# IV.B. ELECTROLYTES & THEIR DYSFUNCTION

## B.a. GENERAL

### B.a.A. FUNCTIONS OF ELECTROLYTES

Table IVB-1. Functions of Electrolytes in the Body

IVB-1

| (M)ajor/(L)esser Role in/as | $Na^+$ | $K^+$ | $Ca^{++}$ | $P0_4^{-3}$ | $H^+$ | $HC0_3^-$ | $NH_4^+$ | $Mg^{++}$ | $Cl^-$ | Proteins$^-$ |
|---|---|---|---|---|---|---|---|---|---|---|
| 1a. Regulating body fluids | M[a] | L | L | L | L | L | L | L | L | M |
| b. Maintaining intracellular osmolality | | M | | | | | | | | |
| c. Determining normal intracellular $K^+$ levels | | | | | | | | M | | |
| d. Acid-base regulation | M | L | | M[b] | M | M | L | | M[c] | |
| | | | | | | | | | | |
| 2a. Coenzyme/cofactor | | L | M | M[d] | | | | M[e] | | |
| b. Anabolic metabolism of carbohydrates & proteins | | M | | | | | | | | |
| c. Energy for anabolic processes, membrane transport, fibril contraction | | | | M[f] | | | | | | |
| | | | | | | | | | | |
| 3a. Major component of macromolecules & organelles (unit membrane & nucleic acids) | | | | M | | | | | | |
| b. Numerous vital chemical reactions | M | | | | | | | | | |
| | | | | | | | | | | |
| 4a. Second messengers | | | M[g,h] | | | | | | | |
| b. Controlling synaptic release of **ACH** | | | M | | | | | | | |
| c. Nerve/muscle impulse | M | M | | | | | | | | |
| d. Initiation/inhibition of nerve/muscle impulse in post synaptic cells | M | M | L | | | | | | | |
| e. Maintains refractability of cardiac muscle | | | M | | | | | | | |
| | | | | | | | | | | |
| 5a. Blood clotting | | | M | | | | | | | |
| b. Normal function of white blood cells & platelets | | | | M | | | | | | |
| c. Component of HCl in the stomach | | | | | M | | | | M | |
| d. Component of alkaline digestive juices | | | | | | M | | | | |
| e. Absorption of vitamin $B_{12}$ & intrinsic factor in small & large intestine | | | M | | | | | | | |
| | | | | | | | | | | |
| 6. Component of bone matrix & otoliths | | | M | M | | M[i] | | L | | |

a major determinant of extracellular volume
b major buffer in blood; buffer in renal excretion of $H^+$
c chloride shift
d essential in enzymes for metabolism of glucose, fat, & protein
e essential in all enzyme systems known to be catalyzed by **ATP**; replication, transcription & translation; fibril contraction & glycogen metabolism
f **ATP** + 2,3 **DPG**
g best example: $Ca^{++}$ binds to troponin on troponin-tropmyosin complex, → altered position of tropomyosin, → exposure of active sites on actin, → attraction of the head of the myosin filament, → the power stroke.
h $K^+$ & $Mg^{++}$ can bind to $Ca^{++}$ receptors
i as $CO_3^=$

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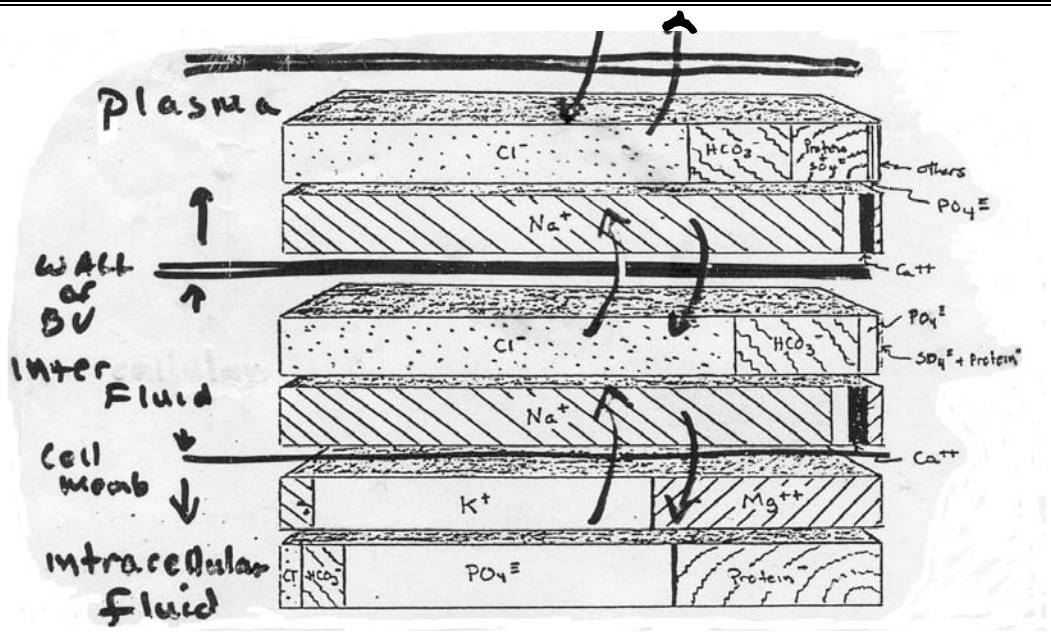
### B.a.B. TERMINOLOGY

| | | | | | | |
|---|---|---|---|---|---|---|
| | 3) -natr- - | | | 3) | | |
| 1) hypo- | 4) -kal- | | 1) | 4) | | |
| 2) hyper- | 5) -calcem- | 8) –emia | 2) | 5) | | 8) |
| | 6) -phosphat- | | | 6) | | |
| | 7) -magnes- | | | 7) | | |

B.a.C. RELATIVE CONCENTRATIONS




IVB-2

Critical Figure IVB-1. Relative Concentrations of Electrolytes in Three Fluid Compartments

B.b. SODIUM

B.b.A. NORMAL GAINS & LOSSES (**MDR** = 300 mg//day) (normal intake: 12-30 times this)

| GAINS | LOSSES | KIDNEY ACTIONS |
|---|---|---|
| Diet | kidneys (90%) | ↑ $Na^+$ → ↑ $Na^+$ excretion |
| | | ↓ $Na^+$ → ↑ $Na^+$ retention |
| Meds | skin (≤ 15-30 mg//day, except during profuse sweating) | |
| | gi tract (normally actively absorbed in lower bowel, so that in stools: 32 mEq $Na^+$//ℓ) | |

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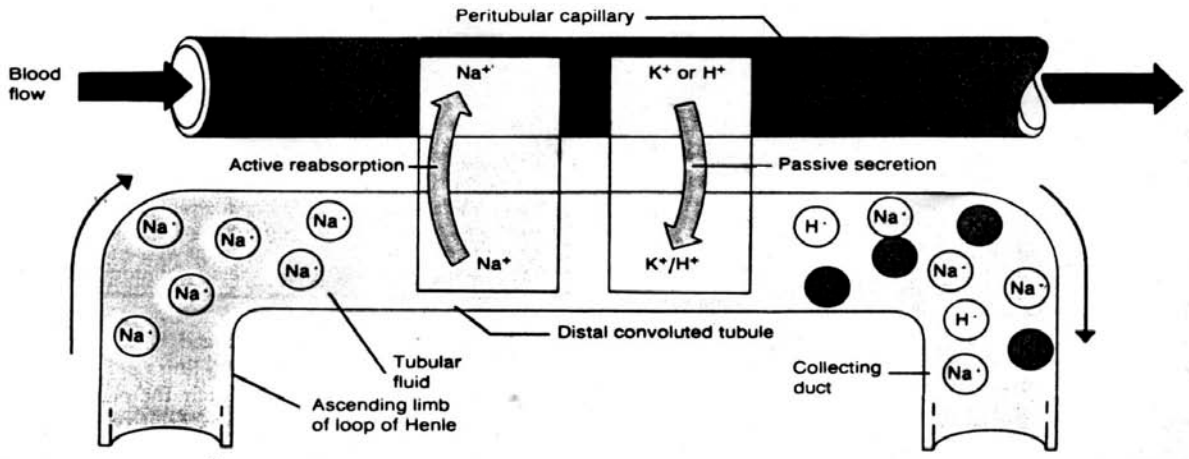
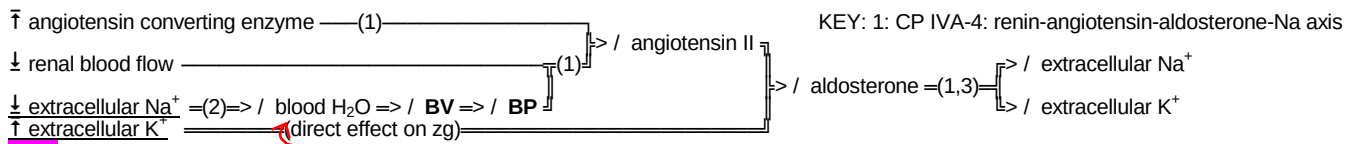
B.b.B. RENAL RETENTION [normal serum = 136-145 mmol//ℓ (200, p 676) = < > mEq//ℓ]




IVB-3

Critical Figure IVB-2. The Coupling of $K^+/H^+$ Secretion to $Na^+$ reabsorption (22, p 767)




Critical Path IVB-1. Mechanisms of Sodium Regulation

## B.b.C. HYPONATREMIA [serum $Na^+$ < 135 mEq/ℓ < 120 mEq/ℓ is serious (200, p 676)

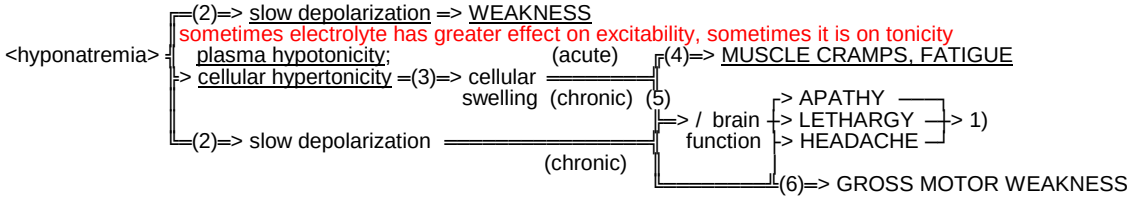
### B.b.C.a. CONDITIONS

1) normal vomiting &/or diarrhea =(iso-osmotic fluid loss)=> no Δ $Na^+$
2) ↑ $Na^+$ secretion in kidney
3) ↑ $Na^+$ loss through skin
4) dilution of existing serum $Na^+$ via other osmotically active substances (↑ sugar –> ↑ $H_2O$ –> ↓ $Na^+$)
5) ↓ $Na^+$ gain w/ ↑↑ $H_2O$ gain
6) ↑↑ $Na^+$ loss w/ ↑ $H_2O$ loss
7) ↑ $Na^+$ loss to **GI** tract

### B.b.C.b. ETIOLOGIC FACTORS

kidney: ↑↑ diuretics, salt wasting kidney disease, Addison's Disease –> )
skin: 3rd degree burns –> ); heat exhaustion –> )
endocrine: diabetes –> )
**GI** tract: water intoxication –> ); frequent tap water enemas, frequent **GI** irrigation w distilled $H_2O$ –> )

water intoxication –(1)–> acute hyponatremia –> / $Na^+$ filtration –> / urine osmolality –> / URINE SPECIFIC GRAVITY*




1) => DISORIENTATION (110 mOsm//kg)
=> CONFUSION –> SEIZURES –> COMA

KEY: 1: P IVA-5: WVE path
2: Table IVB-1: 4c: role of $Na^+$ in action potential
3: CF IIIA-5: osmosis & $H_20$ –> hypertonic soln
4: CP IIIA-2: mild hypoxia-> / **ATP** –> / sarcoplasmic $Ca^{++}$
5: CP IIIA-9: cellular swelling –> / mitochondrial function
6: CF IIIA-3: role a of **ATP** in the cell: microfibril contraction

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Path IVB-2. Manifestations of Hyponatremia

## B.b.D. HYPERNATREMIA [serum $Na^+$ > 148 mEq/ℓ: > 160 mEq/ℓ is serious (200, p 676)]

### B.b.D.a. CONDITIONS

1) rapid, hypertonic $Na^+$ ingestion/input
2) defect in thirst mechanism
3) inability to drink/get water
4) $H_2O$ input < $H_2O$ output
5) ↓ Na output

### B.b.D.b ETIOLOGIC FACTORS

taking excess salt tablets, near drowning in salt water, rapid $NaHCO_3$ administration during **CPR**, osmotically active (hypertonic) tube feeding w/out adequate $H_2O$, therapeutic abortion w saline solution placed intravenously rather than intraamniotically –> )
head trauma –> )
oral trauma, severe laryngopharyngitis, unconsciousness, bed ridden, infancy –> )

fever, watery diarrhea, tracheobronchitis, diuretic therapy, strenuous exercise in heat, diabetes insipidus, –> )

<congestive heart failure>, most forms of kidney disease, <Cushing's syndrome>* –> )

## B.c.. POTASSIUM

### B.c.A. NORMAL GAINS & LOSSES (**MDR** = 50-100 mg//day) (↑ demands during trauma & stress)

| GAINS | STORAGE | LOSSES |
|---|---|---|
| diet | cells | kidneys (80-90%), skin, stools |

### B.c.B. REGULATION (normal serum = 3.5-5.0 mEq//ℓ) ($K^+$ in plasma = 2% of total body $K^+$)

### B.c.B.a. RENAL MECHANISMS (review: (1) CP IVB-1: r,a,aI,aII,a axis & (2) CF IVB-2: action of aldos on dct)

1) **aldosterone** (1,2): (↑ in serum $K^+$ **≥ 1 mEq//ℓ** –> 3X / in aldosterone)
2) DCT (2): ↑ serum $K^+$ –(2)–> / $K^+$ secretion –> / $H^+$ secretion –> / $H^+$ retention –> metabolic acidosis
3) DCT (2): ↓ serum $K^+$ –(2)–> / $K^+$ secretion –> / $H^+$ secretion –> / $H^+$ retention –> metabolic alkalosis

4) metabolic alkalosis –(3)–> / plasma $HCO_3^-$ –> / $KHCO_3$ secretion –> // serum $K^+$ levels [(3) S. IV.C.c.C.]

### B.c.B.b. REDISTRIBUTION BETWEEN FLUID COMPARTMENTS (review: (4): CF IIIA-5: cell lysis)

1) **insulin** (↑ serum $K^+$ ≥ 1 mEq//ℓ –> / serum insulin –> / $K^+$ into cells)
2) injury to cells –(4)–> / serum $K^+$
3) cellular anabolism > cellular catabolism ($K^+$ necessary for glycogen synthesis & storage, & protein synthesis) –> ↓ serum $K^+$ & *visa versa*
4) $K^+/H^+$ exchange (cells vs secretion into **DCT**) (Table IVB-1, 2b)
   ↑ $K^+$ into cells, ↑ $H^+$ out of cells & ↑ $K^+$ out of cells, ↑ $H^+$ into cells
   acidosis –> / $H^+$ into cells –> / $K^+$ out of cells (1:1 ratio); alkalosis, just the reverse
5) **epinephrine** (↑ epinephrine –> ↑ $K^+$ into cells)
6) ↓ $Mg^{++}$ –??–> ↓ intracellular $K^+$ (Table IVB-1, 1c)

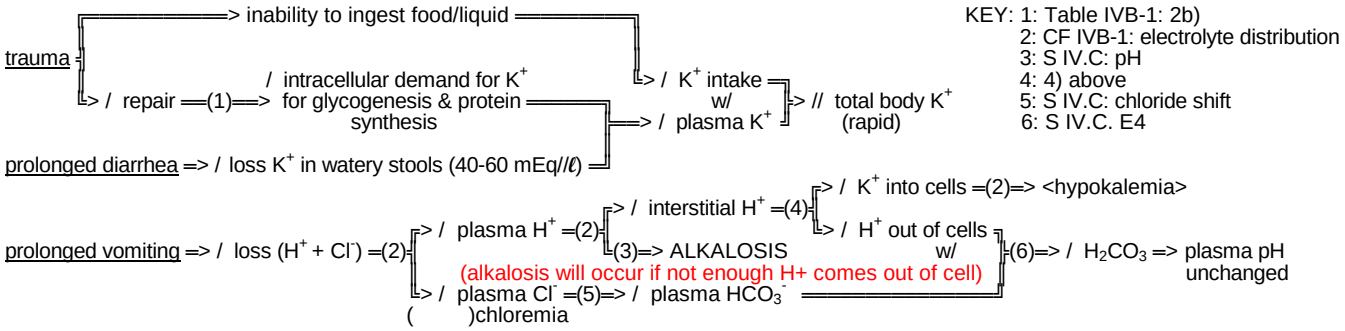
### B.c.C. HYPOKALEMIA [serum $K^+$ < 3.5 mEq//ℓ]

### B.c.C.a. ETIOLOGIC FACTORS

1) redistribution between intracellular & extracellular compartments
2) inadequate intake
3) excessive intestinal losses
4) excessive renal losses

### B.c.C.b. PATHOPHYSIOLOGY

### B.c.C.b.(A.) ETIOLOGY OF HYPOKALEMIA **NB**: kidneys have no mechanism for conserving $K^+$ during acute $K^+$ loss, ∴:)




Conn's syndrome –T–> ⇓ total body K – (slow)
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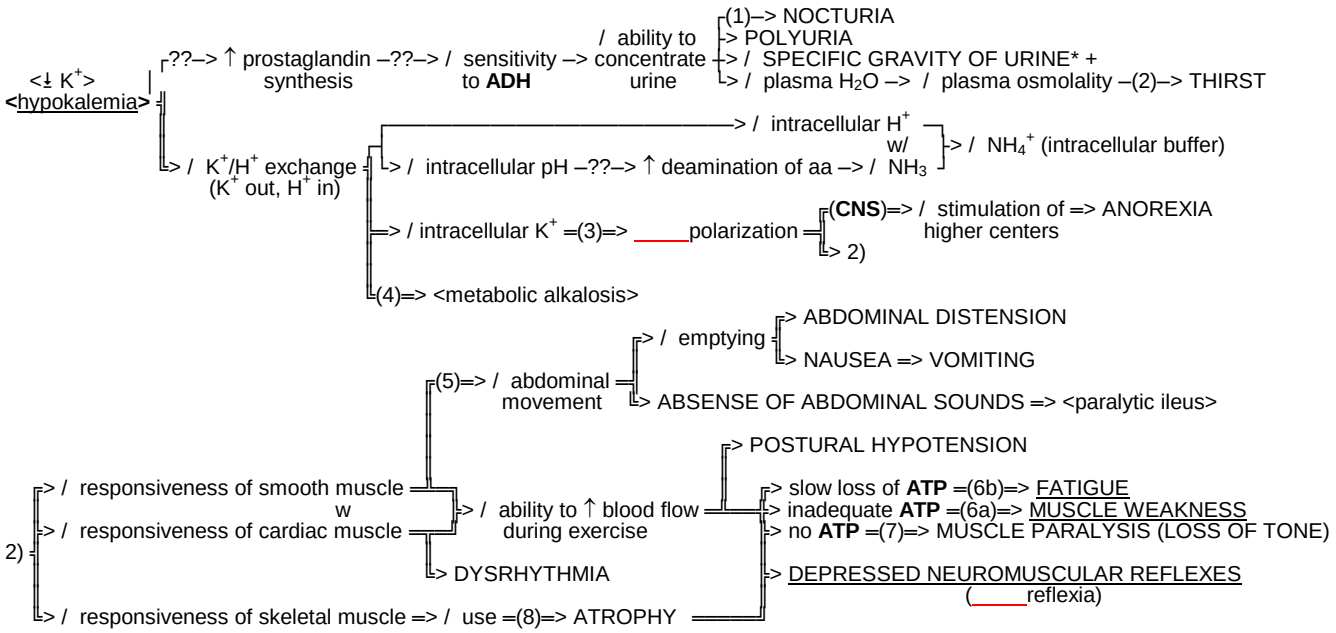
Path IVB-3. General Etiology of Hypokalemia

B.c.C.b.(B.) MANIFESTATIONS OF HYPOKALEMIA (< 3.5 mEq//ℓ: < 2.5 mEq//ℓ is serious (200, p 578))



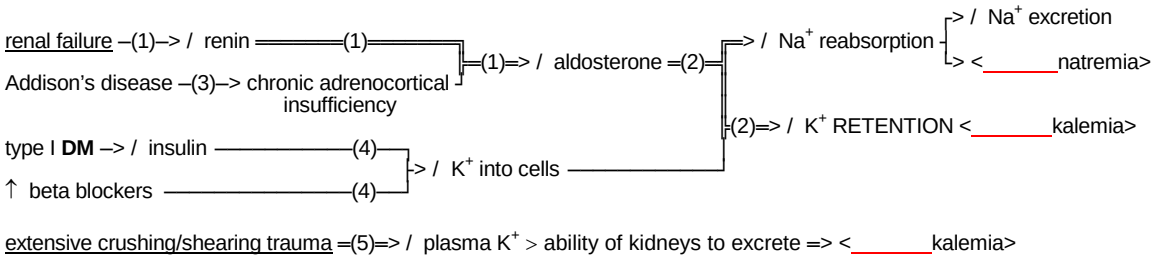

Key: 1: F II-1: diurnal patterns (↑ **ADH** at night)
2: CP IVA-2: high serum osmolality & thirst receptors in hypothalamus
3: P IVC-1: ↓ intracellular $K^+$ –> lowering of resting potential –> _____polarization
4: S IVC.b.C.: ↓ interstitial $H^+$ –> metabolic alkalosis
5: S VIII.A.: gastrointestinal functions
6: CP IIIA-3: b: role of **ATP** in anabolism; a: role of **ATP** in neurofibril contraction
7: CP IIIA-2: effect of ↓ **ATP** on $Ca^{++}$ uptake by sarcoplasmic reticulum
8: P IIIA-4: effect of ↓ use on **ATP** & protein synthesis

IVB-4
Path IVB-4. Manifestations of Hypokalemia

B.c.D. HYPERKALEMIA [serum $K^+$ > 5.0 mEq// ℓ] (manifestations appear at > 6.5 mEq//ℓ (200, p 578))
B.c.D.a. ETIOLOGIC FACTORS difficult to create, but potentially life-threatening

1) excess $K^+$ gains by trauma,cancer treatment, extensive hemolysis/blood transfusion of old blood/rapid parenteral perfusion
2) renal failure
3) Addison's disease (insufficient aldosterone)
4) conditions that decrease $K^+$ uptake by cells

B.c.D.b. PATHOPHYSIOLOGY
B.c.D.b.(A.) ETIOLOGY OF HYPERKALEMIA




extensive crushing/shearing trauma =(5)=> / plasma $K^+$ > ability of kidneys to excrete => <_____kalemia>

KEY: 1: CP IVA-4: Renin, angiotensinogen, angiotensin, aldosterone axis
2: CF IVB-2: $Na^+/K^+$ exchange at **DCT**
3: S VIID: Endocrine
4: S IVB.c.B., above
5: CF IIIA-7: cellular swelling & lysis

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Path IVB-5. General Etiology of Hyperkalemia

KEY: 1: CF IVB-1: electrolyte distribution
2: F IIIA-6: electrochemical gradient & cell
3: P IVB-4: effect of ↑/↓ intracellular $K^+$ on resting potential

<$\bar{\uparrow}$ $K^+$> =(1)=> / $K^+$ outside of cells =(2)=> / flow of $K^+$ into cells =(3)=> (____polarization) => / excitability/irritability => (6 mEq//ℓ) => PAR\ESTHESIA {\G sensation}; (3) => ARRHYTHMIAS*; (3) => CHANGED **ECG*** (F 16.15, p 417); T=(if: $\bar{\uparrow}\bar{\uparrow}$ $K^+$ => 1)

(201, p 106)

1) => resting potential above threshold potential => CARDIAC ARREST

IVB-6

Path IVB-6. General Manifestations of Hyperkalemia

## B.d. CALCIUM & PHOSPHATE BALANCE

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### B.d.A. BACKGROUND

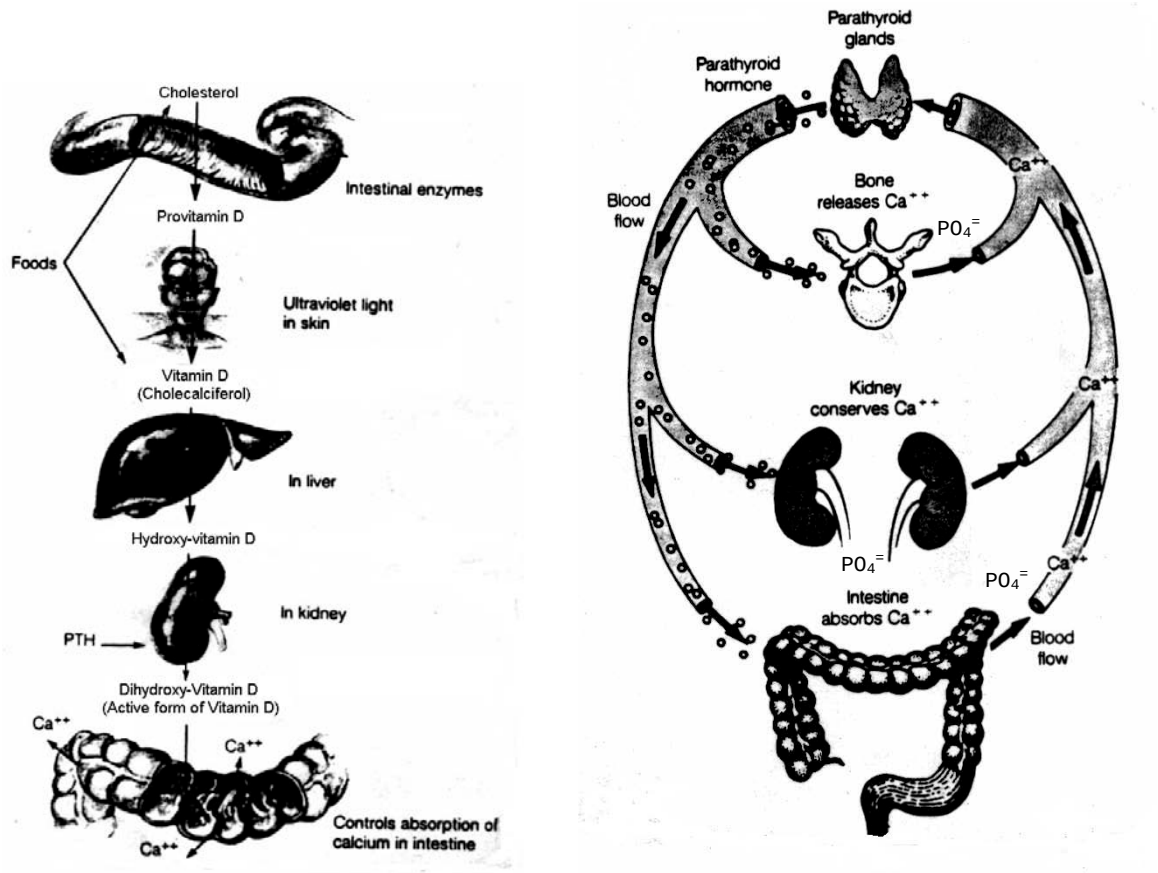
1) $Ca^{++}$ & $PO_4^{-3}$ are linked because main reservoir is bone which has 70% crystalline salts, most of which are $Ca_3(PO_4)_2$
2) in adults, normal serum $Ca^{++}$ = 8.8-10.0 mg//dℓ (4.4-5.0 mEq/ℓ); normal serum $PO_4^{-3}$ = 2.7-4.5 mg//dℓ (0.85-1.4 mEq//ℓ)
3) concentration in extracellular fluids is regulated such that their products in mg//dℓ = 35 (to prevent precipitation of $Ca_3(PO_4)_2$ into tissues)

### B.d.B. NORMAL GAINS, STORAGE & LOSSES

| GAINS | STORAGE | LOSSES[a] |
|---|---|---|
| gastrointestinal[a] | bones | kidneys |
| | | feces |

[a]30-50% of $Ca^{++}$ ingested is absorbed in duodenum & upper jejunum; remainder eliminated through bowels; all of $PO_4^{-3}$ ingested is absorbed.

### B.d.C. REGULATION




IVB-6

Figure IVB-3. Roles of Vitamin D & **PTH** in $Ca^{++}$ & $PO_4^{-3}$ regulation (22, p 482)

↓ serum $Ca^{++}$ below critical level
↑ serum $PO_4^{-3}$ above critical level
=> / **PTH** =(1)=> / $Ca^{++}$ excretion => / serum $Ca^{++}$
=(1)=> / $PO_4^{-3}$ excretion => / serum $PO_4^{-3}$
=? (_____)

Key: 1: F IVB-3: role of **PTH** on kidney

IVB-7a

Path IVB-7. Normal Mechanisms for Calcium & Phosphate Regulation

## B.e. CALCIUM [normal serum = 8.8 - 10 mg//dℓ]

### B.e.A. EXTRACELLULAR $Ca^{++}$ LEVELS (99% in bones & teeth, 1% in tissue cells & extracellular fluid)

ef => ↓ serum $Ca^{++}$ below normal levels (nl) =(1)=> / **PTH** => / activity of osteoclasts => / $Ca^{++}$ erosion from bone => / serum $Ca^{++}$ to nl

ef => ↑ serum $Ca^{++}$ above nl => / calcitonin => / activity of osteoblasts => / $Ca^{++}$ deposition to bones => / serum $Ca^{++}$ to nl

=? (_____)

IVB-7b

Path IVB-8. Mechanisms of Calcium Regulation

Key: 1: P IVB-7: response of parathyroid gland to low calcium

of total serum $Ca^{++}$

1) 40% bound to plasma proteins ∴ can't leave plasma
   36% bound to albumin; 4% bound to globulin ∴ Δ albumin –> Δ total serum $Ca^{++}$
   (total serum $Ca^{++}$ ↓ 's 0.75-1 mg//dℓ for every 1 g//dℓ ↓ in serum albumin)
   ↑ pH –> ↑ binding of $Ca^{++}$ to plasma protein (serum $Ca^{++}$ ↓'s 0.16 mg//dℓ for every 0.1 ↑ in pH)
2) 10% bound to citrates, phosphates & sulfates (citrates used to inhibit coagulation in blood transfusions;
   cleared by liver in minutes; citrates –> ↑ $Ca^{++}$ binding –> ↓ free $Ca^{++}$ –(S V.I.)–> ↓ coagulation)
3) 50% as free $Ca^{++}$ which can leave the plasma

i.e. total serum $Ca^{++}$ = $Ca^{++}$•albumin + $Ca^{++}$•cit/phos/sulfates + free $Ca^{++}$ ∴ ↓ in any –> ↓ serum $Ca^{++}$ but only free $Ca^{++}$ is of critical importance

### B.e.B. HYPOCALCEMIA [serum $Ca^{++}$ < 8.5 mg//dℓ]

### B.e.B.a. ETIOLOGIC FACTORS

impaired ability to mobilize $Ca^{++}$ from bones
   hypoparathyroidism (–> impaired mobility)
abnormal $Ca^{++}$ binding (too much in unionized form)
   ↑ pH, ↑ free fatty acids, rapid transfusion of citrated blood, acute pancreatitis
   (**NB**, since Δ serum albumin –> no Δ in free serum $Ca^{++}$, ↓ serum albumin rarely –> manifestations)
abnormal losses
   renal failure
decreased absorption from intestine
   inactivity or vitamin D deficiency

### B.e.B.b. PATHOPHYSIOLOGY

### B.e.B.b.(A.) ETIOLOGY OF HYPOCALCEMIA

hyperventilation =(1)=> respiratory alkalosis => / pH =(1)=> / binding of $Ca^{++}$ to plasma protein => no Δ in total serum $Ca^{++}$
renal failure => / responsiveness of kidneys to **PTH** =(2)=> / $Ca^{++}$ absorption from gut => / free $Ca^{++}$ <_____calcemia>

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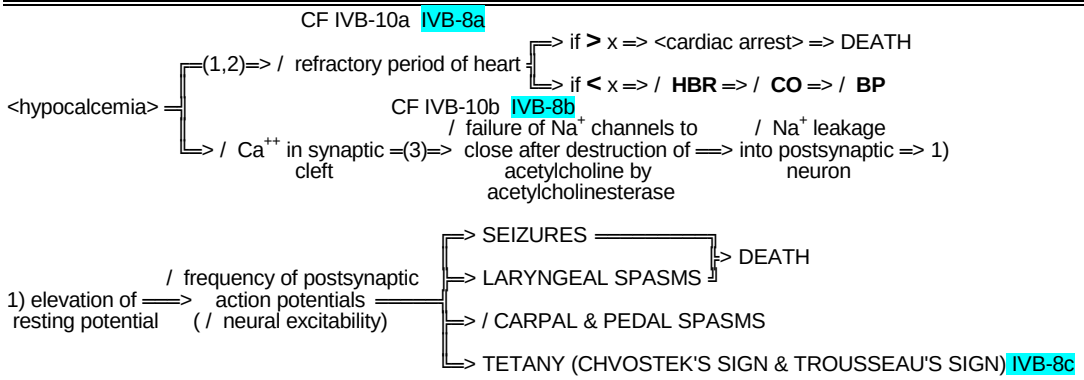
Path IVB-9. General Etiology of Hypocalcemia

Key: 1: S IV.C: acid-base balance
2: F IVB-3: role of **PTH** on $Ca^{++}$ absorption from sm intestine

## B.e.B.b.(B.) MANIFESTATIONS OF HYPOCALCEMIA




KEY: 1: Table IVB-1; 4e: $Ca^{++}$ maintains cardiac refractivity
2: S VII.D.: cardiac function & dysfunction
3: Table IVB-1; 4d: role of $Ca^{++}$ in **EPSPs** & **IPSPs**

IVB-8

Path IVB-10. General Manifestations of Hypocalcemia

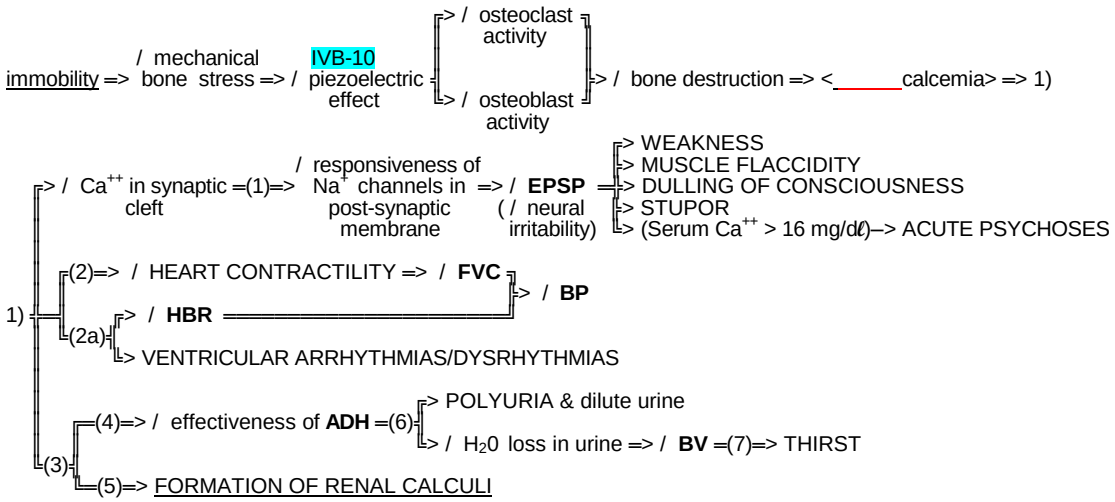
## B.e.C. HYPERCALCEMIA [total serum $Ca^{++}$ > 10.5 mg//dℓ]

### B.e.C.a. ETIOLOGIC FACTORS

1) excess osteoclast activity:
malignant neoplasms, ↑ bone destruction: immobility, thiazide diuretics, post menopausal, hyperparathyroidism,
2) **GI** tract: (sources: milk, egg yolk, shellfish, green-leafy vegies)
↑ intestinal absorption, excessive vitamin D, excessive $Ca^{++}$ in diet, milk-alkali syndrome

### B.e.C.b. PATHOPHYSIOLOGY

manifestations results from:
1) ↓ neuromuscular activity
2) resorption of $Ca^{++}$ from bone
3) exposure of kidneys to high $Ca^{++}$ concentrations




KEY: 1: Path IVB-10: / $Ca^{++}$ in synaptic cleft necessary for $Na^{+}$ channels to open
2: Table IVB-1: 4a: binding of $Ca^{++}$ to troponin-tropomyosin complex *et seq.;* S VII.D: cardiac function & dysfunction
2a: Table IVB-1; 4e: $Ca^{++}$ maintains cardiac refractivity
3: S IX.A: renal function & dysfunction
4: $Ca^{++}$ somehow interferes w/ activity of **ADH**
5: F IVA-3: $PO_4^{-3}$ excreted by kidney; S B.d.A: 3): if product of $Ca^{++}$ & $PO_4^{-3}$ > 35, –> precipitation of $Ca_3(PO_4)_2$
6: CP IVA-3: **ADH** & urine volume
7: Fig 16.8: p 429: ↓ **BV** & thirst

IVB-9 & HWA

Path IVB-11. Pathophysiology of Hypercalcemia