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Potassium Disorders

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Research Focus: Urate transport
Clinical Focus: Glomerulonephritis, Electrolyte disorders, Gout, Consultative Nephrology

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– Gout: Allena Pharmaceuticals, Horizon Pharma/Amgen, Alnylam Pharmaceuticals, ANI Pharmaceuticals, Shanton Pharma
– ANCA-associated vasculitis: Amgen

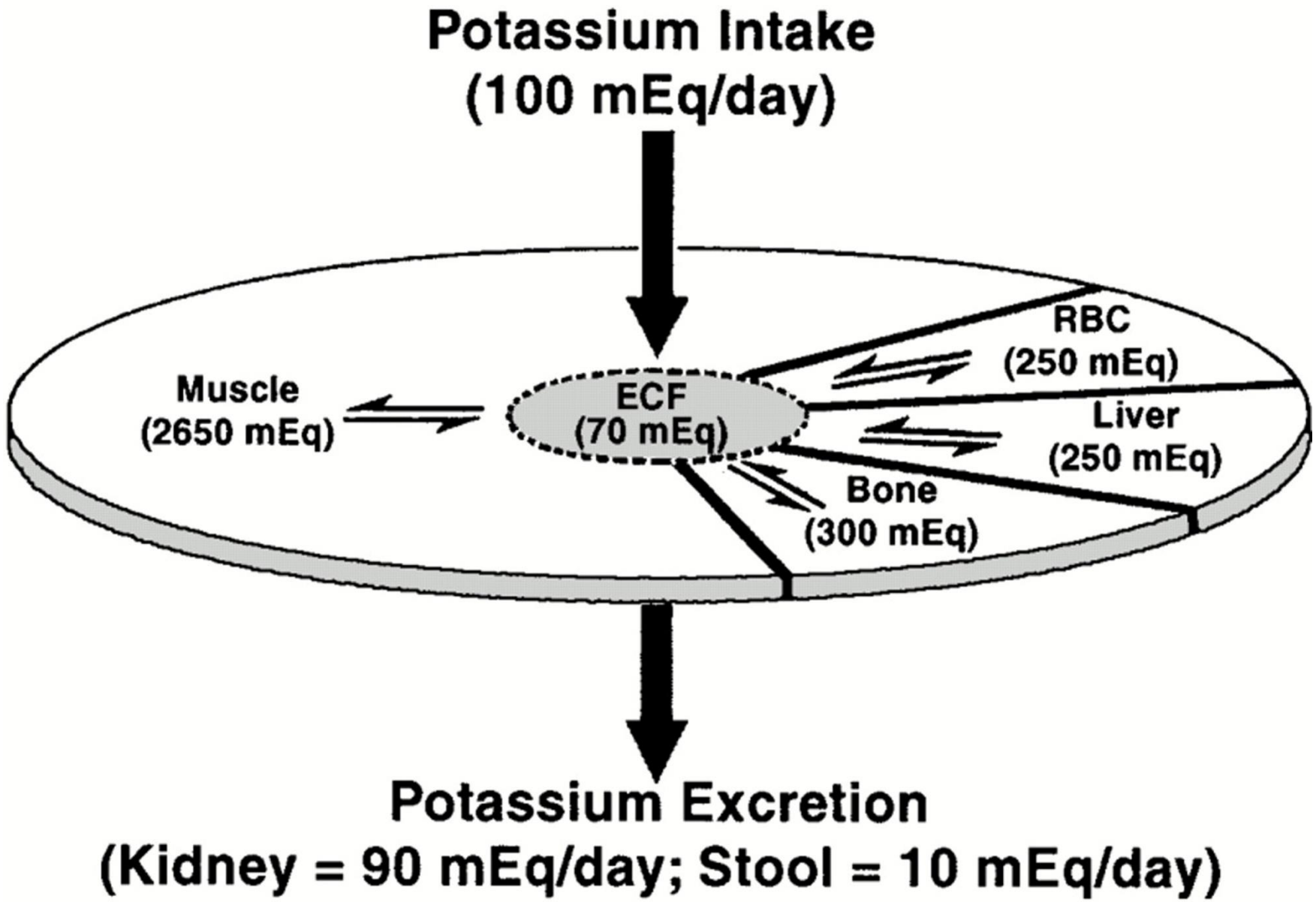
A Physiological Approach to Potassium Disorders

Overview of the relevant physiology

- Regulated K^+ secretion by the distal nephron
- Renal and adrenal RAS and K^+ homeostasis

Hyper/hypokalemia

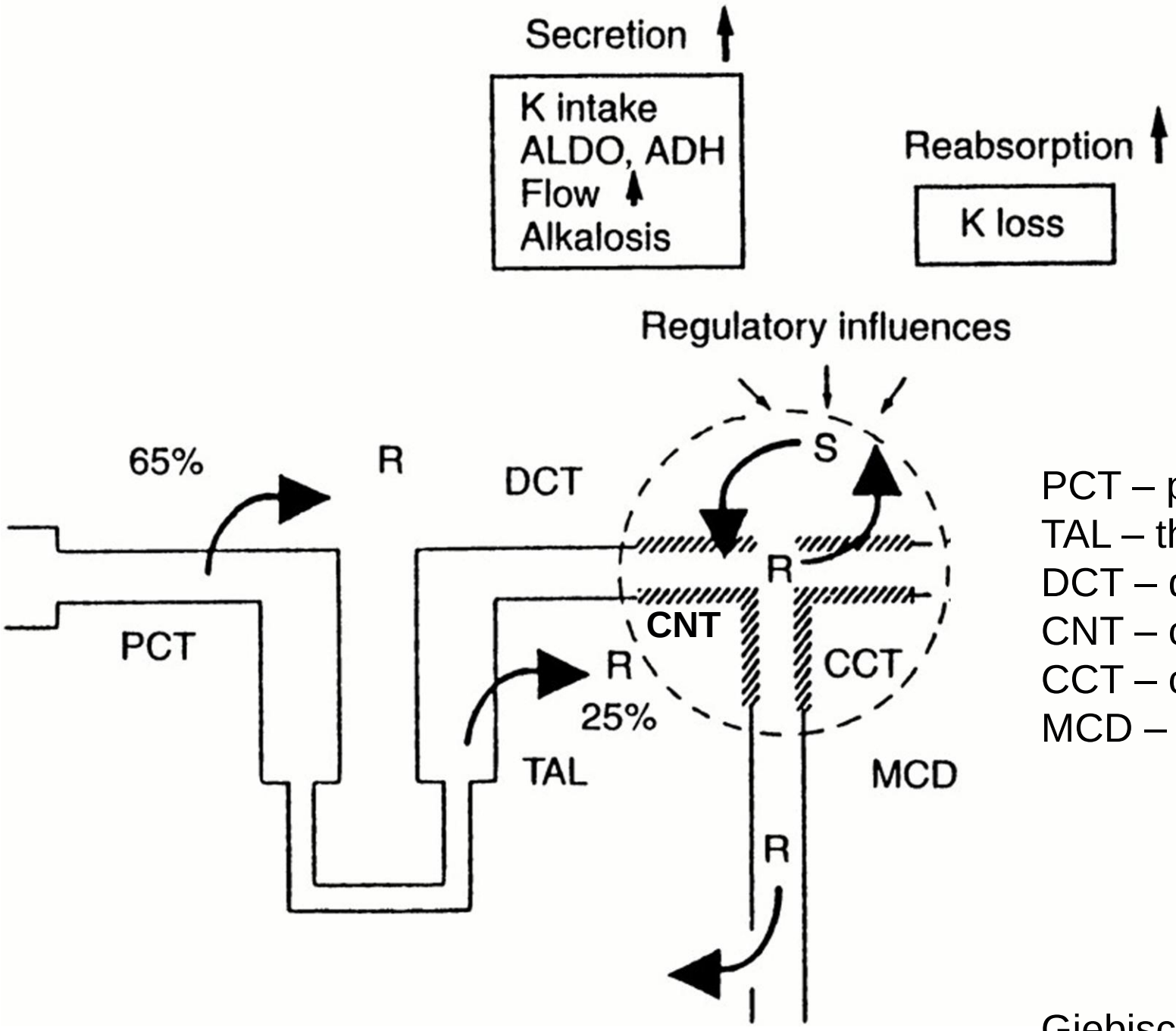
- Urinary indices and other diagnostic tests
- Clinical consequences
- Treatment of both disorders
- DD_x of both disorders



Giebisch, *AJP-Renal*, 274, 1998

Factors Affecting K^+ Shift

Factor	*Transmembrane K^+ Shift*
Insulin	↑ uptake
***β*-catecholamine**	↑ uptake
***α*-catecholamine**	↓ uptake
Acidosis	↓ uptake
Alkalosis	↑ uptake
Hyperosmolarity	↑ efflux

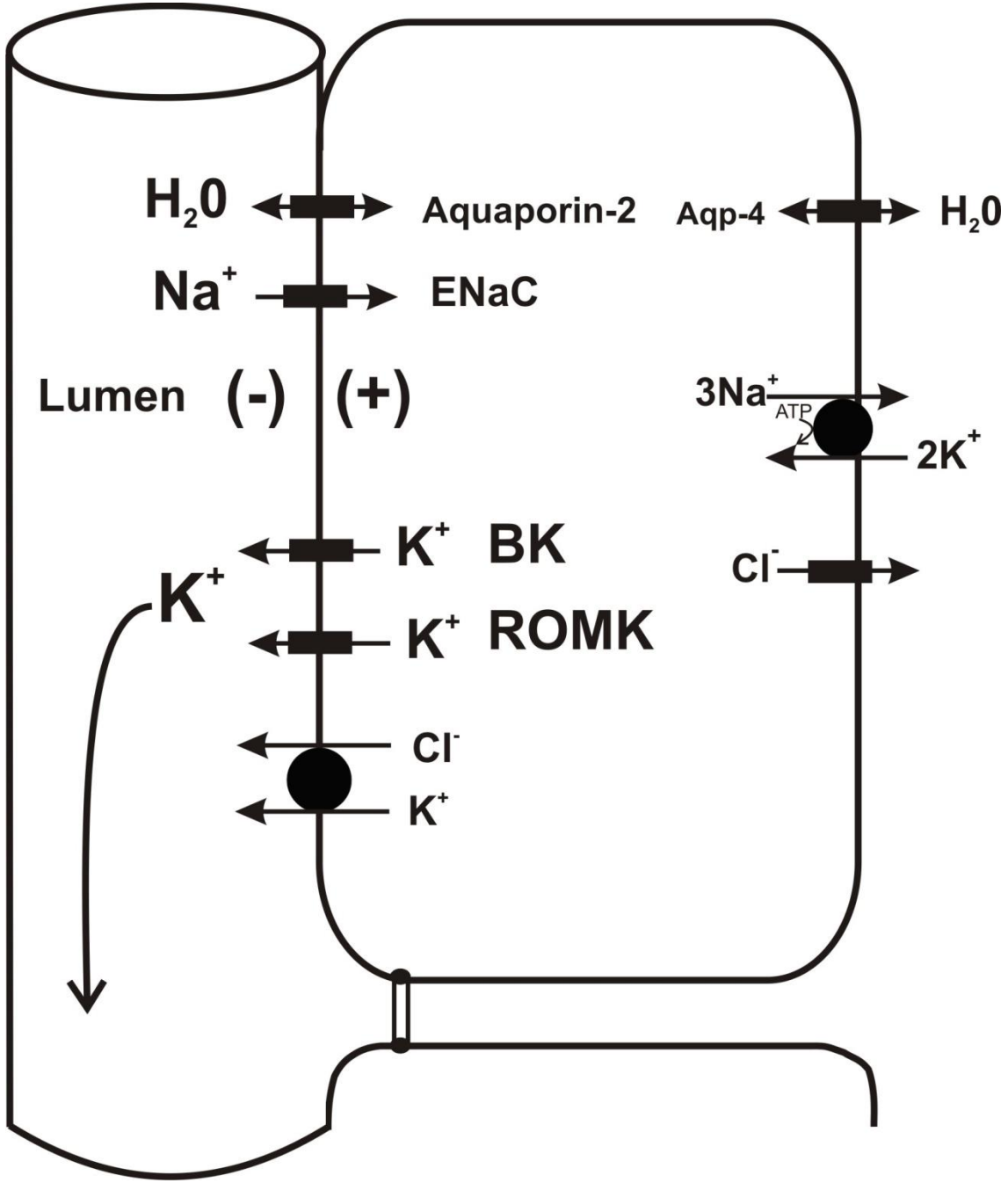


PCT – proximal convoluted tubule
TAL – thick ascending limb
DCT – distal convoluted tubule
CNT – connecting tubule
CCT – cortical collecting tubule
MCD – medullary collecting duct

Giebisch, *AJP-Renal*, 274, 1998

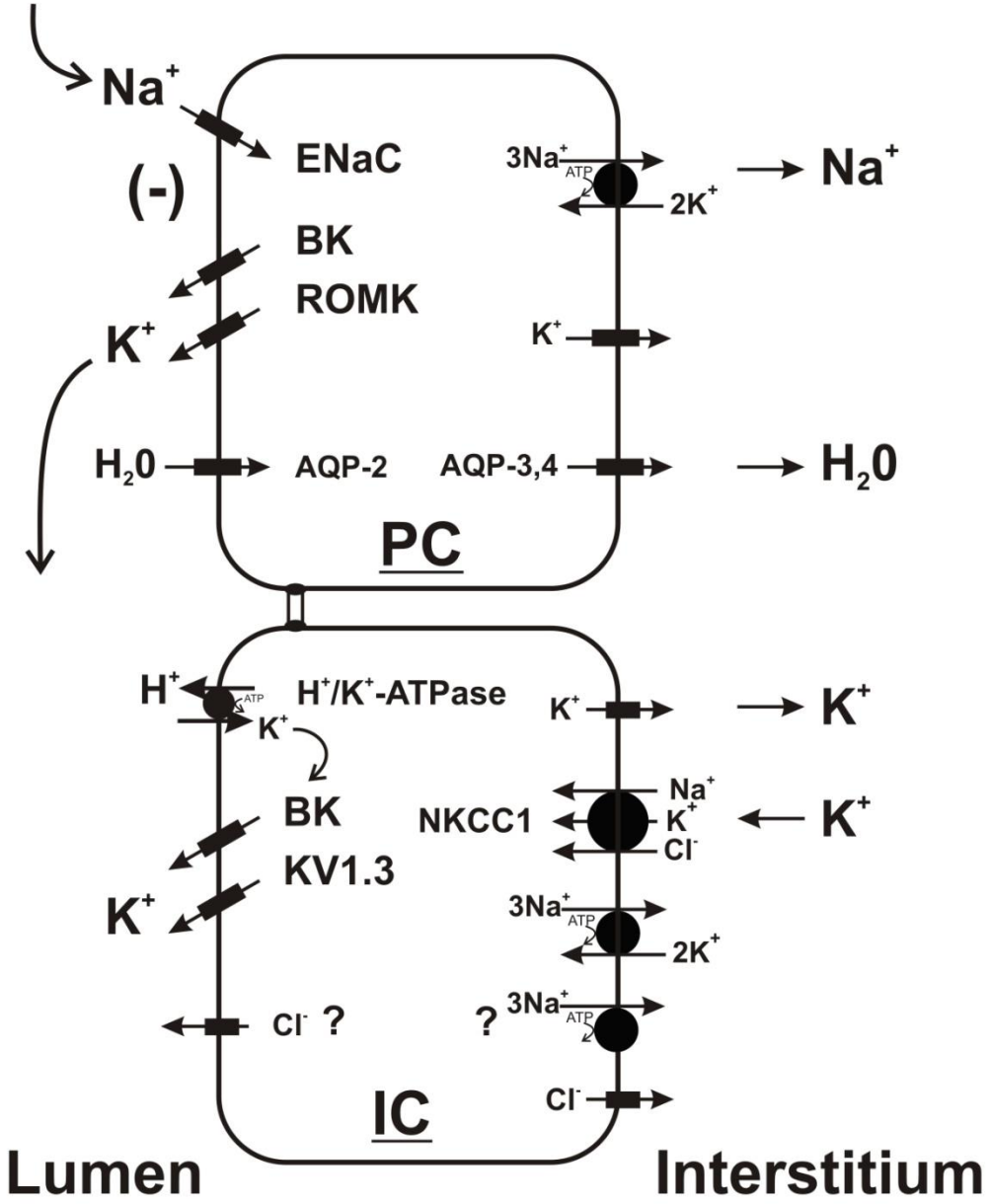
Na^+, K^+ and H_2O Transport in Principal Cells

ENaC – epithelial Na^+ channel
ROMK – secretory K^+ channel
Maxi-K/BK – flow-activated K^+ channel

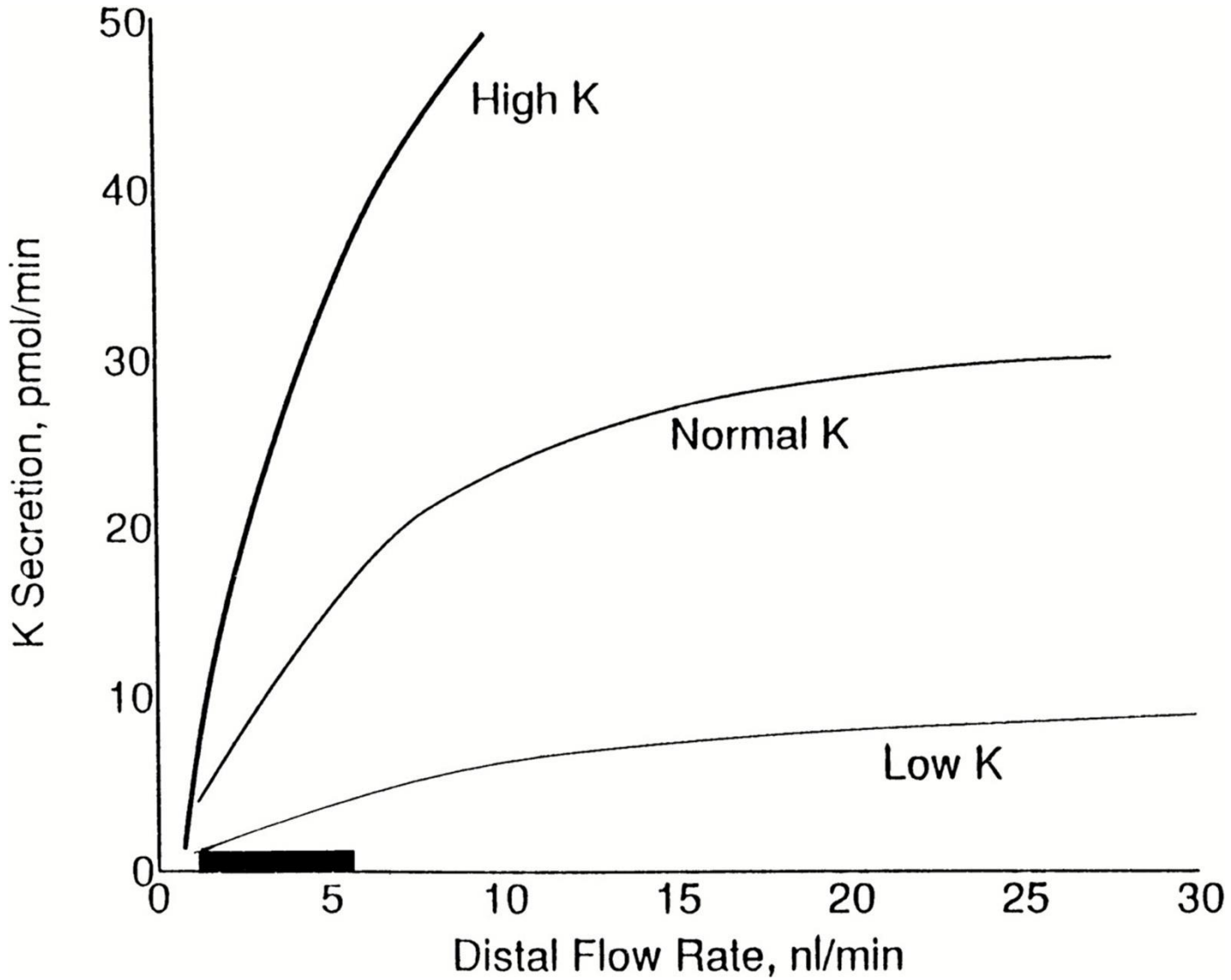


K^+ in Intercalated Cells (IC) and Principal Cells (PC)

TAKE-HOME MESSAGE:
K^+ excretion also involves ? electroneutral secretion by intercalated cells.



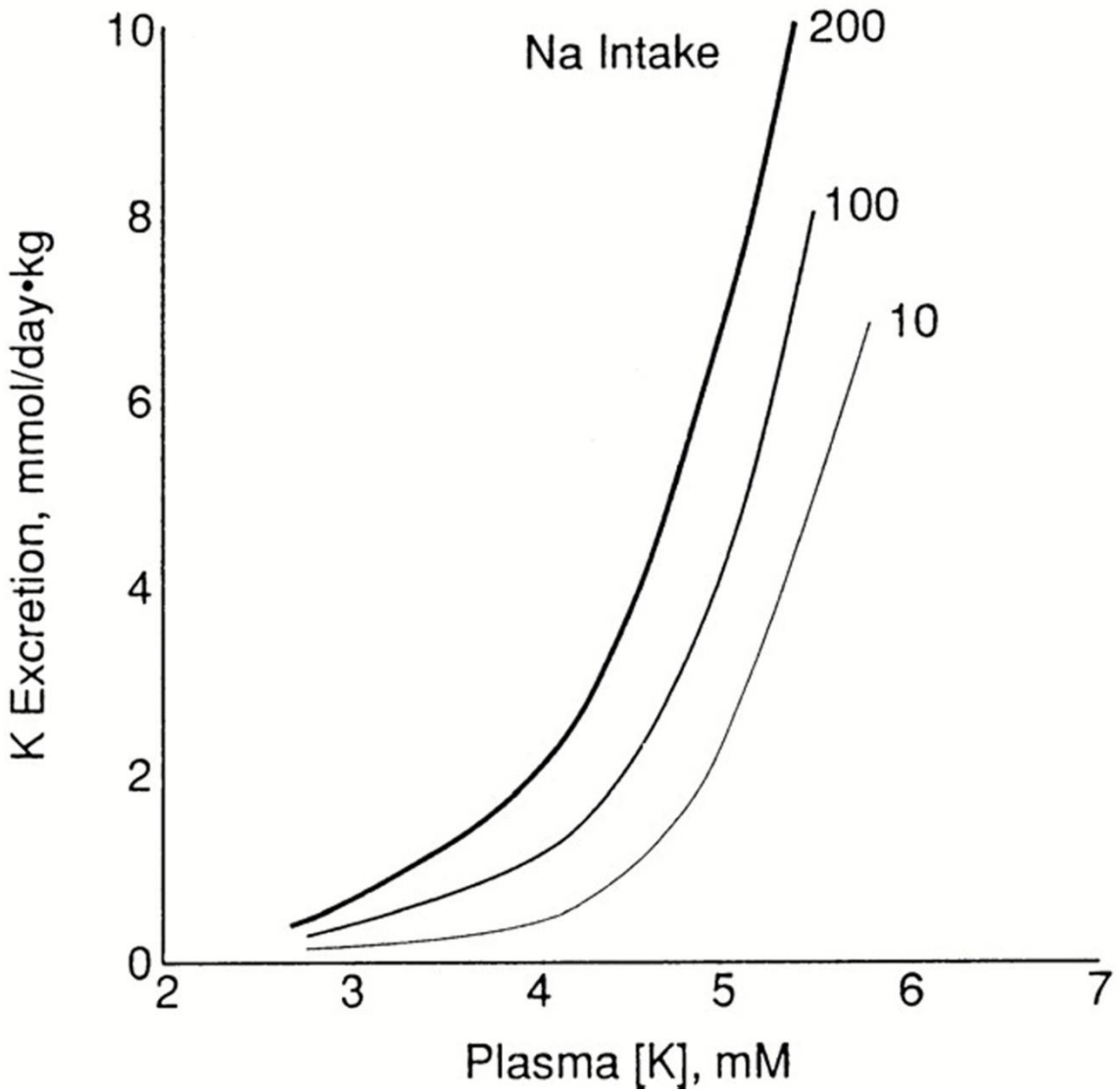
K^+ Secretion is Proportional to Distal Flow



Animals on different K^+ diets

Giebisch, *AJP-Renal*, 274, 1998

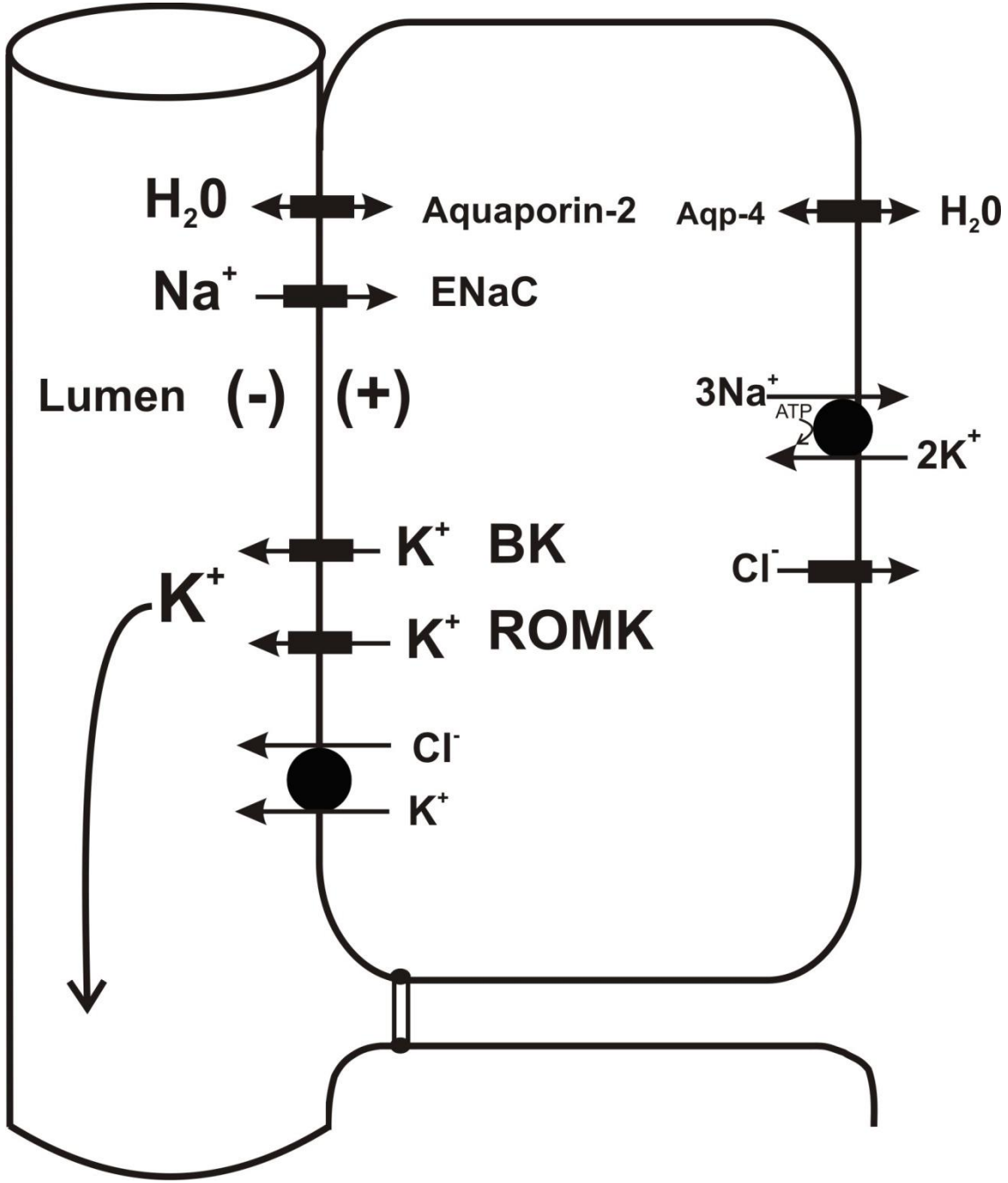
K^+ Excretion is Dependent on Na^+ Intake



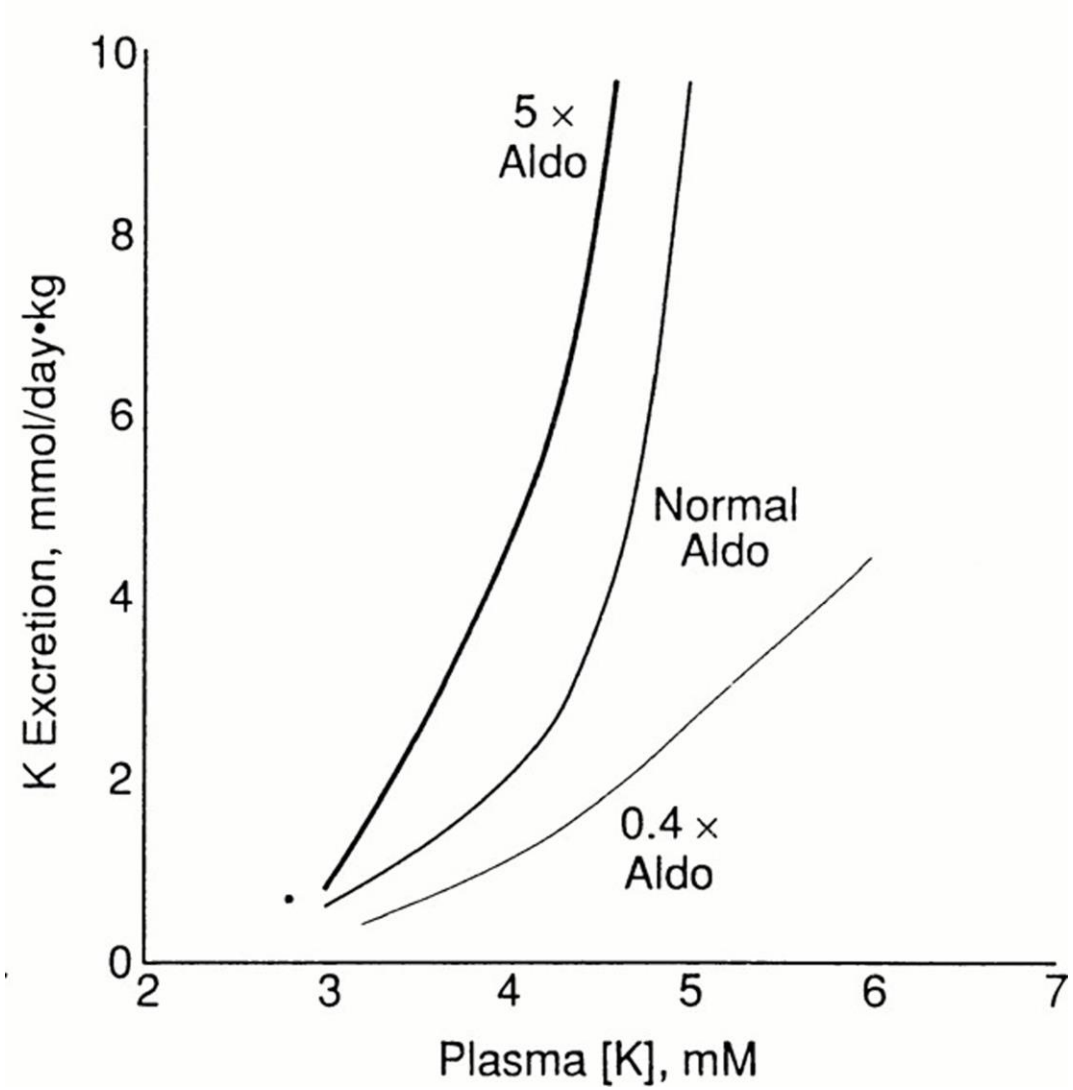
Young et al, *AJP-Renal*, 246, 1984

Na^+, K^+ and H_2O Transport in Principal Cells

TAKE-HOME MESSAGE:
K^+ excretion requires delivery of Na^+ to the distal nephron, to generate a lumen-negative potential difference



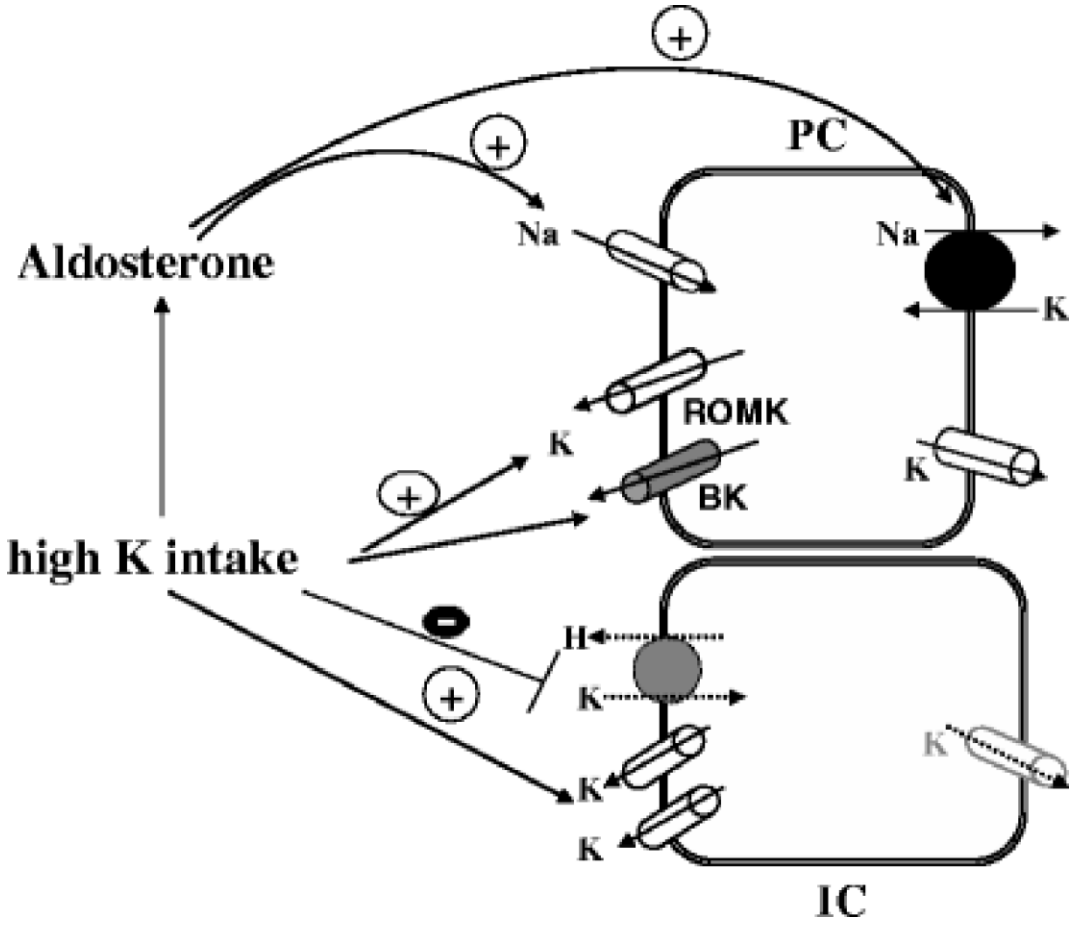
K^+ Excretion as a Function of Plasma K^+ and Circulating Aldosterone



Adrenalectomized with different levels of aldo replacement

Young et al, *AJP-Renal*, 255, 1988

Aldo-Dependent and Aldo–Independent Regulation of K^+ Excretion



TAKE-HOME:
K^+ channels are mostly regulated by K^+ intake, whereas aldosterone mostly regulates ENaC, and thus the "driving force" for K^+ excretion.

Wang and Giebisch, Eur J Physiol, 2009

Causes of Hyperkalemia

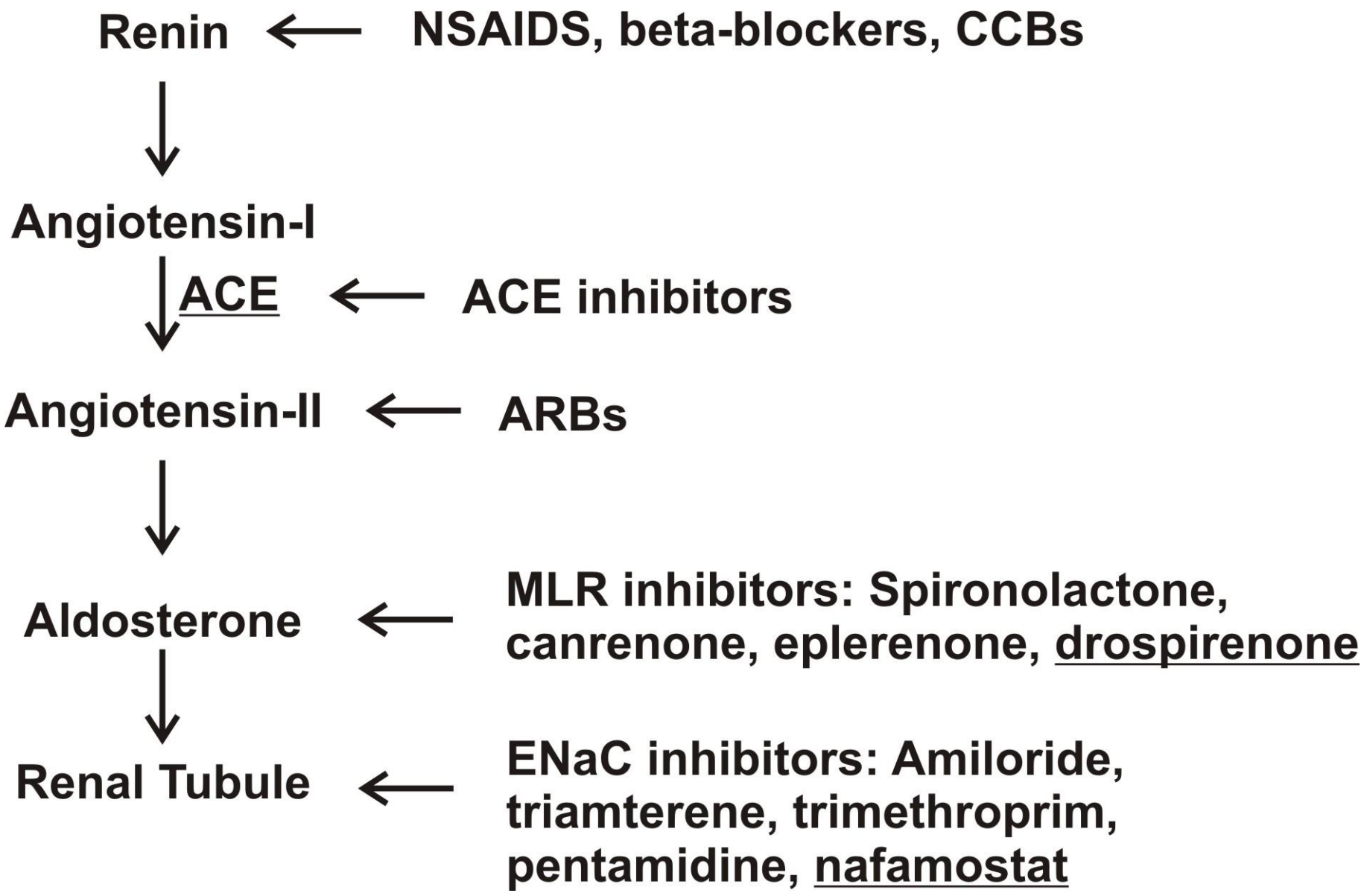
Increased intake
- K^+ supplements, diet, transfusions, iatrogenic

Decreased renal excretion
- Renal disease, particularly with type IV RTA
- DRUGS
- Adrenal insufficiency – hyperkalemia is not universal

Intra $\rightarrow$ extracellular shifts
- Hyperosmolarity
- Insulinopenia
- Metabolic acidemia – but NOT with AG acidosis
- DRUGS – Amicar, lysine, K^+ channel blockers

Artifactual
- *in vitro* hemolysis, leukocytosis, thrombocytosis
- “pseudohyperkalemia”

Drugs and the RAS



Take A Dietary History!

Consider both ***quantity*** and potassium content:

Highest content (>25 mmol/100 g)

- Dried figs, molasses, seaweed

Very high (>12.5 mmol/100 g)

- Dried fruits, nuts, avocados, bran cereals, wheat germ, lima beans

High content (>6.2 mmol/100 g)

- Vegetables: spinach, tomatoes, broccoli, beets, carrots, potatoes
- Fruits: bananas, kiwis, oranges, mangos, kiwis
- Meats: ground beef, steak, pork, veal, lamb

Gennari, *NEJM*, 1998

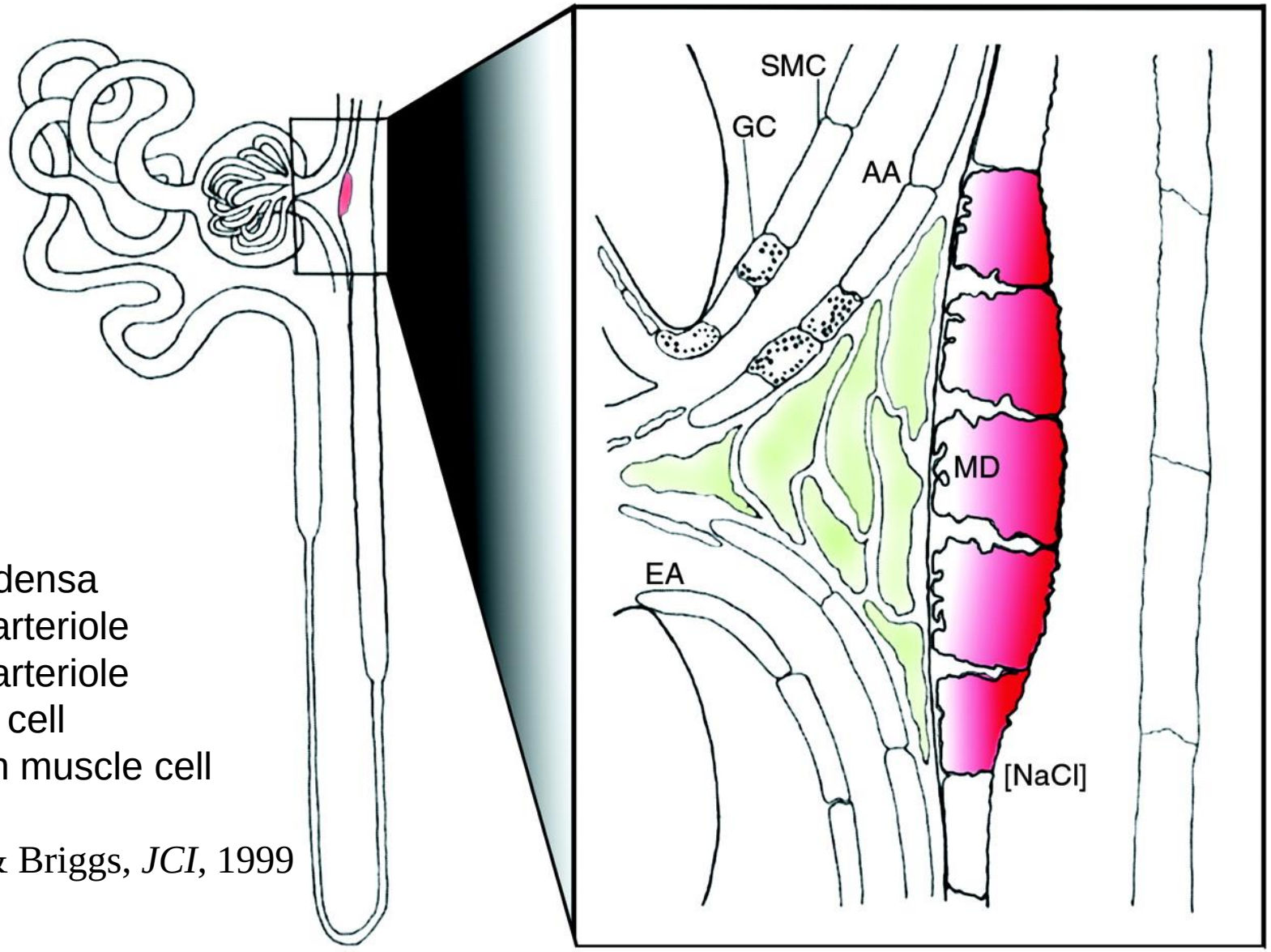
Hyporeninemic Hypoaldosteronism

Hyperchloremic acidosis in ~50%, with urine pH classically < 5.5
Hyperkalemia
↓ Plasma renin activity (PRA) and ↓ aldosterone
↓ Response of PRA to stimuli such as furosemide and captopril
Commonly with ↑ age and ↓ GFR, classically in diabetics
Often hypertensive, with clinical ↑ ECFV

Causes of Hyporeninemic Hypoaldosteronism

Diabetic nephropathy
Acute GN, i.e. nephritic syndrome
[Tubulointerstitial nephropathies, eg. Sickle cell disease] – mostly tubular damage
Drugs, e.g. NSAIDS, COX-2 inhibitors, cyclosporin, tacrolimus
Hereditary causes, e.g. pseudohypoaldosteronism type II

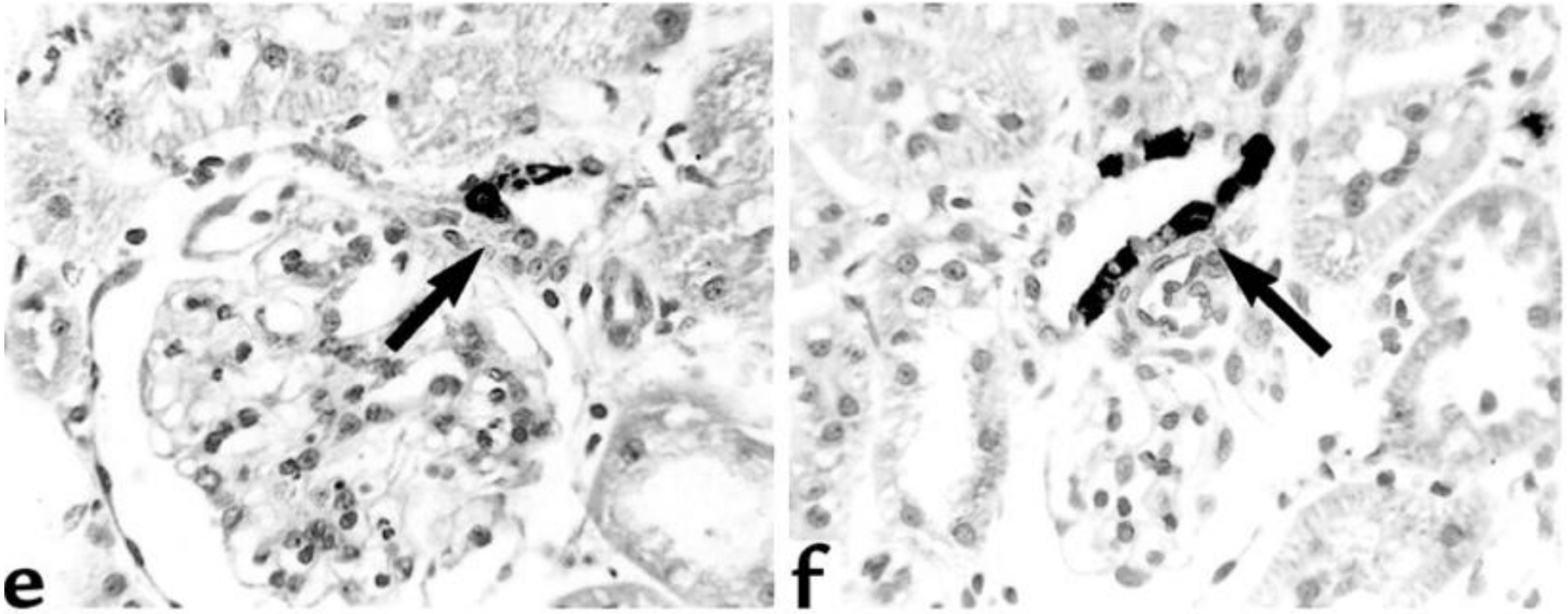
The Juxtaglomerular Apparatus, Intra-Renal Source of Renin

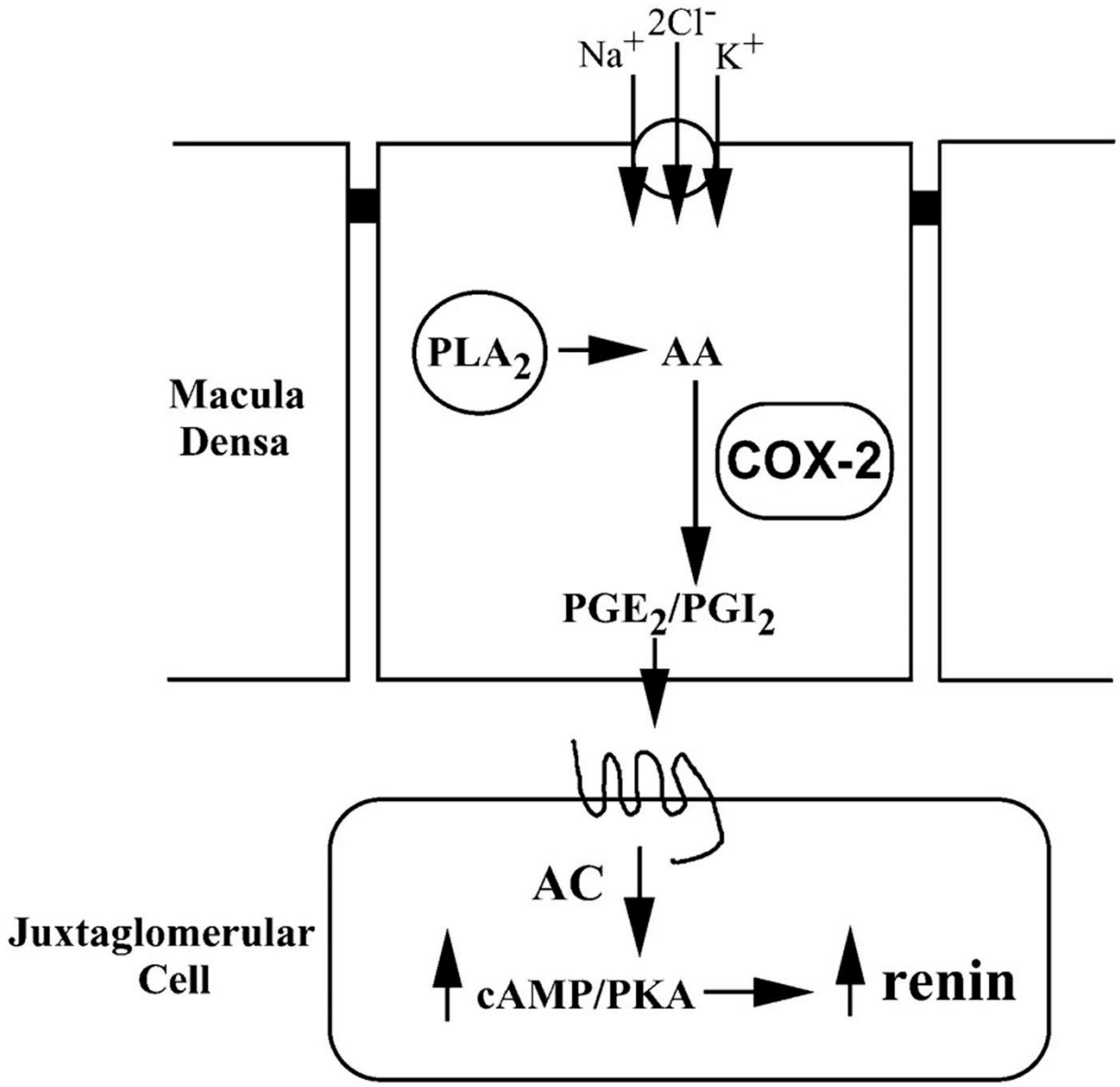


MD, macula densa
AA, afferent arteriole
EA, efferent arteriole
GC: granular cell
SMC: smooth muscle cell

Schnermann & Briggs, *JCI*, 1999

COX-2 is Expressed in the Macula Densa

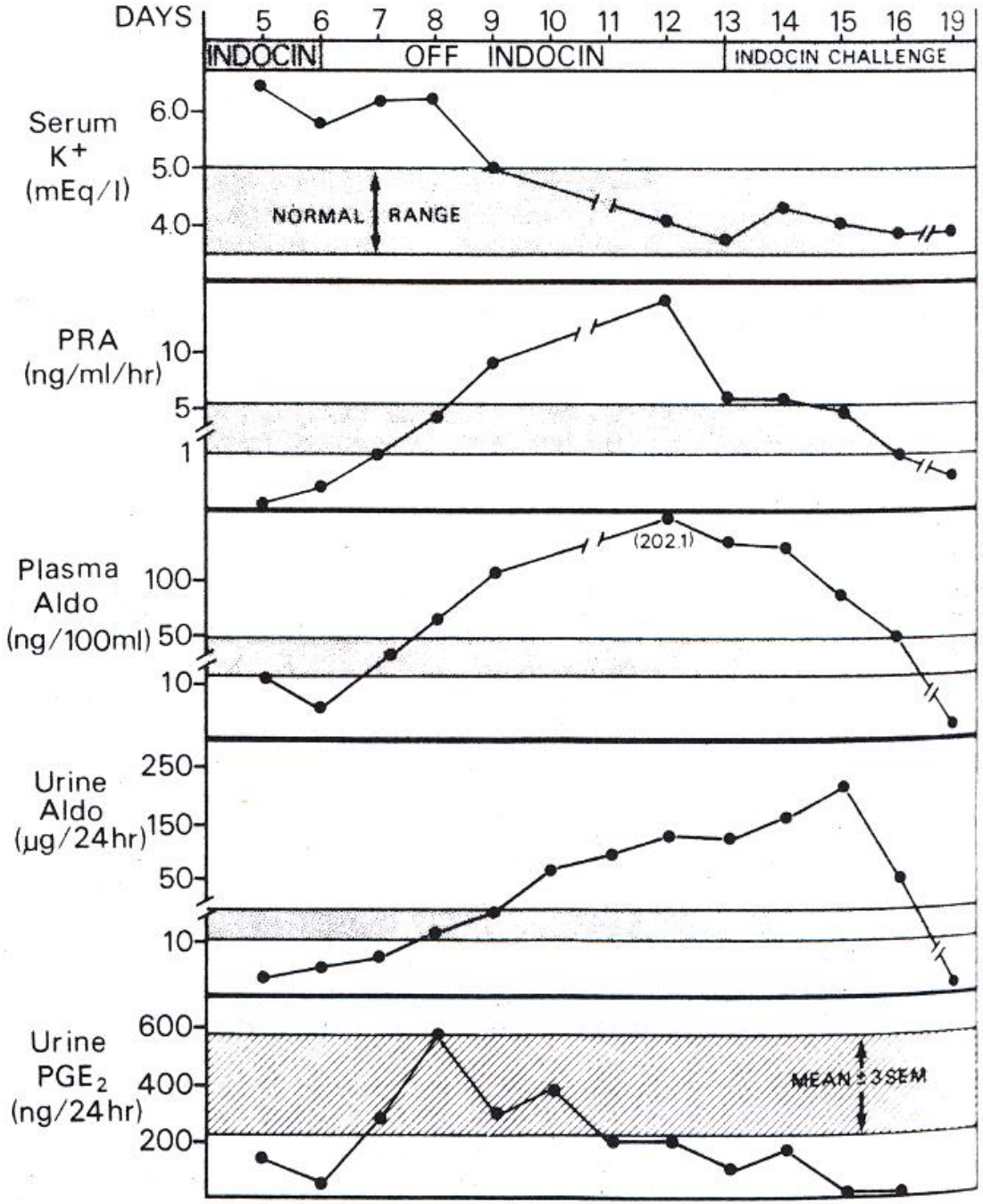




COX-2 and Paracrine Regulation of Renin Release by the JGA

Harris and Breyer, *AJP-Renal*, 281, 2001

NSAIDs and Type IV RTA



K^+

PRA

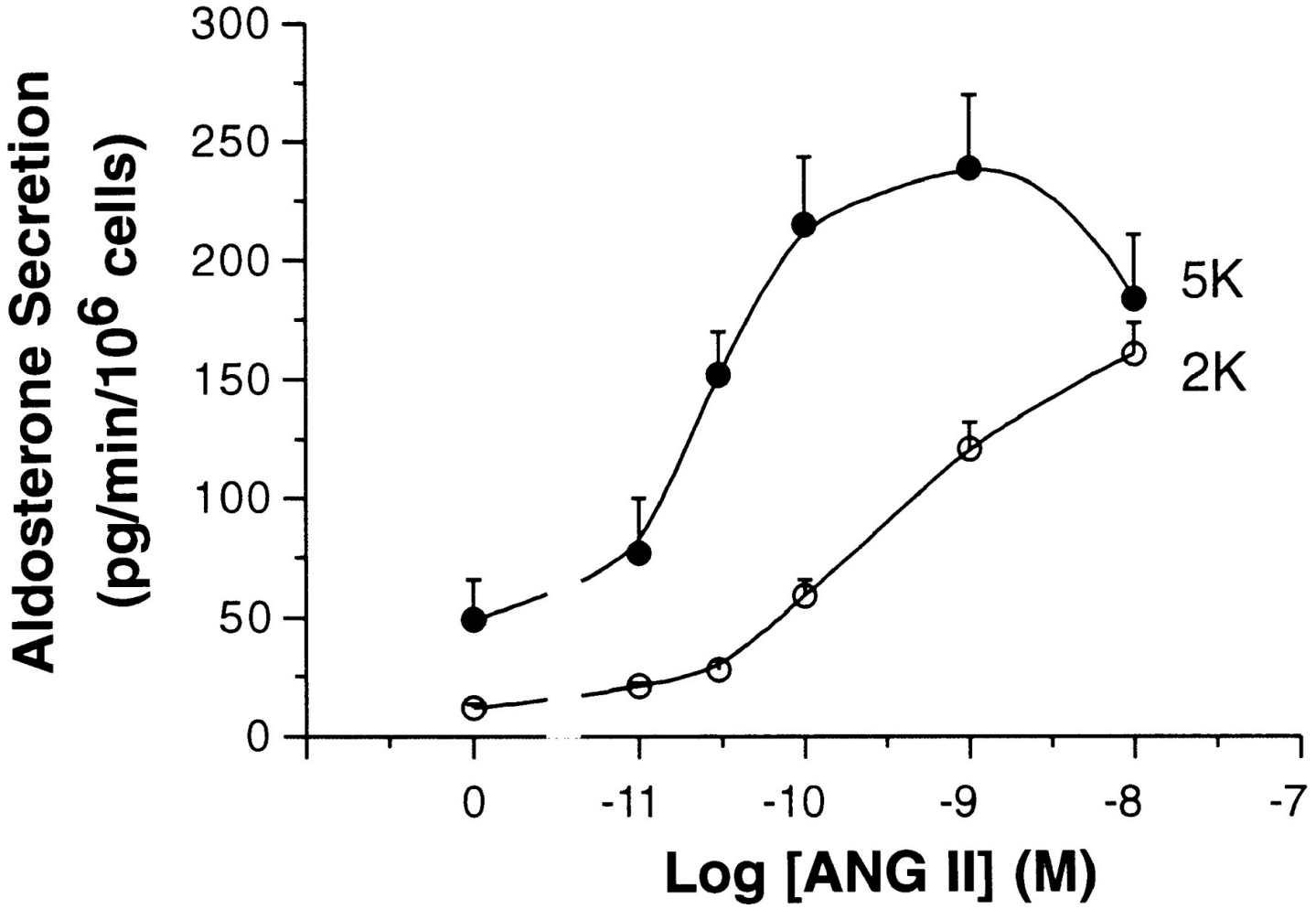
Plasma aldo

Urine aldo

Urine PGE_2

Tan et al, *Ann Int Med*, 90, 1979

Adrenal Aldosterone Release due to ↑[K^+] is Modulated by ANG-II



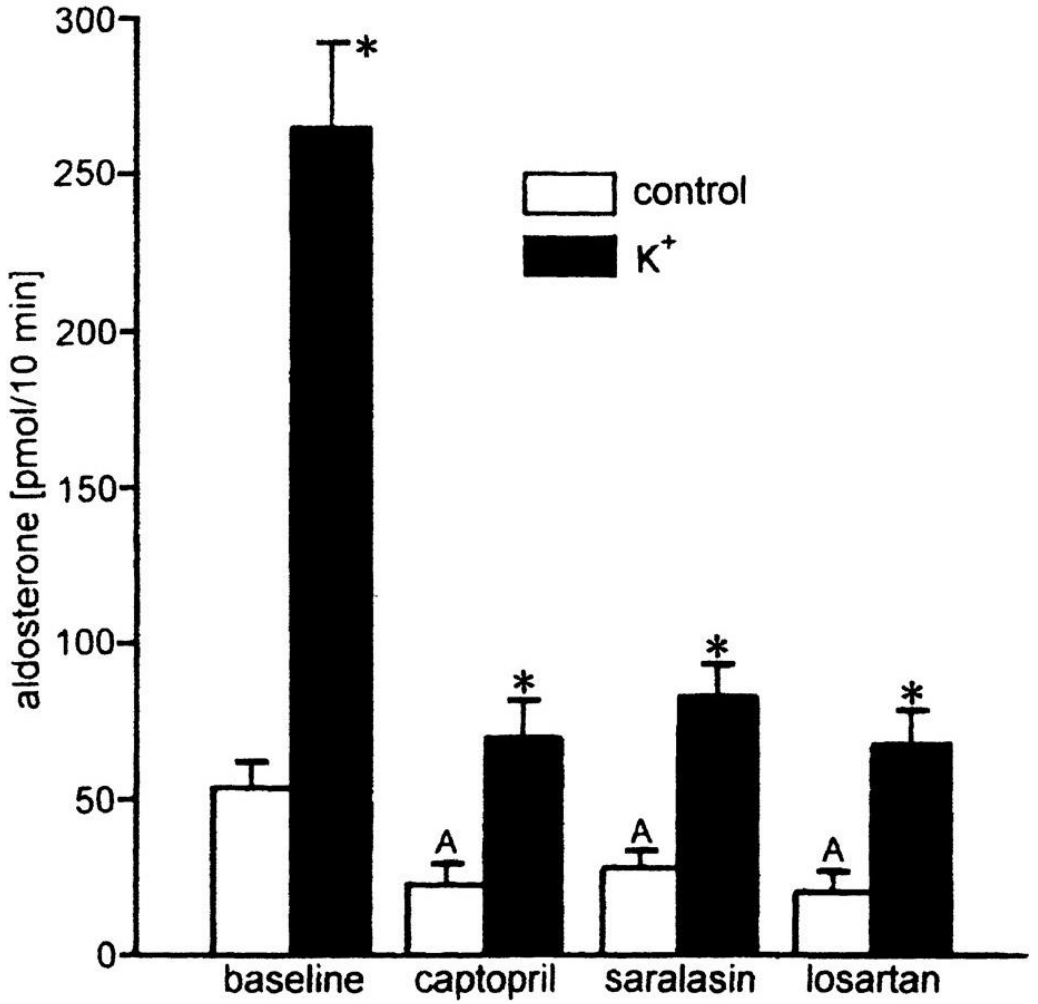
Aldo release by adrenal cells, in response to K of 5 vs. 2 mM

Chen et al, *AJP-Renal,* 276, 1999

An Intact Adrenal RAS is Required For the Response to Hyperkalemia

Aldo release from perfused adrenals, NaCl-restricted animals

<u>TAKE-HOME MESSAGE:</u>
RAS inhibition blunts adrenal response to hyperK



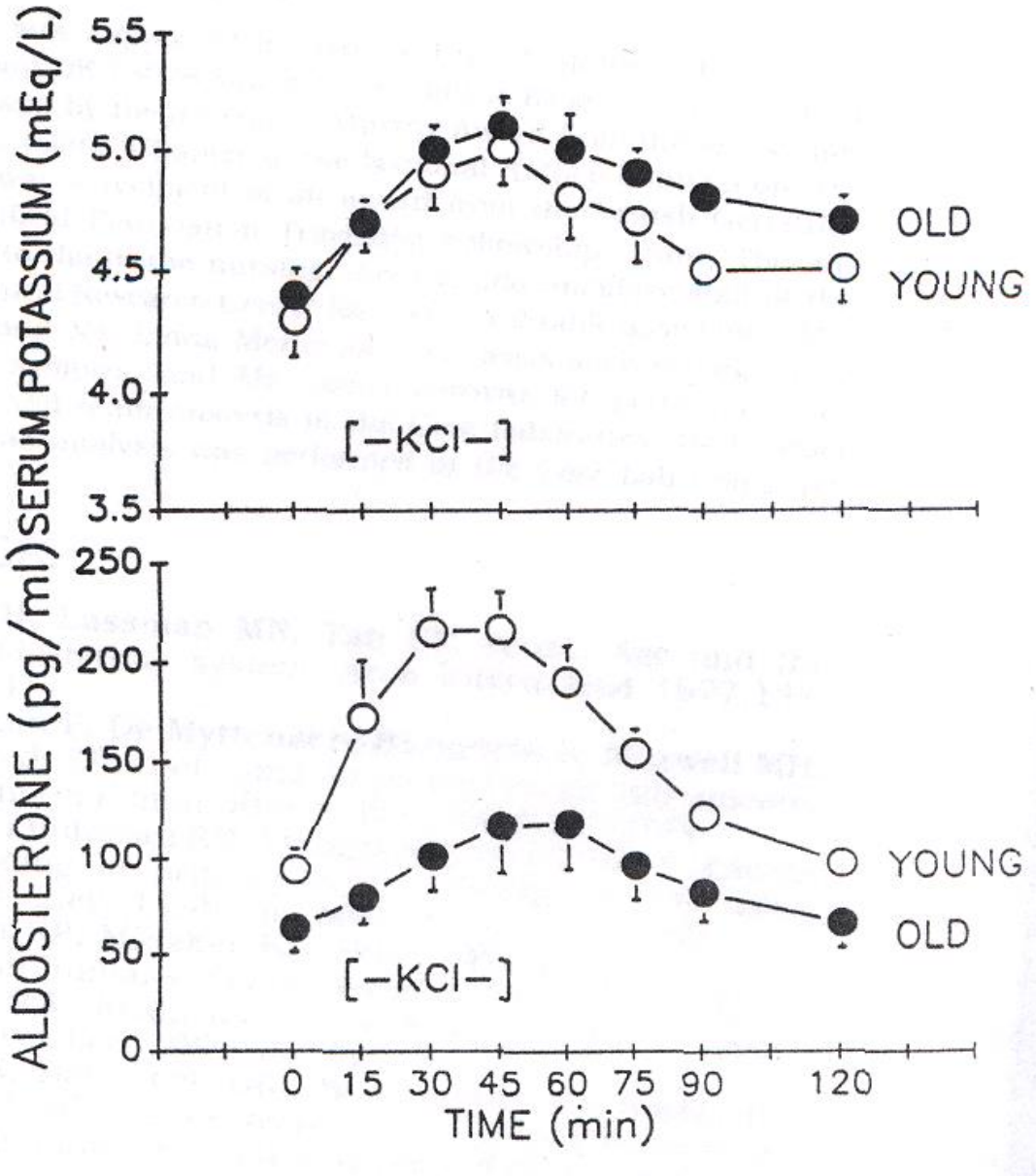
Mazzocchi et al, AJP-Renal, 278, 2000

Hyporeninemic Hypoaldo in the Elderly: Correlation with Increased ANP

Age	*K^+*	*Creat (μM)*	*Aldo (pM)*	*PRA (ng/L/s)*	*ANP (pM)*
Patients:					
81	5.7	265	<65	0.14	3000
94	4.9	88	302	0.06	321
83	5.3	71	202	0.58	1107
84	5.1	115	83	0.06	387
Mean :83	5.3	147	216	0.34	1186
Healthy:					
Mean: 75	4.1	106	211	0.17	91

Clark et al, *J Clin Endocrinol Metab*. 1992 Aug;75(2):399-403.

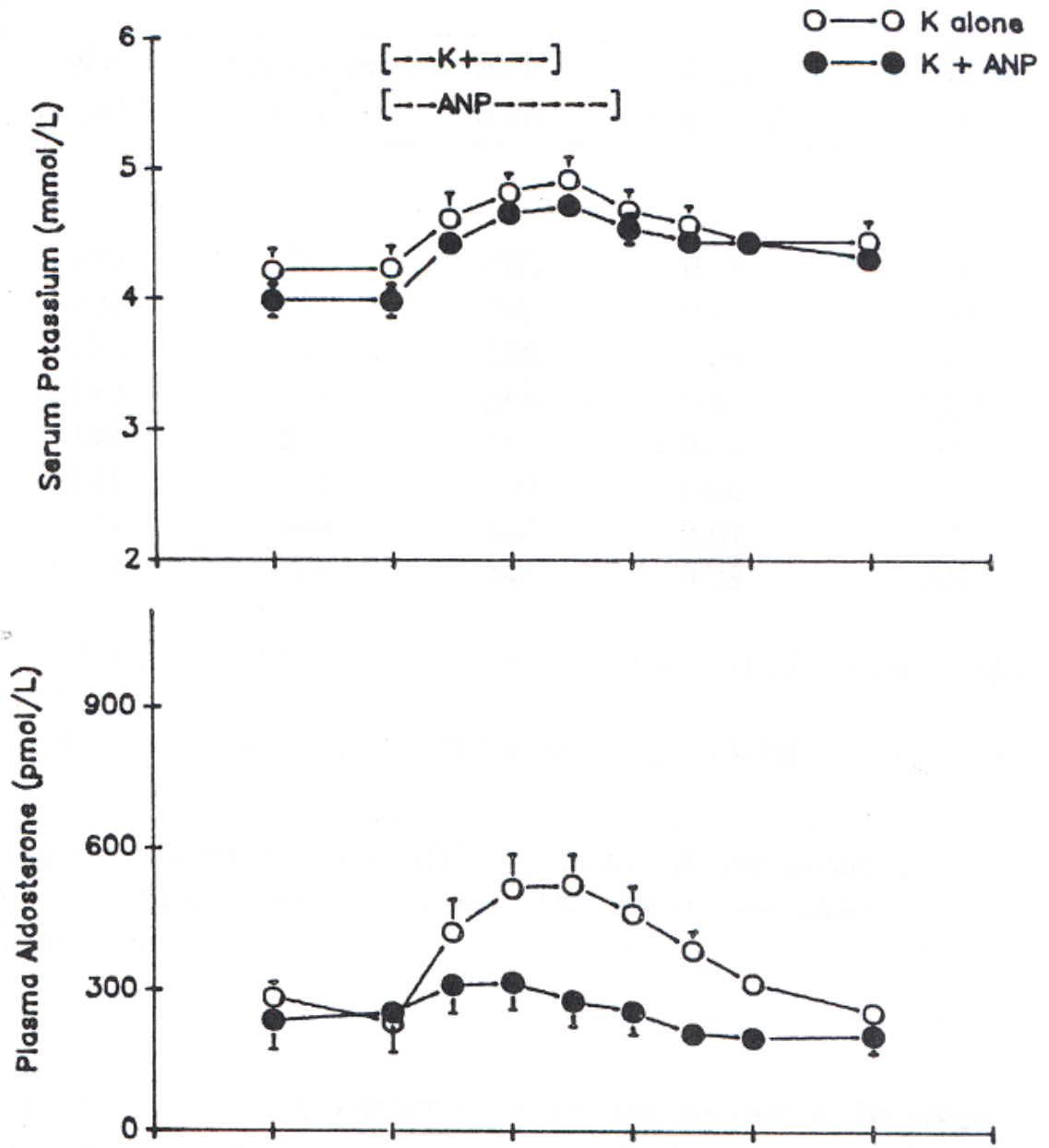
Aldo Response to K-Cl Infusion



Clark et al, *J Am Soc Nephrol*. 1995 Nov;6(5):1459-62

ANP Blunts the ↑Aldo from ↑K^+

Healthy young subjects, infused With K +/- ANP



Clark et al, *J Am Soc Nephrol*. 1995 Nov;6(5):1459-62

TAKE HOME MESSAGES: The Renin-Angiotensin-Aldosterone Axis and Hyperkalemia

ANP, systemic and local RAS, and prostaglandins all affect renal renin release **AND** adrenal aldosterone release, i.e. remember the *adrenal* effect

The role in hyporeninemic hypoaldosteronism of volume expansion and ↑ ANP/BNP

→ ↓ renal renin and ↓ adrenal aldosterone release

Question #1

You are referred a 17 year-old high school student for management of high blood pressure. He has not seen a physician since childhood, is on no medications.
He denies drug abuse, including cocaine.
FH: His 50 year-old father is also hypertensive, with a history of renal stones.
Since you have access to a clinical research center, you admit the father and son for biochemical profiling while ingesting a diet with rigorously controlled salt content.

Parameter	Son		Father	
Dietary Na^+ (mmol/day)	200	10	200	10
BP	150/90	**110/64**	142/90	**110/70**
K^+	6.0	4.5	5.6	4.6
Cl^-	119	102	114	102
HCO_3^-	18	25	21	27
pH	7.33	7.41	7.36	7.38
PRA	0.2	6.3	0.4	2.6
Aldo	15	61	13	41
ANP	48	9	32	14
FE_K (%) basal	7.8	10.3	8.5	7.8
FE_K (%) saline	8.1	**33.8**	8.2	**15.0**

Which of the following is the most appropriate therapy for this patient?

A. Aggressive K restriction
B. NaCl restriction to 10 mEqu/day
C. Nifedipine
D. Amiloride
E. Hydrochlorothiazide

Pseudohypoaldosteronism Type II (PHA-II)

Also known as Gordon's syndrome or the "chloride-shunt" disorder, familial hypertension with hyperK

The "mirror image" of Gitelman's syndrome due to loss of function in the thiazide-sensitive NaCl cotransporter:

- hypertension
- hyperkalemic acidosis
- suppression of plasma renin, aldosterone
- ***hypercalciuria***, nephrolithiasis

Responsive to thiazides

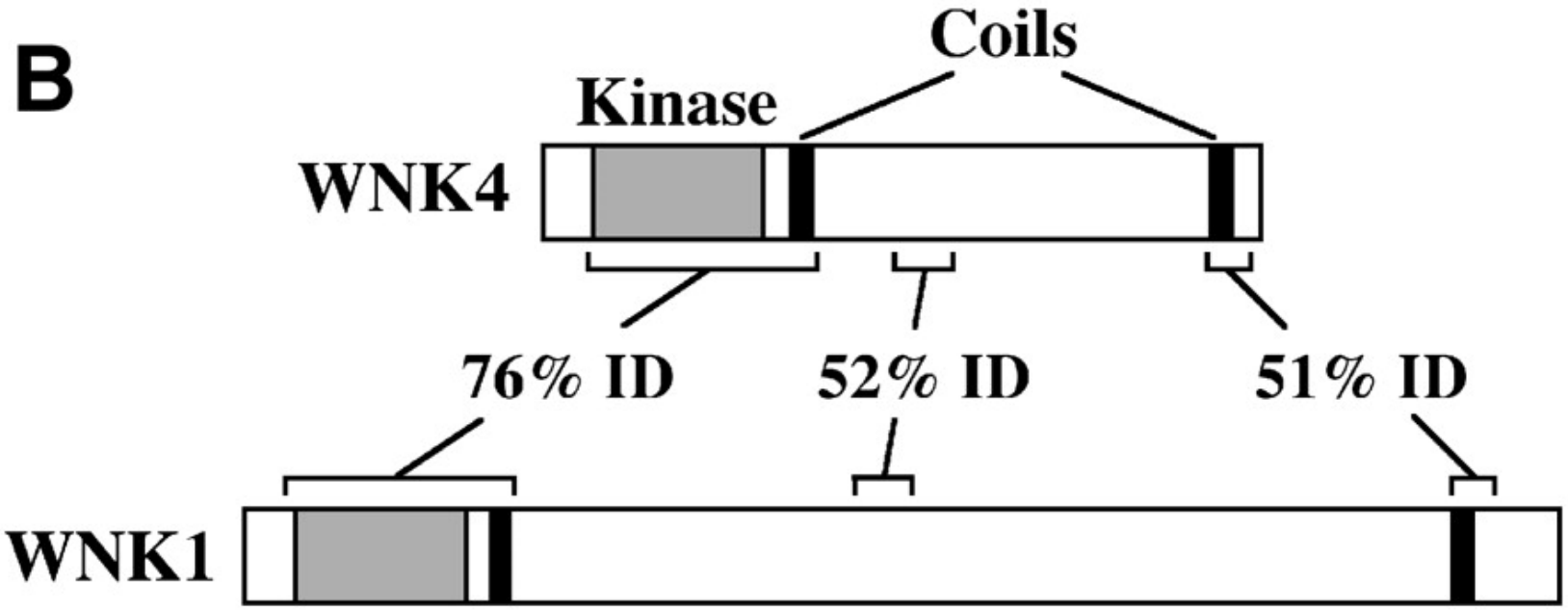
Autosomal dominant transmission, rarely recessive; five different genes, four characterized

Human Hypertension Caused by Mutations in WNK Kinases

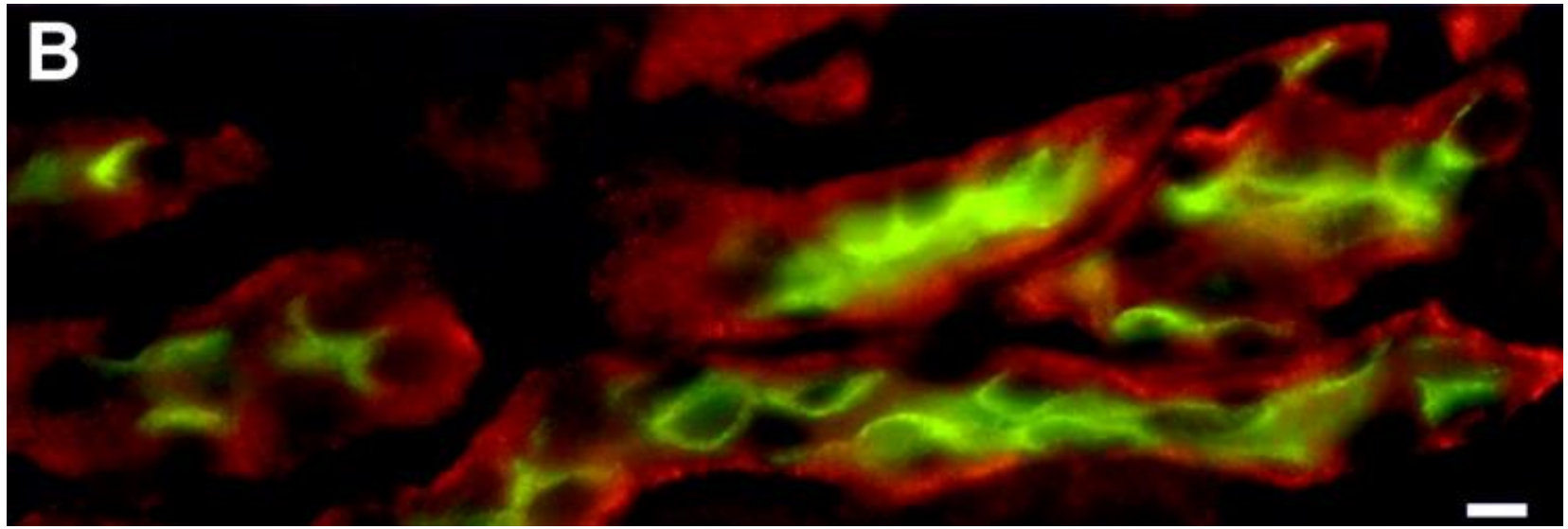
Frederick H. Wilson,[1] Sandra Disse-Nicodème,[2*]
Keith A. Choate,[1*] Kazuhiko Ishikawa,[1*] Carol Nelson-Williams,[1]
Isabelle Desitter,[2] Murat Gunel,[1] David V. Milford,[3]
Graham W. Lipkin,[4] Jean-Michel Achard,[5] Morgan P. Feely,[6]
Bertrand Dussol,[7] Yvon Berland,[7] Robert J. Unwin,[8]
Haim Mayan,[9] David B. Simon,[1] Zvi Farfel,[9] Xavier Jeunemaitre,[2]
Richard P. Lifton[1†]

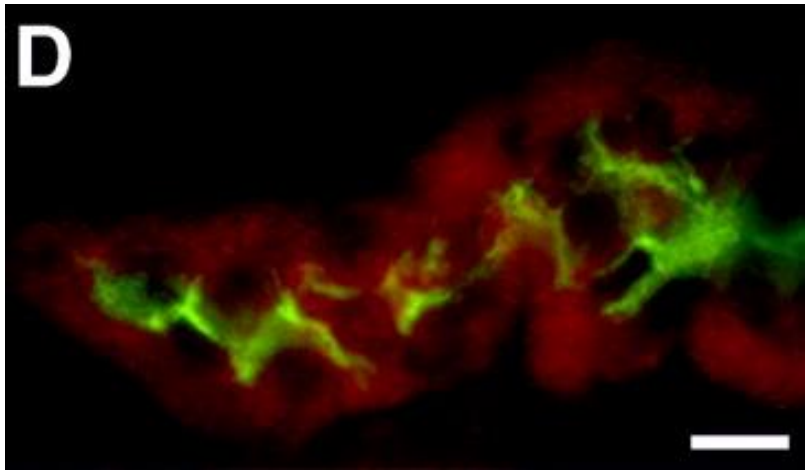
SCIENCE VOL 293 10 AUGUST 2001

WNK1 and WNK4 are Homologous Serine/Threonine Kinases



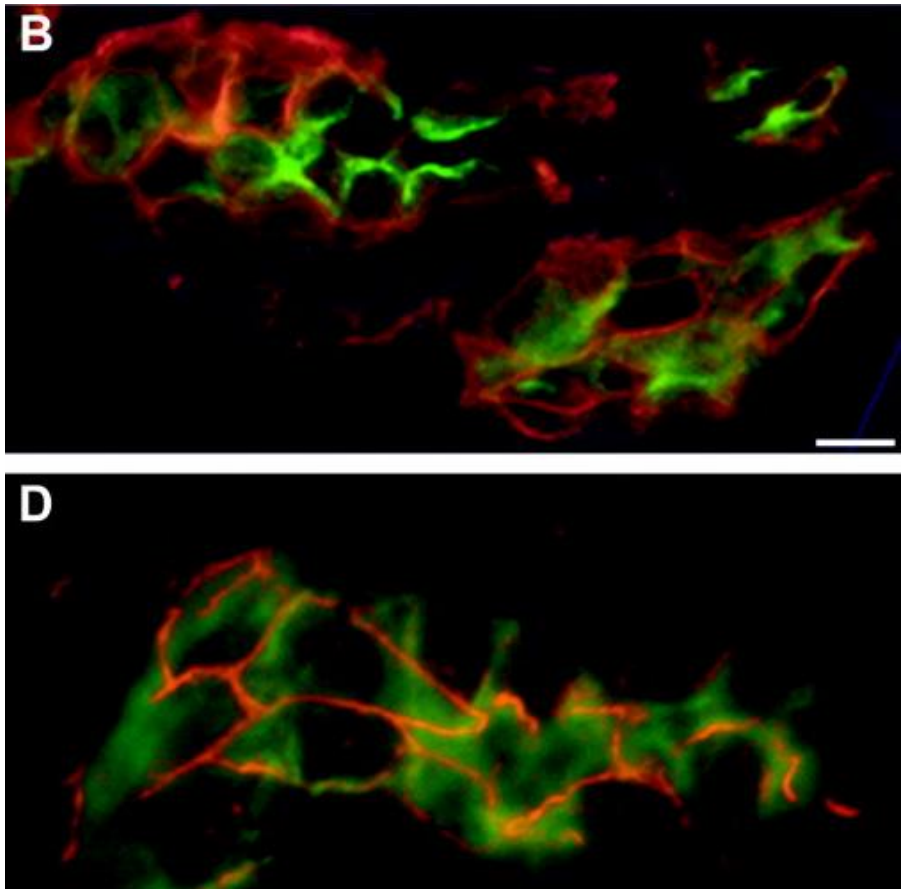
WNK1 is Expressed in the DCT and CCD





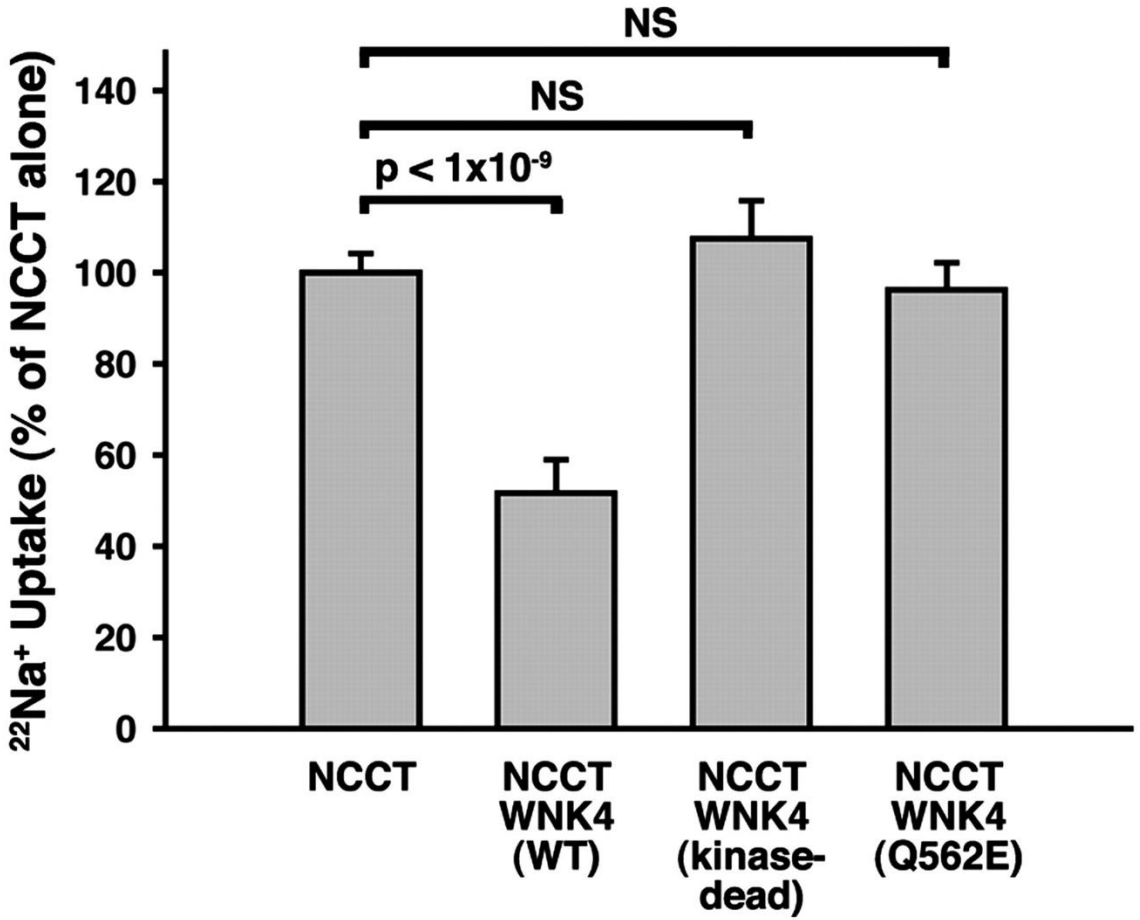
B) WNK1 (red) and Aqp-2 (green)
D) WNK1 (red) and NCC (green)

WNK4 is Expressed in the DCT and CCD



B) Co-expression of WNK4 (red) and Aqp-2 (green)
D) Co-expression of WNK1 (red) and NCC (green)

PHA-II Mutations in the WNK4 Kinase Abrogate Its Inhibition of the Thiazide-Sensitive Na-Cl Cotransporter



NCCT – Na-Cl cotransporter

Choate et al, *PNAS*, 100, 2003

The Aldosterone Paradox: Integrated Distal Na^+ and K^+ Transport

↑ in Ang-II by hypokalemia/K^+ restriction → inhibition of apical secretory K^+ channels (ROMK)

K^+-dependent regulation of the NCC Na^+-Cl^- cotransporter in DCT → Na^+ delivery to principal cells.

- suppression of NCC by hyperkalemia/K^+ loading
- Ang-II-dependent ↑of NCC in hypokalemia/K^+ restriction.

K^+-dependent modulation of WNK kinases.

Aldo-dependent induction of *electroneutral* Na^+-Cl^- transport (coupled Na^+-anion exchangers) in the CCD → no effect on electrogenic K^+ secretion.

Electroneutral, ENaC-independent K^+ secretion, ? primarily in intercalated cells.

Hypokalemia - Causes

Pseudohypokalemia – leukocytosis, with uptake of K^+ by WBCs, e.g. in AML

Redistribution

- Insulinopenia → DKA
- Sympathomimetics
- β_2-agonists, dopamine, theophyline
- Hypokalemic periodic paralysis, incl. thyrotoxic
- Acute anabolic state → pernicious anemia

Non-renal loss → skin, stomach (suctioning), intestine (diarrhea, laxatives, K^+ secretion)

Question #2

You are asked to evaluate a female patient with intestinal pseudo-obstruction (Ogilvie's syndrome), with diarrhea and profound hypokalemia.
Meds include metoprolol, risperidone, insulin
Exam and imaging notable for signs of colonic distension.

Laboratory Studies:

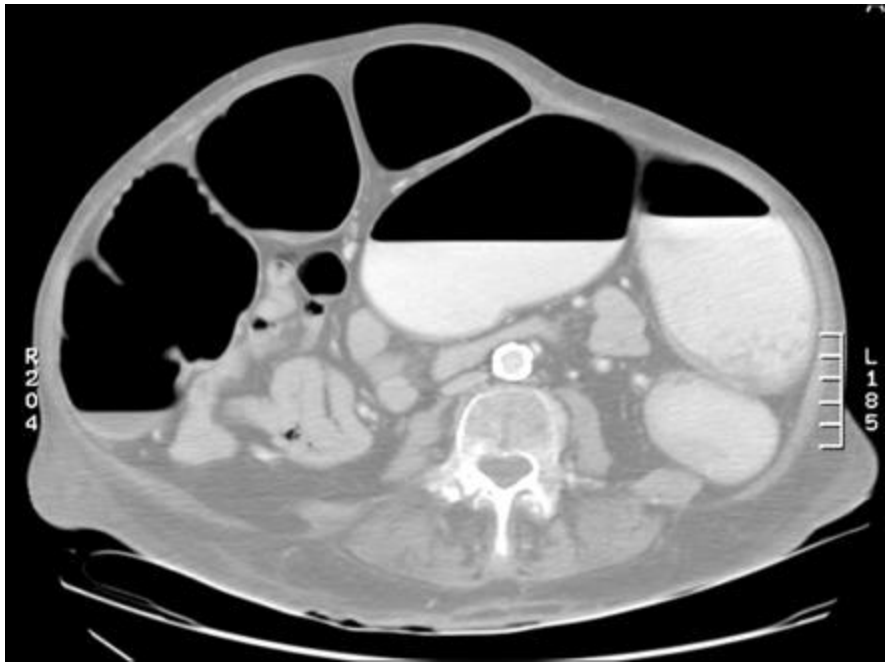
Na^+	151	BUN	30
K^+	2.5	creatinine	1.5
Cl^-	115	TTKG	3
HCO_3^-	15	stool K^+	100 mEqu/kg
		stool Na^+	10 mEqu/kg

Which of the following is the most likely cause of this patient's hypokalemia?

A. Ischemic bowel
B. C diff colitis
C. Activation of colonic K^+ secretion
D. Osmotic diarrhea
E. Sympathetic activation with redistributive hypokalemia

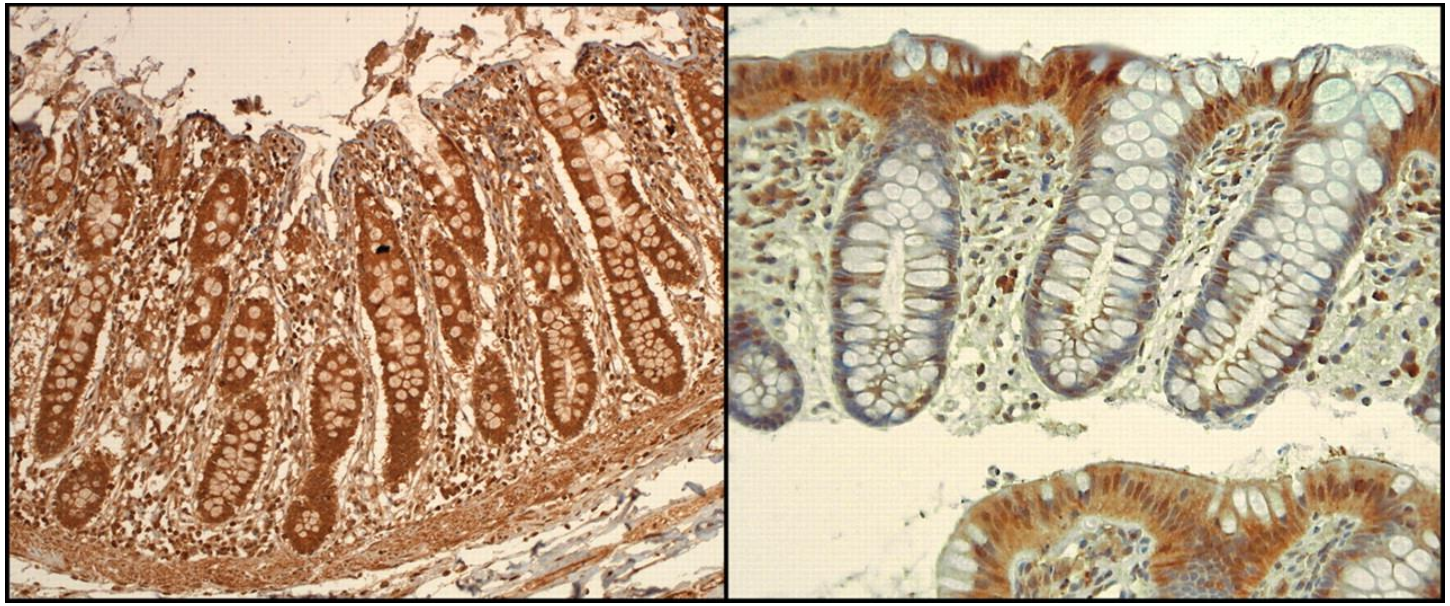
Ogilvie's Syndrome and Hypokalemia

There is an association between (Ogilvie's syndrome) and hypokalemia due to secretory diarrhea with an abnormally high K^+ content. In one patient with concomitant ESRD, immunohistochemistry revealed massive upregulation of the apical BK channel throughout the surface-crypt axes. ? Active stimulation by catecholamines induced by colonic pseudo-obstruction.



Nephrol. Dial. Transplant. (2008) 23 (10): 3350-3352

Upregulation of BK secretory K channel



BK Staining: Patient Control

Renal Loss and Hypokalemia

Drugs
- Diuretics
- Antibiotics
  - Non-reabsorbable anions, e.g. Penicillin

Aldosterone excess

Bicarbonaturia

Magnesium deficiency – inhibition of muscle Na/K-ATPase and ↓ Mg^{2+}-dependent block of ROMK →↑ distal K^+ excretion

Tubular damage
- ATN
- Cisplatin, aminoglycosides, amphotericin

Intrinsic renal transport defects
- Liddle's syndrome
- Bartter's syndrome
- Gitelman's syndrome
- Hereditary dRTA

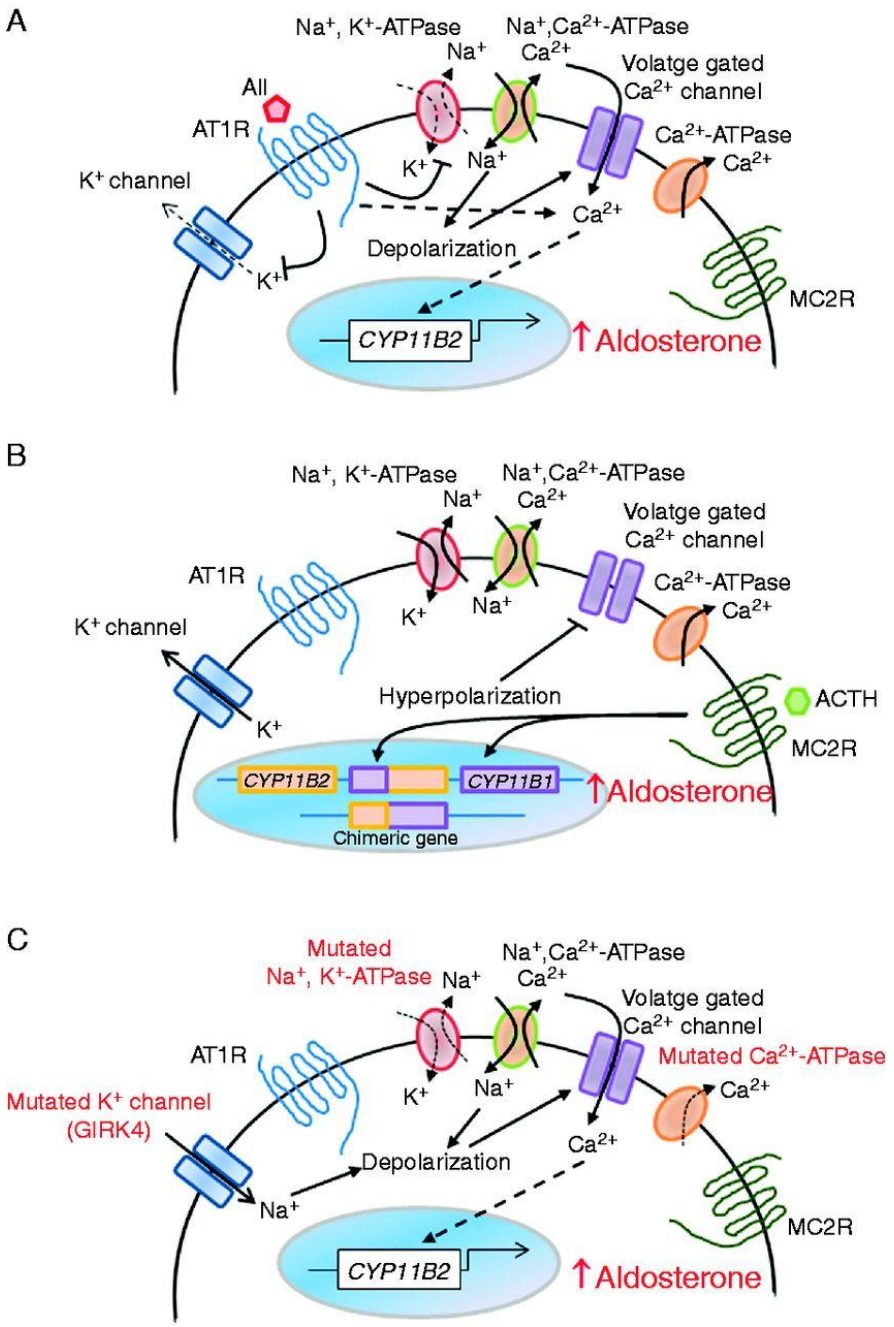
Hypokalemia and Hypertension

Common

- aldosterone-producing adenoma, bilateral adrenal hyperplasia

< Common

- familial hyperaldosteronism, including GRA (Glucocorticoid remedial aldosteronism)
- adrenocortical carcinoma
- renovascular disease
- Liddle's syndrome
- 11βHS2 inhibition/deficiency – licorice/S.A.M.E.
- Ectopic ACTH

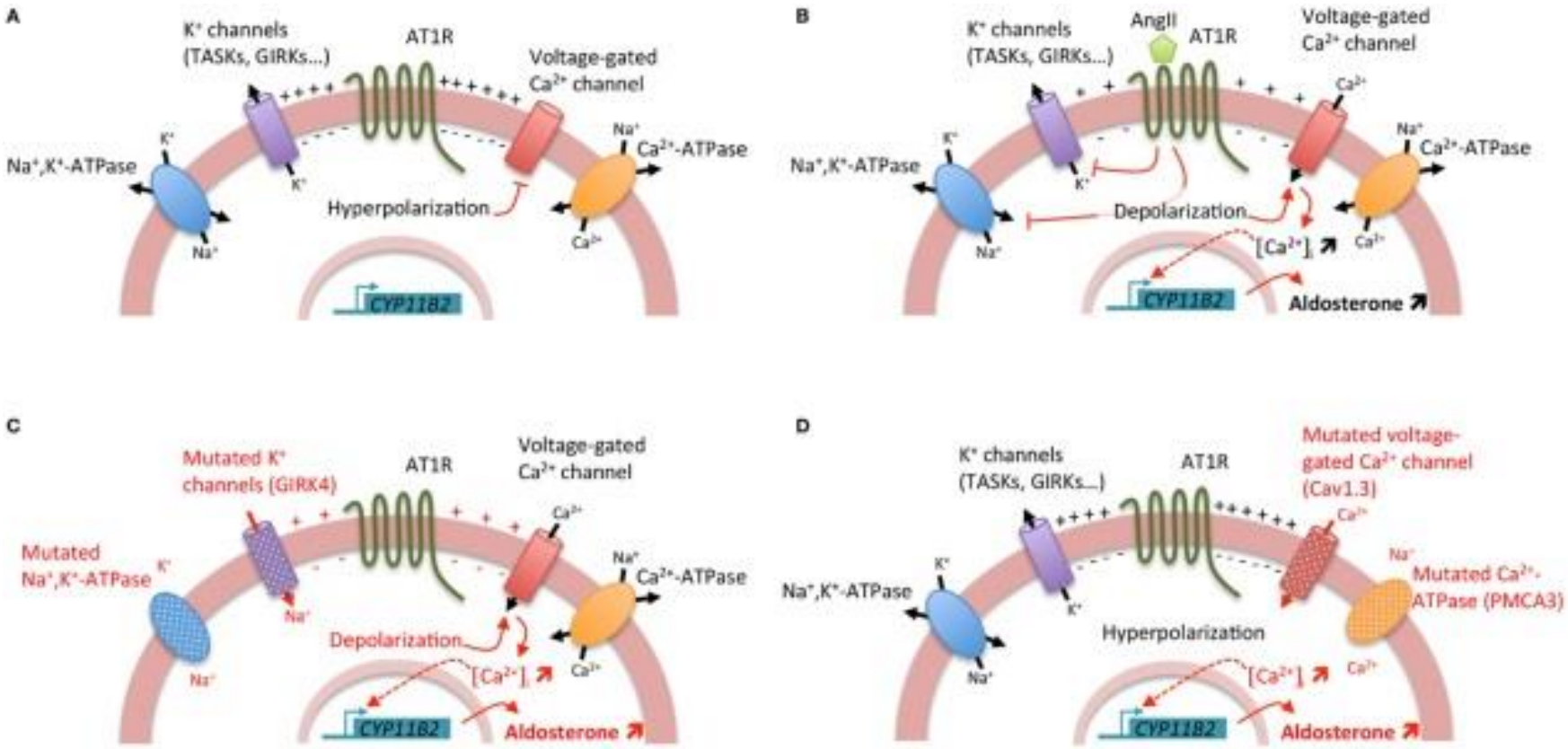


A) Physiological activation of aldo synthesis by ATII

B) Aldo synthesis in GRA, glucocorticoid remedial hyperaldosteronism (FH-I)

C) Genetic abnormalities in membrane transport proteins in FH-III (GIRK4/KCNJ5) and/or adrenal adenomas

Eur J Endocrinol 2013, 169, R15-R25



A) Zona glomerulosa cells are strongly hyperpolarized (-80 mV) due to K channel activity
B) Ang-II depolarizes cells by inhibiting K channels and Na/K-ATPase, leading to depolarization. Depolarization activates Ca^{2+} channels, increasing intracellular Ca^{2+} and activating CYP11B2 transcription to generate more aldo.
C) Acquired mutations in GIRK4/KCNJ5 induce Na^{+} conductivity, depolarizing the cell. Acquired mutations in Na/K-ATPase have the same effect.
D) Acquired mutations in calcium transport proteins increase intracellular Ca^{2+}

Screening and Confirmatory Testing, Primary Hyperaldosteronism

Aldosterone (PAC) to renin (PRA) ratio

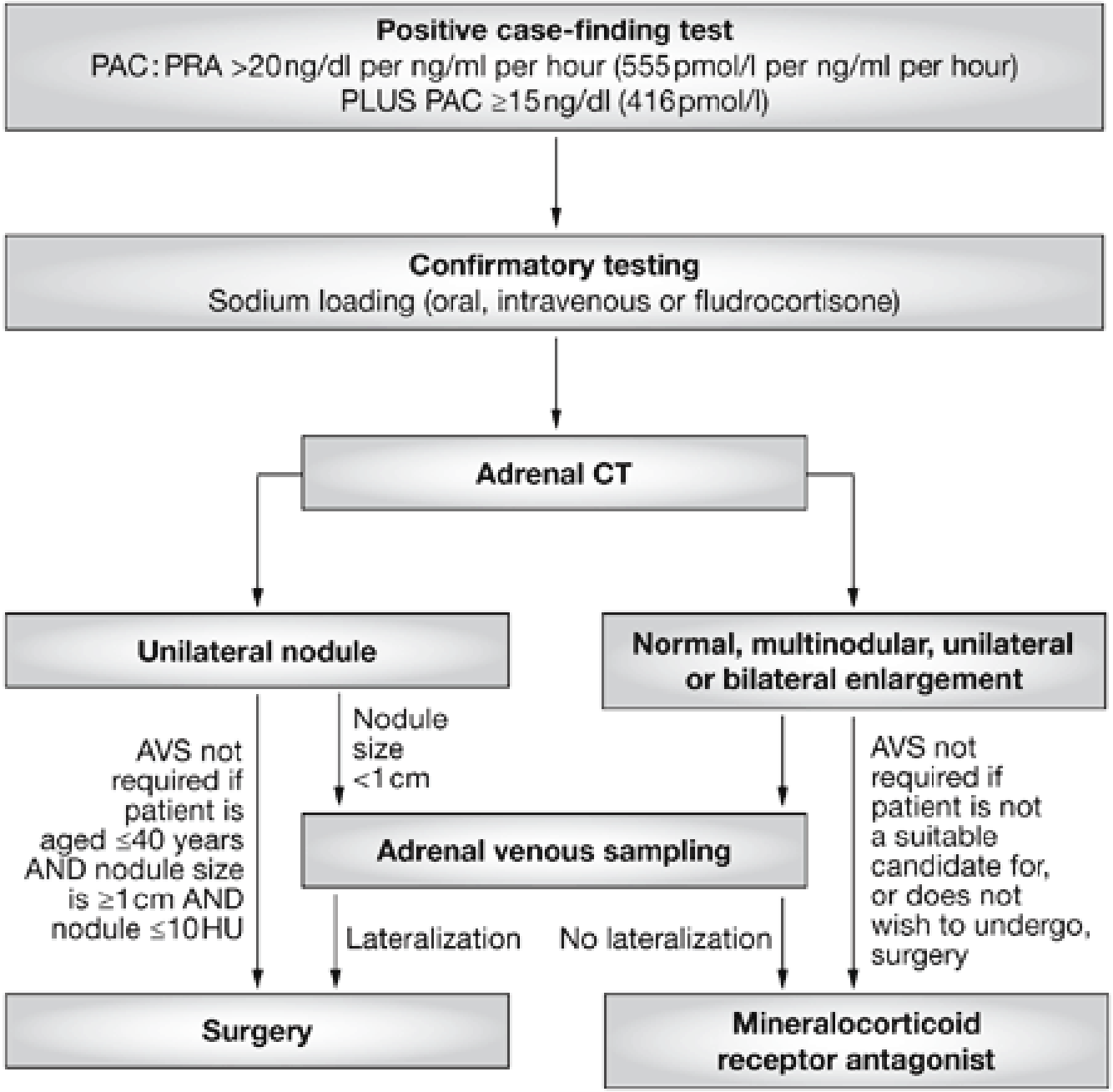
- Check when normokalemic, [K^+]>4.0 mEqu/L
- Beware of drug effects during evaluation, switch to RAAS-neutral drugs (verapamil, alpha blockers, hydralazine)

24 hour aldosterone secretion

Salt suppression testing

- Oral to >200 milliEqu/day for 3 days, followed by PAC:PRA and 24 hr urine aldo
- IV saline, 2 liters/4 hours, pre- and post-PAC:PRA

Imaging +/- adrenal vein sampling (AVS)



Nature Clinical Practice Nephrology (2006) 2, 198-208

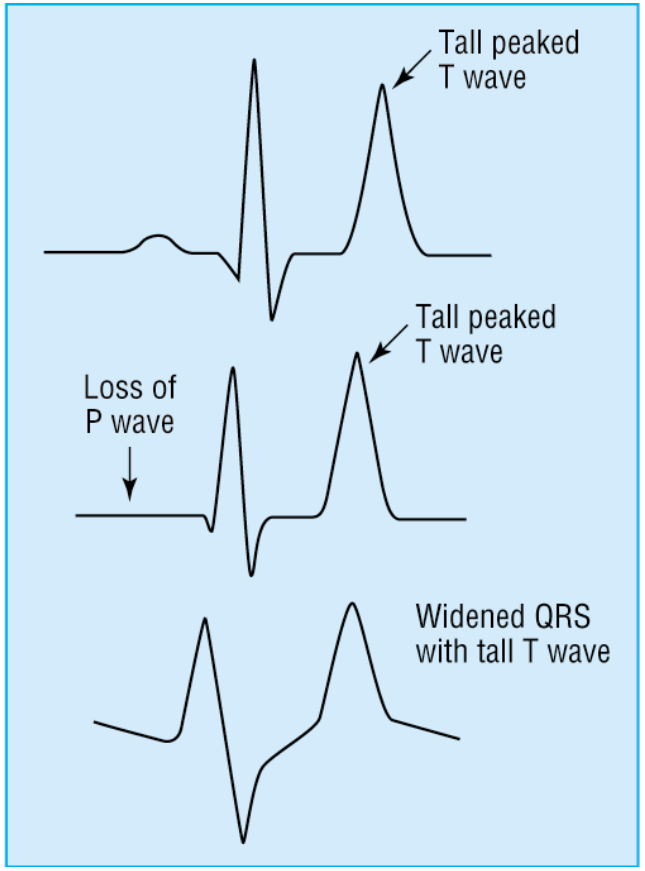
Consequences of Hyperkalemia

Excitable tissue – change in resting membrane potential

- Cardiac, decreased myocardial conduction velocity, ↑PR and ↑QRS and increased rate of repolarization (T wave changes)
- Skeletal muscle – weakness, fatigue, paralysis

Kidney – decreased ability to secrete NH_4^+ → acidosis

Typical Electrocardiographic Features of Hyperkalemia



Serum K+	*Major change*
5.5-6.5	Tall peaked T waves
6.5-7.5	Loss of P waves
7.0-8.0	Widening of QRS
8.0-10	Sine wave, ventricular arrhythmia, asystole

Caveats: ECGs and Hyperkalemia

Remember, “the first symptom of hyperkalemia is death…..”

ECG changes are not sensitive, particularly in ESRD

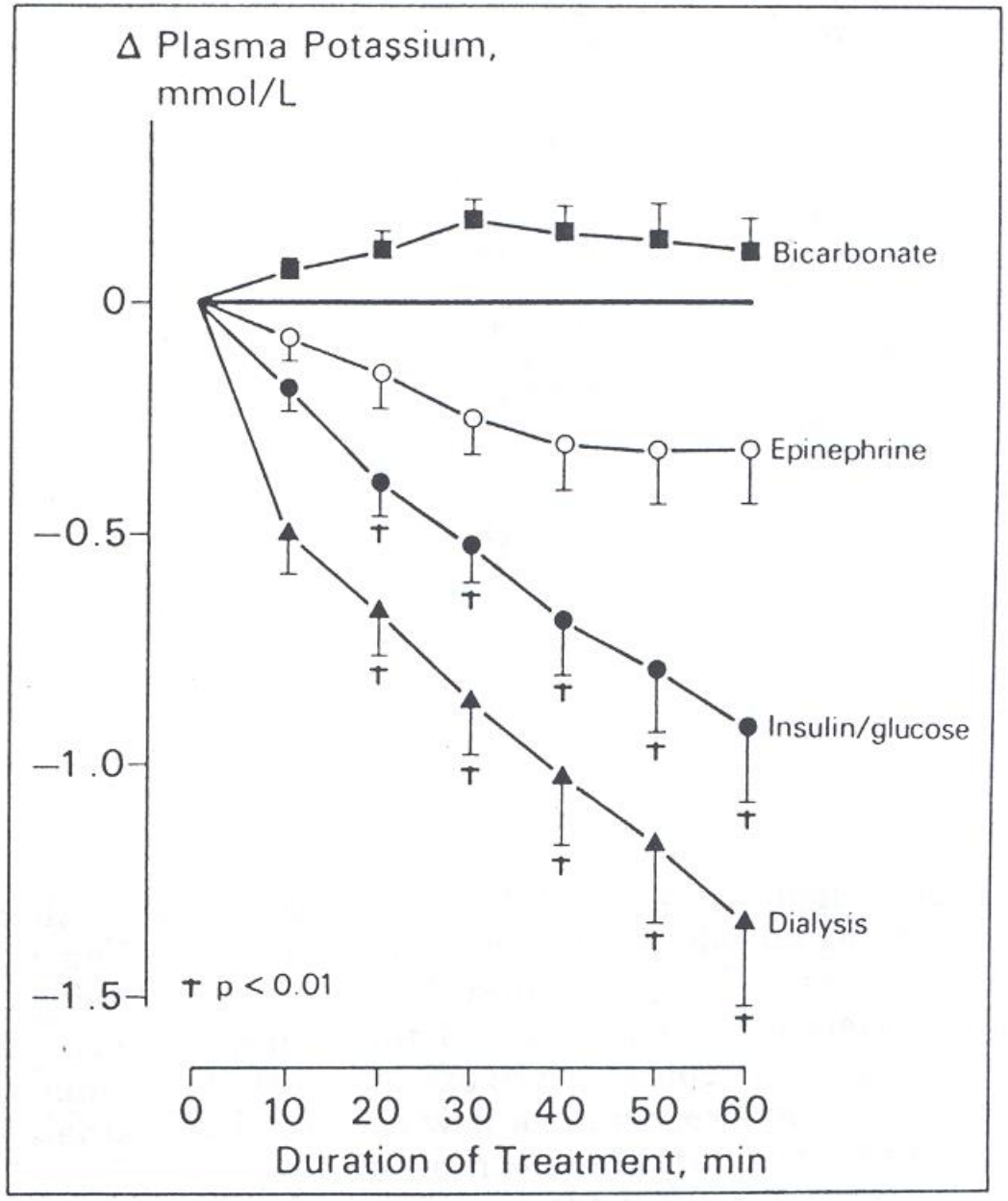
Peaked T’s in other disorders

Atypical ECGs

- Complete heart block
- Intraventricular conduction delays
- QRS axis shift
- Brugada sign - pseudo-RBBB and “coved” ST ↑

Treatment of Hyperkalemia

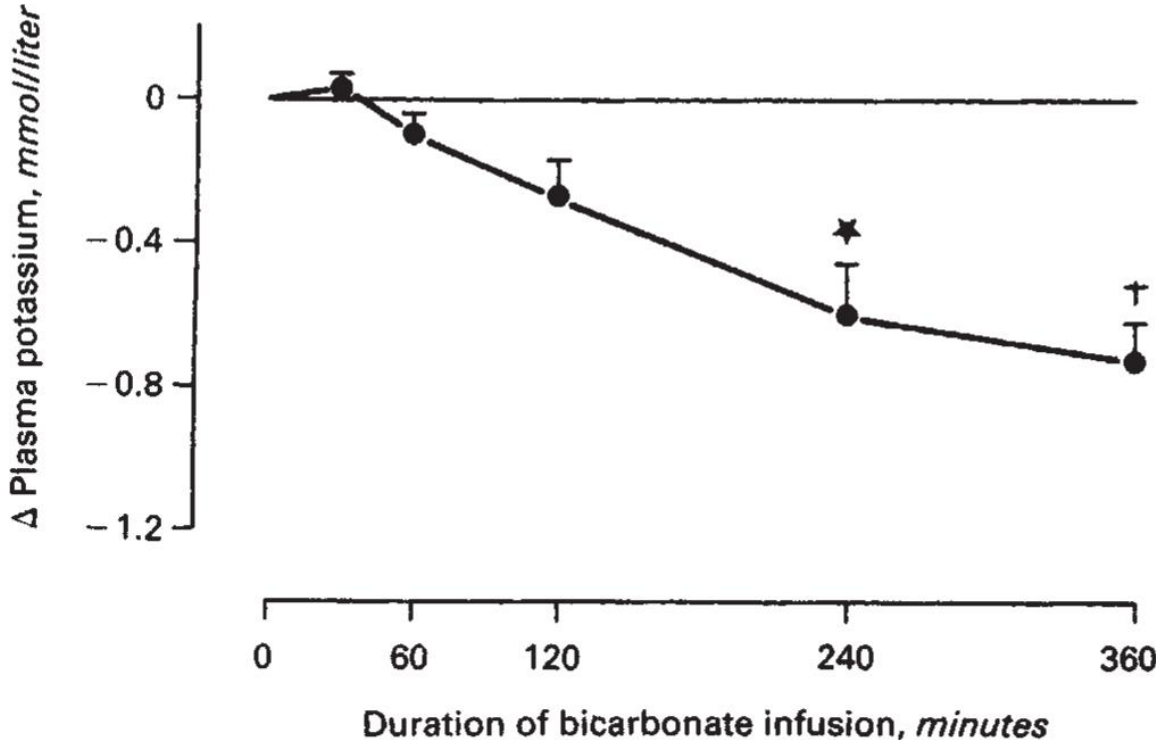
Mechanism	*Therapy*	*Dose*	*Onset*	*Duration*
Stabilize membrane potential	Calcium	10% Ca-gluconate, 10 ml over 10 min.	1-3 min.	30-60 min
Cellular K^+ uptake	Insulin	10 U R with 50 ml of D50, if BS<250	30 min.	4-6 h
	β_2-agonist	nebulized albuterol, 10 mg	30 min.	2-4 h
K^+ removal	Potassium Binders	Agent-specific	hours	?
	Hemodialysis		Immediate	



Hypertonic Bicarb Is Acutely Ineffective

Blumberg et al, *Am J Med,* 85, 1988

Sustained, Isotonic Bicarbonate Infusions are Modestly Effective in ESRD



ESRD patients.
mean [K] 6.0 mEqu/l,
mean [HCO_3] 17 mEqu/l

Hypertonic → isotonic infusion, 390 mmole in 1190 ml

Blumberg et al, *Kidney International*, 42, 1992

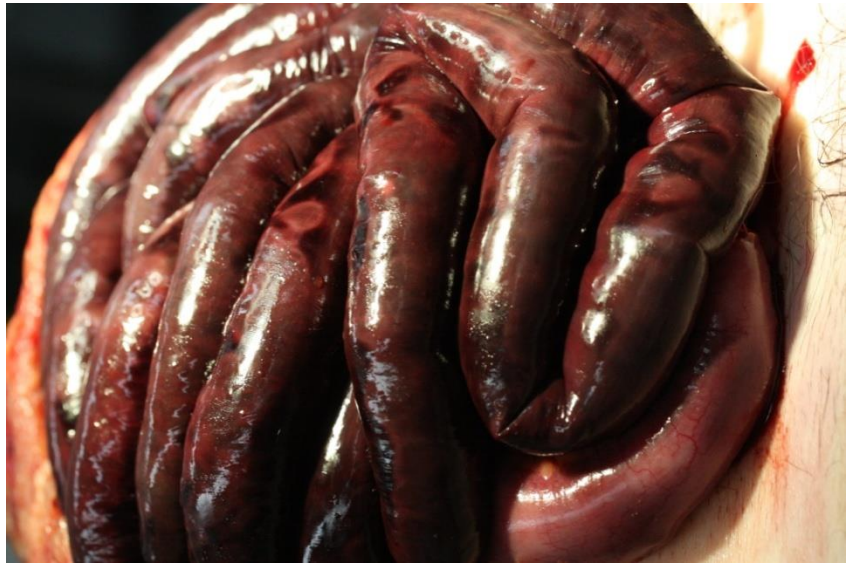
Insulin and Glucose

Threshold of >6.5 mEqu/L without ECG changes.
Recommended dose is 10 units of regular insulin followed by 25 g of 50% glucose
Followed by 10% dextrose infusion at a rate of 50-75 ml/hour (to prevent hypoglycemia)
In hyperglycemic patients (glucose > 200-250 mg/dl) insulin alone is enough
D50W alone should be avoided → hyperosmolality
can increase K^+, primarily in predisposed patients (e.g. DM with type IV RTA)

β_2-Adrenergic Agonists (Inhaled)

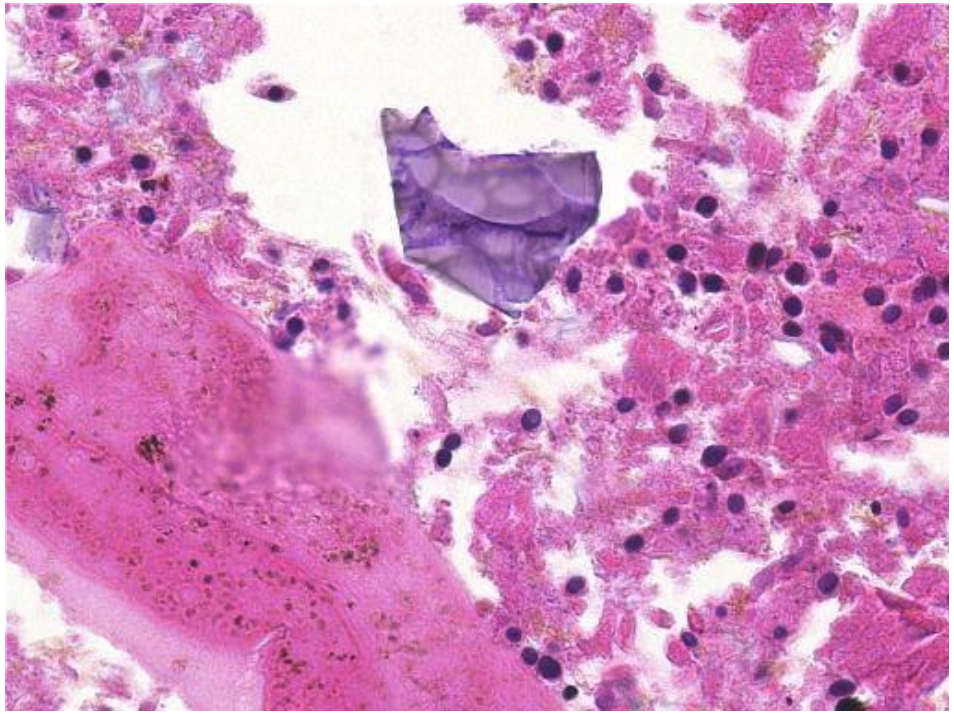
10-20 mg of nebulized albuterol in 4 ml of normal saline, inhaled over 10 minutes
Hypokalemic effect starts in 30 minutes, peaks at 90 minutes and lasts for 2-6 hours
Reduces K^+ level by 0.5-1.0 mmol/L
Synergistic with insulin, but ineffective as the sole agent in ESRD
Use with caution in ischemic HR, monitor HR closely

Sodium Polystyrene Sulphate (Kayexalate) Can Cause Bowel Necrosis



necrotic small bowel

Boston case, 2011



SPS crystal, duodenum

Concerns re Sodium Polystyrene Sulphate (SPS)

Slow onset of effect → SPS unnecessary in most patients with acute hyperkalemia.

Intestinal necrosis due to SPS in sorbitol is often a fatal complication, **NOT** restricted to post-op setting.

FDA advisory September, 2009 – do **NOT** administer SPS with sorbitol.

Yet… SPS with sorbitol remains a very popular "reflex" mechanism of therapy for hyperkalemia, and is often the only formulation of SPS available.

Increasing reports and an animal model of necrosis w/o sorbitol; **it's the SPS, sorbitol isn't necessary for necrosis.**

The Available Alternatives….

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 15, 2015 VOL. 372 NO. 3

Patiromer in Patients with Kidney Disease and Hyperkalemia Receiving RAAS Inhibitors

Matthew R. Weir, M.D., George L. Bakris, M.D., David A. Bushinsky, M.D., Martha R. Mayo, Pharm.D., Dahlia Garza, M.D., Yuri Stasiv, Ph.D., Janet Wittes, Ph.D., Heidi Christ-Schmidt, M.S.E., Lance Berman, M.D., and Bertram Pitt, M.D., for the OPAL-HK Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Sodium Zirconium Cyclosilicate in Hyperkalemia

David K. Packham, M.B., B.S., M.D., Henrik S. Rasmussen, M.D., Ph.D., Philip T. Lavin, Ph.D., Mohamed A. El-Shahawy, M.D., M.P.H., Simon D. Roger, M.D., Geoffrey Block, M.D., Wajeh Qunibi, M.D., Pablo Pergola, M.D., Ph.D., and Bhupinder Singh, M.D.

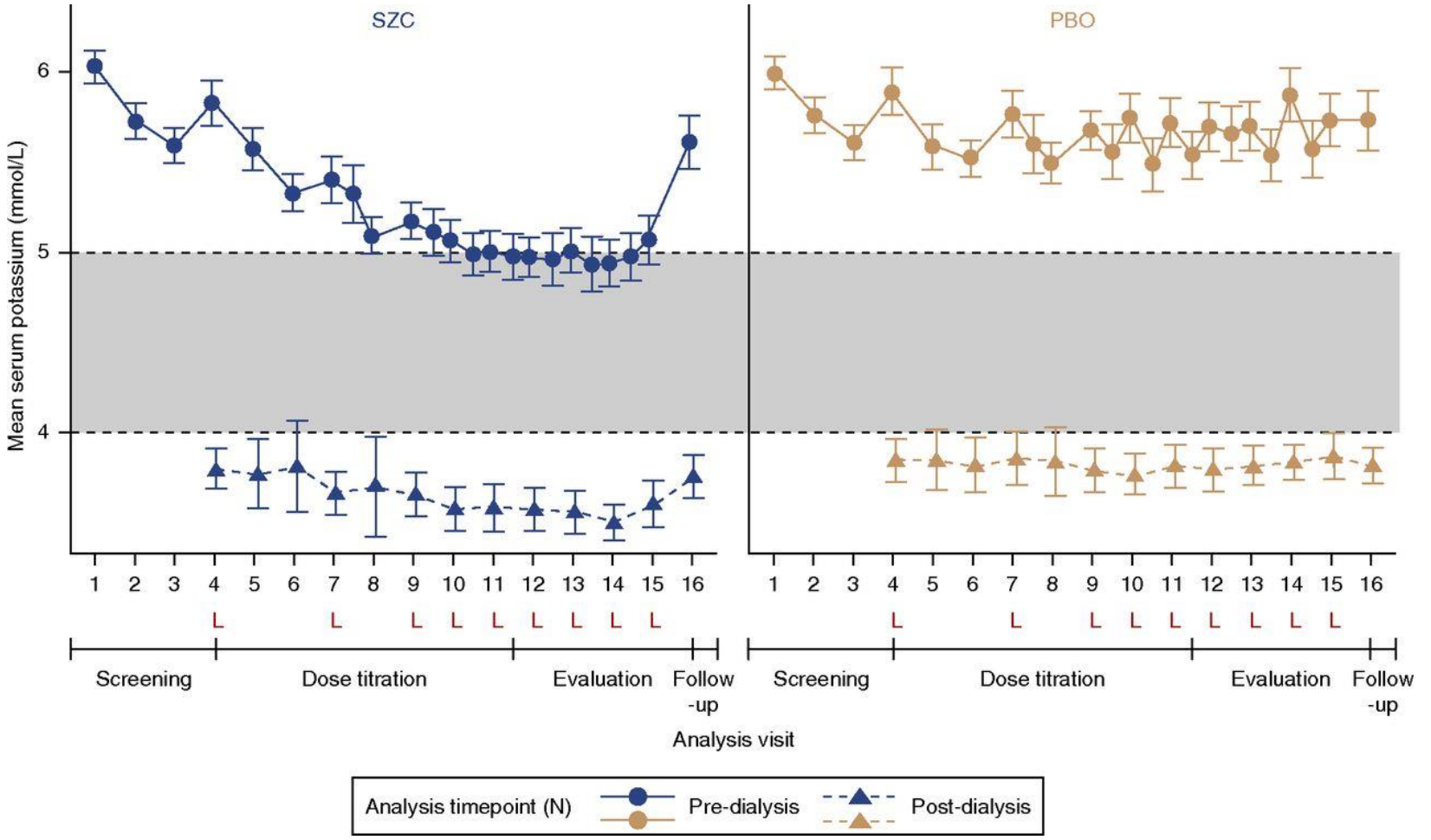
Patiromer

Chief adverse event is hypomagnesemia (4.3% incidence of magnesium <1.2 mg/dL in AMETHYST-DN)
Concerns re drug interactions, but only documented for ciprofloxacin, metformin, and thyroxine; can obviate if dosed 3 hours between/before other drugs
Demonstrated to reduce circulating aldosterone; ? role in managing aldosterone breakthrough

Sodium Zirconium Cyclosilicate (SZC, ZS-9)

Selective for K^+ and NH_4^+ - no binding to magnesium or calcium.
Associated increase in serum bicarbonate.
No drug interactions.
Rapid onset: After one 10-g dose serum [K^+] declines by ~0.4 mEqu/L at 1 hour, by ~0.6 mmol per liter at 2 hours, and by ~0.7 mEqu/L at four hours.
May contribute to edema, presumably due to Na^+ load.

SZC in Hyperkalemic HD Patients



RCT of 196 patients Fishbane et al, JASN 2019

Hemodialysis

The only therapy that can reliably normalize hyperK within 4 hours.
Serum K^+ reaches a nadir at ~3 hours, but removal continues to end of HD Rx.

The amount of K^+ removed depends on:

- type and surface area of the dialyzer
- blood flow rate
- dialysate flow rate
- dialysis duration
- <u>serum:dialysate K^+ gradient</u>

The Serum - Dialysate Gradient

Dialysates with lower K^+ concentration are more effective, but may lead to rebound hypertension

Dialysates with very low K^+ concentration (0 or 1 mmol/L) should be used cautiously, given the risk of arrhythmia

Graded reduction in K^+ concentration is effective, with ↓ arrhythmia, and is the standard of care at BWH

Continuous cardiac monitoring is recommended when using very low K^+ concentration dialysates

Consequences of Hypokalemia

Arrhythmias
Muscles – weakness, paralysis, myopathy
Metabolic alkalosis
Insulin resistance

HYPERTENSION
Polydipsia, polyuria, nephrogenic DI
Structural renal disease – AKI, ESRD
Predisposition to
- Rhabdomyolysis
- Hepatic encephalopathy

QTc and Serum [K^+]

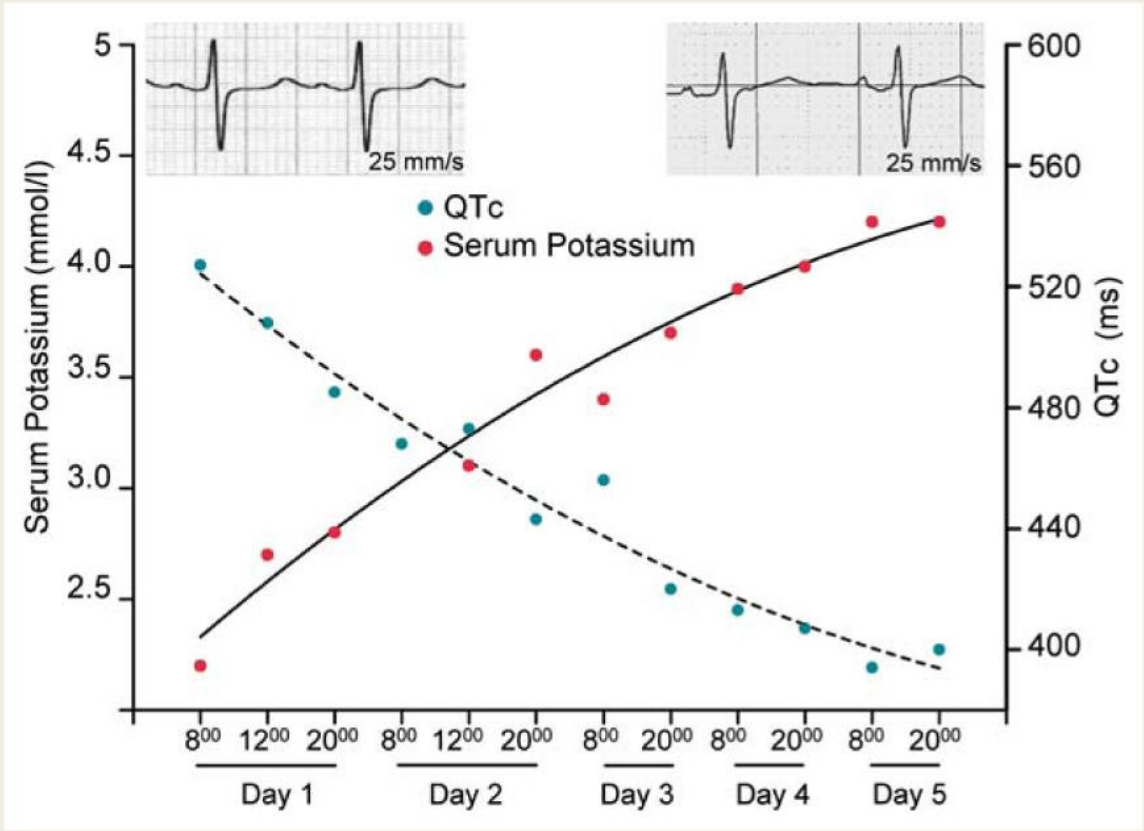
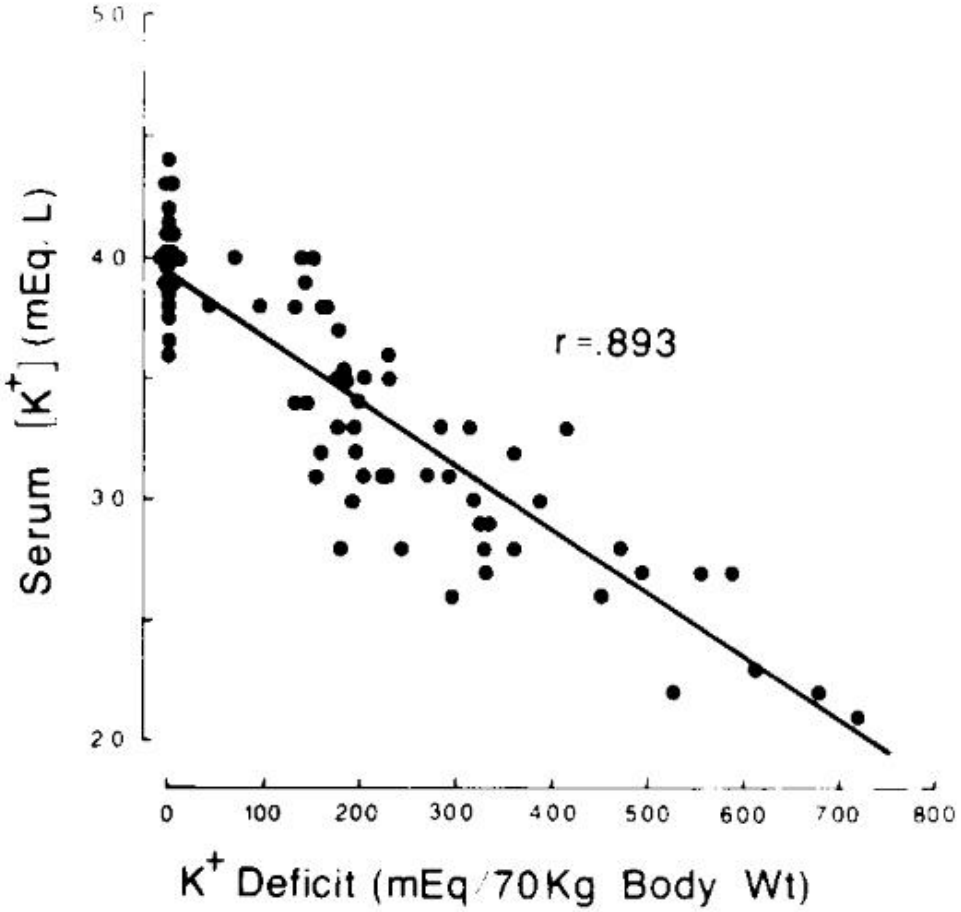


Figure 1 Continuous measurement of corrected QT interval, over 5 days during potassium supplementation; exemplified electric cardiac beats demonstrating prolonged QT interval on admission (left) and normalized at discharge (right).

Case report, hypokalemia with LQT

Nia et al, *Europace*. 2011;13(9):1352-3

Estimate the Deficit!



↓ in $[K^+]$ of 0.27 mM per 100 mEqu deficit

Pooled studies of K+ deprivation

Sterns et al, *Medicine*, 1981

Treatment of Hypokalemia

Look for sequelae – ECG, motor power, etc., → **telemetry** for ECG changes, symptomatic hypokalemia requiring aggressive Rx

First replete magnesium

Usually oral therapy, preferably K-Cl

Replete deficit over days, monitor [K^+] q4-6h to monitor Rx and avoid transient hyperkalemia

IV can be given safely at 10 mEqu/hour, but up to 40-60 mEqu/hr in a monitored setting – need central line, ? preferably femoral

DO NOT USE DEXTROSE SOLUTIONS

→ acute ↓ in K^+, due to the induced insulin release

Question #3

32 yo Latin American male admitted with weakness and a K of 2.0

HPI: The patient has been very healthy until 2 months PTA, when he developed leg weakness. This weakness has fluctuated, and is more severe at night-time. He denies drug abuse, laxative abuse, is on no medications.
ROS: no nausea, no vomiting or diarrhea.
SH: Taxi driver, married with one child
FH: 10 siblings, mother has DM, one sister has thyroid disease.

Physical Exam

Temp 97.2 bp 176/96 HR 102, RR 16
HEENT normal
JVP visible and not elevated, good peripheral pulses, no edema
S1, S2 normal, no murmurs
Abdomen – soft, non-tender, no organomegaly
Neuro – decreased DTRs, otherwise normal

	Admission:	5 months PTA:
Na	139	143
K	**2.0**	3.8
Cl	105	107
HCO_3^-	26	29
BUN	11	16
Creat	0.6	1.0
Glu	145	136
PO4	**1.2**	
Ca	8.8	8.8
Mg	**1.3**	1.9
Alb	3.8	
Posm	290	TTKG = 2.0
UOsm	590	
UK	10	

Which of the following is likely to be abnormal in this patient?

A. TSH level
B. Genetic sequence of the gene encoding the Na/K-ATPase alpha-1 subunit
C. Genetic sequence of the gene encoding a muscle-specific K^+ channel
D. A & C
E. A, B & C

Mutations in Potassium Channel Kir2.6 Cause Susceptibility to Thyrotoxic Hypokalemic Periodic Paralysis

Devon P. Ryan,[1,2,14] Magnus R. Dias da Silva,[2,14,15] Tuck Wah Soong,[4,8] Bertrand Fontaine,[5] Matt R. Donaldson,[2,16] Annie W.C. Kung,[6] Wallaya Jongjaroenprasert,[7] Mui Cheng Liang,[8] Daphne H.C. Khoo,[10] Jin Seng Cheah,[9] Su Chin Ho,[1(] Harold S. Bernstein,[11] Rui M.B. Maciel,[12] Robert H. Brown, Jr.,[13] and Louis J. Ptáček[1,2,3,*]

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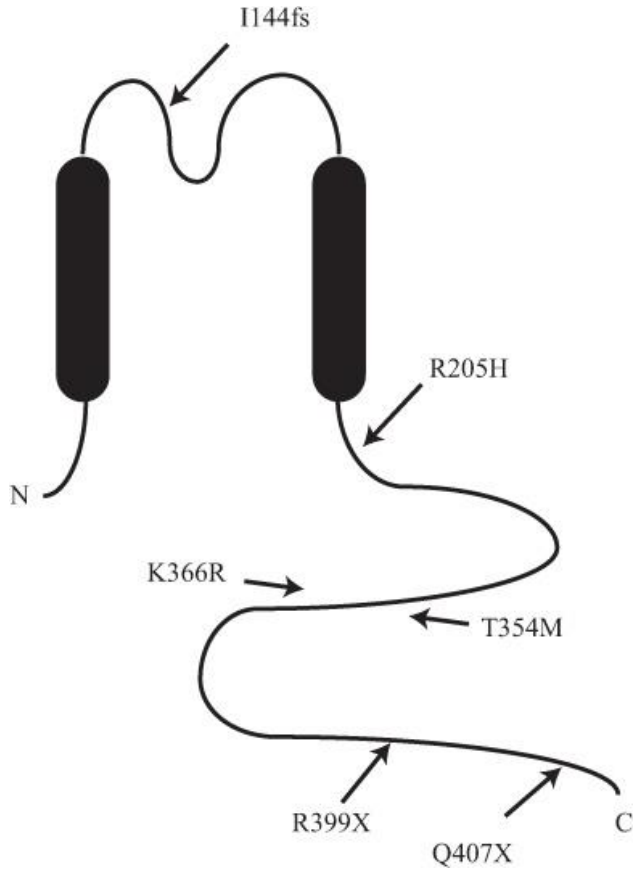
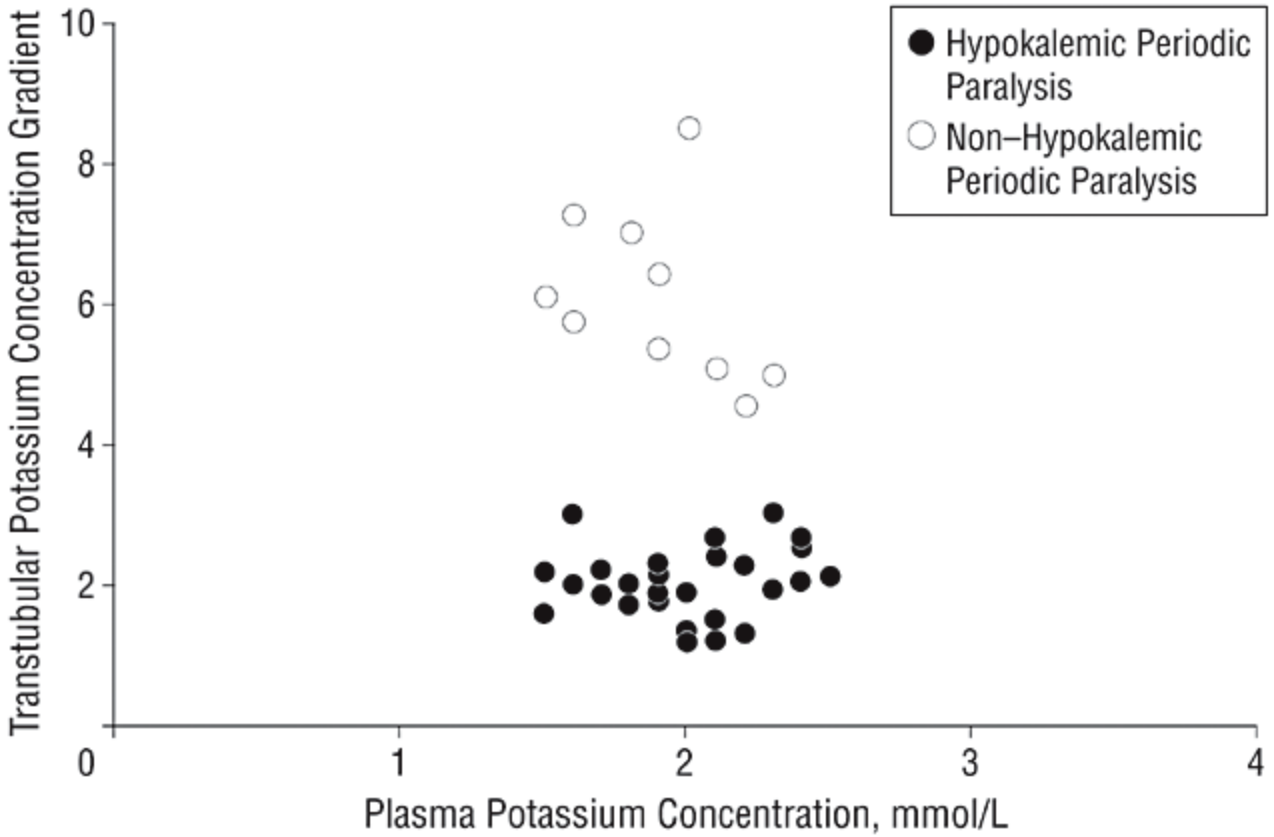
DOI 10.1016/j.cell.2009.12.024

Cell *140*, 88–98, January 8, 2010 ©



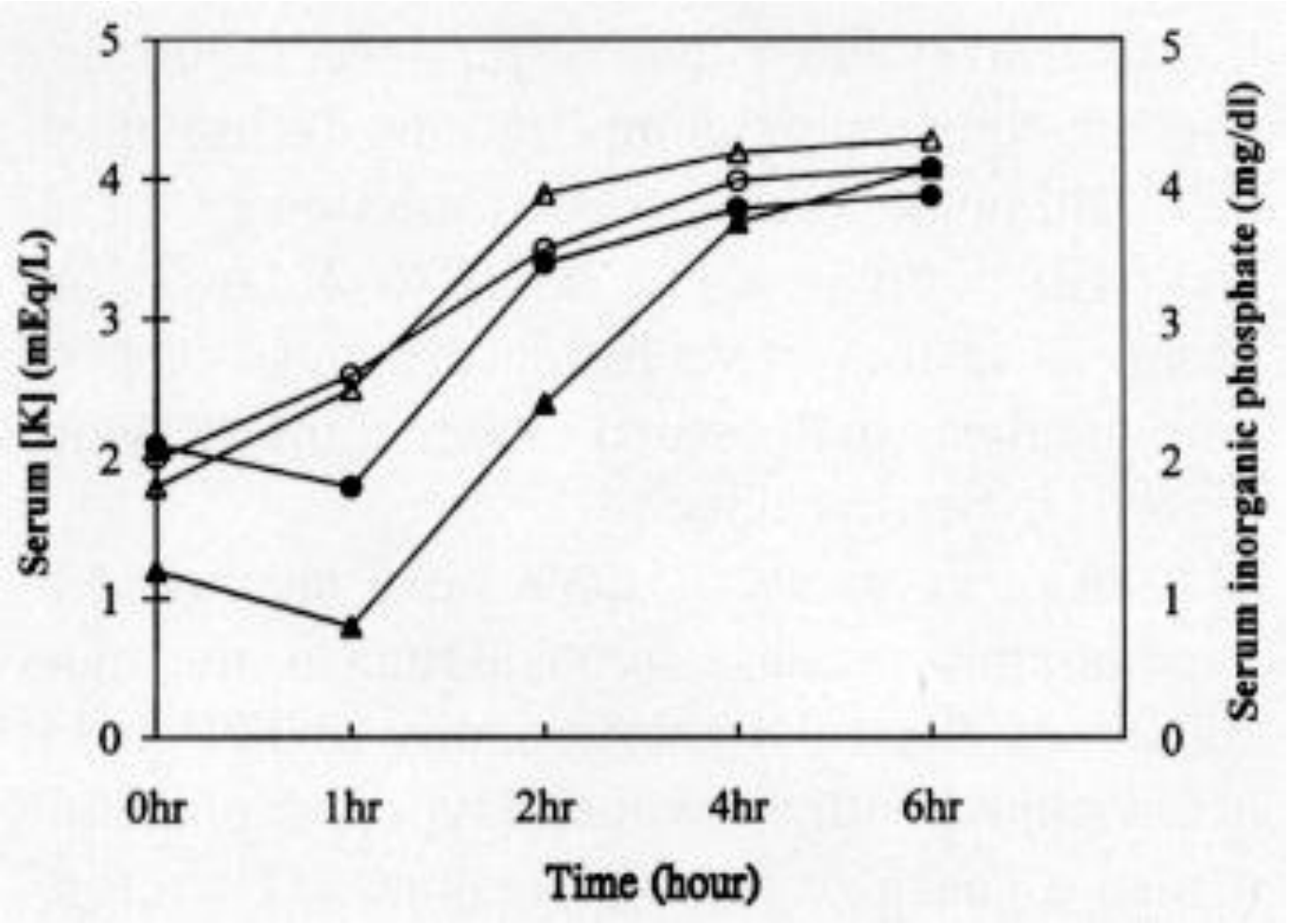
Point mutations in a muscle-specific, thyroid-induced K^+ channel detected in multiple un-related patients with TPP, primarily non-Asian in origin.

Use of the TTKG in Hypokalemic Paralysis



Lin et al, *Arch Int Med*, 2004

Response of Serum K^+ and Phosphate to High-Dose Propranolol in TPP



Lin and Lin, *AJKD*, 2001

TAKE HOME MESSAGES

Regulation of renal renin release and adrenal aldosterone release.
The aldosterone paradox.
New developments in hyperaldosteronism and thyrotoxic periodic paralysis.
Treatment issues in hypokalemia.
New K^+ binders for hyperkalemia.

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