Disorders of Sodium and Water Metabolism

Homeostasis

- The maintenance of normal volume and normal composition of the extracellular fluid.
- Homeostasis: the various physiologic arrangements, which serve to restore the normal state, once it has been disturbed
  - Fluid balance
  - Electrolyte balance
  - Osmotic balance
  - Acid-base balance

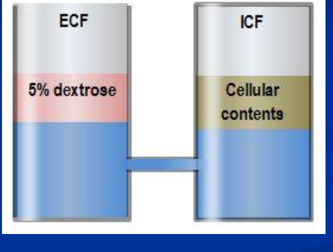
General principles

- Diffusion: movement of the particles in a solution from the area of high concentration to the area of lower concentration
- Electrolyte: inorganic substance that dissociates into ions
- Osmosis: diffusion of solvent molecules (water) into region in which there is a higher concentration of a solute (electrolyte) to which the membrane is impermeable
- Osmotic pressure: the pressure necessary to prevent solvent migration

General principles

- Osmolarity : number of osmoles per liter of solution
- Osmolality: number of osmoles per kilogram of solvent
  - Measurement: depression of freezing point
  - Calculation (plasma): 2x(Na+K)+glucose+BUN (mmol/l)
  - **Osmolality is the same in the ICF and the ECF**.
- Tonicity: effective osmolality of a solution relative to plasma
  - tonicity is only influenced by solutes that cannot cross this semipermeable membrane, because these are the only solutes influencing the osmotic pressure gradient.

Iso-osmolar solutions and isotonic?



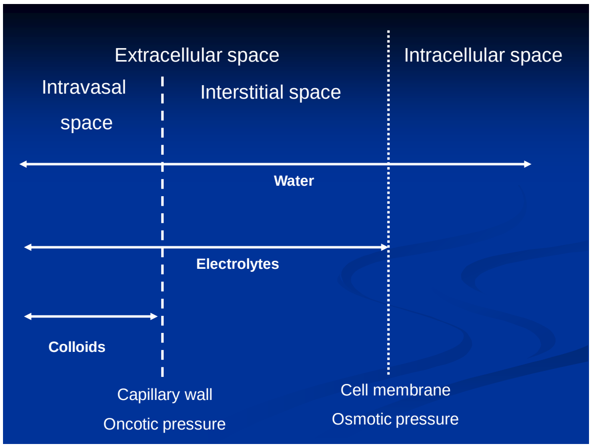
Dextrose penetrates the cells so easily - it cannot contribute to tonicity. Thus, the infused dextrose is iso-osmolar but hypotonic.

General principles

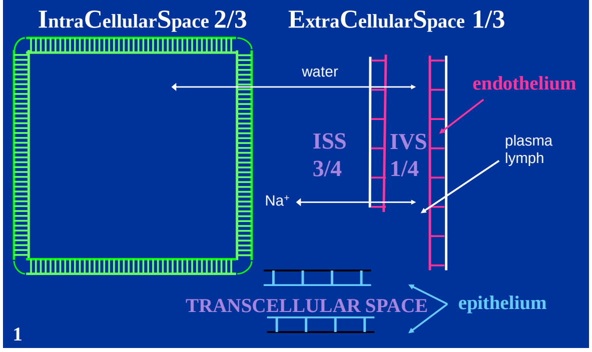
- Colloids: high molecular weight particles (> 20000 D)
- Oncotic pressure (colloid osmotic pressure): the pressure necessery to prevent diffusion of solvent molecules (water) into region in which there is a higher concentration of a colloid to which the membrane is impermeable

Compartments of body fluids

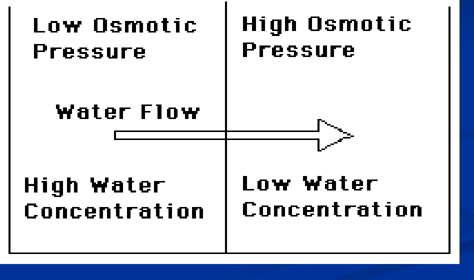
- Total body water averages about 60% of body weight
- Aproximate volume of body fluids compartments:
- 60% intracellular water
- 40% extracellular water
  - 31%interstitial fluid
  - 7% plasma
  - 2% transcellular fluids (saliva, bile, etc.)



Compartements of body fluids



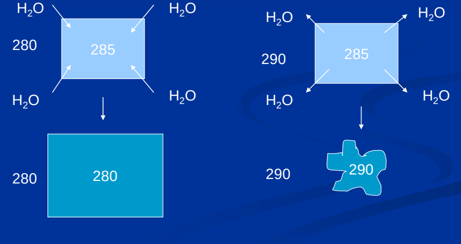
Osmosis



Change of the cell volume in response to change in extracellular osmolality

Decrease of osmolality

Increase of osm.



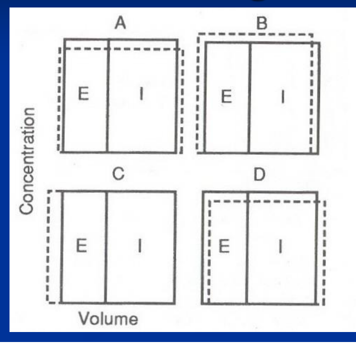
Blood plasma

- Osmolality 280-290 mosm/kg
- Osmotic pressure 745 kPa
- Onkotic pressure 3,3 kPa
- Na 135-145 mmol/l

Note: Normal plasma Na concentrations → roughly normal plasma osmolality → normal osmolality of the cells. The electrolyte content in the cells is roughly fixed → normal volume of liquid in the cells (IC space)

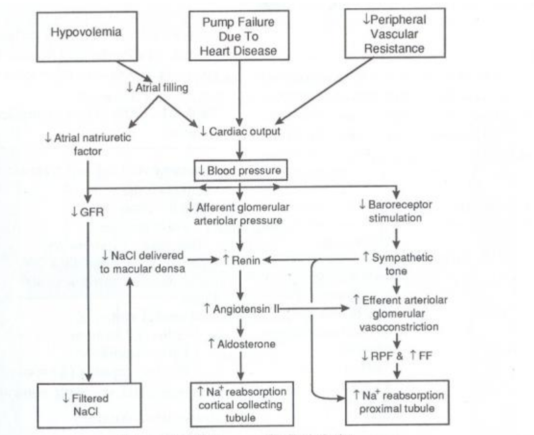
A large quantity of water is exchanged between an organisms and the environment via kidneys and a gut → a small percentual derangement has large consequences for the whole-body water and electrolyte balance

Fluid compartment volume and osmolar changes



Normal regulation of sodium balance

- Extracellular fluid volume is controlled by the amount of sodium in the body
- The kidneys regulate the sodium excretion or retention
- The changes in osmolality are detected by hypothalamus → changes in ADH secretion → water secretion or reabsorption



Normal regulation of water balance

- Extracellular fluid osmolality is controlled by the amount of water in the body
- The kidneys regulate the water excretion

Water intake

- Food
- Metabolic water
- **Drinking is the most important way of water intake regulated by the thirst**

Water excretion

- Skin (perspiratio insensibilis, sweat)
- Respiratory system (perspiratio insensibilis)
- Stool
- **Urine excretion is the most important way of water loss regulation - ADH**

Daily Water Balance (liters)

INPUT		OUTPUT	
FLUID INTAKE	1.5	INSENSIBLE	0.8
IN FOOD	0,8	SWEAT	0.1
METABOLIC	0.3	FECES	0.2
Total	2.6	URINE	1.5
		Total	2.6

Volume and tonicity regulation

- **Tonicity is ultimately regulated by water, the circulating volume by sodium**
- Tonicity – hypothalamic osmoreceptors → neurohypophysis, thirst and ADH → renal water reabsorption
- Volume – baroreceptors, more sluggish feedback than osmoreceptors, under extreme conditions:

  Volume overrides tonicity

Water Deficit

- INCREASED OSMOLARITY SENSED BY HYPOTHALAMIC RECEPTORS
- FALL IN ECF VOLUME
- FALL IN ARTERIAL BLOOD PRESSURE

RELIEVES

STIMULATION OF HYPOTHALAMIC NEURONS

INCREASED THIRST ↓ INCREASED WATER INTAKE ↓ DECREASED PLASMA OSMOLARITY

INCREASED VASOPRESSIN

OPEN PORES IN COLLECTING DUCT

ARTERIOLAR VASOCONSTRICTION

MORE WATER REABSORBED ↓ FALL IN URINE OUTPUT ↓ DECREASED PLASMA OSMOLARITY

RELIEVES

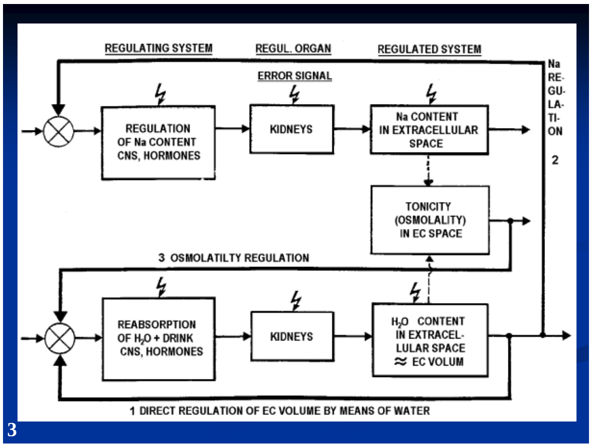
Blood pressure and renal handling of sodium

FALL IN SODIUM LOAD ↓ FALL IN ARTERIAL PRESSURE

RELIEVES

FALL IN GFR ↓ FALL IN FILTERED SODIUM → FALL IN EXCRETION OF SODIUM, CHLORIDE, AND FLUID ↓ INCREASED CONSERVATION OF SODIUM AND FLUID

INCREASE IN ALDOSTERONE SECRETION ↓ INCREASE IN SODIUM ABSORPTION



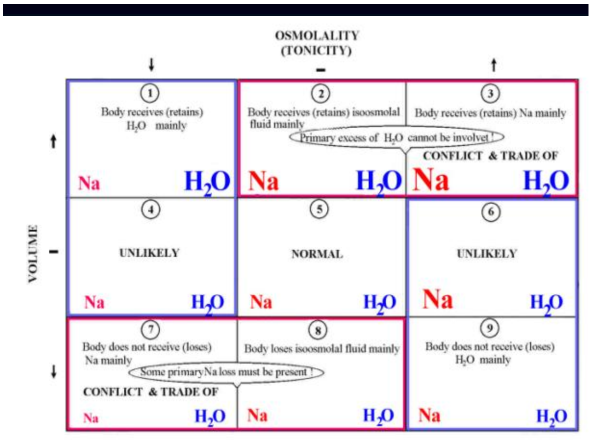
Regarding adiuretine and thirst regulation: osmoreception (feedback No. 3) is functioning more sensitively, volumoreception (feedback No. 1) more sluggish, later more forcefully, however → “volume overrides tonicity” when the large deviations of volume and tonicity from a norm take place. It is a consequence of the type of dependency of the ADH production on both these factors. A circulatory failure is apparently evaluated to be more dangerous acutely than the CNS disturbances.

Disturbances of fluid homeostasis

- Disturbance of fluid balance (intake≠output)
  - Dehydraton, Overhydration (hyperhydration)
- Disturbance of osmolarity (electrolyte intake≠water intake)
  - Isonatremic (isotonic)
  - Hyponatremic (hypotonic)
  - Hypernatremic (hypertonic)

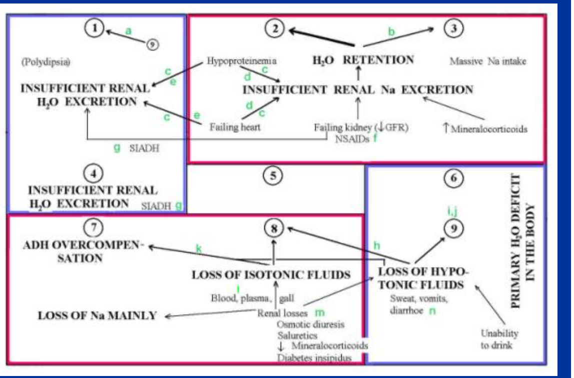
Dehydration

- Signs: increased thirst (except: advanced age, hypotonic dehydration), weakness, decreased skin turgor, dry mucous membranes, empty neck veins, decreased urine output, elevated Htk, fever, tachycardia, hypotension, decreased CVP,lethargy, stupor, coma
  - Mild (loss: 4% of body weight): decresed skin turgor, sunken eyes, dry mucous membranes
  - Moderate (loss: 5-8 % of body weight): + oliguria, orthostatic hypotension, tachycardia
  - Severe (loss: 8-10 % of body weight): + hypotension, decreased level of consciusness, stupor



Tonicity disorders ⇔ disorders of water: states 1, 4, 6, 9

Volume disorders ⇔ sodium disorders: states 2, 3, 8, 7



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Explanatory notes

a – overshooting compensation of hyperosmolality (state 9) by water

b – a trade off by means of ADH: hypervolemia does not rise so much with a considerable Na_{EC} enhancement that isoosmolality could be maintained

c – loss of effective blood volume

d – three factors of Na retention (GFR, aldosterone, 3rd factor)

e – by means of ADH

f – **nonsteroid antiphlogistics** (acetylosalicylic acid, sodium salicylate, phenacetin, paracetamol) depress the protective prostaglandins in the kidney → decline of GFR

g – **SIADH** is euvolemic clinically, hypervolemic subclinically

h – by means of thirst and ADH, some loss of salt is presupposed, however

i – although body dehydration may be considerable with the loss of hypotonic fluids, loss of circulating volume used to be negligible in this condition (loss of water is compensated in 90% from stores outside the circulating volume)

j – if the water loss is much higher than loss of salt, Na_{EC} lowering may be attended by P_{Na} rise

k – an organismus has lost salt and water massively, it tries, however, to maintain predominantly the volume by the quick feedback by means of thirst and ADH in this extreme situation (salt losses are compensated only by drinking); it succeeds only partially, however, and it is paid by hypotonicity (a trade-off again);

l – Na in urine < 10mmol/L

m – Na in urine > 20 mmol/L – the urine itself is effective in the Na loss

n – with a small urine volume Na in urine > 600 mmol/L

CONDITION 3 Na

The body receives (retains) Na mainly - **hyperosmolal hyperhydratation**

RdS: *massive Na intake (per os, sea water)*
RgS: *primary surplus of mineralokorticoids*
RgO: *acute glomerular diseases*
billateral parenchymatous
renal diseases with chronic
renal failure (GFR < 10mL/min)

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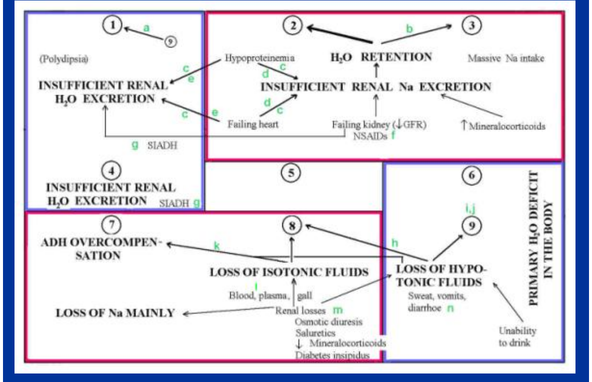
Fig. 10 – hyperosmolal hyperhydration (state 3) Renal failure with the GFR value higher than 10 mL/min is not connected with a deranged G-T balance → under the lowered GFR, reabsorption is lowered, too. G-T balance is disturbed in acure nephritic syndrome, however



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CONDITION 2 Na

Body receives (retains) isoosmolal fluid mainly - **isoosmolal hyperhydratation**

RdS: *i.v. infusion of isoosmolal fluids*
nephrotic syndrome
cirrhosis
RgS: *cardiac failure*
RgO: *non-steroid antiphlogistics*
failing kidney (↓ GFR!)
acute & chronic, esp. when isoosmotic solutions are administered

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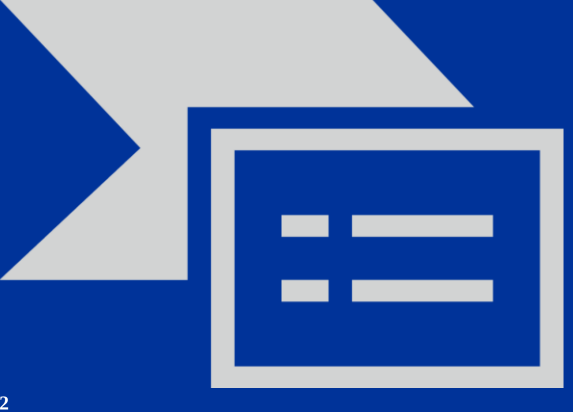
Fig. 11 – isoosmolal hyperhydration (state 2)

Heart failure: a decline of effective blood volume is signalized, RAS and SAS are activated (Fig. 11), ↓GFR, "3rd factor"



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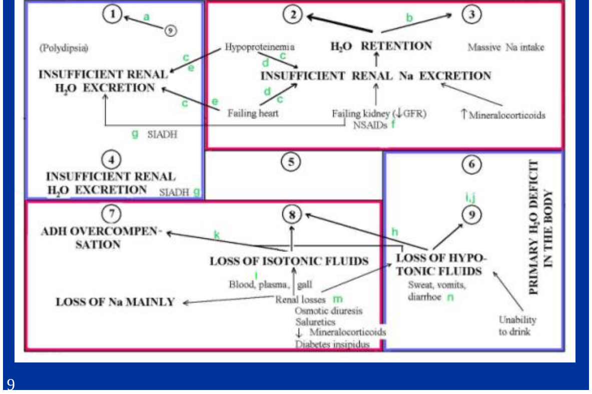

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CONDITION 1 Na

The body receives (retains) H_2O mainly - **hypoosmolal hyperhydratation**

RD: *infusion of glucose solutions, nephrotic syndrome*
cirrhosis
RS: *psychogenic polydipsia*
renal oligo/anuria when ↑tubular H_2O reabsorption with SIADH, chlorpropamid
cardiac failure
RO: *renal oligo/anuria*
↓ GFR
esp. in combination with H_2O or glucose solution administration

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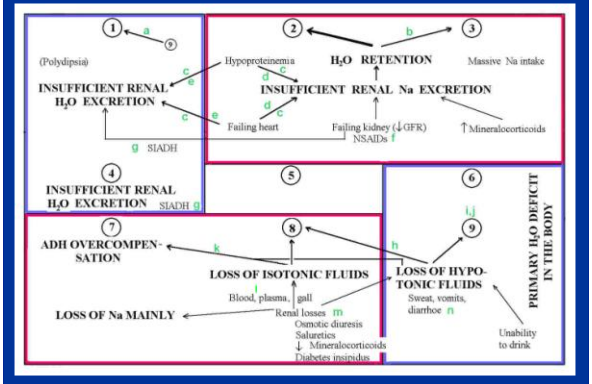

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Consequences of hypervolemia:

Hypervolemia → enhanced left ventricle preload → enhanced cardiac output

↑cardiac output * unchanged peripheral resistan-ce = ↑arterial pressure

↑arterial pressure → ↑hydrostatic capillary pres-sure → ↑filtration into the IC space → edema

CONDITION 9 Na

The body does not receive (loses) H_2O mainly - **hyperosmolal dehydratation**

RdS: *vomiting*
diarrhoe
sweating
insesible losses
hyperventilation, fever, hot environment
hyperglycemia in diabetes mellitus
mannitol

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RgS: ↓ *thirst*
unconsciousness
newborns
diabetes insipidus (central)

RgO: *osmotic diuresis in diabetes mellitus*
diabetes insipidus (nephrogenic)
polyuria in acute renal failure

If the water supply is not disturbed and Na is normal, state 9 cannot last long

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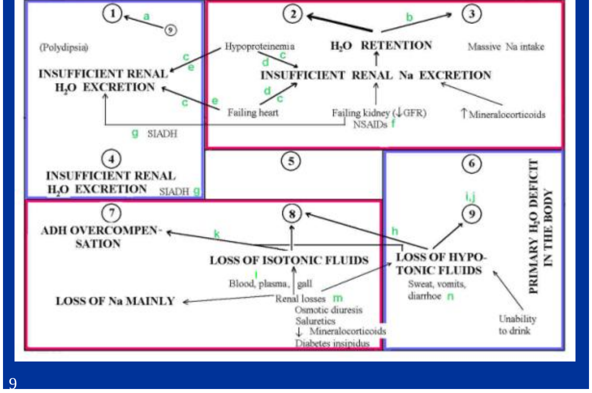

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CONDITION 8 Na

Body loses isoosmolal fluid -
isoosmolal dehydratation

RD: *loss of blood or plasma*
burns, ascites draining
diarrhoe, gall drains, fistulas
escape into interstitium or 3rd space
crushing of tissues, intestinal obstruction, pancreatitis
hemorrhage into body cavities
RO: *abusus of saluretics*
and many other renal loss types

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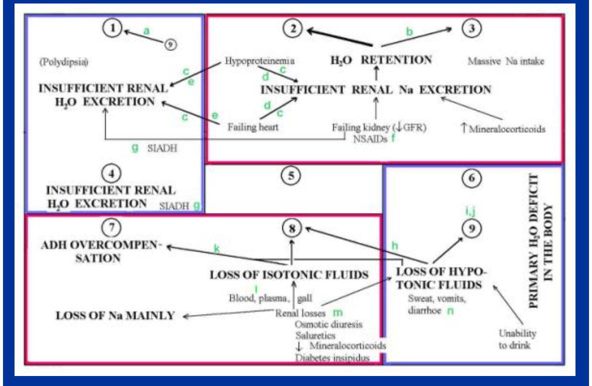

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CONDITION 7 Na

Body does not receive (loses) Na mainly - **hypoosmolal dehydratation**

RD: *alimentary lack of salt in combination with loses*

RS: *primary lack of mineralocorticoids*

RO: *renal salt losses:*

- *polyuria in acute renal failure*
- *loss of hypotonic fluids → trade off preferring volume*
- *pressure diuresis in extemely enhanced blood pressure*
- *BARTTER syndrome*
- *abusus of diuretics*

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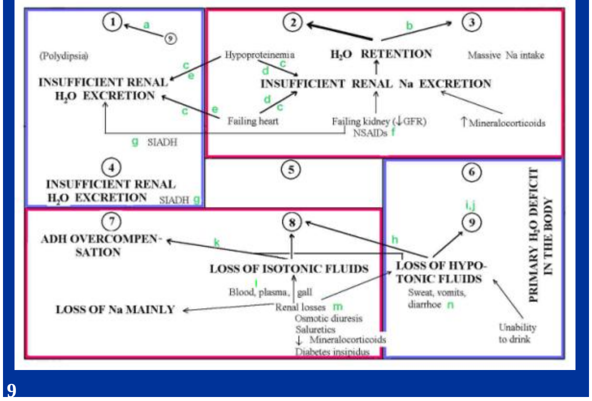

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A survey of the influence of renal pathology on volume and osmolality Fig. 17

Na AND H_2O EXCRETION IN VARIOUS PATHOLOGIC RENAL CONDITIONS

CONDITION	Na	H_2O
ACUTE GLOMERULAR DISEASES	RETENTION	RETENTION
STENOSIS OF ART. RENALIS CONSIDERABLY ENHANCED BP PRESSURE DIURESIS	RETENTION ↑EXCRETION	RETENTION ↑EXCRETION
PRERENAL AZOTEMIA	RETENTION AIMED AT CORRECTING BP OR VOLUME	RETENTION

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CONDITIOON	Na	H_2O
ACUTE RENAL FAILURE INITIAL PHASE (ANURIA, OLIGURIA) PREREN. AZOTEMIA MOST OFTEN RESTITUTION PHASE (POLYURIC) - SALT WASTING KIDNEY	RETENTION ↑EXCRETION	RETENTION ↑EXCRETION
CHRONIC RENAL FAILURE (TO THE ADVANCED PHASE) GFR < 10 - 20 mL/min	WITHOUT DISTURBAN-CES RETENTION	WITHOUT DISTURBAN-CES RETENTION
TUBULOINTERSTITIAL DISEASES, ADRENAL INSUFICIENCY, DIURETICS, „WASTING SALT" NEPHROPATHY (i.g. CHRF)	↑EXCRETION	↑EXCRETION

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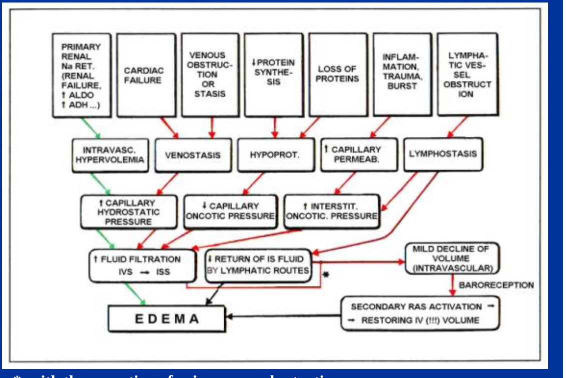
Control of Interstitial Fluid

- Hydrostatic pressure
- Oncotic pressure
- Endothelial integrity
- Lymphatic system

2.2 Edematous conditions



* with the exception of primary renal retention

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Movement Of Fluid Across Capillaries

- Capillary (hydrostatic) pressure
- Interstitial fluid (hydrostatic) pressure
- Plasma oncotic pressure
- Interstitial fluid oncotic pressure

Capillary Pressure

- Forces fluid from capillary to interstitium
- Arterial end higher than venous end
- Arterial approx. 30 mmHg
- Venous approx. 10 mm Hg

Interstitial Fluid Pressure

- Maybe positive or negative
- Negative - forces fluid into interstitium
- Positive - forces fluid into capillary
- Approx. minus 3 mm Hg in loose connective tissue
- Higher in denser connective tissue

Plasma Oncotic Pressure

- Proteins are the only solutes which do not pass freely between plasma and interstitium
- Thus it is only proteins which exert a significant osmotic effect across capillary walls
- Albumin is the most abundant plasma protein
- Approx 28 mm Hg (Albumin = 21.8)

Interstitial Oncotic Pressure

- A small amount of protein is present in the interstitium
- Tends to force fluid out of capillary
- Concentration is approx 40 % of that in plasma
- Approx 8 mm Hg

Lymphatic System

- The lymphatic system provides a route for the transport of fluids and protein away from the interstitium
- System of fine lymphatic channels throughout the body passing via lymph nodes to thoracic duct
- Valves ensure one-way flow

Oedema

- Hydrostatic pressure
- Oncotic pressure
- Endothelial integrity
- Lymphatic integrity

Oedema

- Definition

  An increased volume of interstitial fluid in a tissue or organ

  May be localised or generalised (systemic)

Causes of Oedema

- Raised capillary pressure
- Reduced oncotic pressure
- Endothelial damage (inflammation)
- Impaired lymphatic drainage

Raised Capillary Pressure

- Cardiac failure
  - right ventricular failure - systemic oedema
  - left ventricular failure - pulmonary oedema
  - congestive cardiac failure - both
- Local venous obstruction
  - deep vein thrombosis
  - external compression
  - SVC obstruction

Reduced Oncotic Pressure

- Renal disease
  - loss of albumin across glomerulus
- Hepatic disease
  - inadequate albumin synthesis
- Malnutrition
  - inadequate albumin synthesis

Lymphatic Obstruction

- Tumours
- Fibrosis
- Inflammation
- Surgery
- Congenital abnormality

Generalised Oedema

- Congestive cardiac failure
- Right ventricular failure
- Renal disease
- Liver disease

With the exception of the “primary” hypervolemia conditioned by **primary renal Na retention**, **RAS is activated secondarily** (possibly **secondary hyperaldosteronismus** may be elicited) → Na retention → edema

Not in Fig. : Cardiac failure → distortion of baroreception → RAS, SAS, 3rd factor activation, ↓GFR