Nephrology Quiz and Questionnaire: Electrolyte Cases

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Case 1

- A 35 year old woman is admitted with left flank pain and fever for the last 2 days. Physical examination showed a toxic appearing thin woman. Vital signs showed a blood pressure of 100/68 mmHg, pulse 110, and respiratory rate of 24. Right sided costovetebral tenderness was present. An ultrasound of the abdomen showed normal sized kidneys and no evidence of hydronephrosis. Renal function and serum electrolytes on admission were normal. Right sided pyelonephritis was diagnosed. The patient was treated with intravenous ticarcillin/clavulanate, gentamicin, and tetracycline and the patient's clinical condition gradually improved over the next several days. After a two week course of parenteral antibiotics she was discharged on no medications.

Case 1-continued

- One week after discharge the patient presented with the complaint of weakness, and paresthesias. Physical examination showed downbeat nystagmus and carpal pedal spasm could be elicited. An ECG showed prominent U waves and Q-T prolongation

Case 1-Laboratory studies

- Creatinine 0.9 mg/dl, BUN 14 mg/dl
- Serum electrolytes (mEq/l)
  - Na^+ 139
  - K^+ 2.3
  - Cl^- 92
  - HCO_3 34
- Urine electrolytes (mEq/l)
  - Na^+ 110
  - K^+ 35
  - Cl^- 106
- Serum Mg^{++} 0.9 mg/dl
- Urine Ca^{++}/creatinine (mg/mg) 0.53
- Plasma renin activity 2.4 ng/ml/hr (Normal 0.8-2.5), aldosterone 235 ng/dl (Normal 35-240)

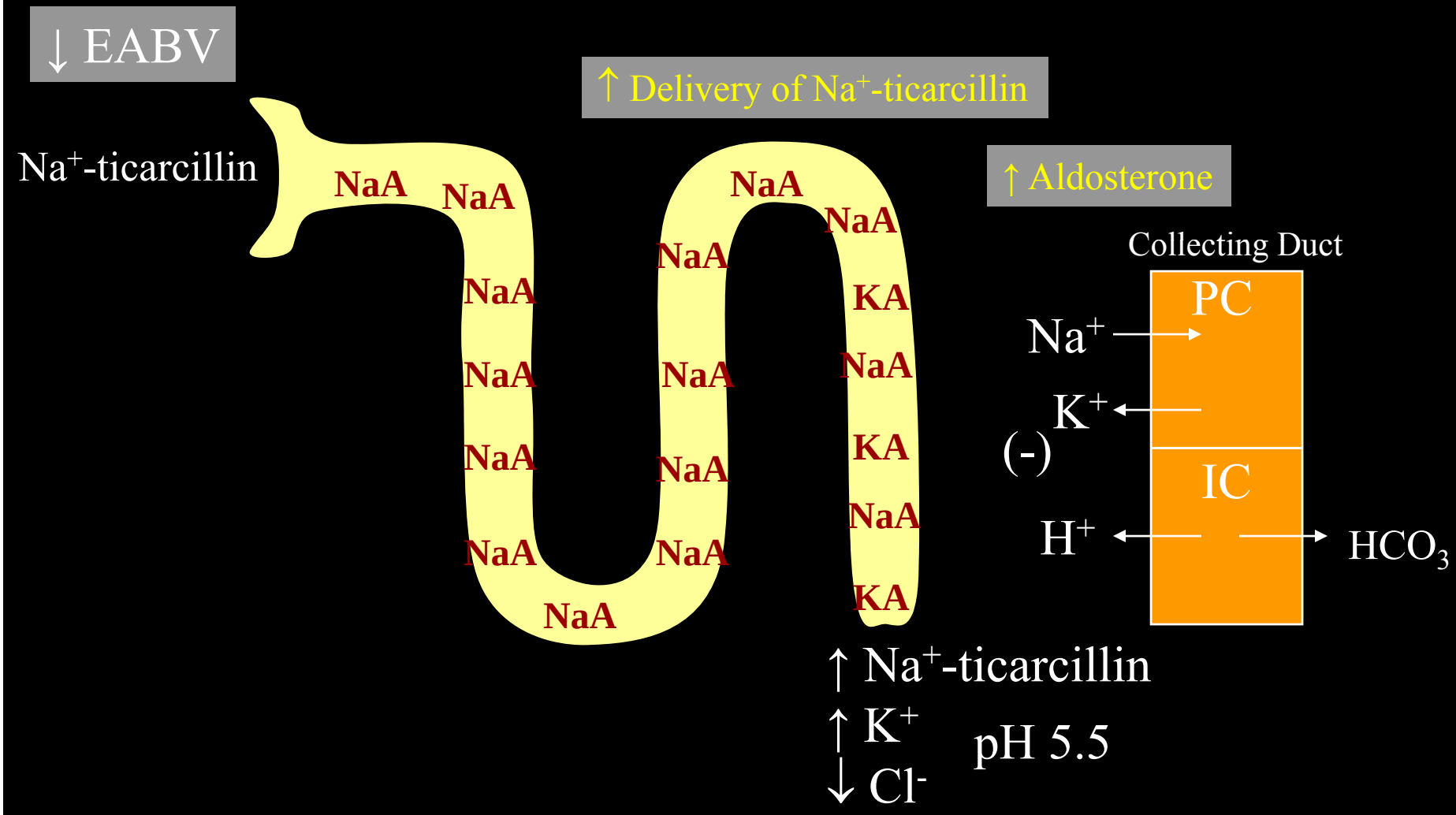
Which One of the following is the Most likely cause of the electrolyte abnormalities?

1. Complication of ticarcillin/clavulanate
2. Surreptitious diuretic use
3. Tetracycline nephrotoxicity
4. Aminoglycoside nephrotoxicity
5. Gitelman syndrome

Case 1

- Features to account for:
  - New onset hypokalemic metabolic alkalosis with normal blood pressure
  - High urine Na^{+}, K^{+}, Cl^{-}, and Ca^{++}
  - Hypomagnesemia
  - Down beat nystagmus

Renal K^+ Handling in Setting of a Non-reabsorbed Anion (Ticarcillin)



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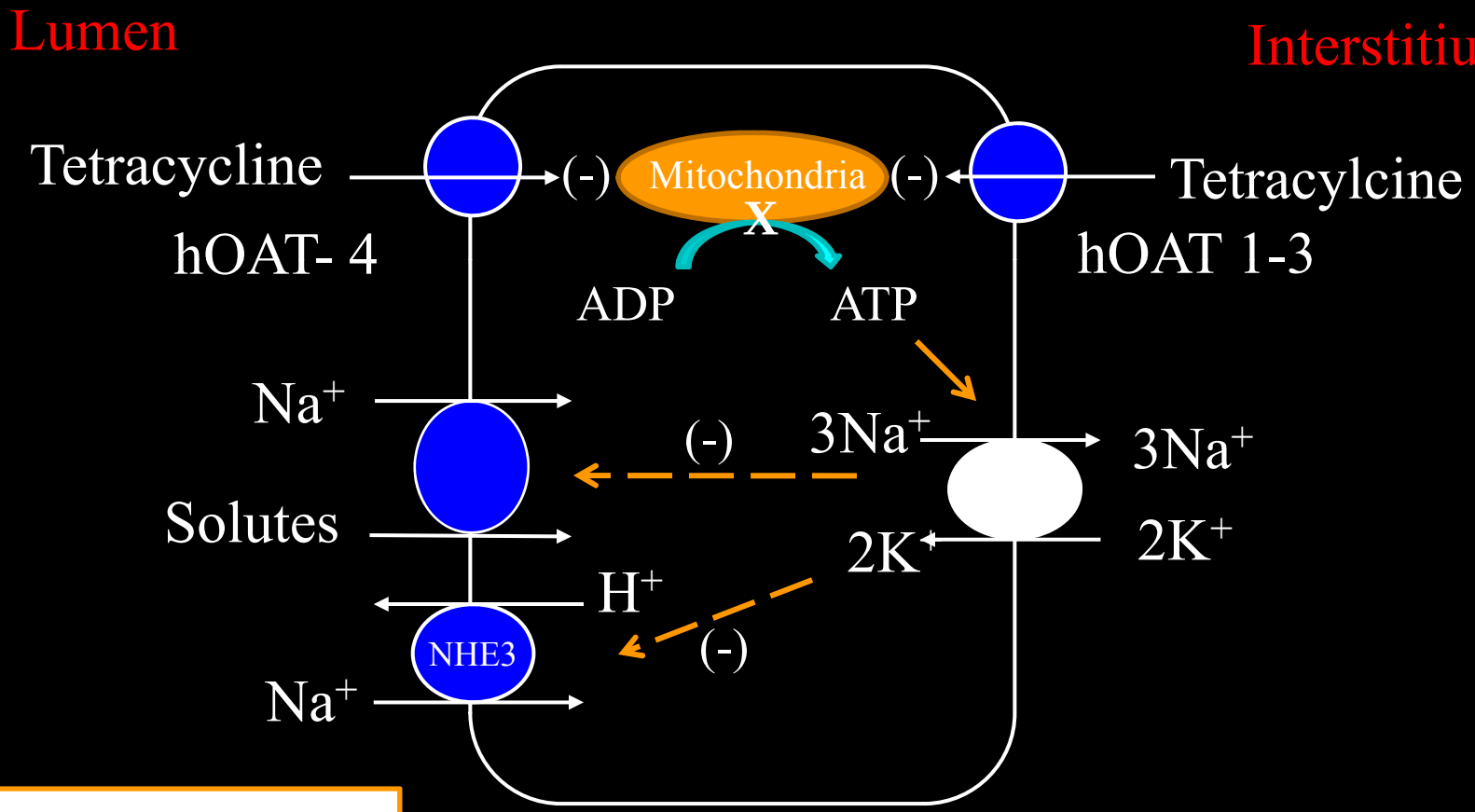
Tetracycline Entry and Effects on Proximal Tubular Cells



Type II RTA
Fanconi syndrome

Jpn J Pharm 88:69-76, 2002
Nat Rev Nephrol 5:193-202, 2009

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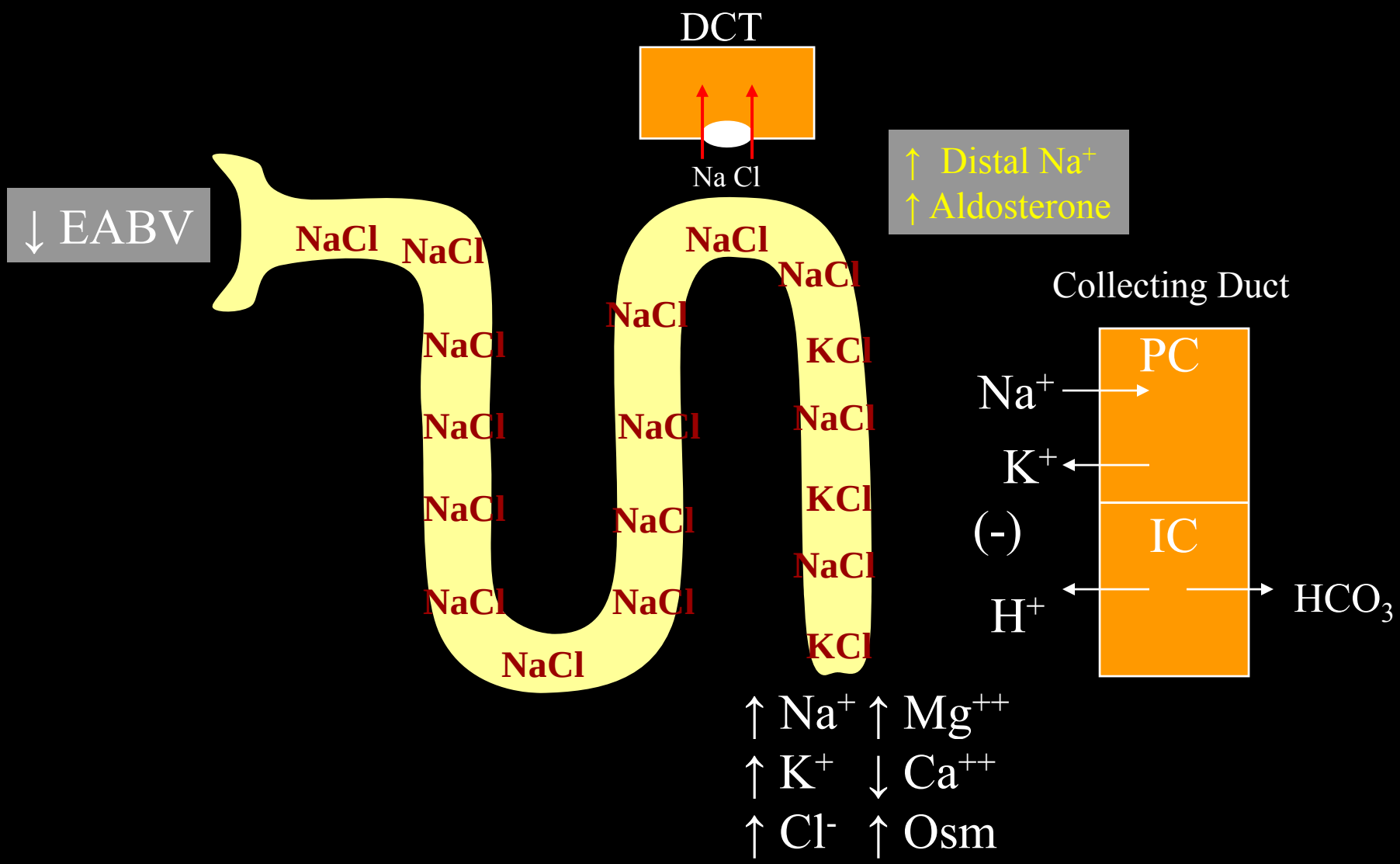
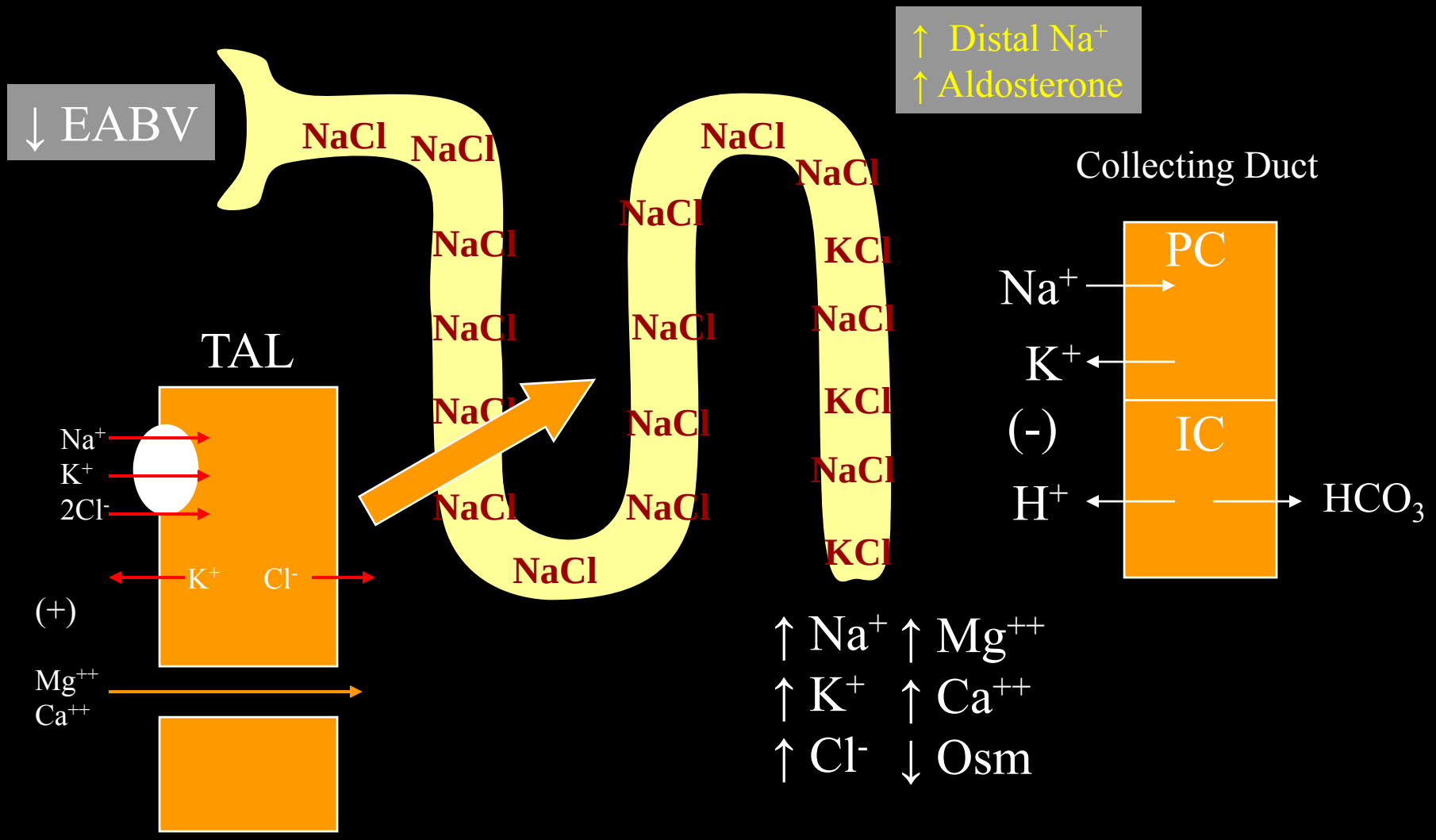
Thiazide Diuretic or Gitelman Syndrome



Loop Diuretic or Bartter Syndrome



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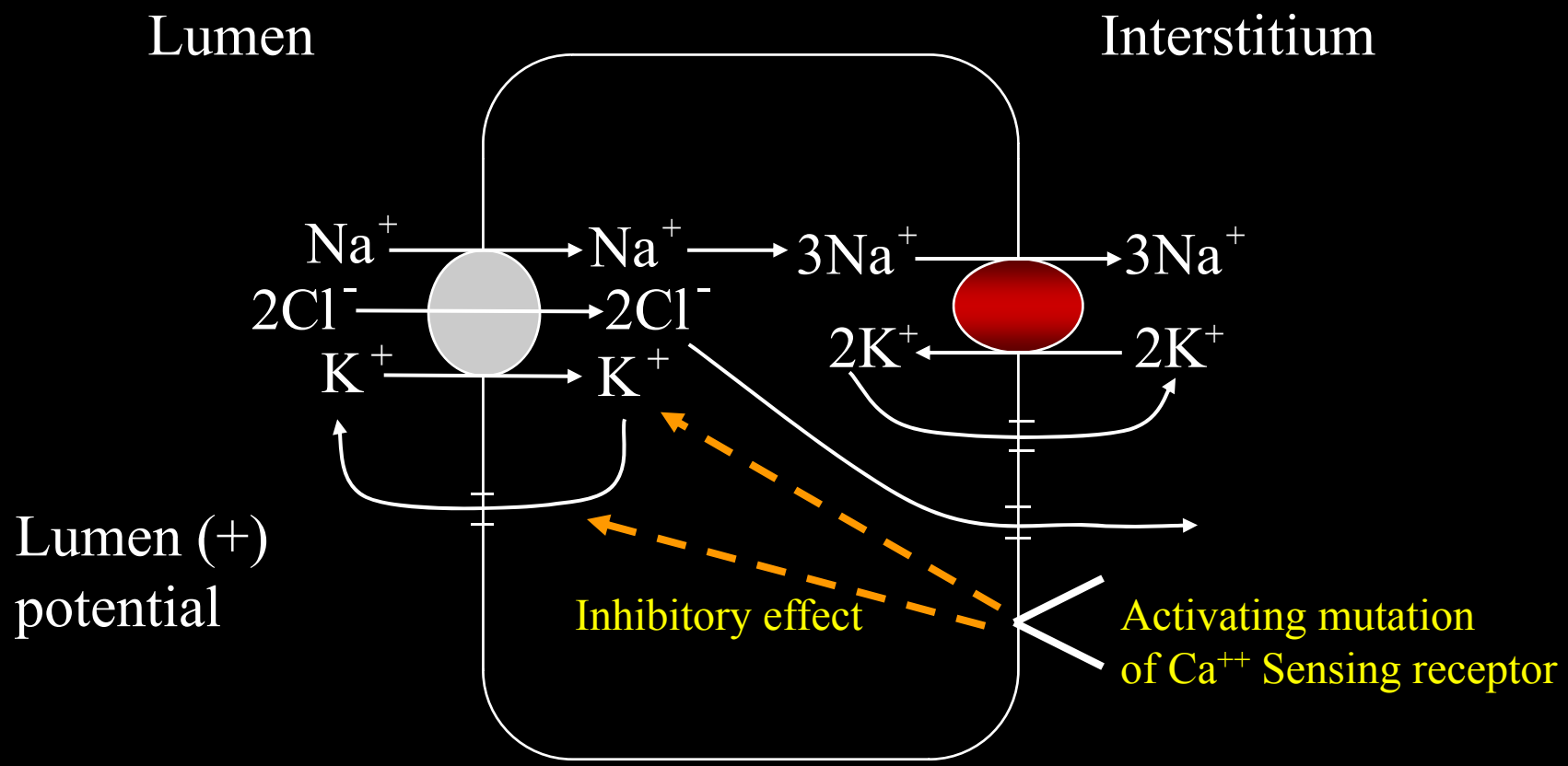
Acquired Bartter-Like Syndrome Associated with Gentamicin Administration

- 4 patients with gentamicin induced Bartter-like syndrome*
- Hypokalemic alkalosis with hypomagnesemia, hypermagnesuria, hypocalcemia, hypercalciuria, normal BP
- Total dose of gentamicin 1.2-1.6 gm
- Abnormalities resolve 2-6 wks after d/c of drug

*Am J Med Sci 329:144-149,2005
Pediatr Nephrol 11:737-40, 1997
Clin Pediatr 39:529-33, 2000

Gentamicin-induced Bartter-like Syndrome May be Due to Activation of Basolateral Ca^{++} Sensing Receptor

Gentamicin is a divalent cation



Nat Rev Nephrol 5:193-202, 2009

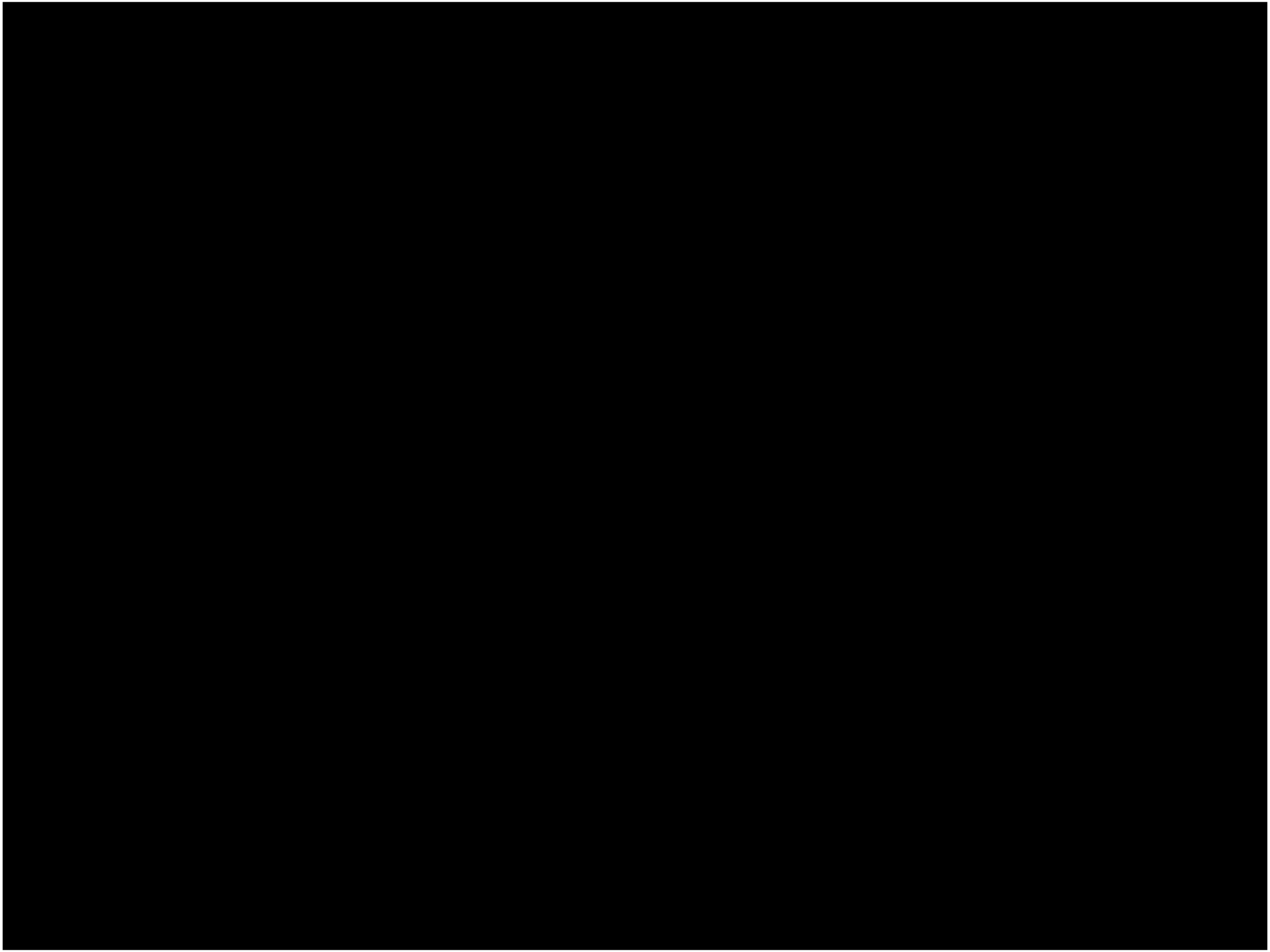
Nystagmus and Hypomagnesemia

- Downbeat nystagmus can be a manifestation of hypomagnesemia

Arch Neurol 38:650-2, 1981
Neurology 51:1478-80, 1998

Conclusion

- Aminoglycosides can cause a reversible Bartter-like syndrome characterized by hypokalemia and metabolic alkalosis in the setting of normal blood pressure.
- Interaction and stimulation of the basolateral Ca^{++} sensing receptor may be involved in the genesis of this disorder



Case 2

- A 33 year old black woman is admitted with right flank pain radiating to the groin in association with gross hematuria. Her history is noteworthy for 1 previous episode of nephrolithiasis 6 months ago. The patient works as a fashion model and as such she has always been concerned about her body weight. She admitted use of diuretic in the past but denies recent use of diuretic, laxatives or vomitus. Physical examination shows a BP of 122/78 mm Hg with no orthostatic changes. The remainder of the exam is normal.

Case 2-Laboratory studies

- Creatinine 1.1 mg/dl, BUN 14 mg/dl
- Serum electrolytes (mEq/l)
  - Na^+ 139
  - K^+ 2.3
  - Cl^- 92
  - HCO_3 34
- Urine electrolytes (mEq/l)
  - Na^+ 10
  - K^+ 15
  - Cl^- 80
- Urinalysis: SG 1.024, pH 6.8, + blood on dipstick, 20 rbc/hpf, 5-10 wbc/ hpf
- Urine culture: no growth at 24 hours
- Stone composition is found to be ammonium urate

Which One of the following can Best account for the clinical findings and electrolyte abnormalities in this patient?

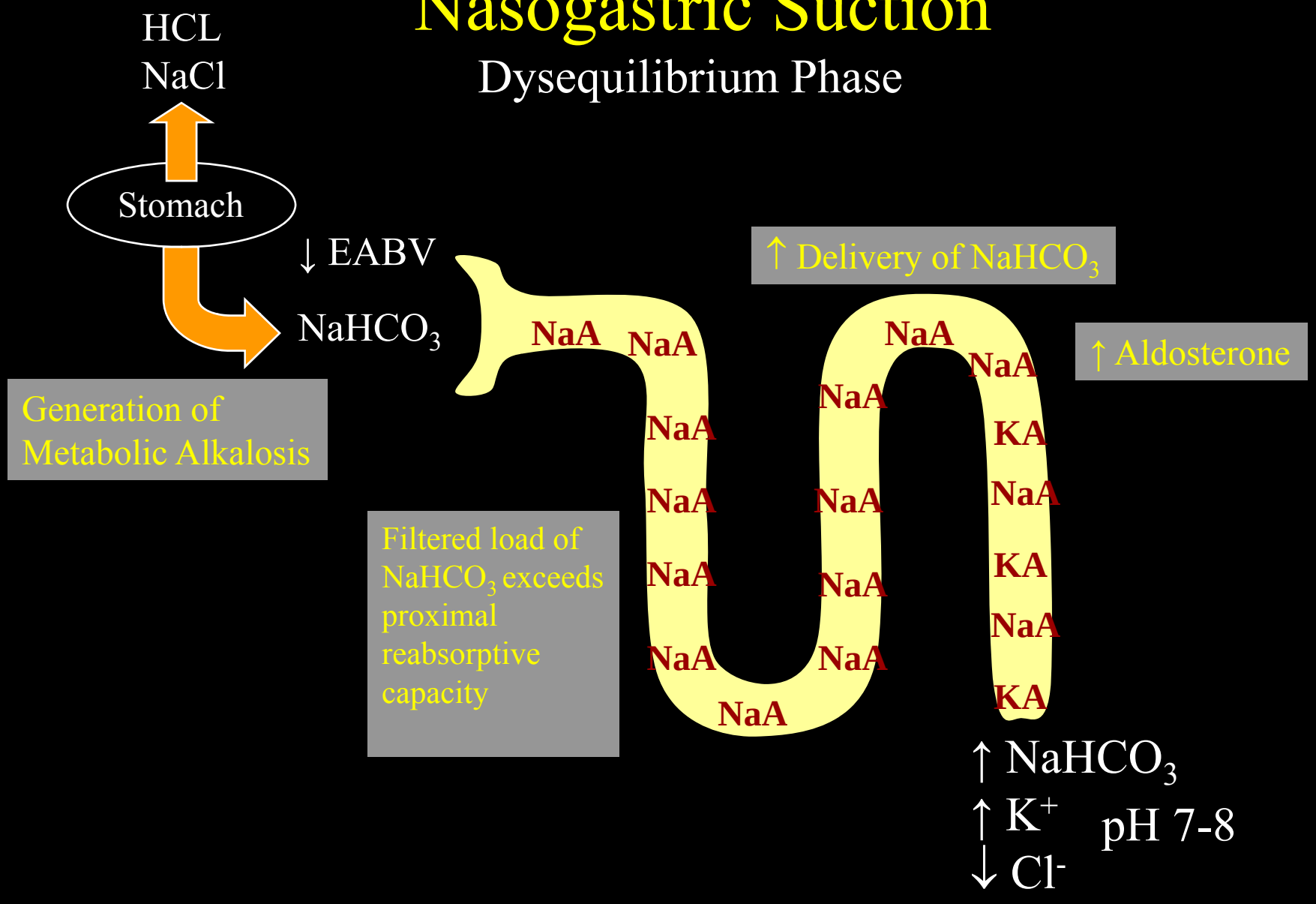
1. Vomiting
2. Surreptitious laxative abuse
3. Bartter syndrome
4. Sjogren syndrome
5. Surreptitious diuretic abuse

Case 2

- Features to account for:
  - Hypokalemic metabolic alkalosis with normal blood pressure
  - Low urine Na^+, K^+
  - High urine Cl^-
  - Ammonium urate stone

Renal K^+ Handling in Vomiting or Nasogastric Suction

Dysequilibrium Phase



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- Sjogren syndrome
- Surreptitious diuretic abuse

Which One of the following can Best account for the clinical findings and electrolyte abnormalities in this patient?

- Sjogren syndrome
  - More common in young black women
  - Associated with nephrolithiasis and nephrocalcinosis
  - Renal manifestations
    - Nephrogenic diabetes insipidus
    - Type 1 renal tubular acidosis

Which One of the following can Best account for the clinical findings and electrolyte abnormalities in this patient?

- Vomiting
- Surreptitious laxative abuse
- Bartter syndrome
- Sjogren's syndrome
- Surreptitious diuretic abuse

Which One of the following can Best account for the clinical findings and electrolyte abnormalities in this patient?

- Surreptitious diuretic abuse
  - Thiazides and loop diuretics associated with hypokalemia and metabolic alkalosis
  - Urine electrolytes:

	Na^+	K^+	Cl^-
Active use	↑	↑	↑
Remote use	↓	↓	↓

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- Sjogren's syndrome
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Gastrointestinal K^+ Losses

- Hypokalemia with metabolic alkalosis
  - Congenital chloridorrhea
  - Villous adenoma
  - Chronic laxative abuse (Colon effect) (Am J Gastroenterol 74:451-8, 1980, Pharmacology 47 Suppl 1:138-45, 1993)

Surreptitious Laxative Abuse

- Prevalence of 4-26% of patients with chronic diarrhea
- Colonic stimulants most widely used
  - Phenolphthalein (no longer available OTC)
  - Bisacodyl: Dulcolax, Ex-Lax, Correctol
  - Anthraquinone
    - Senna (Senokot, Castoria, Black Draught)
    - Aloin
    - Cascara
    - Frangula

Composition of Intestinal Secretions

	Volume (ml)	Na^+ (mEq/L)	K^+ (mEq/L)	Cl^- (mEq/L)	HCO_3 (mEq/L)
Early Jejunum	9000	60	15	60	15
Late Jejunum	3000	140	6	100	30
Ileum	1000	140	8	60	70
Colon	100	140	90	30	30

Chronic Laxative Abuse

Laxative effect in colon

↓

K^+ Depletion

↓

Intracelluar acidosis

↓

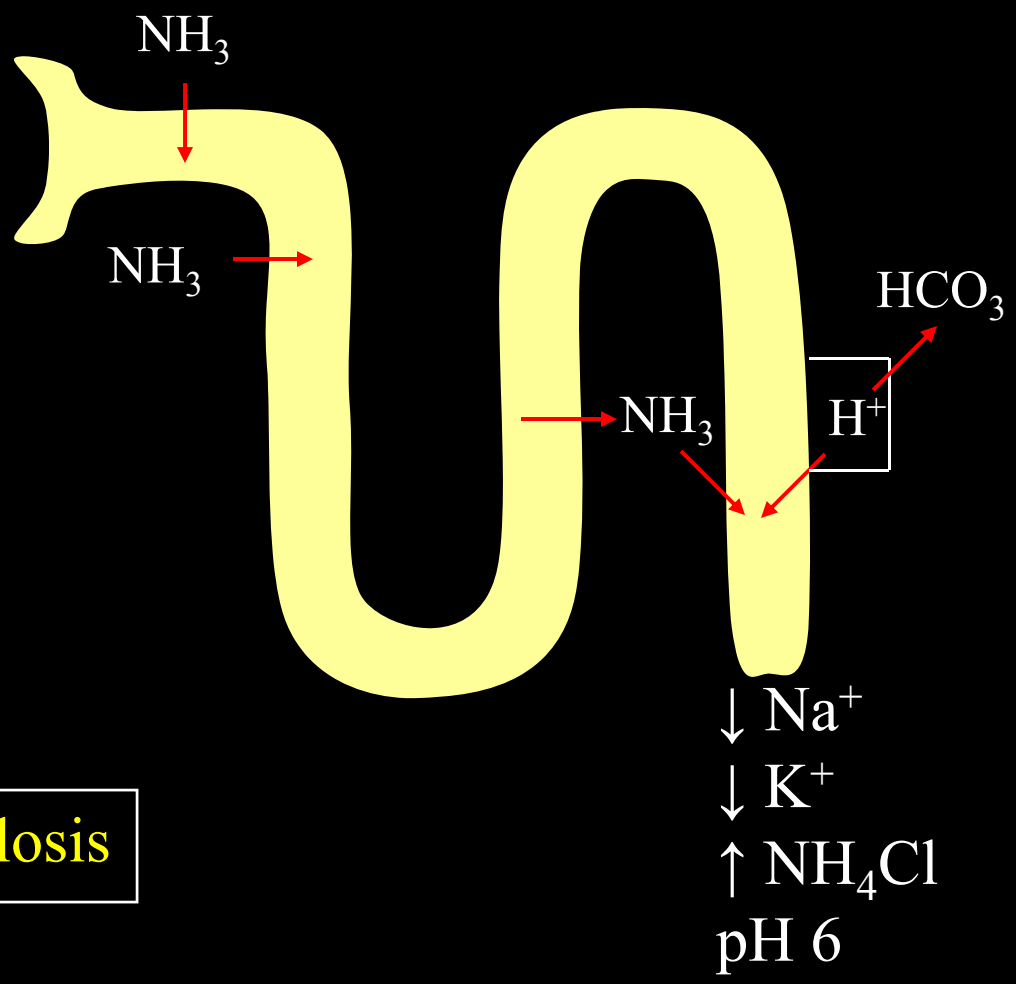
↑ Renal NH_3 production

↓

↑ Urinary excretion of NH_4Cl

↓

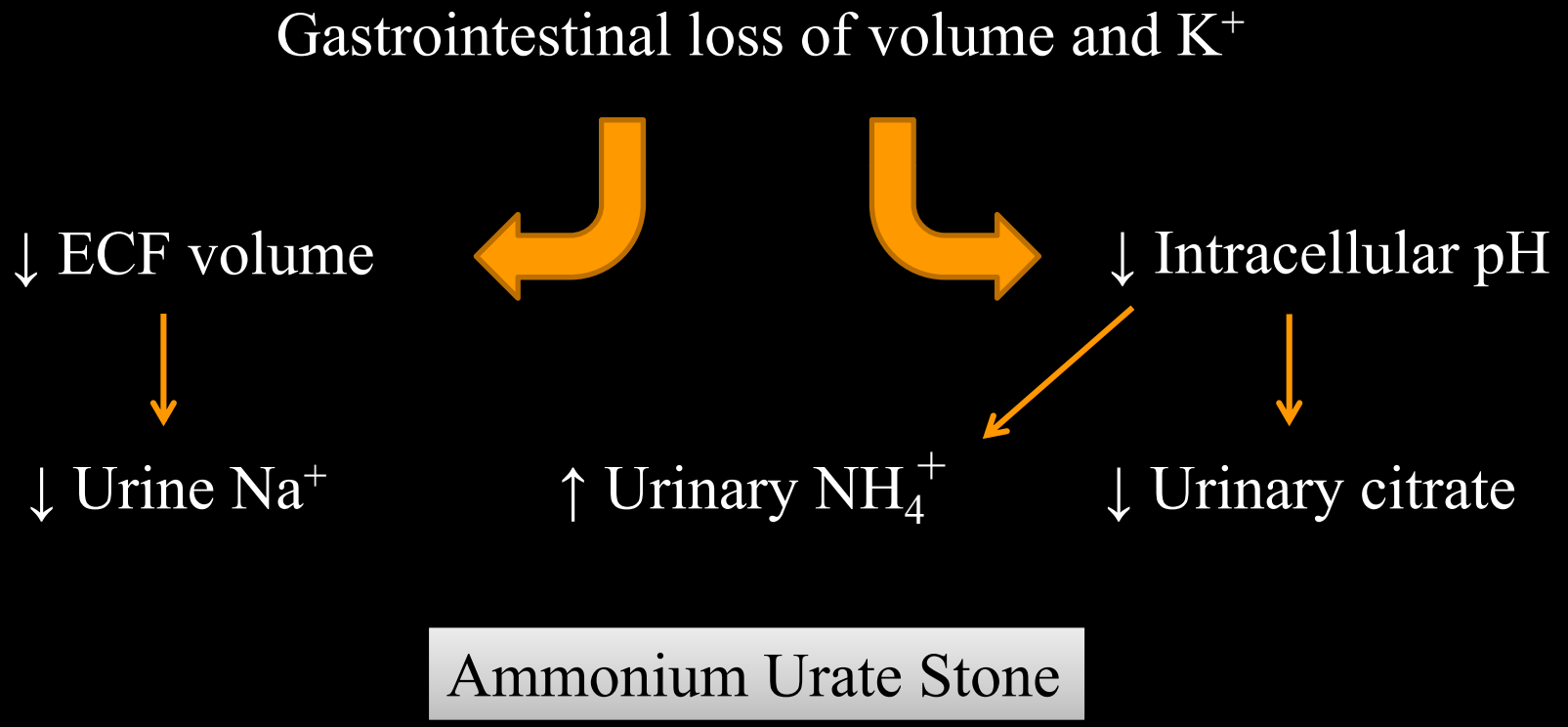
Generation of Metabolic Alkalosis



Surreptitious Laxative Abuse and Metabolic Alkalosis

- Metabolic alkalosis results when the stimulatory effect on renal acidification exceeds the loss of actual and potential HCO_3 in the stool

Nine women with laxative abuse and ammonium urate renal calculi*



*J Urology 143:244-247, 1990

Endemic Bladder Stones Composed of Ammonium Urate

- Bladder stones composed of ammonium urate in third world countries
- Low milk/high cereal diet is acidogenic and low in phosphate resulting in low urinary phosphate and increased ammonium
- Low urine volumes (poor water supply and high ambient temperatures) contribute to concentration of uric acid

Semin Nephrol 23:77-87, 2003

Summary

- Chronic use of laxatives that primarily effect the colon can result in metabolic alkalosis
- Metabolic alkalosis results when the stimulatory effect on renal acidification exceeds the loss of actual and potential HCO_3 in the stool
- The high concentration of urinary ammonium can lead to ammonium urate stones