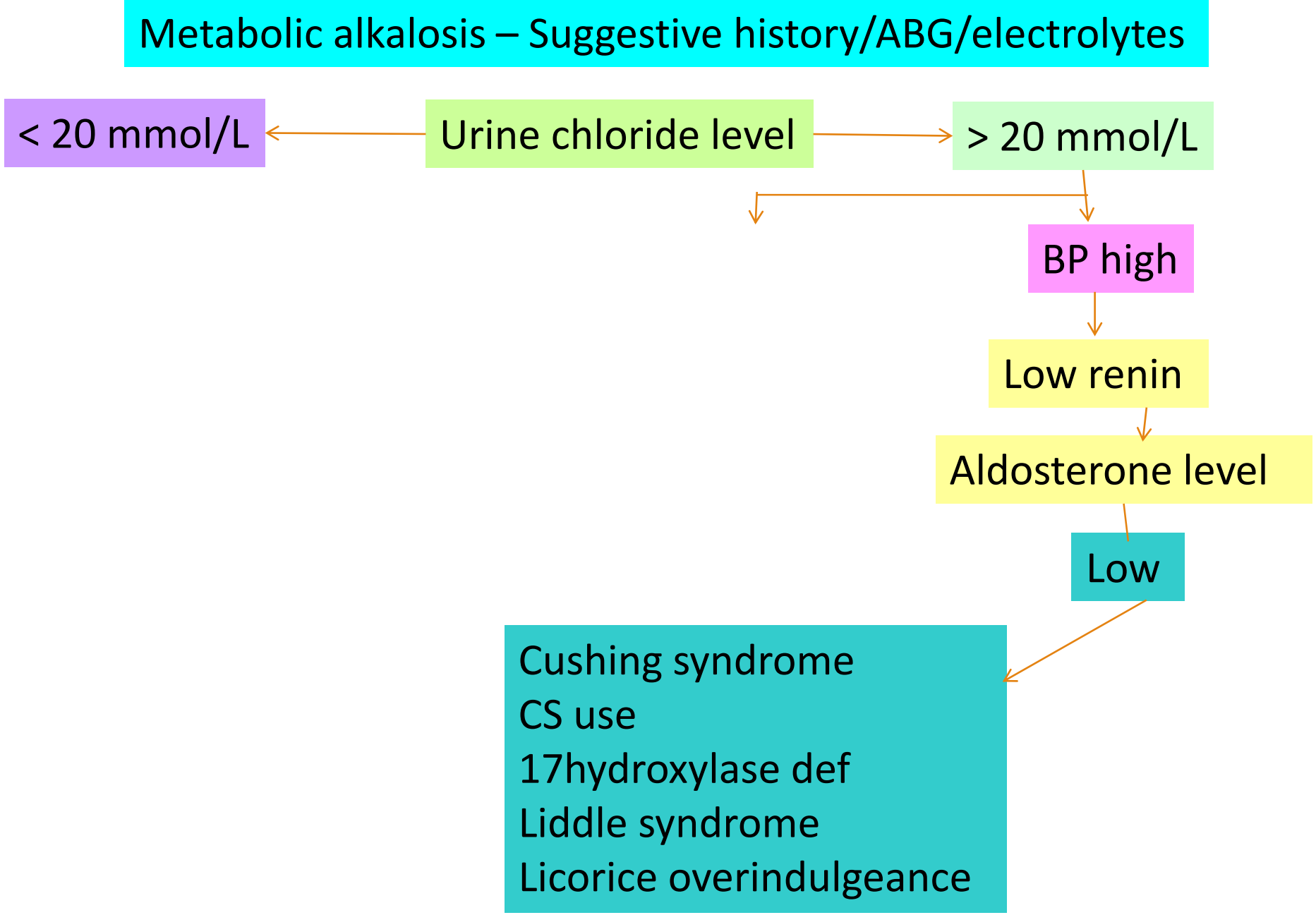
Dehydroepiandrosterone sulfate
Dehydroepi-
androsterone
17β-HSD
Androstenediol
3β-HSD
3β-HSD
3β-HSD
Progesterone
17α-hydroxylase
17-OH progesterone
17,20 Lyase
Androstenedione
17β-HSD
Testosterone
21-Hydroxylase
21-Hydroxylase
Aromatase
Aromatase
Deoxycorticosterone
11-Deoxycortisol
Estrone
17β-HSD
Estradiol
11β-Hydroxylase
11β-Hydroxylase
Corticosterone
Cortisol
18-Hydroxylase
18-OH corticosterone
18-Oxidase
Aldosterone


Metabolic alkalosis – Suggestive history/ABG/electrolytes
< 20 mmol/L
Urine chloride level
> 20 mmol/L
BP high
Low renin
Aldosterone level
Low
Cushing syndrome
CS use
17hydroxylase def
Liddle syndrome
Licorice overindulgeance

Case Scenario-4

14 year old girl with headache, dizziness, blurred vision and involuntary twitching movement of face and spasm of hands. Found to have Stage 2 HTN, normal development.

Family history of early-onset hypertension in the mother

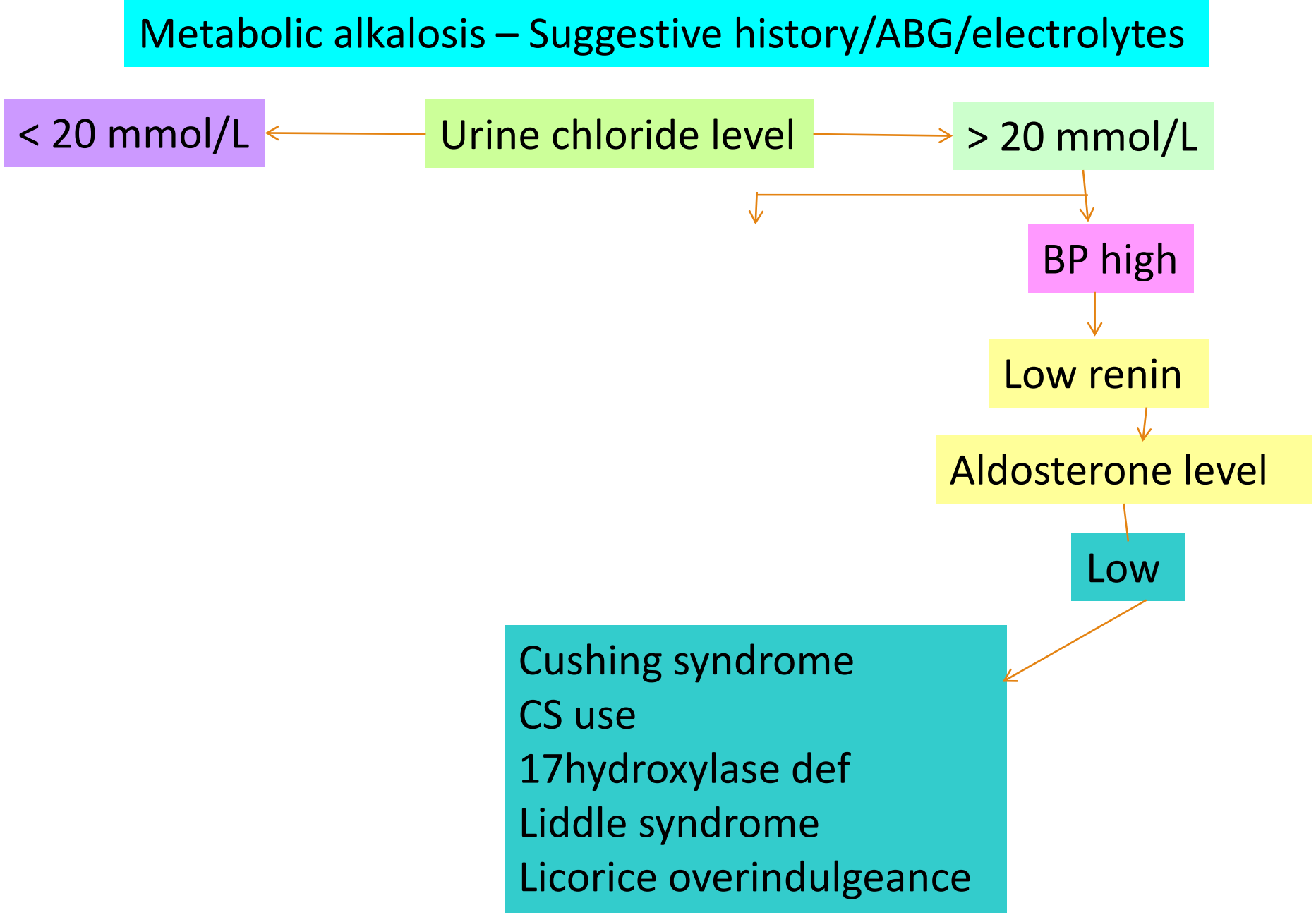
Investigations : elevated Na-149 mmol/L and hypokalemia (3.1 mmol/L) with a increased bicarbonate (32 mmol/L), normal urea and creatinine with ica- 0.7 and S. calcium 9.0

Further HTN workup – LVH in EKG and echocardiogram, normal renal ultrasound and MAG-3 renal scan without evidence of renal artery stenosis.

Renin was low at < 0.1 ng/mL/h and aldosterone low at < 3.0 ng/dL. (Thyroid function, metanephrines, and free cortisol - Normal)

Hypertension not controlled with low salt diet or mineralocorticoid antagonist but responded well to amiloride

Child with hypertension-hypokalemic metabolic alkalosis- significant family history of early onse HTN- Decreased renin and aldosterone normal cortisol- A monogenic hypertension – HTN controlled with amiloride -genetic panel was sent SCNN1B mutation s/o LIDDLE SYNDROME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Case Scenario-4

Why this child present with features of hypocalcemia?

Case Scenario -5

14 yr girl found to be hypertensive

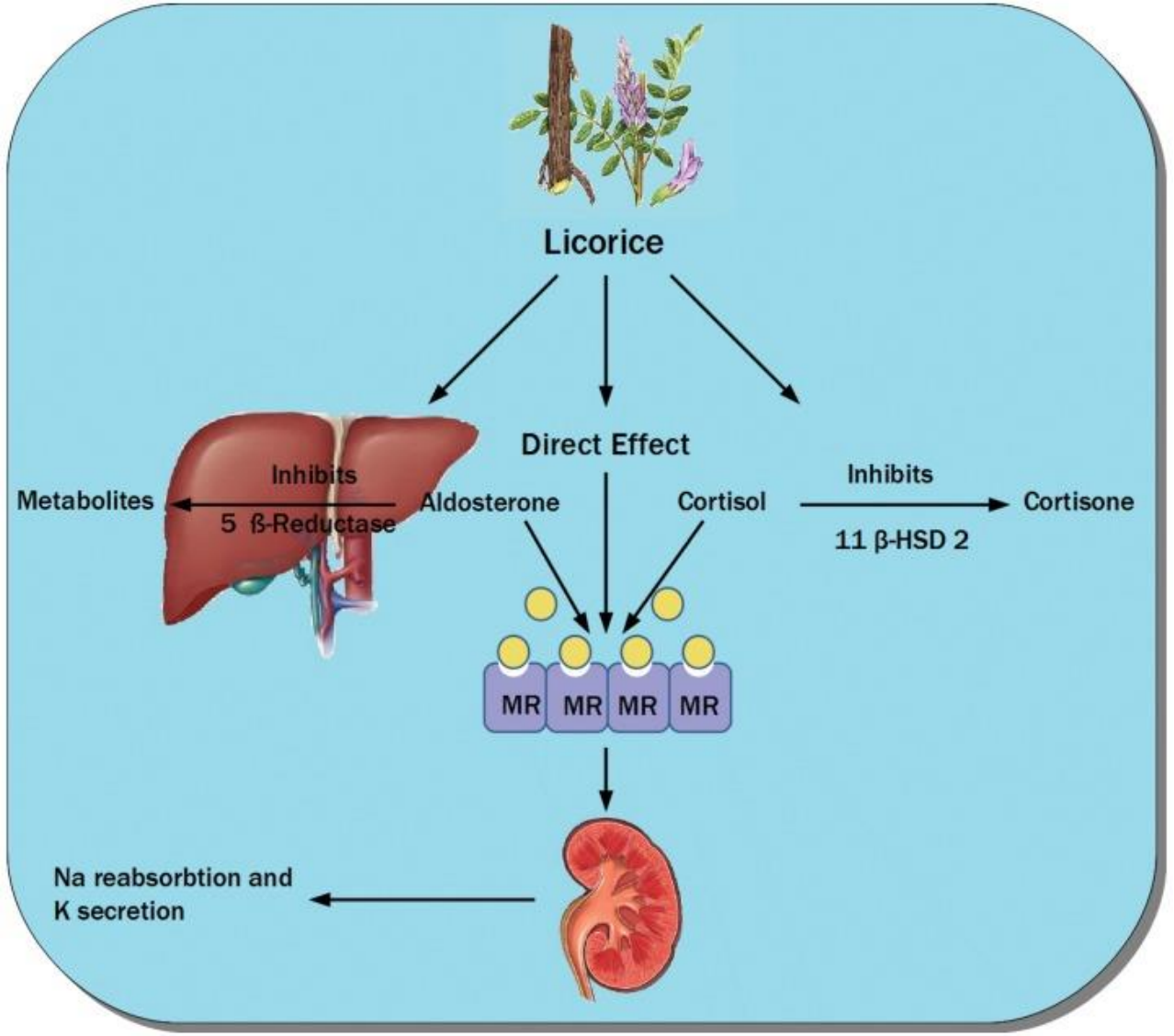
Well thriving, normal sexual development

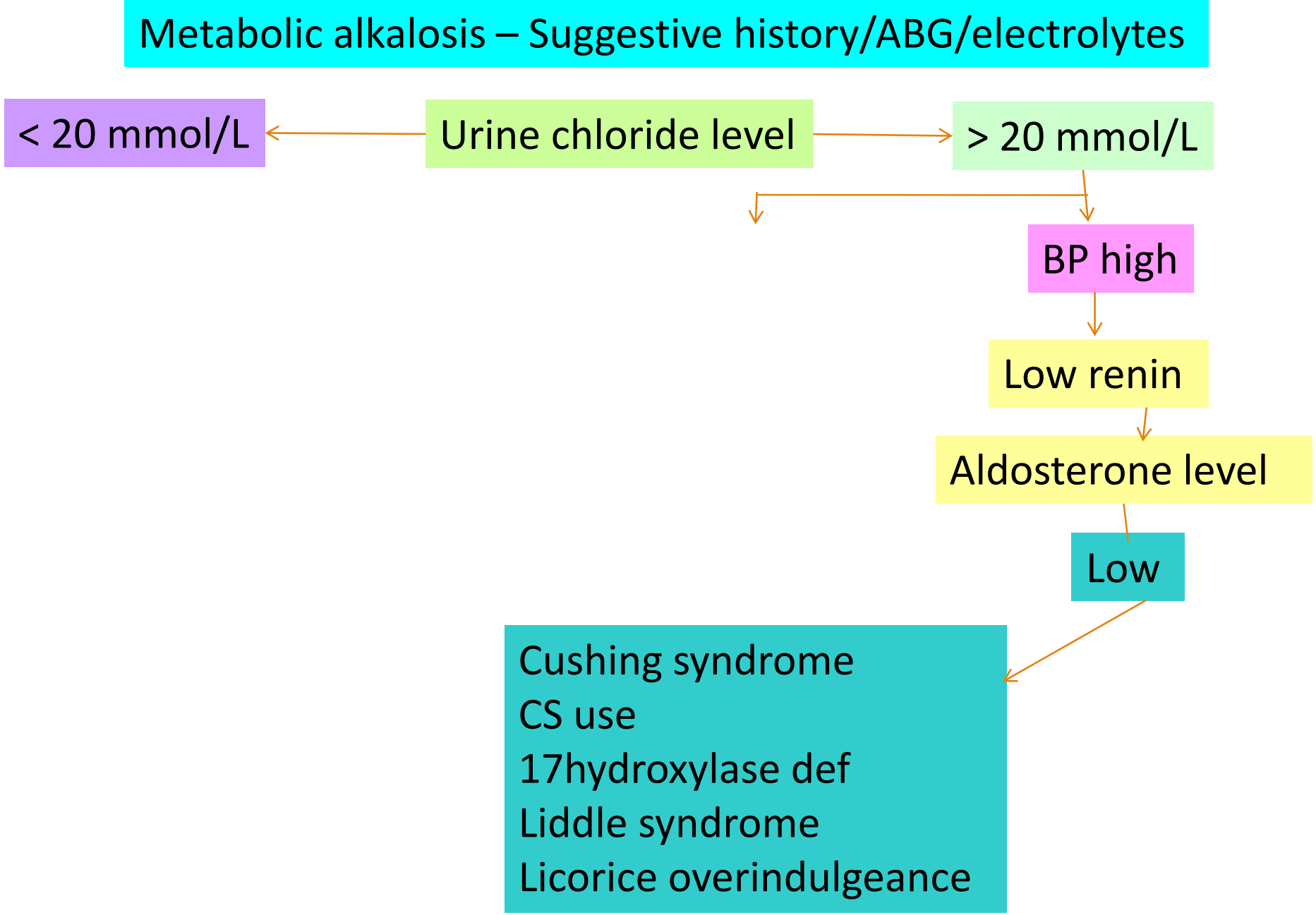
Evaluation – hypernatremia, hypokalemia , metabolic alkalosis, low renin and aldosterone levels, renal functions normal

Normal BP 1 month back during regular health visit

On probing found to have cough cold and taken kashayam made of adhimadhuram for 2 weeks

Licorice intoxication !!

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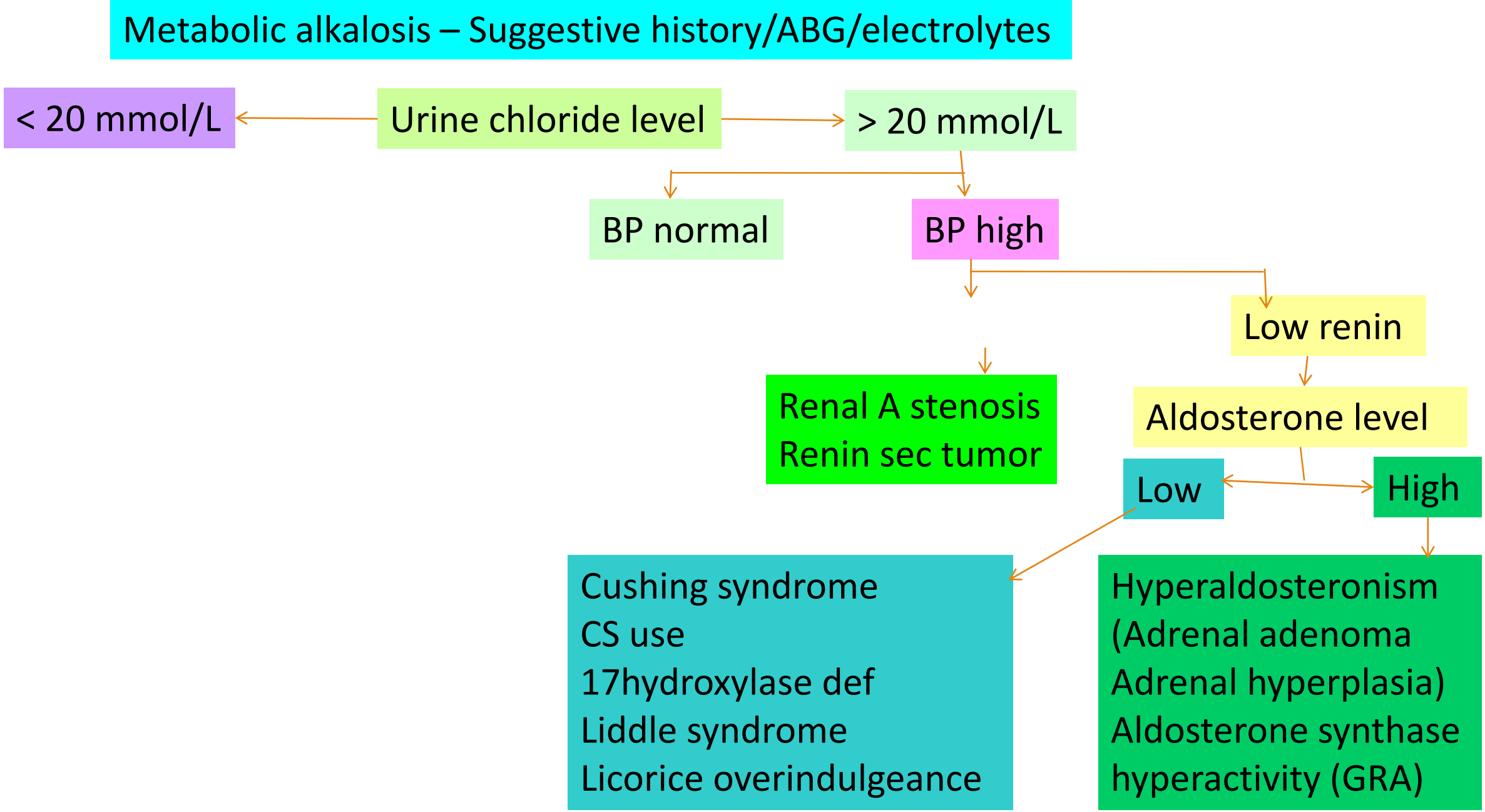
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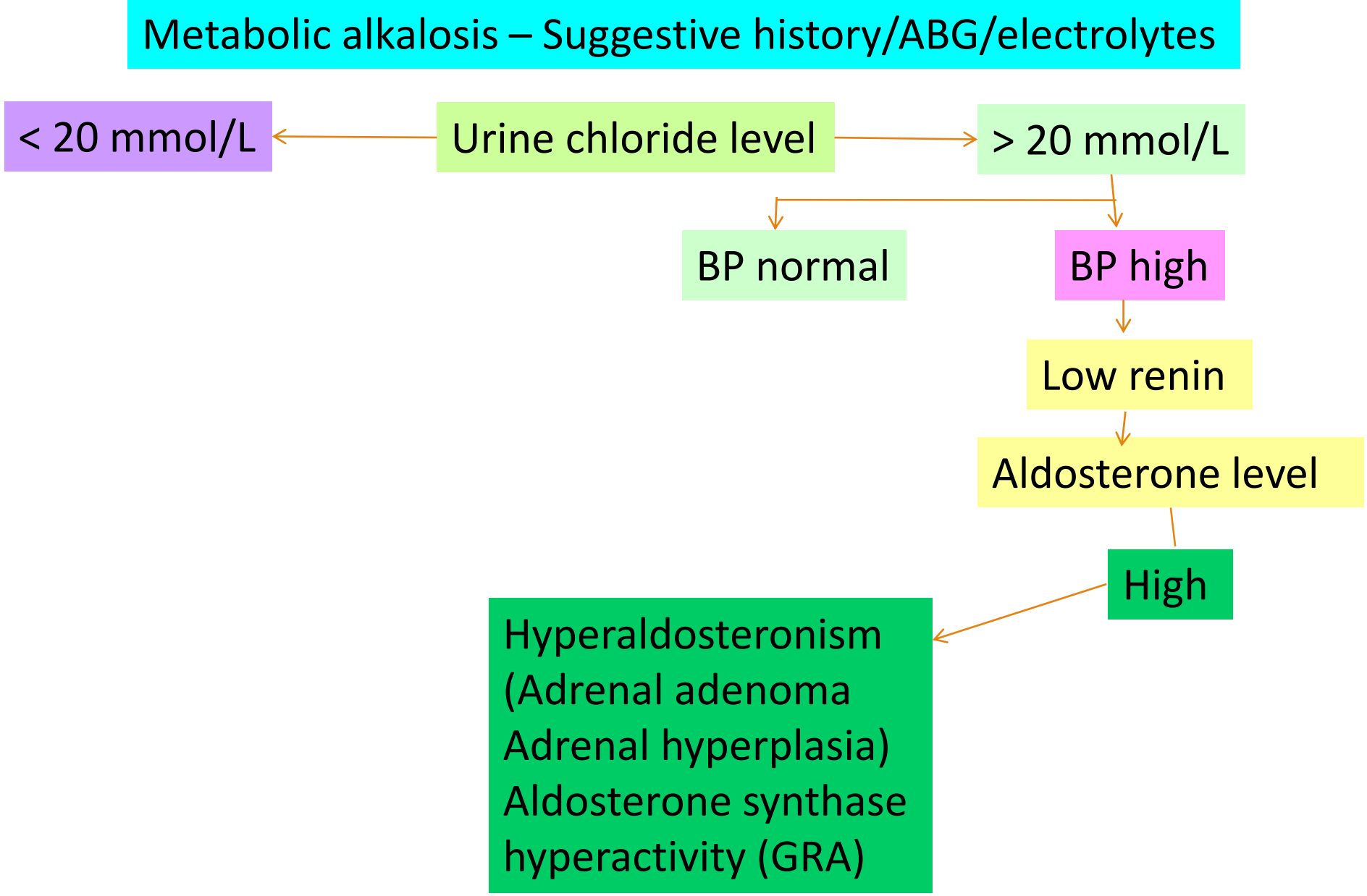
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hyperactivity (GRA)

Thumb rules in Metabolic alkalosis

- Fluid and acid base balance – closely linked – Fluid status given preference
- **↓ Effective circulatory volume (ECV)-** Renin Angiotensin Aldosterone axis – controlled reciprocal physiologic balance
- Urine Chloride – indicator of ECV
- Correction of

  Volume contraction/Hypochloraemia/Hypokalaemia/Hypomagnesaemia/Increased adrenocorticoids improves Metabolic alkalosis

Thank you !!!