IV. - ALTERATIONS IN BODY FLUIDS & ELECTROLYTES

IV.A. - BODY FLUIDS & THEIR DYSFUNCTION (most body fluids are at least 90% water)

A.a. PHYSIOLOGY OF BODY FLUID VOLUMES, COMPOSITION & DISTRIBUTION

A.a.A. GENERAL [fluid = water (solvent) + solutes (proteins, electrolytes, blood gases, nutrients, vitamins, hormones)]

↑ intake
↓ intake
} ═(regulatory mechanisms)═ { => homeostatic fluid volumes
=> homeostatic composition

Path IVA-1. General Homeostasis of Body Fluid Volumes & Composition

A.a.B. DISTRIBUTION

Critical Table IVA-1. Body Fluid~Water Compartments

TP IVA-1

<table>
<tr><td colspan="4">TOTAL BODY
FLUID
43ℓ - 62% OF BODY WEIGHT
100 % OF BODY FLUID
WATER
40ℓ - 60% OF BODY WEIGHT
100 % OF BODY WATER</td></tr>
<tr><td>INTRACELLULAR
FLUID 32ℓ, 46%
74%
WATER 30ℓ, 45%
75%</td><td colspan="3">EXTRACELLULAR
FLUID 11ℓ, 16%
26%
WATER 10ℓ, 15%
25%</td></tr>
<tr><td rowspan="2">1ST SPACE</td><td rowspan="2">INTERSTITIAL~
INTERCELLULAR
FLUID 7.2ℓ,10%
17%
65%</td><td rowspan="2">PLASMA*
3ℓ, 4%
7%
27%</td><td>TRANSCELLULAR
FLUID 0.8ℓ 2%
2%
8%</td></tr>
<tr><td>LYMPH
NEPHRON FILTRATE
CSF
SYNOVIAL FLUID
TEARS
HUMOR OF EYE</td><td>3RD SPACE**:
SECRETIONS OF
GI TRACT
SEROUS FLUID
FLUIDS OF BURNS</td></tr>
<tr><td colspan="2">2ND SPACE</td></tr>
</table>

I'll use BV from now on, bv = blood vessel

*When formed elements are added to the plasma, the blood~vascular volume (**BV**) is obtained which ≅ 5 ℓ.
**So-called third space fluids are singled out because 1) they have the potential to be significant &/or
2) water is not easily returned to the interstitial fluid or is easily lost once it enters the third space,
thus the regulation of third space fluids can become a significant factor in certain pathologies.

Critical Table IVA-2. Distribution of Water in the Three Most Important Compartments

Compartment	% Water	% Protein	% Others
Plasma	91.5	7 (plasma proteins)	1.5
Interstitial	92	5 (albumin)	3
Intracellular	90	6 (enzymes & structure)	4

TP IVA-2

A.a.C. ELECTROCHEMICAL PROPERTIES

Solute particles move across cell membrane on the basis of:
1) size (F IIIA-6)
2) lipid/water solubility
3) concentration gradient
g% = g solute//100mℓ solvent/soln
mg% = mg solute//100mℓ solvent/soln
1 molar soln = 6.023×10^{23} molecules//ℓ soln
4) charge
1 equivalent soln = 6.023×10^{23} charges//ℓ soln

To convert X mg% (X mg//100 mℓ) (mg//dℓ) to Y mEq//ℓ,

$$\frac{\text{X mg}}{\text{100 mℓ}} \times \frac{\text{valence}}{\text{g ionic wt}} \times \frac{\text{1000 mℓ}}{\text{1 ℓ}} = \frac{\text{Y mEq}}{\text{ℓ}} :: = \text{X mg\%} \times 10 \times \frac{\text{valence}}{\text{g ionic wt}} \quad \text{(E1)}$$

To convert X mmol//ℓ to Y mEq//ℓ,

$$\frac{\text{X mmol}}{\text{ℓ}} \times \frac{\text{valence}}{\text{1}} = \frac{\text{Y mEq}}{\text{ℓ}} \quad \text{(E2)}$$

To convert X mEq//ℓ to Y mg//ℓ,

$$\frac{\text{X mEq Y}}{\text{ℓ}} \times \frac{\text{0.001 Eq Y}}{\text{1 mEq Y}} \times \frac{\text{Z g Y}}{\text{1 Eq Y}} \times \frac{\text{1000 mg Y}}{\text{1 g Y}} = \frac{\text{X x Z mg Y}}{\text{ℓ}} \quad \text{(E3)}$$

5) pressure gradient: fluid pressure & osmotic pressure (mmHg) (CF IVA-2)

A.a.D. OSMOSIS [movement of water across semipermeable membrane] (Review CF IIIA-5 & F IIIA-6) (F 16.2, p 424) TP IVA-3

1 osmolar soln = 6.023×10^{23} non-diffusible solute particles//ℓ soln) not quite correct, but close enough for us
1 osmolal soln = 6.023×10^{23} non-diffusible solute particles//ℓ H_2O)

What are non-diffusible solute particles of note?

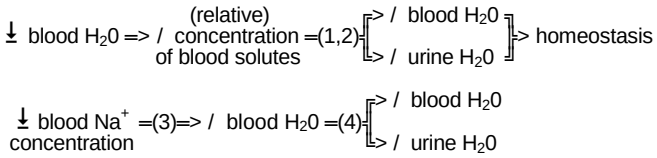
1) intracellular: K^+, $HPO_4^=$ & protein$^-$ & protein
2) interstitial: Na^+ & Cl^- & albumin
3) plasma: Na^+ & Cl^- (90-95%), plasma proteins (< 7%), **BUN** (blood urea nitrogen) & glucose (< 5%)

A.b. ALTERATIONS IN TOTAL FLUID VOLUME

A.b.A. NORMAL GAINS (beverages, water in food, metabolic water) (CF IIIA-1) (F 16.3, p 424) TP IVA-3

A.b.A.a. METABOLIC WATER (150 - 300 mℓ //day, depending upon rate of metabolism)

A.b.A.b. NORMAL MECHANISMS

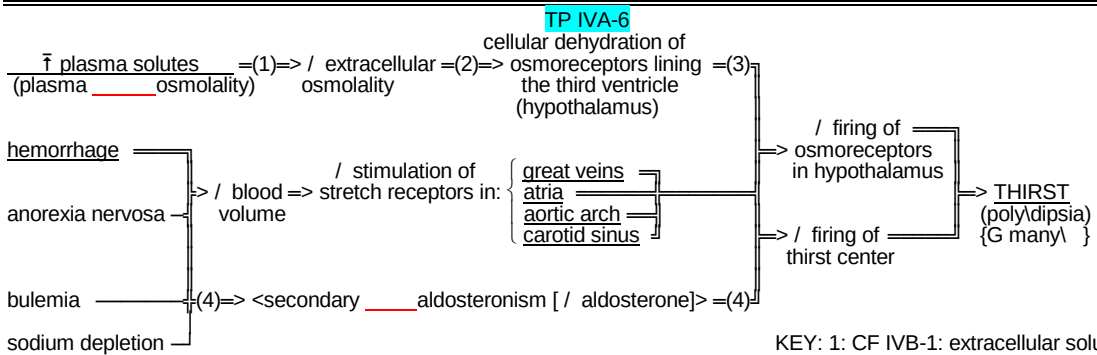


KEY: 1: CP IVA-3: osmoreceptors & **ADH**
2: CP IVA-2: role of thirst drive
3: CF IIIA-5: Osmosis
4: CP IVA-4: **RAAA** axis

Critical Path IVA-!a. Mechanisms Controlling Blood Water

A.b.A.c. THIRST (F 16.8, p 429) TP IVA-4

ef's: high extracellular solute concentration, hemorrhage, anorexia nervosa, bulimia, sodium depletion



KEY: 1: CF IVB-1: extracellular solute concentrations depend upon plasma solute concentrations
2: CF IIIA-5: mechanism of osmosis
3: F IVA-1: osmoreceptors in hypothalamus
4: CP IVA-4: renin-angiotensin-aldosterone axis

Critical Path IVA-2. Important Mechanisms for Stimulation of Thirst TP IVA-5

A.b.A.d. URINE CONCENTRATING MECHANISM

Antidiuretic Hormone (**ADH**) (vasopressin) (F 16.8, p 429, F 17.30, p 477) (Fig IVA-a, next page)

TP IVA-6

Figure IVA-1. Centers of the Hypothalamus & Pituitary Gland Involved in Water Balance (adapted from 32, p 596)

i.e. if ↓ BP is 5-10% → ↑ firing of osmoreceptors

normal physiology: **PVN**[a] & **SON**[b] in **HT** make **ADH** => movement to & storage in posterior pituitary => / blood **ADH** => 1)

↓ blood H_2O => / **BP** (if by 5-10%) => / **BV** (if by 10-15%) => / extracellular solute concentration => / osmolality (if by 1-2%) then ↑ alcohol inhibits / firing of (1)=> osmoreceptors in hypothalamus => / firing **PVN** & **SON**

1) => / H_2O reabsorption from distal convoluted tubules & collecting ducts => / blood H_2O => (_____) achieved; (2)=(_____)=> / **ADH**

=> / URINE OUTPUT

KEY: [a]paraventricular neurons
[b]supraoptic neurons
1: CP IVA-2: thirst 2: CF IIIA-5: Osmosis explained

HWA

Critical Path IVA-3. The Normal Action of **ADH**

A.b.A.d. RENIN-ANGIOTENSIN-ALDOSTERONE-Na^+-H_20 AXIS~SYSTEM (F 16.9, p 429) TP IVA-7

TP IVA-8

↓ BV => / **BP** =(1)=> / blood flow => / plasma CO_2 =(2)=> / HCO_3^- =(3)=> / Cl^- shift => / plasma Cl^- => / filtrate Cl^- in **DCT** => 1)

=> / **GFR** => / filtrate flow => / dwell time in renal tubule => / NaCl reabsorption

model: 1) / stimulation of Cl^- sensors in macula densa of juxtaglomerular apparatus =??=> / renin

lungs: angiotensin converting enzyme

<cat adrenal gland> (**Z G** of) (adrenal cortex)

liver => angiotensinogen => angiotensin I => angiotensin II => / aldosterone => 2)

2) (4)=> / Na^+ reabsorption in distal convoluted tubule; => / Na^+ absorption in stomach => / blood Na^+ =(5)=> / osmotic pressure of plasma =(5)=> / osmosis of H_2O => / **BV** into blood

KEY: 1: S VII.B.c.D.: Poiseuille's Law (e.g. perfusion w 8 % of CO vs 25%)
2: acid base considerations, formula E-2, S IV.C.a.B.a.
3: F 12.7. p 312 as modified in S IV.C.a.E.b. (chloride shift)
4: CF IVB-2: Action of aldosterone on Na^+ reabsorption in **DCT**
5: CF IIIA-5: Osmosis explained, water goes to hypertonic solution

Critical Path IVA-4. The Impact of the Renin-Angiotensin-Aldosterone Axis on Blood Volume

A.b.B. PATHOPHYSIOLOGICAL FLUID GAINS

A.b.B.a. FLUID vs WATER VOLUME EXCESS

(↓ excretion of Na & H_2O) –> (retention of Na & H_20)

renal insufficiency w/ low **GFR** (> 70% loss of glomeruli)

↑ intake of Na^+ & H_2O => isotonic expansion of extracellular fluid both interstitial & vascular components) <fluid volume excess> (**FVE**~_____volemia) may be an an important component of essential hypertension

↑ H_2O intake —> / solute dilution –> hypotonicity of extracellular compartment <water volume excess> (**WVE**~water overload)

<water intoxication>

psych patients & military/OCS esp critical for electrolytes

Path IVA-5. General Pathophysiology of Volume Excess HWA

A.b.C. NORMAL LOSSES - ATRIAL NATRIURETIC PEPTIDE (**ANP**)

HWA

↑ **BV** =(1)=> / stretching of atrial walls => / **ANP** secretion by atrial endocrine glands ⟹ => blocks effects of renin (CP IVA-4); => blocks effects of aldosterone (CP IVA-4); => 1)

1) / Na^+ secretion into tubular filtrate ⟹ => _____tonic filtrate =(2)=> / H_2O in filtrate ⟹ => / H_2O in blood => / **BV** (_____ achieved); => / H_2O in urine; => / Na^+ in urine (natriuretic)

Path IVA-6. Normal Physiology of Atrial Natriuretic Peptide

KEY: 1: CP IVA-2: role of stretch receptors in blood-volume sensors
2: CF IIIA-5: Osmosis explained, water goes to hypertonic solution

A.b.D. PATHOPHYSIOLOGICAL FLUID LOSSES - FLUID VOLUME DEPLETION~DEFICITS (**FVD**)

↓ intake, ↑ loss ⟹ => <**FVD**> (_____volemia)

Path IVA-7. General Etiology of **FVD** (F 16.10, p 432)

↓ intake:
1) inability to get H_20
2) difficulty swallowing
3) impaired thirst

↑ loss:
1) skin losses
(sweating in hot weather ≥ 2 ℓ//hr)
(fever ≥ 3 ℓ//day)
2) third space losses (includes gastrointestinal losses (S VIII.A) & burns) (Fig 16.10) TP IVA-9

cell injury =(1)=> / capillary permeability => / protein out of **BV** ⟹ => / protein in 3rd space =(_____)=> / water loss to 3rd space

Path IVA-8. General Etiology of Third Space Fluid Loss

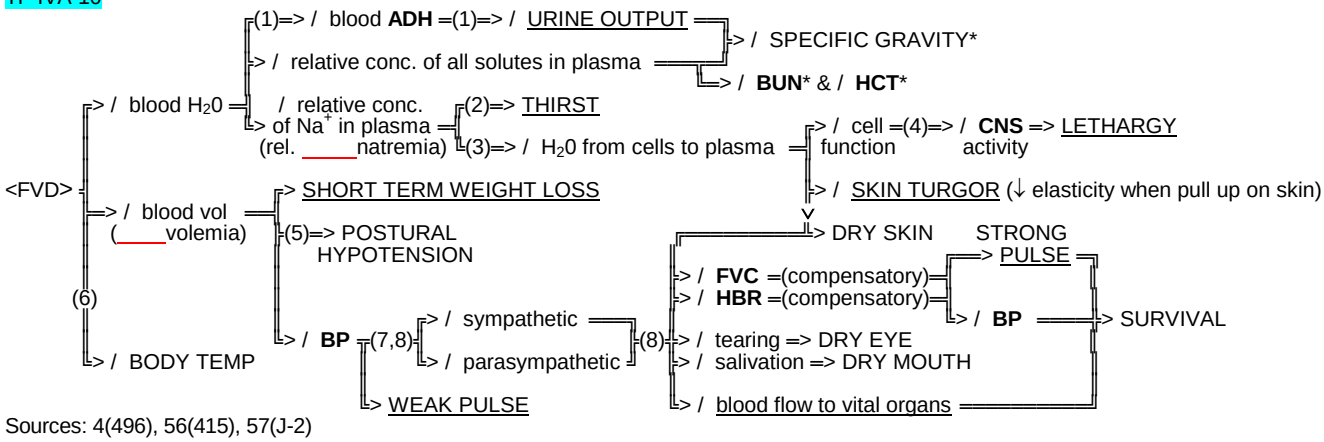
Key: 1: CP VE-1: inflammation

3) urine losses (S IX, includes diabetes insipidis)

A.b.D.a. DEHYDRATION

Manifestations: / URINE OUTPUT, THIRST, LETHARGY, / SKIN TURGOR, SHORT-TERM WEIGHT LOSS, / BODY TEMP / **BP**, / **BP,** WEAK PULSE, STRONG PULSE

TP IVA-10



Sources: 4(496), 56(415), 57(J-2)

KEY: 1: CP IVA-3: hypothalamus & **ADH**
2: CP IVA-2: mechanisms for stimulating thirst
3: CF IIIA-5: Osmosis & consequences of cell being hypotonic to interstitium
4: CF IIIA-1: importance of H_20 to cell & CT IVA-1: importance of intracellular H_20
5: S VIIC: blood pressure
6: P VD-8: ↓ H_20 → ↓ evaporative cooling, *et al.*
7: P VD-11: / blood vol → hypoxia → / sympathetic
8: F VA-2: consequence of stress on **ANS**

Critical Path IVA-9. Manifestations of **FVD** (DEHYDRATION)

A.c. ALTERATIONS IN INTERSTITIAL FLUID VOLUME & EDEMA

A.c.A. FUNCTION

1) transport vehicle for gases, nutrients, wastes, hormones & cytokines between vascular & intracellular compartments

2) reservoir for vascular volume during hemorrhage & other losses

A.c.B. REGULATION OF INTERSTITIAL FLUID VOLUME [**IFF** - **IFR** = **IFV**] (E4)

A.c.B.a. INTERSTITIAL FLUID (TRANSUDATE) FORMATION (**IFF**)

1) occurs at the level of the precapillary arteriole, capillary & post-capillary venule (CF IVA-2, p IVA-6) TP IVA-11

2) gel in interstitium absorbs H_2O

3) factors that can affect the rate of interstitial fluid formation (**IFF**): envelope & separates TP IVA-11

1) arterial pressure: ↑ **a p** –> / **IFF**
2) venous pressure: ↑ **v p** –> / **IFF**
3) **BP**: ↑ **BP** –> ↑ **a p** & ↑ **v p** –> / **IFF**
4) vascular volume - affects both arterial & venous pressure: ↑ **v v** –> / **a p** + / **v p** –> / **IFF**
5) hydrostatic pressure: in standing person, gravity causes the weight of the blood in the vascular column to increase by 1 mm Hg for every 13.6 mm (1/2 in) of distance below the heart, recumbent - no change; dependent –> edema in certain pathologies
6) blood colloidal osmotic pressure [**OP** due to plasma proteins (mostly albumin) vs crystalline **OP** due to Na^+]: ↓ **bcop** –> / **IFF**
7) interstitial albumin levels: ↑ **ial** –> / **IFF**
8) status of integrity of interstitial fibers: ↓ integrity –> / **IFF**
9) ↓ interstitial fluid pressure –(e.g., -7.5)– ⊔ (larger box, with greater "pulling" pressure) –> / **IFF**

A.c.B.b. INTERSTITIAL FLUID REMOVAL (**IFR**) (LYMPH) (F 16.2, p 424) TP IVA-12

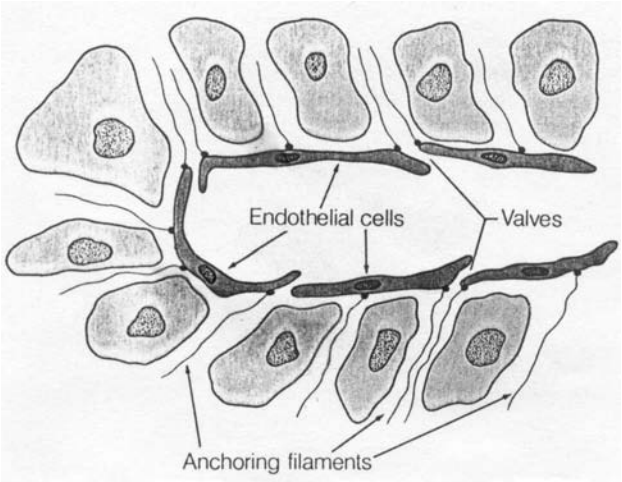
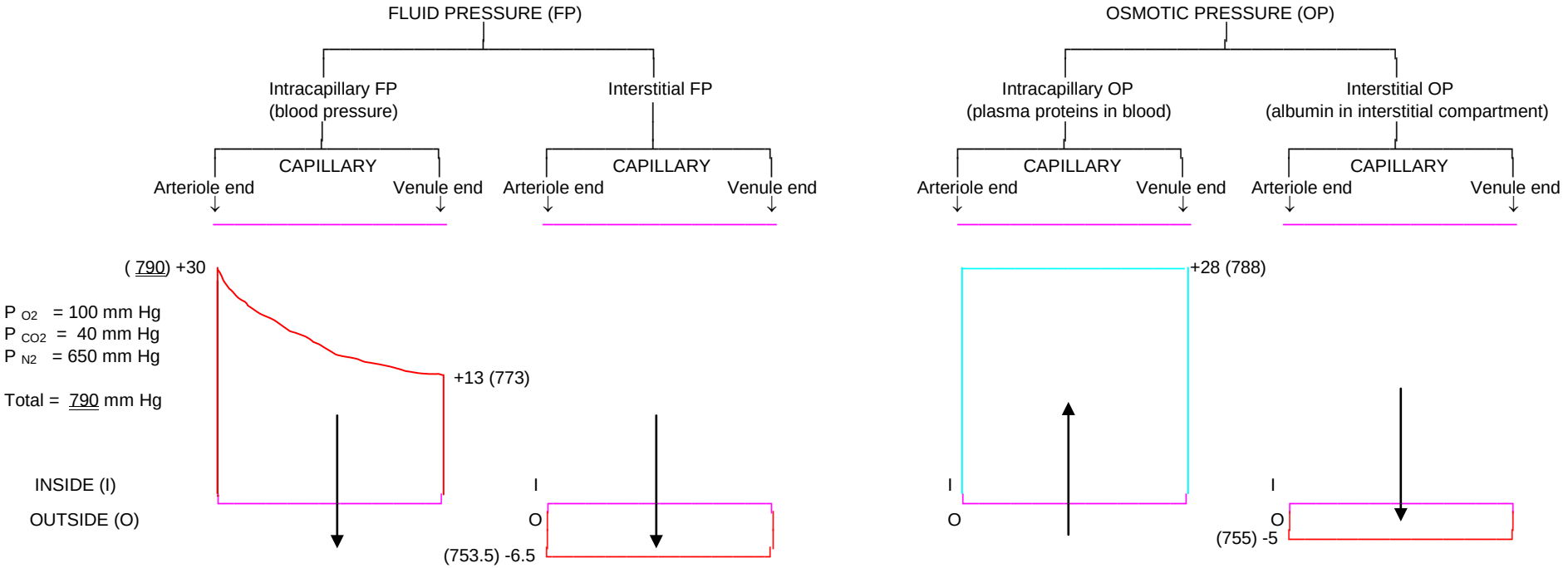


Figure IVA-3. Mechanisms of Interstitial Fluid Removal (**IFR**) (Lymph Formation) (adapted from 32, p 623) TP IVA-12

A.c.B.c. EDEMA [excess interstitial fluid in tissues] (transudation vs exudation)

A.c.C.c.(A.) ETIOLOGIC FACTORS (Table IVA-3, p IVA-7 & factors in A.c.B.a. above)



KEY:

(790): Actual pressure at capillary end at sea level (ASL) in mm Hg
+30: Pressure above atmospheric baseline (760 mm Hg ASL) i.e. 790 = 760 + 30
-6.5: Pressure below atmospheric baseline

NOTE: Total Pressure = FP - OP
NOTE: Intracapillary OP + Interstitial OP: 28-5 = 23 mm Hg = Oncotic Pressure

Key: capillary wall ↓ direction of water movement

Force originating **in**side of capillary

Force originating **out**side of capillary

TP IVA-11

Critical Figure IVA-2. The Four Forces (Starling's Forces) That Influence Interstitial Fluid (Transudate) Formation

Table IVA-3. Causes of Edema (adopted from 32, p 624)

INCREASED CAPILLARY PRESSURE
Local Arteriolar Dilation –> ↑ **BF*** –(__)–> ↑ **IFF**→ ↑ **IFV**
allergic responses Do this one last
inflammation

Venous Obstruction –(__)–> ↑ **IFF**
hepatic obstruction
right-sided heart failure
thrombophlebitis

Increased Vascular Volume –( )–> ↑ **IFF**
left-sided heart failure
increased levels of ACTHs
premenstrual sodium retention
pregnancy
environmental heat stress

Effects of Gravity –(__)–> ↑ **IFF**
prolonged standing

DECREASED BLOOD COLLOIDAL OSMOTIC PRESSURE
Decreased *Production* of Plasma Proteins –(__)–> ↑ **IFF**
liver disease
starvation /severe protein deficiency

Increased *Loss* of Plasma Proteins
protein-losing kidney diseases –(__)–> ↑ **IFF**
extensive burns –(__)–> ↑ **IFF**

INCREASED CAPILLARY PERMEABILITY –(__)–> ↑ **IFF**
inflammation
immune responses
neoplastic diseases
tissue injury & burns

DECREASED INTERSTITIAL PRESSURE
pathologic condition of purpura –(__)–> ↑ **IFF**
obstruction of eustachian tube => air in middle ear reabsorbed => 1)

1) => EAR DRUM BULGES INWARD
=> negative pressure in middle ear => / "interstitial pressure" =(__)=> ↑ **IFF** =T=> EAR DRUM BULGES OUTWARD

OBSTRUCTION OF LYMPHATIC FLOW –> / **?**
HWA disease of lymphatic structures; surgical removal of lymph nodes; adjacent hard tumor; chronic stasis KEY: *blood flow

A.c.B.c.(B.) MANIFESTATIONS

MANIFESTATIONS: NECROSIS, PITTING EDEMA, NON-PITTING EDEMA~BRAWNY EDEMA

HWA

<edema> =>
- in brain, larynx, lungs => DEATH
- around eyes => closed eyelids => temporary LOSS OF SIGHT
- in appendages => DIFFICULTY MOVING; DEFORMED APPENDAGE => DIFFICULTY GETTING CLOTHES; PSYCHOLOGICAL EFFECTS
- in finger –> relatively inflexible skin –> / blood flow to finger acting as a tourniquet — blood diffusion picture
- in tissues –> / distance for diffusion =(1)=> / oxygen; / nutrients; / wastes; / susceptibility to damage from other ef's (as, e.g., occurs in pressure sores) =(2)=> NECROSIS

<pitting>: **IFF** > ability of gel –> displacement of excess H_2O with finger –> slow return of displaced H_2O to site –> PITTING EDEMA (sponge)
to absorb H_2O

<chronic>: permanently stretched intercellular fibers =(__)=> (/ integrity) (/ **IFF** > **IFR**)–> / **IFP**–> new equilibrium –> **intractability**
↓ chronic stasis goes to here??

<nonpitting>: local infection; trauma =(3)=> / capillary permeability => / interstitial albumin =(__)=> 1)

1) =(4)=> <coagulation necrosis> => FIRM, DISCOLORED AREA <NON-PITTING~BRAWNY EDEMA> sponge becomes a brick

Key: 1: CF IIIA-1: essential inputs & outputs for cell function
2: CP IIIA-9: / **ATP** –> cell swelling –> cell bursting –> necrosis
3: CP VE-1: vascular responses to inflammation
4: CP IIIA-9: the roles of extracellular conditions & release of cellular proteins in coagulation necrosis

Critical Path IVA-10. The Manifestations of Edema