
# Approach to a child with hypokalemic metabolic alkalosis

**Dr Sriram Krishnamurthy**

Professor

Department of Pediatrics,

Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER),

Pondicherry

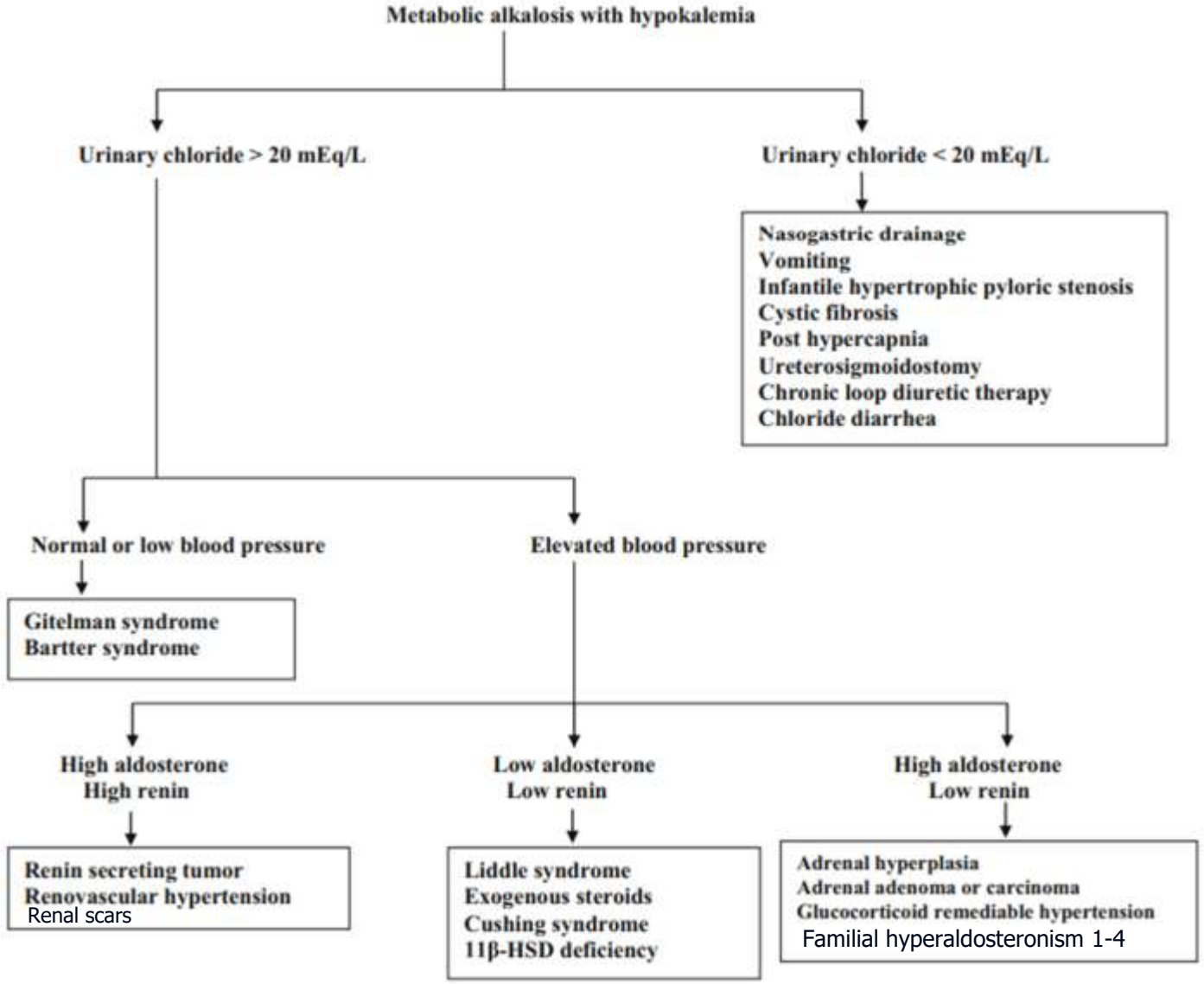
# Specific learning objectives

- Differential diagnosis of conditions presenting with hypokalemic metabolic alkalosis with special emphasis on Bartter syndrome
- Clinical case based scenarios illustrating the wide diversity in phenotypic spectrum of hypokalemic metabolic alkalosis
- Management of these conditions

# Case 1

- PJ, 8-month-old girl; non-consanguineous parents; second born
- Poor weight gain since birth (birth weight 2.46 kg; now 4.2 kg)
- Antenatally, no polyhydramnios documented, term delivery at 37 weeks
- History suggestive of polyuria: documented as 6 ml/kg/h; dehydrated at admission
- Serum sodium 129 mEq/L, potassium 2.6 mEq/L, chloride 95 mEq/L; Urine chloride 48 mEq/L
- Serum creatinine 0.15 mg/dL, bicarbonate 34 mEq/L; Serum phosphorus 4.2 mg/dL, calcium 9.4 mg/dL, Mg 1.9 mg/dL
- Plasma renin activity high; BP 64/30 mm Hg

# Approach to metabolic alkalosis



# Final diagnosis

- Homozygous pathogenic mutation in **CLCN-KB** gene: Exon 10: c. 910 C>T; p. Arg304Ter (nonsense variation resulting in a stop codon and premature termination of protein)

- **Final diagnosis: Bartter syndrome type 3**
- KCl supplements (6 mEq/kg/day) and indomethacin (1 mg/kg/day)
- Growth velocity 4.5 cm/year

# Bartter syndrome

- In 1962, F. Bartter et al described 2 African American patients with
  - -hypokalemic metabolic alkalosis with renal potassium wasting
  - -JG apparatus hypertrophy
  - -normotensive hyperaldosteronism and high Plasma renin activity
- Over the years, phenotypic variants based on age of onset, severity, hyposthenuria, hypomagnesemia, hypercalciuria due to involvement of different channels in different nephron segments
- Usually Autosomal recessive, except MAGED2 mutations (XLR) and CaSR mutations (AD)
- Genotypic information important, but weak genotype phenotype correlation reported mostly

Konrad M, et al. Mutations in the chloride channel gene CLCNKB as a cause of classic Bartter syndrome. J Am Soc Nephrol. 2000;11:1449–59.
Jeck N, et al. Salt handling in the distal nephron: lessons learned from inherited human disorders. Am J Physiol Regul Integr Comp Physiol. 2005;288(4):R782–95.

# Salt reabsorption in Thick ascending Limb of Loop of Henle (TAL)

(10-20%)

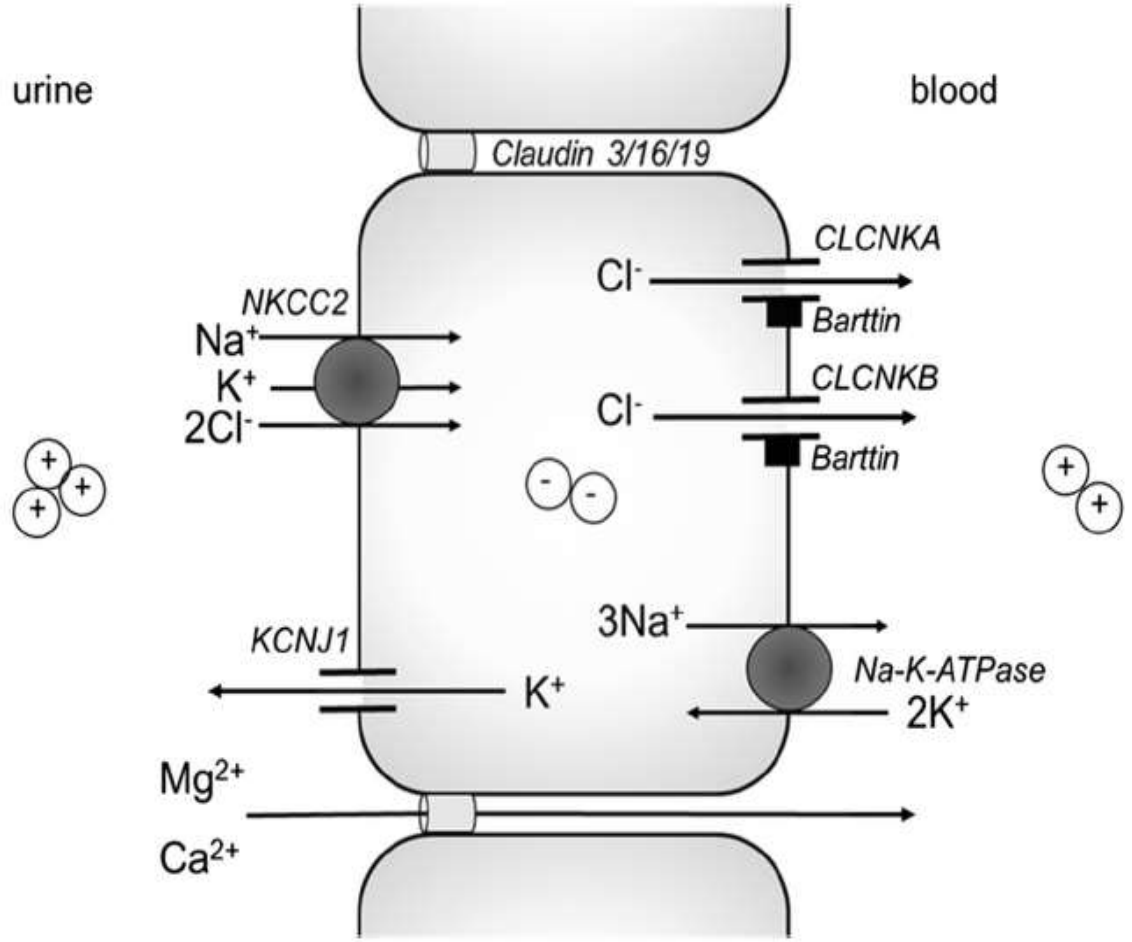
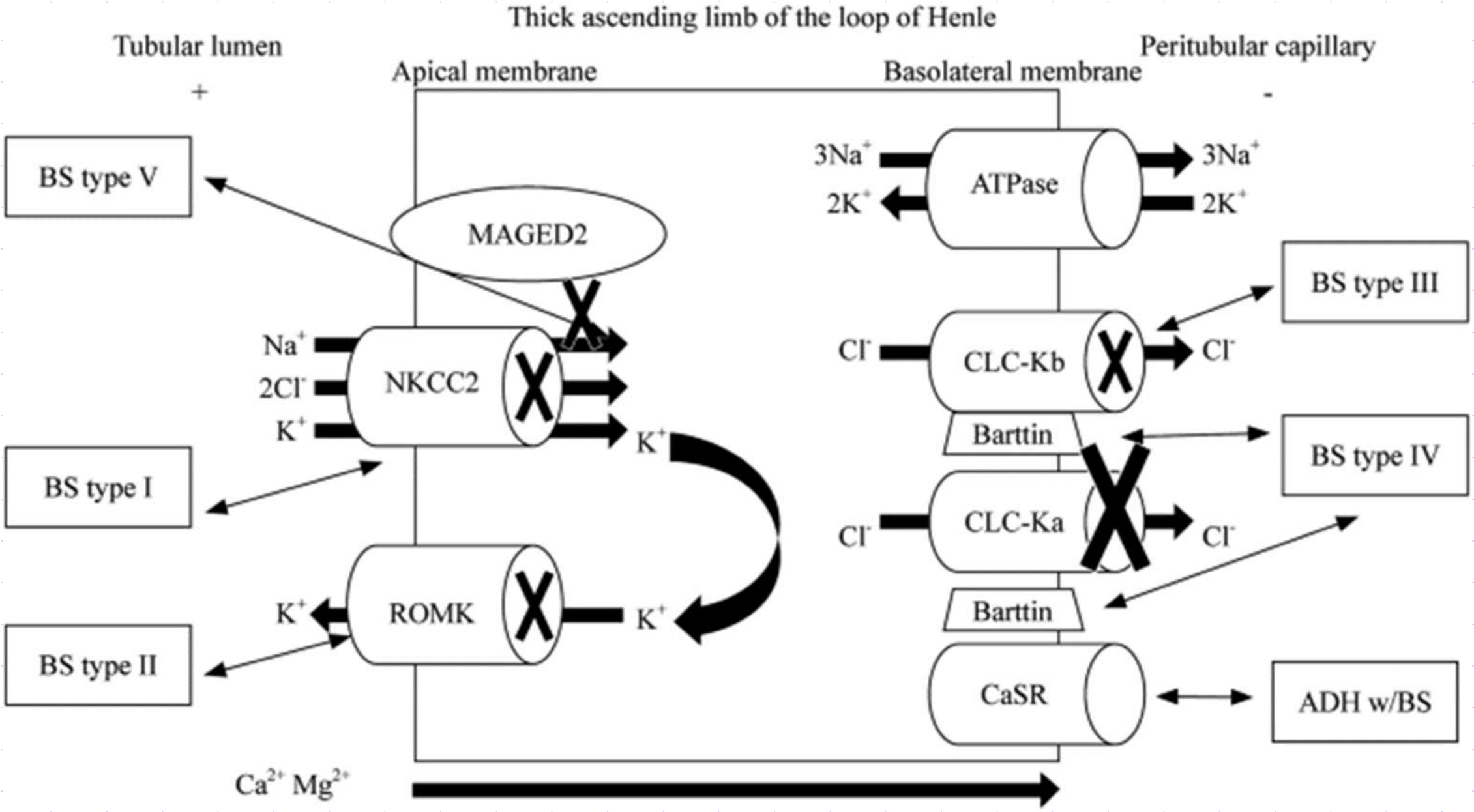



**Fig. 1.** Electrolyte transport in the TAL. The NKCC2 transporter imports one sodium, one potassium, and two chloride ions from the lumen into the cell. This transporter can be blocked by loop diuretics, inherited dysfunction causes Bartter syndrome type 1. Mutations in the gene encoding MAGE-D2 result in a transient decreased expression of NKCC2, thus causing Bartter syndrome type 5. Chloride leaves the cell via the basolateral chloride transporters CLCNKB and, presumably, CLCNKA, both of which need the Barttin subunit in order to function. Mutations in CLCNKB cause Bartter syndrome type 3 and in Barttin

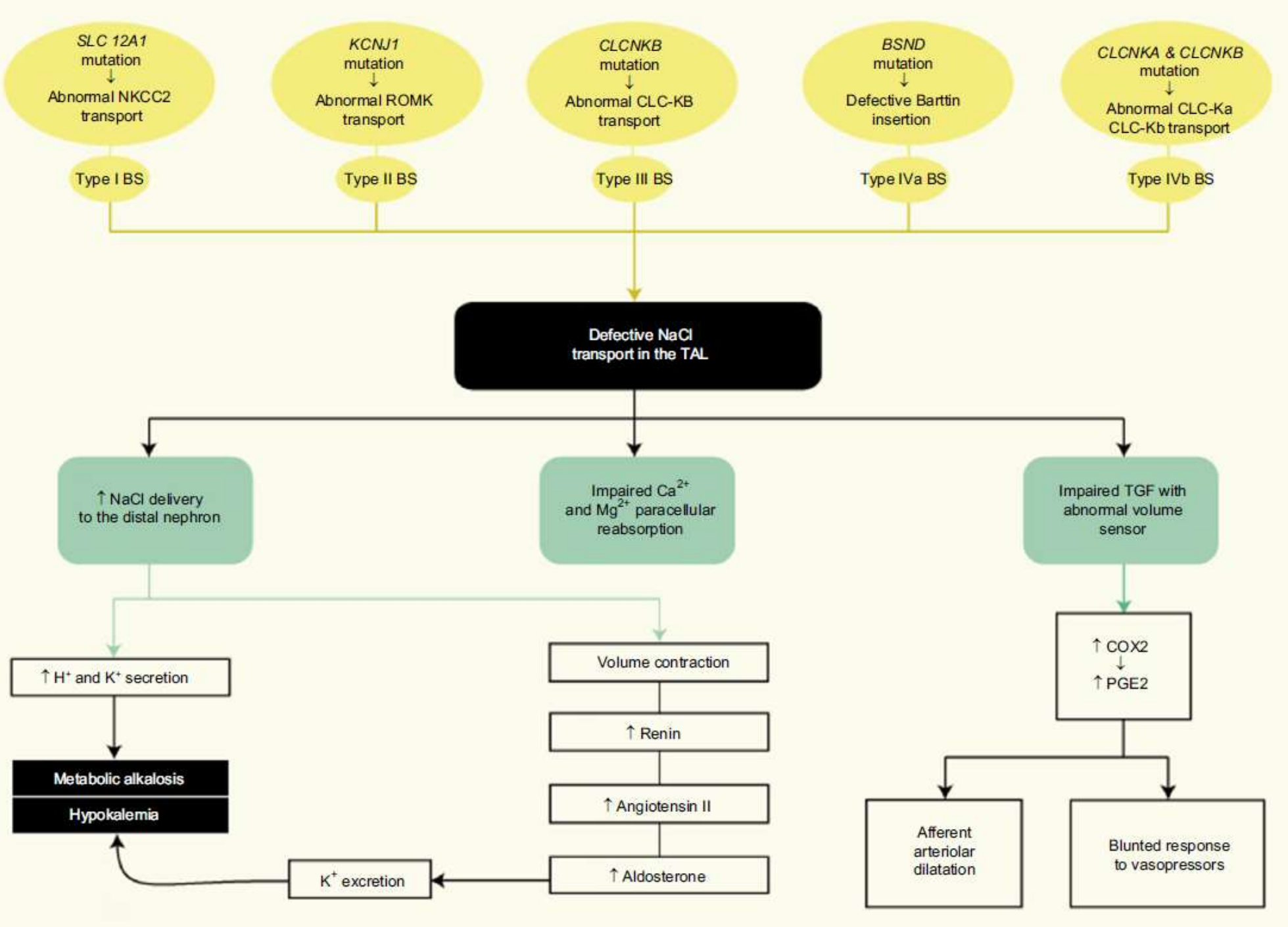
Sodium leaves the cell via the basolateral Na-K-ATPase that actively exports three sodium ions and imports two potassium ions. Potassium subsequently leaves the cell via the luminal KCNJ1 channel, mutations in which cause Bartter syndrome type 2. The luminal potassium concentration is the main driving force for the paracellular uptake of calcium and magnesium, which is facilitated by a lumen-positive transepithelial potential. Therefore, hypercalciuria with nephrocalcinosis and hypermagnesuria is typically seen in Bartter syndromes type 1 (NKCC2), type 2 (KCNJ1), and type 5 (MAGE-D2), while it can be

# Bartter syndrome subtypes



## Gene defects And Pathophysiology In Bartter Syndrome

There is a subset of BS in which no genes are identified yet



# Why metabolic alkalosis in BS?

- **Classical view:** Increased sodium loss in urine stimulates H+ excretion in urine via stimulation of V type H+ATPase
- **Recent views:**
- NHE-3 stimulation in TAL since NKCC2 has loss of function
- CLCN-KB loss of function leads to loss of function of Type b intercalated cells that secrete bicarbonate (this explains higher alkalosis in BS-3 than other types)


de Bruijn PI, et al (2015) Furosemide-induced urinary acidification is caused by pronounced H+ secretion in the thick ascending limb. Am J Physiol Renal Physiol 309(2):F146–F153

Pinelli L, et al (2016) Dual regulation of the native ClC-K2 chloride channel in the distal nephron by voltage and pH. J Gen Physiol 148(3):213–226

Wingo CS (2016) Alkaline activation of ClC-K2 chloride channels switches renal cells from reabsorbing to secreting. J Gen Physiol 148(3):195–199

Cunha TDS, Heilberg IP. Bartter syndrome: causes, diagnosis, and treatment. Int J Nephrol Renovasc Dis. 2018 Nov 9;11:291-301. doi: 10.2147/IJNRD.S155397. PMID: 30519073; PMCID: PMC6233707.

# Genetic defect in BS and phenotype

| | | | | | | |
|---|---|---|---|---|---|---|
| Bartter syndrome type 1 | 601678 | AR | *SLC12A1* | NKCC2 | Antenatal | Nephrocalcinosis |
| Bartter syndrome type 2 | 241200 | AR | *KCNJ1* | KCNJ1 | Antenatal | Postnatal transient hyperkalaemia, nephrocalcinosis |
| Bartter syndrome type 3 | 607364 | AR | *CLCNKB* | ClC-Kb | Variable | Variable |
| Bartter syndrome type 4a | 602522 | AR | *BSND* | Barttin | Antenatal | Sensorineural deafness, severe polyhydramnios |
| Bartter syndrome type 4b | 613090 | AR | *CLCNKA* and *CLCNKB** | ClC-Ka and ClC-Kb | Antenatal | Sensorineural deafness, severe polyhydramnios |
| Bartter syndrome type 5 | 300971 | XLR | *MAGED2* | MAGE-D2 | Antenatal | Transient Bartter syndrome, nephrocalcionsis |
| Gitelman syndrome | 263800 | AR | *SLC12A3* | NCCT | Childhood | Hypomagnesemia, hypocalciuria |
| EAST syndrome | 612780 | AR | *KCNJ10* | Kir4.1 | Infancy | Epilepsy, ataxia, sensorineural deafness |

**-BS4 (aBS with SD) has sensorineural deafness, severe growth retardation, progresses to ESRD faster** (with some exceptions)
-Poorly respond to indomethacin; may have fever, vomiting and bacterial infections
-They may have severe hypomagnesemia
-Occasionally, it may not be antenatal (presentation at 28 years reported with milder manifestations)

# Loop phenotype vs DCT phenotype for classifying BS and GS: proposed new classification

**Loop phenotype**

- SLC12A1 (NKCC2) and KCNJ1 (ROMK)
- Antenatal onset, prematurity, hypercalciuria, nephrocalcinosis

**DCT phenotype**

- CLCN-KB and SLC12A3 (GS)
- Hypo- or normocalciuria, hypomagnesemia
- Later onset in childhood

**Combined phenotype**

- BSND or combined CLCN-KA/CLCN-KB mutations
- Antenatal onset, severe symptoms, variable calcium excretion

Seyberth HW (2008) An improved terminology and classification of Bartter-like syndromes. Nat Clin Pract Nephrol 4(10):560–567

# Case 2

- N, 6 year old boy; referred to us as Bartter syndrome
- Polyuria (5.5 mL/kg/h), refractory rickets, bony deformity in LL
- Weight 11 kg (<3rd centile), Height 95 cm (<3rd centile), BP normal

- Serum bicarbonate 33 mEq/L, serum calcium 9.4 mg/dL, serum phosphorus 1.1 mg/dL
- Serum potassium 2.8 mEq/L
- Hypercalciuria (6 mg/kg/24 h), medullary nephrocalcinosis

WHAT NEXT?

- FeP04 85%, TmPGFR 1.4 mg/dL, eGFR 92 ml/min/1.73 sq.m
- Urine albumin 2+, but 24 hour urine protein 3.1 g/24 hours

# Further investigations

- Urine beta2 microglobulin 10000 mcg/L
- Clinical exome sequencing: CLCN5 (XLR); c.933+1G>A; hemizygous; pathogenic
- FINAL DIAGNOSIS

  Dent disease Type 1

- Treated with neutral phosphate supplements, thiazides
- Mechanism of pseudo-Bartter picture: polyuria with secondary hyperaldosteronism

# Lessons learnt: Pseudo-Bartter phenotype reported in Dent disease-type 1, Dent disease-type 2, cystinosis

CASE REPORT

**Rare Presentation of Cystinosis Mimicking Bartter's Syndrome: Reports of Two Patients and Review of the Literature**

Aysun Çaltik, Sare Gülfem Akyüz, Özlem Erdogan, Mehmet Bülbül, and Gülay Demircin
Dr. Sami Ulus Children Hospital, Pediatric Nephrology Department, Altindag, Ankara, Turkey

Case Report

*Cystinosis Presenting with Findings of Bartter Syndrome*

BMC Nephrology

CASE REPORT Open Access

**Dent-2 disease with a Bartter-like phenotype caused by the Asp631Glu mutation in the OCRL gene**

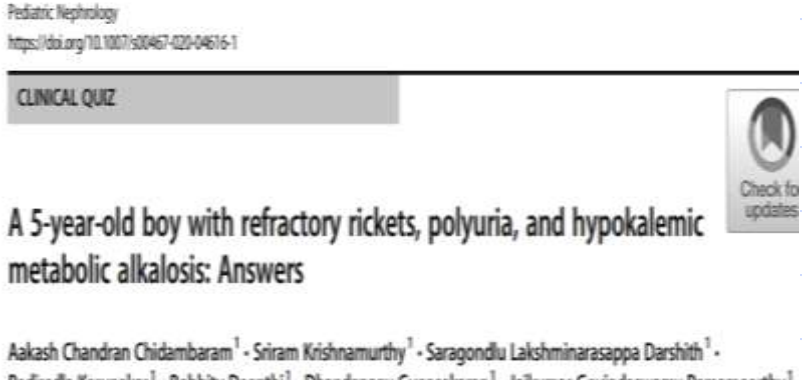
Eleni Drosataki[1], Sevasti Maragkou[1], Kleio Dermitzaki[1], Ioanna Stavrakaki[1], Dimitra Lygerou[1], Helen Latsoudis[2], Christos Pleros[1], Ioannis Petrakis[3], Ioannis Zaganas[4] and Kostas Stylianou[1*]

frontiers in Pediatrics

CASE REPORT

**Bartter-Like Syndrome as the Initial Presentation of Dent Disease 1: A Case Report**

*Qiaoping Chen, Yan Cao, Liyun Xu, Jingqi Liu and Xiaochuan Wu**



Pediatric Nephrology

CLINICAL QUIZ

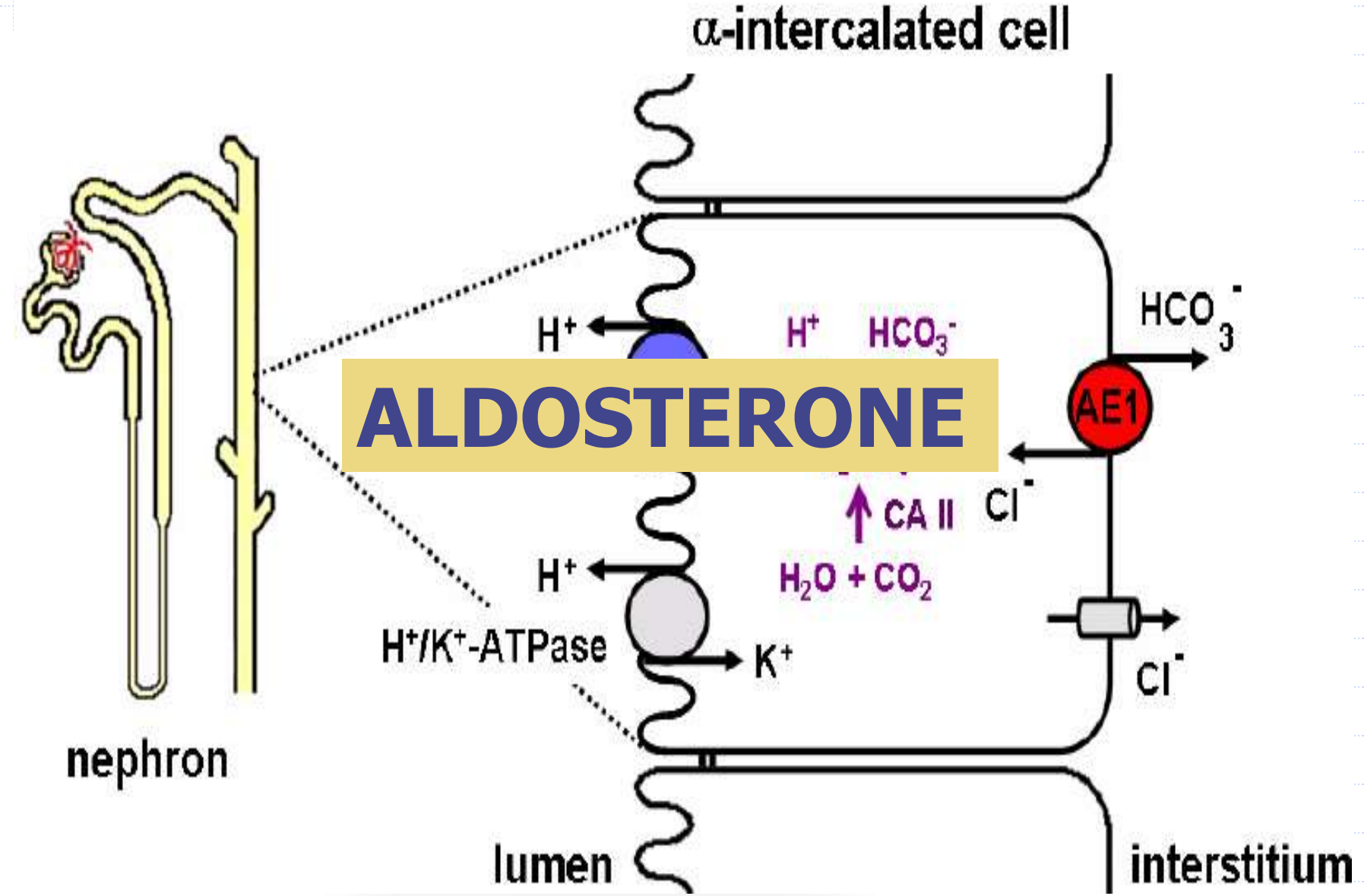
**A 5-year-old boy with refractory rickets, polyuria, and hypokalemic metabolic alkalosis: Answers**

Aakash Chandran Chidambaram[1] · Sriram Krishnamurthy[1] · Saragondlu Lakshminarasappa Darshith[1] · Pediredla Karunakar[1] · Bobbity Deepthi[1] · Dhandapany Gunasekaran[1] · Jaikumar Govindaswamy Ramamoorthy[1]

Received: 30 April 2020 / Revised: 2 May 2020 / Accepted: 11 May 2020
© IPNA 2020

Sjogren syndrome, Mitochondrial disorders, loop diuretic/laxative abuse can cause Bartter like picture

# Cystic fibrosis can present as Pseudo- Bartter syndrome



# CASE 3: A 14-year-old girl

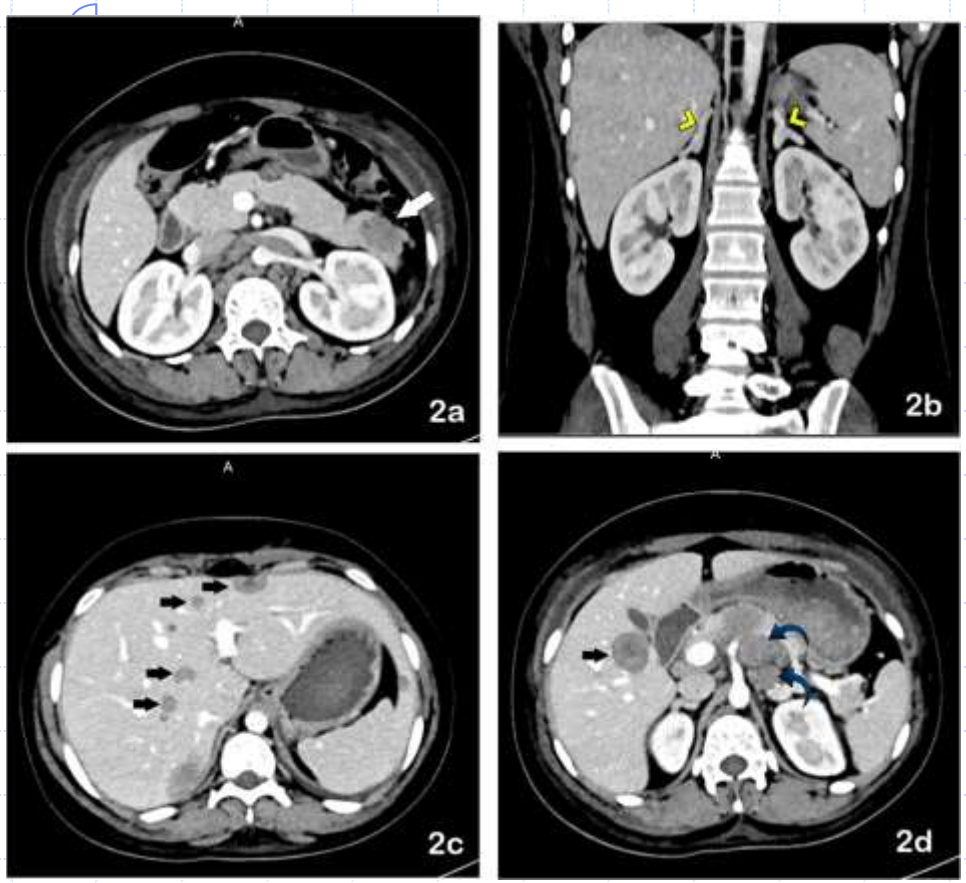
- Excessive weight gain and swelling of both lower limbs for 1 month
- High BP (160/110 mmHg, stage 2 hypertension)
- She denied drugs, traditional medicines, or steroids
- Her face had a Cushingoid appearance, with extensive acneiform eruptions
- Wt 50 kg (0.06 Z) and Ht 151 cm (−1.56 Z)  (Weight was 43 kg 1 month ago)
- No discrepancy in four limb BP, all pulses palpable

# Further work-up

- Serum creatinine- 0.54 mg/dL, urinalysis normal
- Hypokalemic metabolic alkalosis (bicarbonate 45.7, K 2.8)
- Echocardiogram- Concentric LVH
- Plasma cortisol (at 8 am)  > 75 mcg/dL (reference value 4.3–22.4 mcg/dL)
- Plasma ACTH- 363 pg/mL (reference value 10–60 pg/mL)

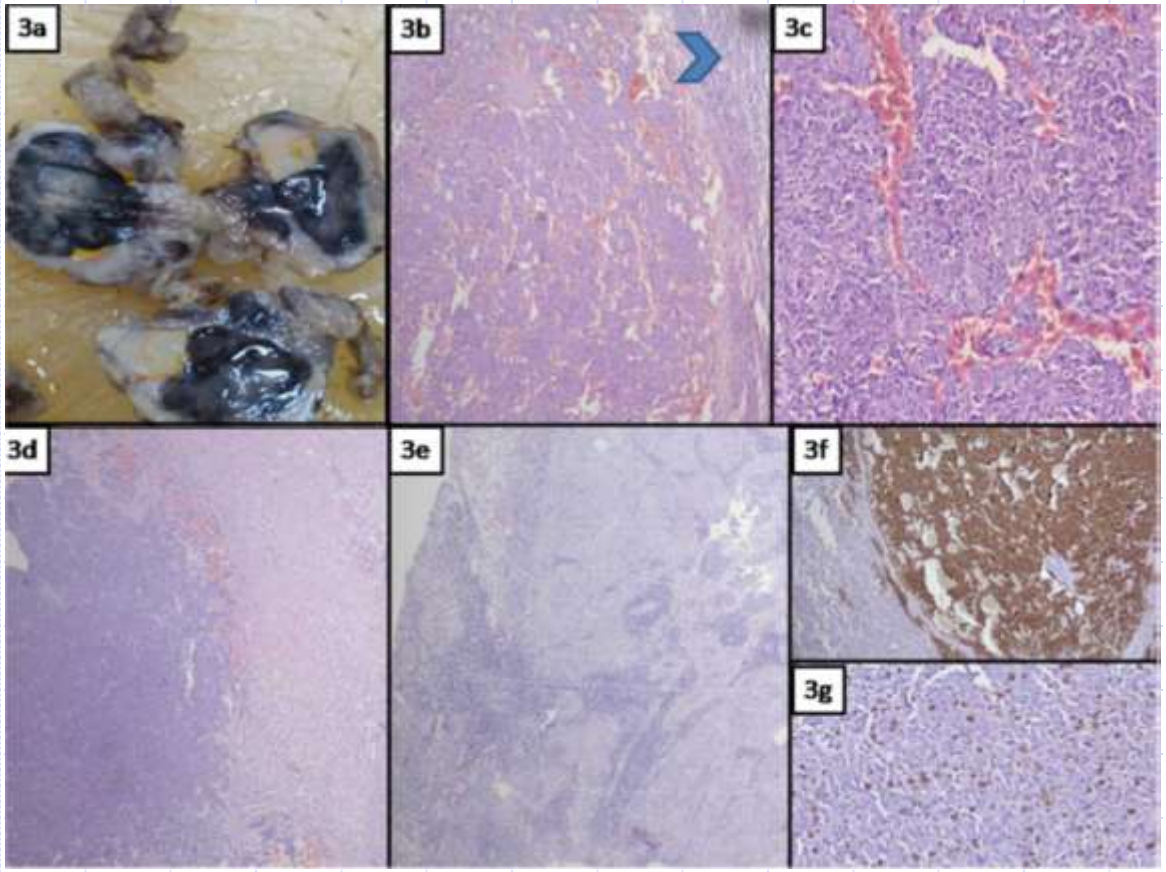
- Diagnosis: ACTH-dependent Cushing syndrome
- MRI cranium showed no evidence of pituitary or hypothalamic lesions

# CECT abdomen



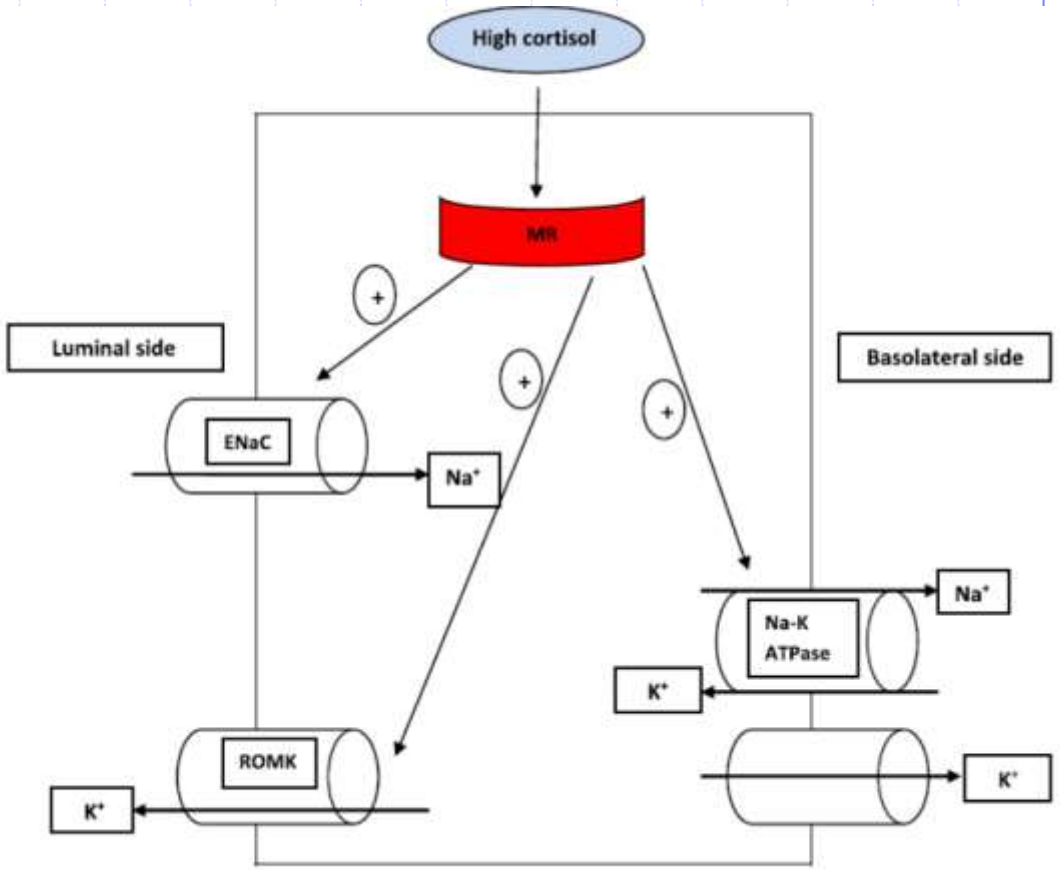

CECT of the abdomen showing a **hypodense poorly enhancing lesion in the tail of the pancreas** (tumor—solid white arrow)

## Distal pancreatectomy specimen: well-circumscribed neuroendocrine tumor



# Mechanism of hypertension in Endogenous Cushing syndrome

- Mineralocorticoid action exerted by supraphysiological levels of cortisol
- Mineralocorticoid receptor (MR) can be chiefly activated by cortisol
- This is kept in check by 11β-HSD
- In cortisol excess, the levels of cortisol would exceed the capacity of 11β-HSD to inactivate it to cortisone, thus making it available to bind to MR, mimicking excess aldosterone.



# Management

- Amlodipine, atenolol and prazosin initially
- **Later spironolactone added**
- Led to much better control of hypertension
- Pancreatectomy: hypertension resolved
- Chemotherapy

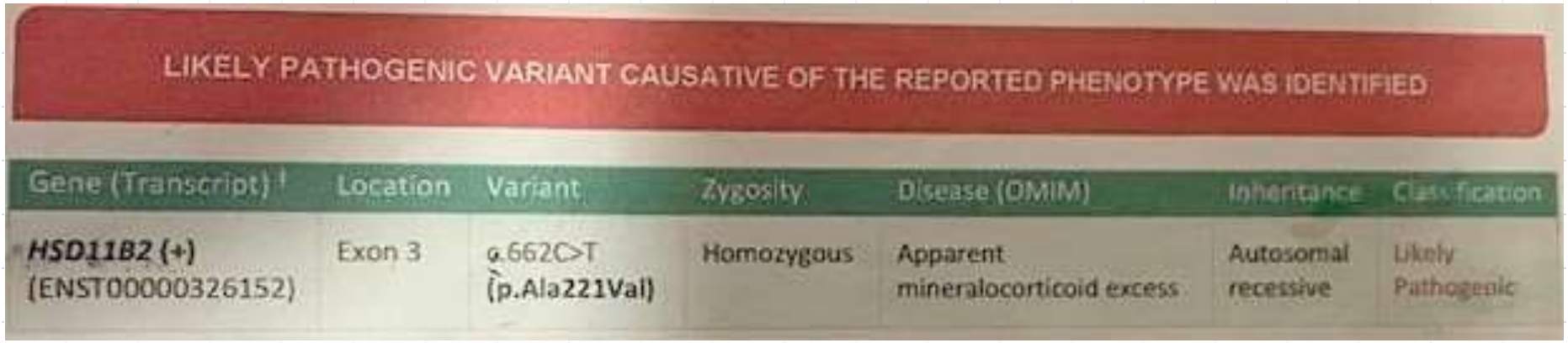
# CASE 4: 18 month old boy

- Presented with acute flaccid paralysis
- Referred as a case of GBS
- Failure to thrive (Weight 7 kg; -2 SD)
- BP- 132/90 (stage 2 hypertension)
- Serum K- 1.8 mEq/L, Na- 136, Cl-94, HCO3 32 mEq/L
- Serum creatinine-0.18 mg/dL
- Review of history- LBW-1.8 kg
- Hypercalciuria (Ca: Cr 1.5), no nephrocalcinosis
- Concentric LVH, Grade 2 hypertensive retinopathy

# Further investigations

- Urine chloride- 60 mEq/L
- Plasma renin activity- 0.3 ng/mL/h (normal for age 3.0–9.0 ng/mL/h) (Low)
- Serum aldosterone- 0.5 ng/dL (1-124 ng/dL) (upright) (Low)
- Elevated 24-h urinary free cortisol-to-cortisone ratio- 4.5 (normal 0.5)

# Next Generation sequencing



LIKELY PATHOGENIC VARIANT CAUSATIVE OF THE REPORTED PHENOTYPE WAS IDENTIFIED

| Gene (Transcript) | Location | Variant | Zygosity | Disease (OMIM) | Inheritance | Classification |
|---|---|---|---|---|---|---|
| ***HSD11B2*** **(+)** (ENST00000326152) | Exon 3 | g.662C>T (p.Ala221Val) | Homozygous | Apparent mineralocorticoid excess | Autosomal recessive | Likely Pathogenic |

HSD11B2 homozygous likely pathogenic variant detected

Diagnosis- 11 Beta hydroxysteroid dehydrogenase deficiency (Syndrome of Apparent Mineralocorticoid excess)

Management: Spironolactone and oral KCl supplements

# Approach to Monogenic hypertension

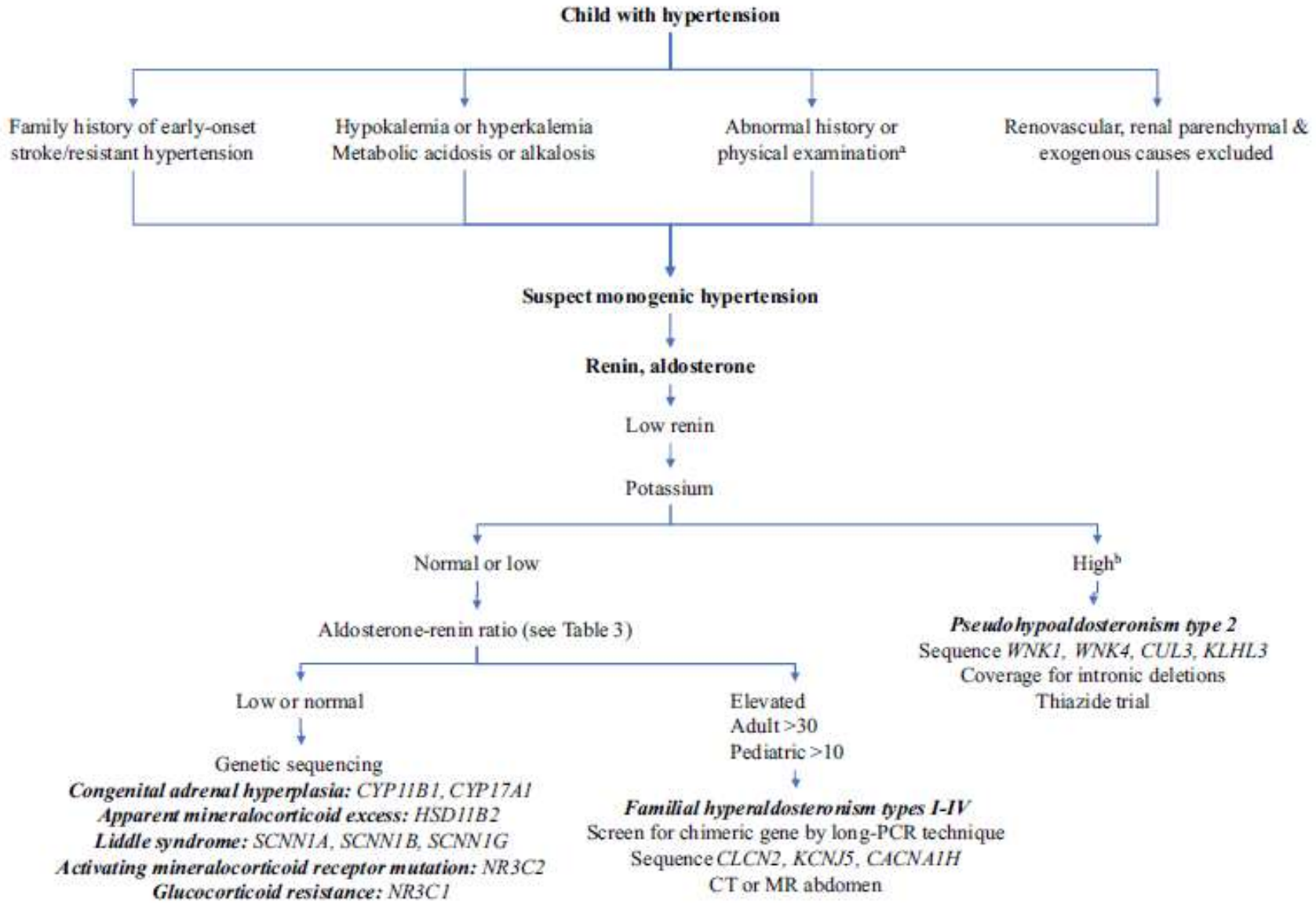
EDUCATIONAL REVIEW

Monogenic forms of low-renin hypertension: clinical and molecular insights

Priyanka Khandelwal[1] · Jaap Deinum[2]

Received: 8 March 2021 / Revised: 16 July 2021 / Accepted: 19 July 2021





# Case 5

- HR, 1.5-year-old boy brought with complaints of:
- FTT (weight 6.1 kg)  and polyuria (urine output 2.1 l/sq.m)
- History of polyhydramnios present in antenatal period, preterm-36 weeks
- Some dehydration present, BP 88/60 mm Hg
- Investigations: serum sodium 131 mEq/L, potassium 2.8 mEq/L, chloride 92 mEq/L
- Serum creatinine 0.26 mg/dL
- Serum bicarbonate 30 mEq/L, urine chloride 30 mEq/L, magnesium 2.2 mg/dL
- Urine calcium: creatinine ratio 0.68, Plasma renin activity High
- USG showed medullary nephrocalcinosis
- Born to third degree consanguineous parents

# Diagnosis

- **Bartter syndrome (Type 2)**
- Homozygous pathogenic mutation (c.772G>T; p.Glu258Ter) in KCNJ1 (ROMK) gene (E258STOP)
- Treatment with Indomethacin and potassium chloride
- (Evidence of hyperkalemia in neonatal period not available in this case)

# Case 6

- EG, 11 month old infant with failure to thrive (3.4 kg), no polyhydramnios
- Past history of **hypernatremia with nephrogenic DI**
- Recurrent dehydration; **later developed hypokalemic metabolic alkalosis**; BP low
- Plasma renin activity high; no hypercalciuria or nephrocalcinosis; hearing assessment normal

Next generation sequencing

**LIKELY PATHOGENIC VARIANT CAUSATIVE OF THE REPORTED PHENOTYPE WAS IDENTIFIED**

**VARIANT INTERPRETATION AND CLINICAL CORRELATION**

**Contiguous regions encompassing the *CLCNKB* gene (ENST00000375679.4) were not covered in the sequencing data of this sample. These regions are usually well covered and hence, could likely be due to homozygous deletion of these regions.**

**The sensitivity of NGS based assays to detect large heterozygous deletions/duplications is low and an alternate method is recommended.**

MLPA

**PATHOGENIC VARIANT CAUSATIVE OF THE REPORTED PHENOTYPE WAS IDENTIFIED**

| Sl. No. | Deletions /Duplications | No. of exons deleted/duplicated ǂ | MLPA probe ratio (Dosage quotient) # | Disease (OMIM) | Inheritance | Classification |
|---|---|---|---|---|---|---|
| 1. | Homozygous deletion | 19 (Exons 1-19) | 0.00 | Bartter syndrome, type 3 (607364) | Autosomal recessive | Pathogenic |

- On KCl supplements (7 mEq/day)
- Progressed to CKD 3B, indomethacin withheld
- Recurrent AKI, hypokalemic tubulopathy and possibly a large gene deletion could account for low eGFR

# Case 7

- K, 1-year-old boy with severe failure to thrive (3.2 kg)
- Polyhydramnios, prematurity, polyuria (12 ml/kg/hour)
- Serum potassium 1.6 mEq/L (acute flaccid paralysis)
- Serum bicarbonate (41 mEq/L), sodium 128 mEq/L, creatinine 0.12
- No hypercalciuria or nephrocalcinosis; serum Mg 1.1
- BP 56/30, urine chloride 54 mEq/L, serum chloride 88 mEq/L

| Gene | Gene/Locus MIM number | Disease (Inheritance) | Exon | Nucleotide change | Amino acid change | Zygosity | Type |
|---|---|---|---|---|---|---|---|
| *CLCNKB* | 602023 | Bartter syndrome, type 3 (AR) | Ex3 | c.226C>T | p.R76* | Homozygous | Pathogenic |

Lesson learnt: Bartter syndrome type 3 has wide phenotypic variability and it too can manifest with polyhydramnios

# Management of Bartter syndrome

- Indomethacin: 1-2.5 mg/kg/d (Doses> 3 mg/kg/d are nephrotoxic)
  -GI complications, ulcer, NEC, AKI
- KCl (usually 1-3 mEq/kg/day)
- Spironolactone can be added (1-1.5 mg/kg/day if higher doses), but concerns regarding aldosterone blockade
- ACE inhibitors controversial (hypotension, AKI)
- If hypomagnesemia, magnesium supplements-typically difficult
- Treatment improves growth, but catch up is often inadequate

# Management of Bartter syndrome

- Thiazides should NOT be added to reduce hypercalciuria; worsen hypokalemia, hypomagnesemia and dehydration
- Correction of hypercalciuria is partial with indomethacin
- Rofecoxib- cardiovascular effects, AKI
- Salt supplementation may be needed: appropriate compensation for salt and fluid wasting
- Gene therapies (to express NKCC2 using adenovirus vector; and to correct KCJN1 folding defects) and Vasopressin (can increase Na uptake via claudin 10b) being investigated

Besouw MTP, Kleta R, Bockenhauer D. Bartter and Gitelman syndromes: Questions of class. Pediatr Nephrol. 2020 Oct;35(10):1815-1824

# Case 8

- 11-year-old boy, **polyuria, salt craving, muscle cramps x 1 yr**
- No polyhydramnios, term baby- birth weight 2.6 kg
- BP-100/70 mm Hg
- **Serum potassium 2.8 mEq/L, bicarbonate 29 mEq/L, S.chloride 89** mEq/L, Na 132 mEq/L, **serum Mg 0.8 mEq/L**
- **Urine calcium: creatinine ratio 0.15**
- **Urine chloride- 56 mEq/L**
- No nephrocalcinosis

| Gene# (Transcript) | Location | Variant | Zygosity | Disease (OMIM) | Inheritance | Classification$ |
|---|---|---|---|---|---|---|
| ***SLC12A3*** **(+)** (ENST00000563236.6) | Exon 24 | c.2800_2803del **(p.Arg934GlyfsTer23)** | Homozygous | Gitelman syndrome (OMIM#263800) | Autosomal recessive | Pathogenic |

Diagnosis: Homozygous frameshift mutation in SLC12A3

**Gitelman syndrome**

On KCl and spironolactone

Polyuria improved

# Salt transport in DCT

(5-10%)

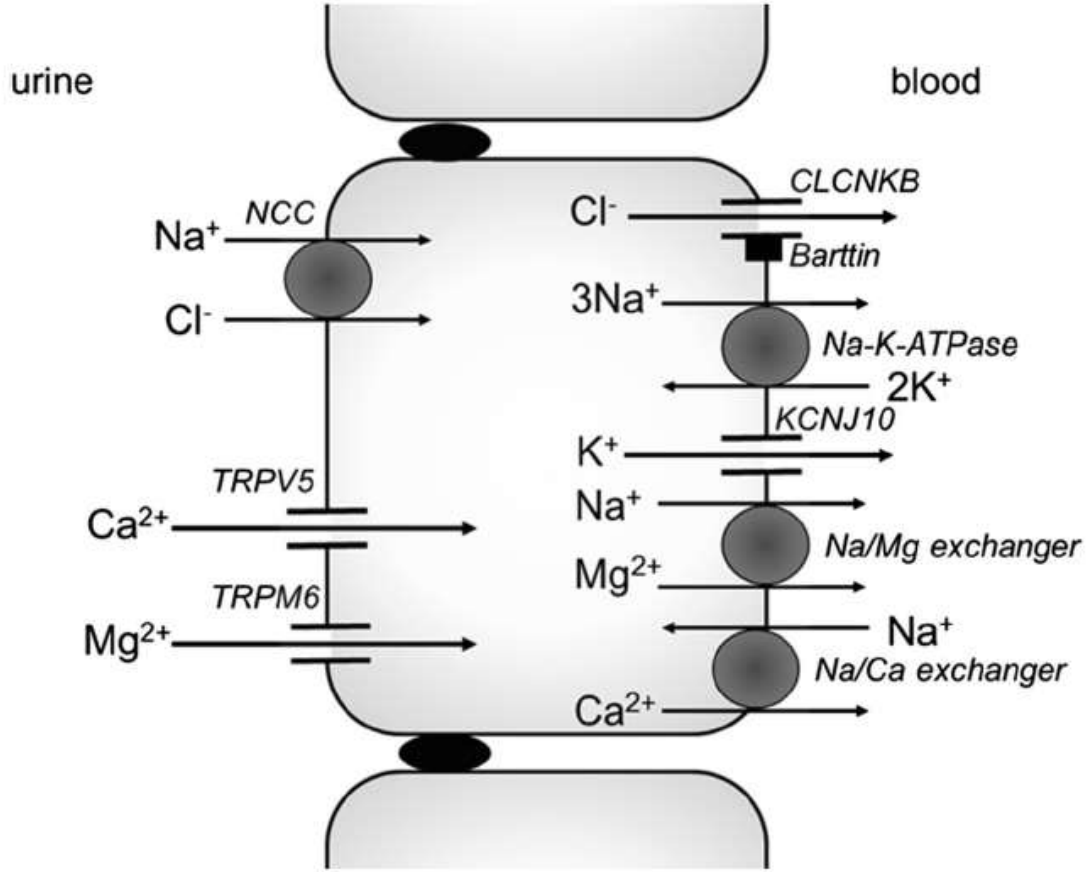
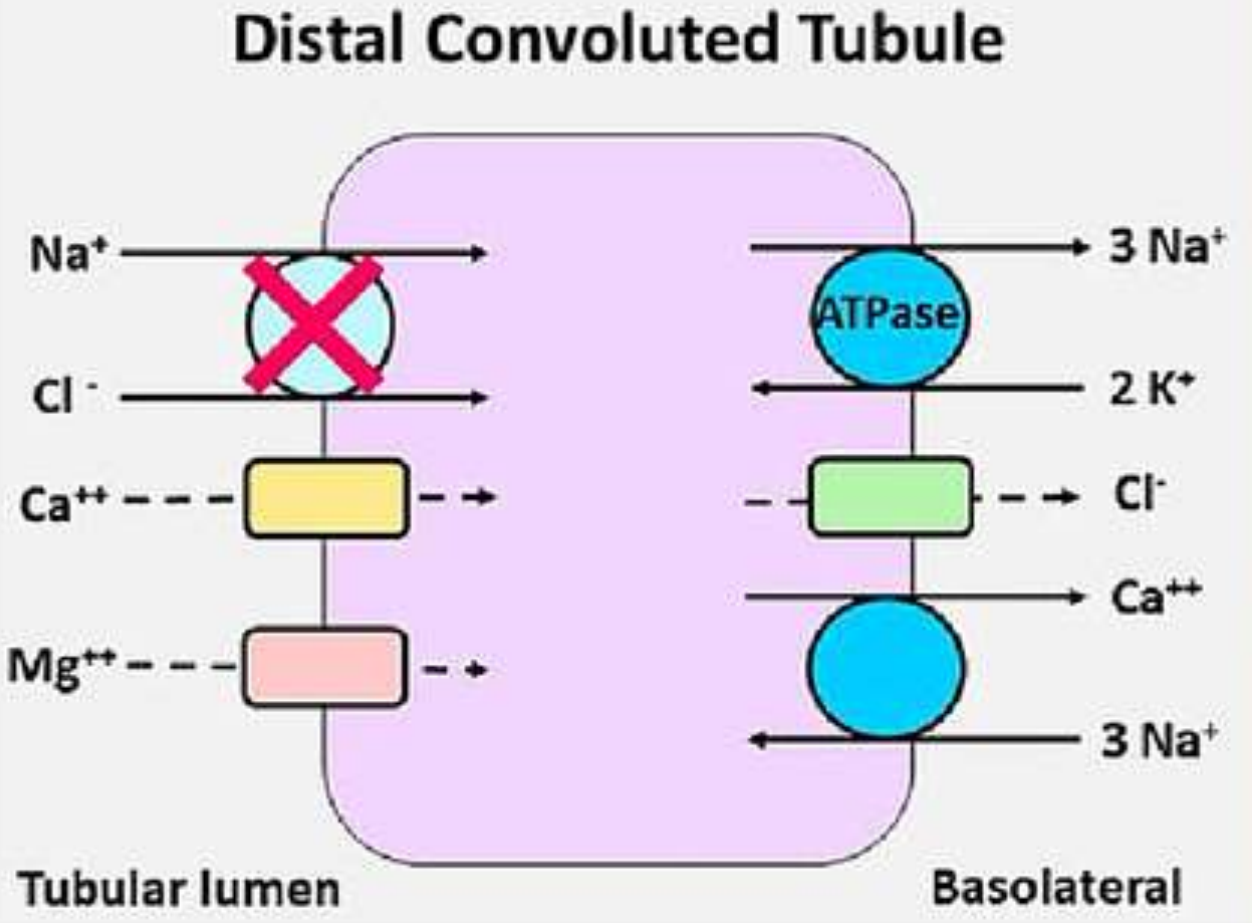



**Fig. 2.** Electrolyte transport in the DCT. The NCC transporter imports one sodium and one chloride ion from the lumen into the cell. This transporter can be blocked by thiazide diuretics. Mutations in the gene encoding NCC cause Gitelman syndrome. Chloride leaves the cell via the basolateral CLCNKB channel, which needs the Barttin subunit in order to function. Both proteins are expressed in both the TAL and DCT, and their decreased function can cause Bartter syndrome (type 3 and type 4a, respectively). Sodium can exit the cell via the basolateral Na-K-ATPase that actively exports three sodium ions while importing two potassium ions. Potassium is immediately recycled and pumped out of the cell by the basolateral potassium channel KCNJ10, mutations in which cause EAST syndrome. Calcium and magnesium are imported by TRPV5 and TRPM6, respectively.

# Gitelman Syndrome : Pathogenesis

Biallelic inactivating mutations in *SLC12A3* which encodes for the thiazide sensitive Sodium Chloride Cotransporter (NCC)



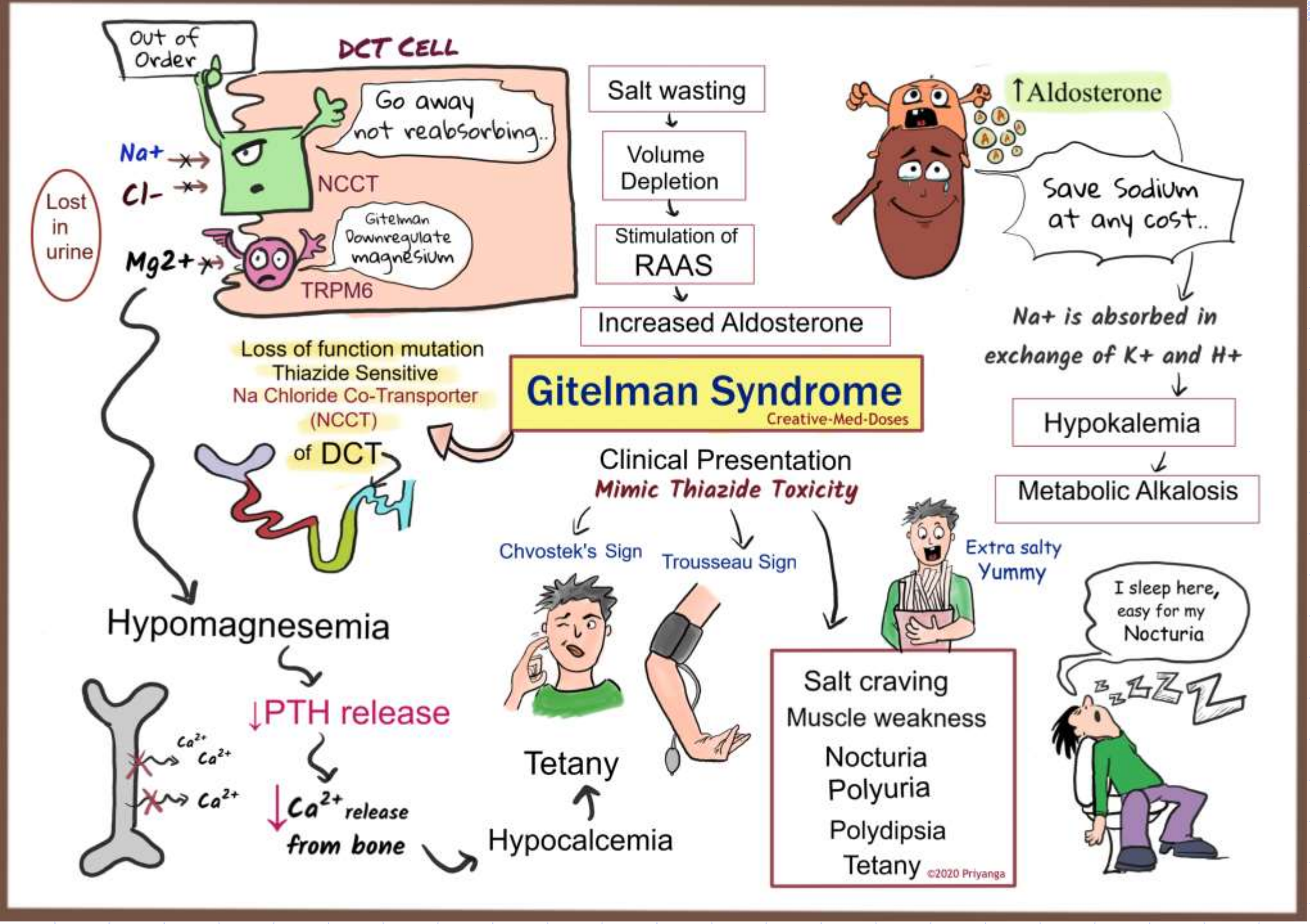

↑ NaCl delivery to distal nephron

↑ $K^+$ and ↑ $H^+$ secretion → Hypokalemia Metabolic alkalosis

Volume Contraction → ↑ Renin

↑ $Ca^{++}$ reabsorption → Hypocalciuria

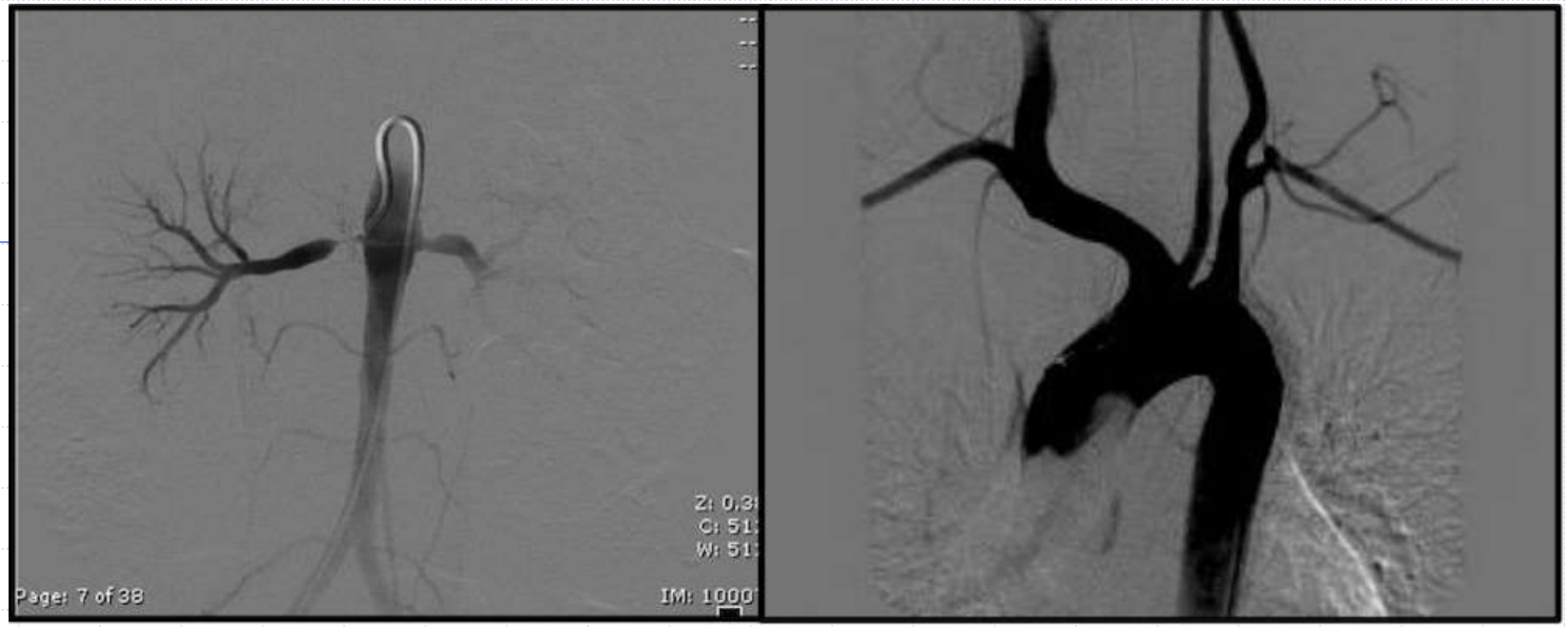
↓ $Mg^{++}$ reabsorption → Hypermagnesuria, Hypomagnesemia




**Spironolactone: Mechanism of action in Gitelman Syndrome**

# CASE 9: A 5-year-old girl

- Referred for evaluation of **metabolic alkalosis with hypertension**
- **She developed dilated cardiomyopathy** (after an episode of CCF)
- **BP- 180/120 mm Hg in Right upper limb**
- Physical examination findings were significant for weak left carotid, brachial, and radial pulses and bilateral carotid bruits.
- Renal ultrasonography with Doppler was performed, suggestive of **renal artery stenosis**
- Serum creatinine-0.35 mg/dL, urinalysis- normal
- Serum bicarbonate 32 mEq/L, K 3.1, pH 7.35
- ESR-80 mm/h
- CRP- 27 mg/L
- **Multiple antihypertensive agents required- Amlodipine, prazosin, hydrochlorothiazide, carvedilol, clonidine, minoxidil**




Angiography of her brain, chest, and abdominal vasculature was performed, revealing **significant narrowing of the left common, external, and internal carotids, and of the bilateral subclavian, hepatic, splenic, and renal arteries;** celiac axis narrowing; asymmetric kidney size; and diffuse thickening of the aorta from the heart through the abdomen, with a bright wall signal.

## Diagnosis- Takayasu arteritis

# EULAR/PRINTO/PRES classification criteria of childhood TA

- Angiographic abnormalities plus 1 of 5 following criteria (sens 100%, spec 99.9%)

1. Pulse deficit or claudication
2. Four limbs blood pressure discrepancy > 10 mmHg
3. Bruit
4. Hypertension >P95$^{th}$
5. Acute phase reactant

- Angiography (conventional, CT, or MRI) of the aorta or **its main branches** and pulmonary arteries showing aneurysm/ dilatation, narrowing, occlusion or thickened arterial wall not due to fibromuscular dysplasia, or similar causes; changes usually focal or segmental

Ann Rheum Dis 2010;69:798-806.

# Further Management

- Methylprednisolone pulses
- Persistent inflammatory activity
- Mycophenolate mofetil with prednisolone
- Antihypertensive drugs (Amlodipine, prazosin, hydrochlorothiazide, carvedilol, clonidine, minoxidil)
- Enalapril avoided due to B/L RAS
- Later, underwent balloon angioplasty of renal arteries
- Better control of hypertension
- Gradual tapering of steroids

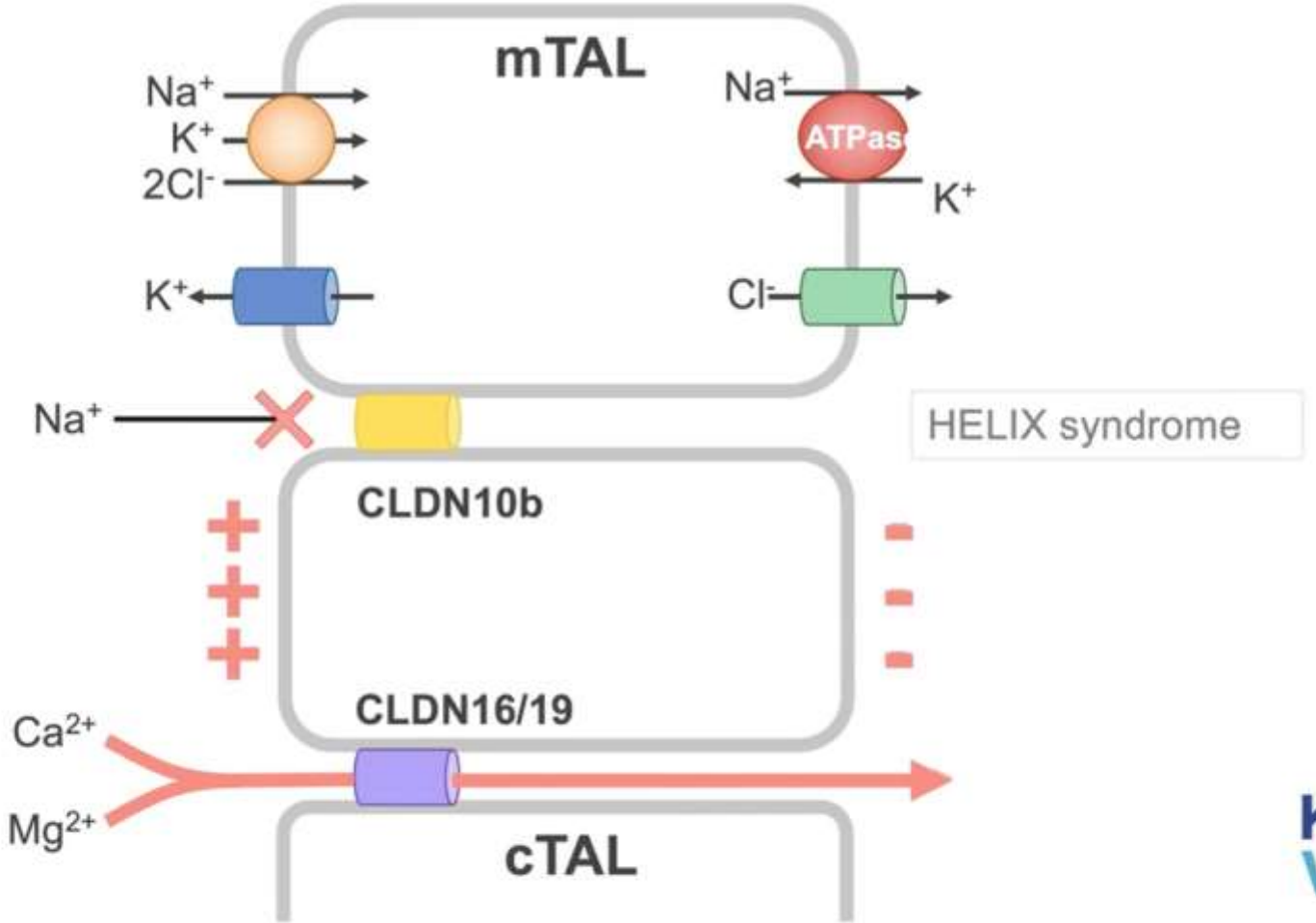
# Rare syndromes with hypokalemic metabolic alkalosis

# Inherited hypermagnesemia: HELIX syndrome

- Autosomal recessive
- Salt wasting with hypokalemic metabolic alkalosis
- Blunted natriuresis to furosemide but exaggerated response to thiazide
- Hypermagnesemia with hypomagnesiuria
- Hypocalciuria
- Hypohidrosis
- Lacrimal gland dysfunction
- Ichthyosis
- Xerostomia

Bongers 2017 JASN 28:3118
Klar 2017 PLoS Genet 13:e1006897
Hadj-Rabia 2018 Genet Med, 20:190-201

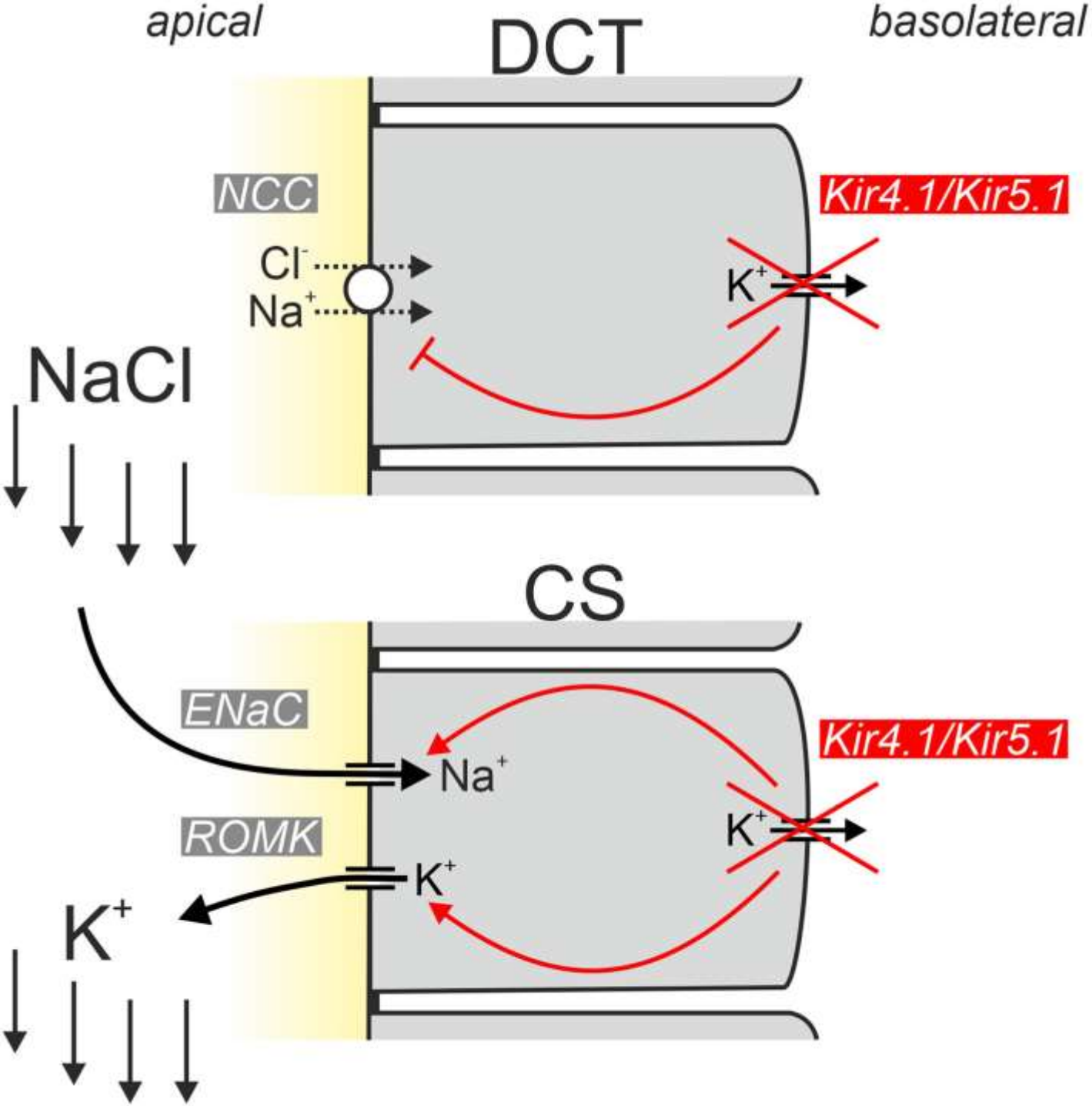
# Separate paracellular channels mediate $Na^+$ divalent cation reabsorption in the TALH

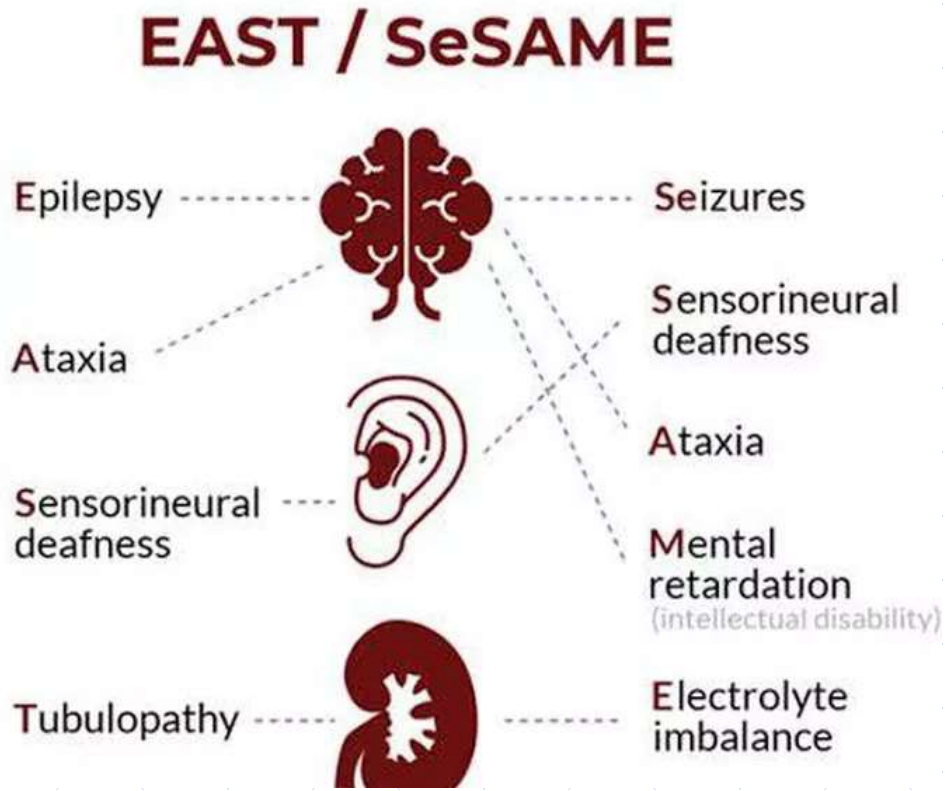



Source: A.Yu

KIDNEY WEEK 2021

# EAST/SeSAME syndrome




**Hypomagnesemia**

# Take home messages

- Every child with hypokalemic metabolic alkalosis should be approached systematically
- BS and GS are important renal tubular causes of hypokalemic metabolic alkalosis
- BS-3 exhibits the widest range of phenotypical variability
- BS-1 and 2 are typically antenatal onset with hypercalciuria
- BS-4 is termed antenatal BS with sensorineural deafness
- The term BS-5 is used to refer to transient Bartter syndrome due to MAGED2 mutations
- As of now, treatment of BS and GS is purely symptomatic; vasopressin and gene therapy are under research
- Hypokalemic metabolic alkalosis with hypertension should prompt search for renovascular hypertension and monogenic hypertension


JAWAHARLAL INSTITUTE OF
POST GRADUATE MEDICAL
EDUCATION AND
RESEARCH
JIPMER

# Thank You


JIPMER WOMEN & CHILDREN'S HOSPITAL