A case of hypokalemia

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Case

57 y.o. male

CC: Weakness

HPI: About 20 years ago, he developed bilateral lower extremity weakness. Laboratory evaluation showed hypokalemia. Since then, he has been receiving potassium supplement, but his serum potassium has remained low or low normal. He did not experience further episode of weakness. He denied vomiting, diarrhea, palpitation, tremor or excessive sweating. He also denied use of over the counter medications or supplements.

PMH: gall bladder polyp, colon polyp, hyperuricemia

FH: Father: hypertension, DM, emphysema, angina pectoris, Grandfather: liver cancer

Mother: subarachnoid hemorrhage

Case

SH: occupation: high school teacher, smoking: 20 cigarettes/day (20y.o. ~ 45 y.o.)

alcohol: none

Medications:

Ursodeoxycol 100mg twice daily

Vitamin B 2

Sustained release potassium chloride 2400mg twice daily

Allopurinol 100mg once daily

Physical Examination

Height 163 cm, BW 76 kg

Well nourished, not in acute distress

BP 136/86 mmHg, HR 66/min, regular

Neck: no goiter

Lung: clear to auscultation

Heart; normal S1, S2 without murmur

Abdomen: soft and flat, normal bowel sound, no bruit

Extremity: no edema

Skin: moist, no rash

Question

What test is the first step in differential diagnoses of hypokalemia?

1. Plasma renin activity and plasma aldosterone concentration
2. Urine electrolytes
3. Arterial blood gas
4. Thyroid function tests

Answer

Rule out pseudohypokalemia.

“Pseudohypokalemia”

- Caused by potassium uptake by cells after venipuncture
- Usually seen in patients with many metabolically active blood cells, such as patients with acute myeloid leukemia
- Can be prevented by rapid separation of the plasma from the cells following venipuncture or storage of the blood at 4 ℃ before assay.

Answer

You eventually need to perform all the tests but the first step is to check urine electrolytes to determine if hypokalemia is from renal or extrarenal potassium loss.

Laboratory Data

ABG		
pH	7.475	
pCO2	42.8	mmHg
HCO3	31.1	mmol/L
CBC		
WBC	8400	/μl
Hb	16.8	g/dL
Hct	48.7	%
Plt	233	$\times 10^3/\mu l$

Chemistry		
Na	139	mEq/L
K	3.2	mEq/L
Cl	99	mEq/L
BUN	9	mg/dL
Cre	0.88	mg/dL
Glu	87	mg/dL
Ca	8.8	mg/dL
P	2.7	mg/dL
Mg	1.1	mg/dL
U-Na	148	mEq/L
U-K	48	mEq/L
U-Cl	145	mEq/L
U-Cr	34.4	mg/dL

S-Osm	286	mOsm/kg
U-Osm	581	mOsm/kg
TSH	1.80	μU/ml
Free T4	1.13	ng/dL
Free T3	3.1	pg/ml
PRA	6.6	ng/ml/hr
PAC	236.6	pg/ml

Laboratory Data

24 hour urine study

Na: 137 mEq/day

K: 137 mEq/day

Cl: 199 mEa/day

Ca: 26 mg/day

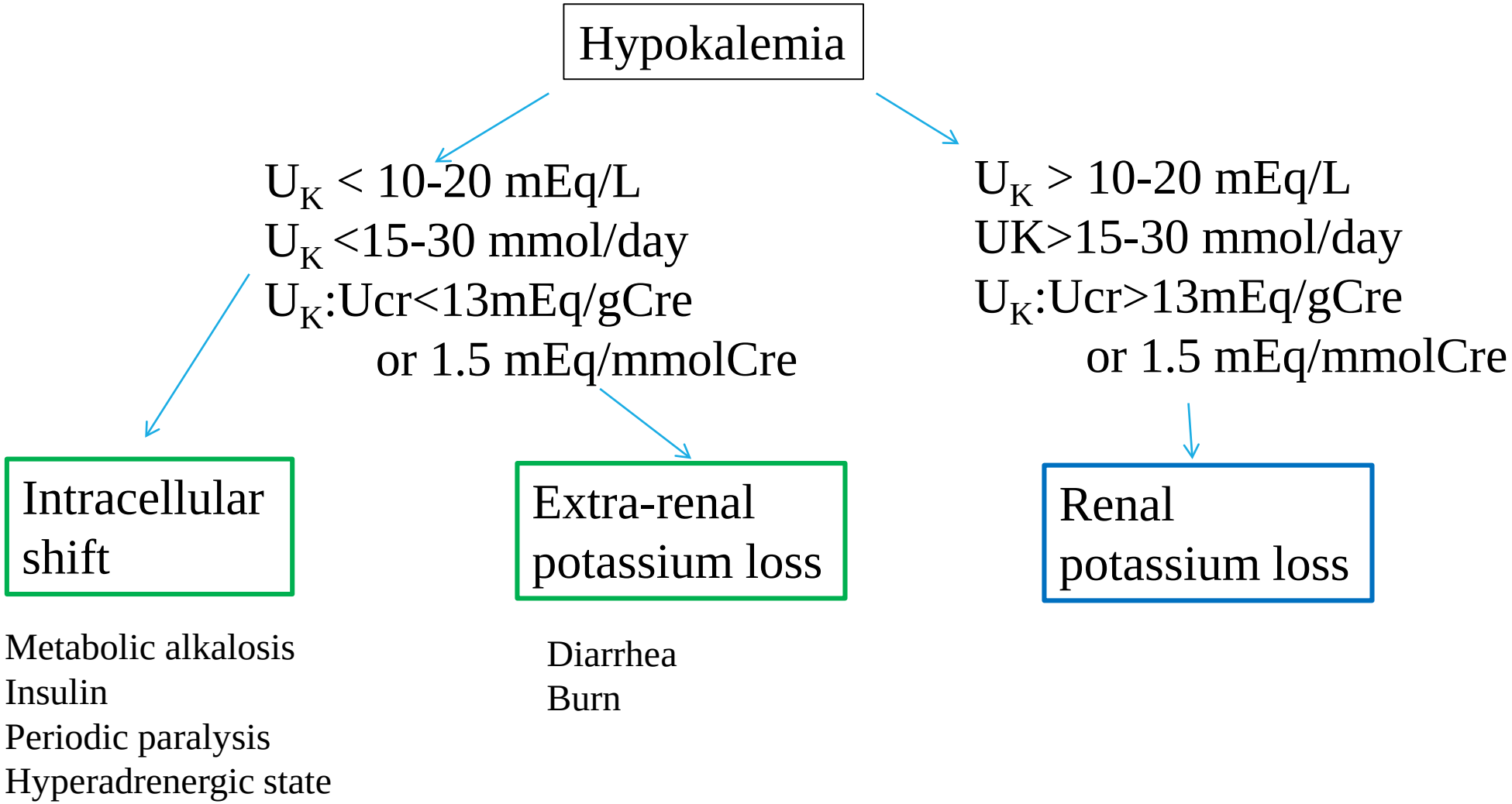
Cre: 1418 mg/day

Question

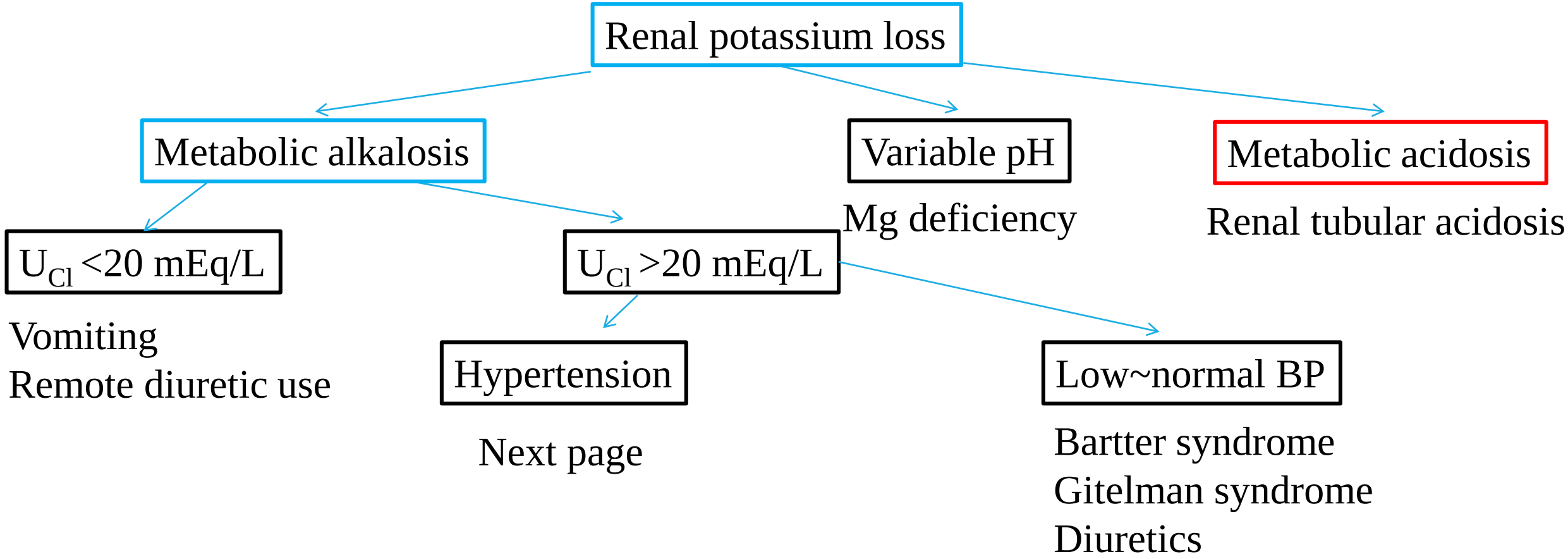
What are the possible causes of his hypokalemia ?

1. Primary aldosteronism
2. Hypokalemic periodic paralysis
3. Diarrhea
4. Renal tubular acidosis
5. Diuretic abuse
6. Vomiting
7. Bartter syndrome
8. Gitelman syndrome
9. Liddle syndrome

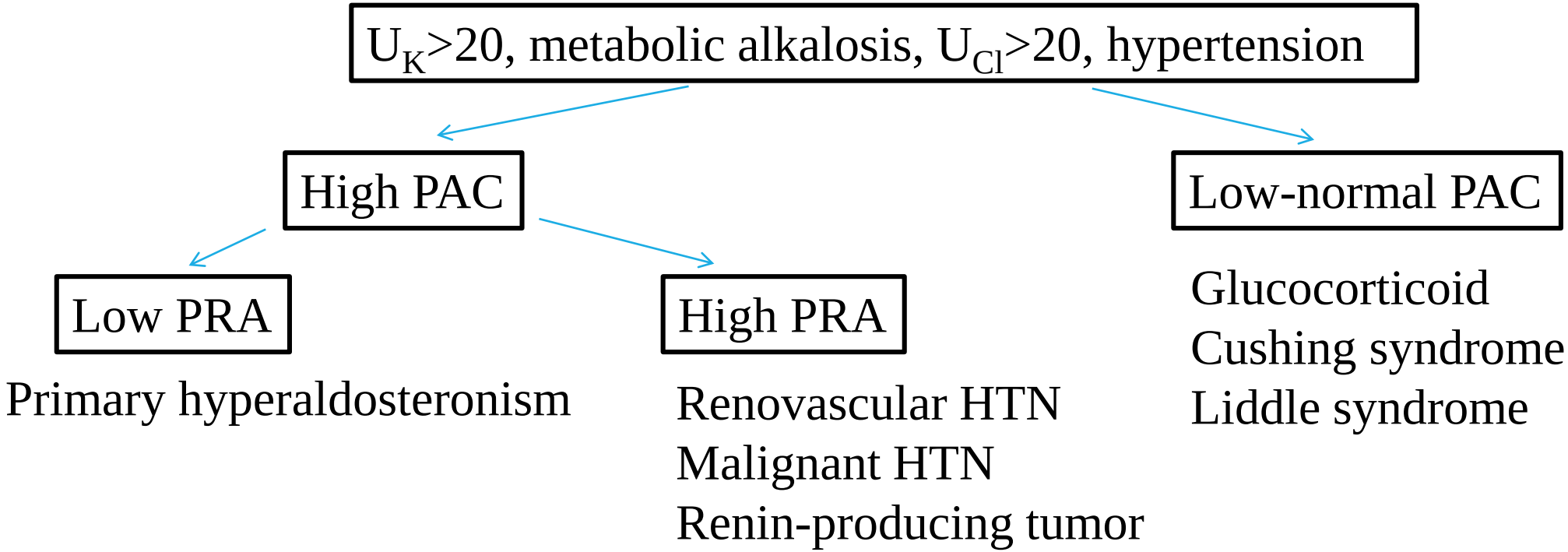
Differential Diagnosis of Hypokalemia



Differential Diagnosis of Hypokalemia



Differential Diagnosis of Hypokalemia



Answer

Step1. His urine potassium was > 20 meq/L, 24 hour urine potassium 137mEq, urine K/Cre 139mEq/gCre →renal potassium loss

Step2. ABG showed metabolic alkalosis. →renal tubular acidosis is unlikely

Step3. His urine chloride was > 20 mEq/L. →vomiting is unlikely

Step4. He is not hypertensive. →Bartter syndrome, Gitelman syndrome, diuretic abuse are the consideration.

Question

His PRA was 6.6 ng/ml/hr and PAC was 236.6 pg/ml. What is the most likely cause of elevated PRA and PAC?

1. He also has primary aldosteronism.
2. He also has renal artery stenosis.
3. He also has renin producing tumor.
4. Secondary aldosteronism from intravascular volume depletion.

Answer

4. Secondary aldosteronism from intravascular volume depletion.

Plasma renin activity (PRA) and plasma aldosterone concentration(PAC)

- Hypokalemia has to be corrected before measurements (hypokalemia suppress aldosterone).
- Many medications can affect the results.

	PAC	PRA	PAC/PRA
ACE-I/ARB	↓	↑↑	↓
β- blockers	↓	↓↓	↑
Direct renin inhibitors	↓	↓↓	↑
Diuretics	↑	↑↑	↓
Aldosterone antagonists	↑	↑↑	↓

Plasma renin activity (PRA) and plasma aldosterone concentration(PAC)

- Mineralcorticoid antagonists (spironolactone, eplerenone) has to be stopped 4-6 weeks before the test
- ACE, ARB, diuretics, beta-blockers may be acceptable. (See next slide.)

Initial aldosterone/renin ratio on antihypertensives among patient with proven aldosterone-producing adenoma

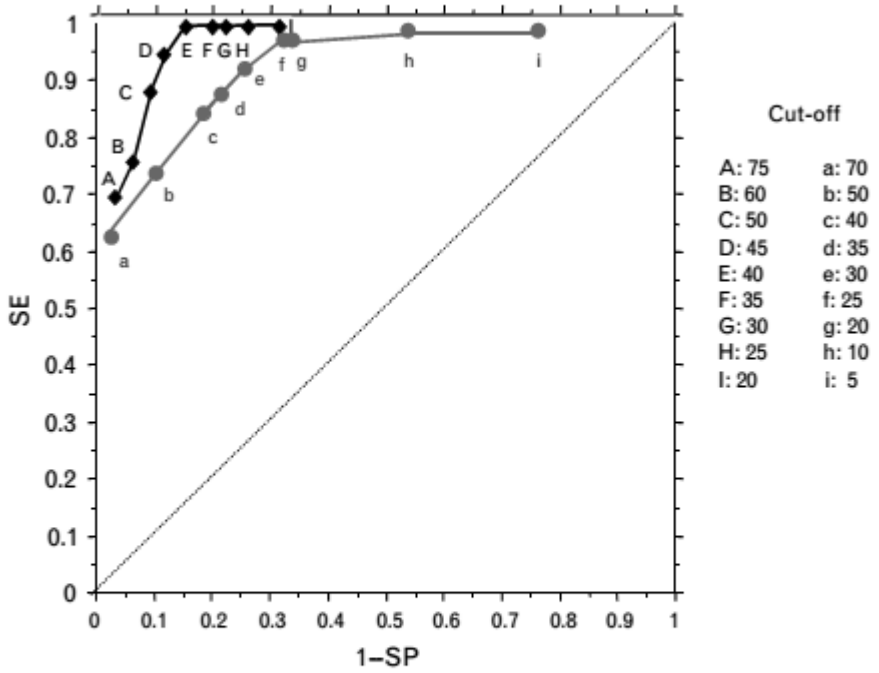
Table 2. Plasma Aldosterone, PRA, ARR, Potassium, and Medications for Each Patient With Adrenal Adenoma

Patient No.	Age (y)/Sex	PA (ng/dL)	PRA (ng/dL/3 h)	Calculated PRA (ng/mL/h)	ARR (ng/dL ÷ ng/mL/h)	K^+ (mEq/L)	Medications
1	48/F	17	<50	0.16	102	4.3	HCTZ, 25 mg/d
2	60/F	19	<50	0.16	114	3.9	Enalapril, 10 mg/d
3	65/F	19	<50	0.16	174	4.0 (3.3)	Lisinopril, 20 mg/d HCTZ/triamterene, 75/50 daily Verapamil, 120 mg/d
4	60/F	67	106	0.35	190	3.5 (2.9)	Nifedipine, 30 mg/d KCl, 30 mEq/d
5	40/F	36	<50	0.16	216	3.3	Labetalol, 400 mg/d
6	47/M	40	<50	0.16	240	3.9 (2.7)	Enalapril, 20 mg/d Atenolol, 100 mg/d HCTZ/triamterene, 75/50 daily
7	42/F	41	<50	0.16	246	3.6	Furosemide, 40 mg/d Nifedipine, 60 mg/d Quinapril, 20 mg/d Metoprolol, 200 mg/d KCl, 20 mEq/d
8	50/M	41	<50	0.16	246	3.3	Nicardipine, 60 mg 3 × d
9	48/M	42	<50	0.16	252	3.5	Labetalol, 200 mg 2 × d Verapamil, 240 mg 2 × d Phenoxybenzamine, 10 mg 3 × d (spironolactone, 50 mg 2 × d)
10	54/F	53	<50	0.16	318	2.8	Enalapril, 10 mg 2 × d KCl, 40 mEq every 4 h

AJKD 2001; 37: 699-705

Sensitivity/Specificity

Fig. 2



Receiver-operating characteristic curve for upright serum aldosterone/plasma renin activity ratio (◆) and supine serum aldosterone/plasma renin activity ratio (●). SE, Sensitivity; SP, specificity.

Aldosterone/renin ratio of 40 (ng/dL/ng/ml/hr) gives the sensitivity of 100 % and specificity of 85 %

(off diuretics, ACE-I/ARB, beta-blocker)

Be careful of unit for aldosterone.

10pg/ml=1ng/dL

J Hypertens 2006; 24: 737-745

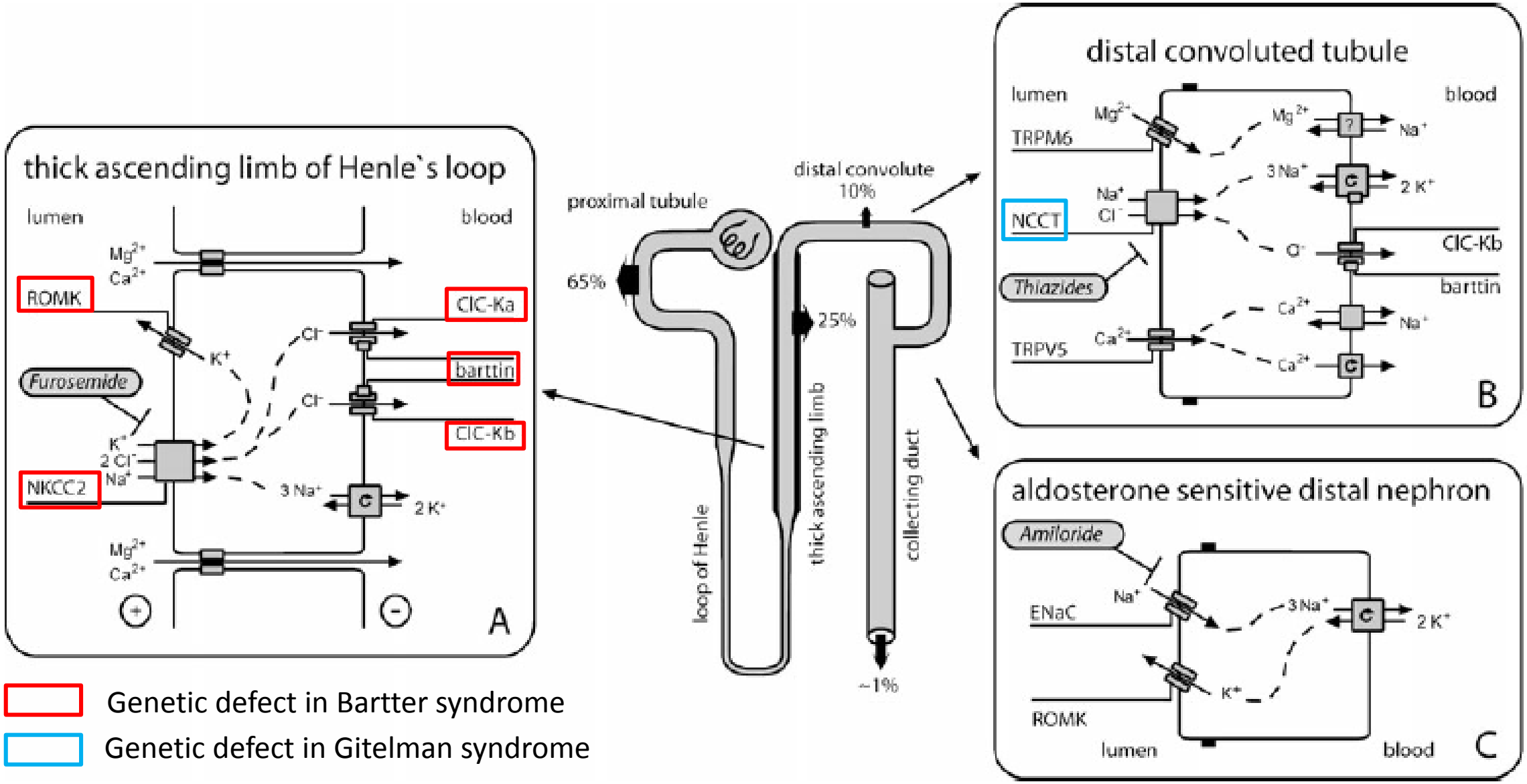
Plasma renin activity (PRA) and plasma aldosterone concentration(PAC)

- The values need to be interpreted in the clinical context.

Case

The patient denied any use of diuretics. He is a school teacher and does not seem to have access to diuretics.

Bartter syndrome and Gitelman syndrome are considered. How can you differentiate these two syndromes?



Genetic defect in Bartter syndrome

Genetic defect in Gitelman syndrome

Table 1 Genetics and presentation of Bartter and Gitelman syndromes

Disorder	Gene affected	Gene product	Clinical presentation
Bartter syndrome type I	SLC12A1	NKCC2	Antenatal Bartter syndrome (hyperprostaglandin E syndrome)
Bartter syndrome type II	KCNJ1	ROMK	Antenatal Bartter syndrome
Bartter syndrome type III	ClC-Kb	CLC-Kb	Hypochloremia, mild hypomagnesemia, failure to thrive in infancy
Bartter syndrome type IVA	BSND	Barttin (B-subunit of CLC-Ka and CLC-Kb)	Antenatal Bartter syndrome (hyperprostaglandin E syndrome) and sensorineural deafness
Bartter syndrome type IVB	ClC-Ka and ClC-Kb	CLC-Ka and CLC-Kb	Antenatal Bartter syndrome (hyperprostaglandin E syndrome) and sensorineural deafness
Bartter syndrome type V	*CaSR* gene	CaSR	Bartter syndrome with hypocalcemia
Gitelman syndrome	SLC12A3	NCC	Hypomagnesemia, hypocalcuria, growth retardation

World J Methodol 2015 June 26; 5(2): 55-61

Bartter and Gitelman syndrome

- Patients with Bartter syndrome would not respond to loop diuretics.
- Patients with Gitelman syndrome would not respond to thiazide diuretics.

Furosemide loading tests

Furosemide 20mg iv

↓

Time	Before	20 min	40min	60 min	80 min	100 min	120 min
Urine volume (L)	0	0.15	0.14	0.14	0.5	0.45	0.35
Urine Na (mEq/L)	80	27	31	32	107	106	102
Urine K (mEq/L)	26	14	11	10	6	4	5
Urine Cl (mEq/L)	90	32	34	34	102	101	95
Urine Cre (mg/dL)	34.4	20.6	14.2	14.5	5.4	4.5	4.9

Thiazide loading test

Trichlormethiazide 8mg po ↓

Time	Before	20 min	40 min	60 min	90 min	120 min	150 min	180 min
Urine Volume (L)		0.13	0.15	0.14	0.2	0.15	0.23	0.22
Urine Na (mEq/L)	29	13	13	12	11	12	13	14
Urine K (mEq/L)	43	18	15	13	13	14	14	15
Urine Cl (mEq/L)	51	23	20	18	17	18	20	21
Urine Cre (mg/dL)	54.2	19.2	13.4	12.8	13.6	14.6	14.4	14.3

Diagnosis

Gitelman Syndrome