Body water
Fluid and electrolyte balance

Biochemistry II
Lecture 8

2008 (J.S.)

Body water

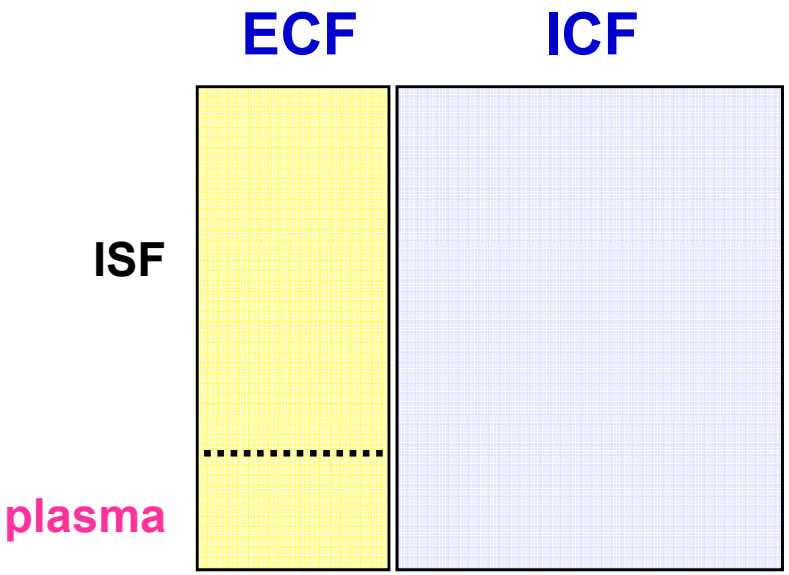
about **60 %** of the body weight (55 % taken usually for women)

2/3 intracellular fluid (ICF, **40 %** b.w.)

1/3 extracellular fluid (ECF, **20 %** b.w.)

interstitial fluid and lymph
(ISF, **15 %** b.w.)

blood plasma (**5 %** b.w.)



The water content of the body changes

– **with age**: about 75 % in the newborn, less than 50 % in the elders,

– **with the total fat content**, there are only 10 % water in adipose tissue.

"Transcellular" fluids

include water that is present at the moment within the GIT, abdominal and pleural cavities, as well as spinal fluid, urine, and bile. In adults, the volume is about 2 litres (2 – 3 % b.w.) under normal conditions.

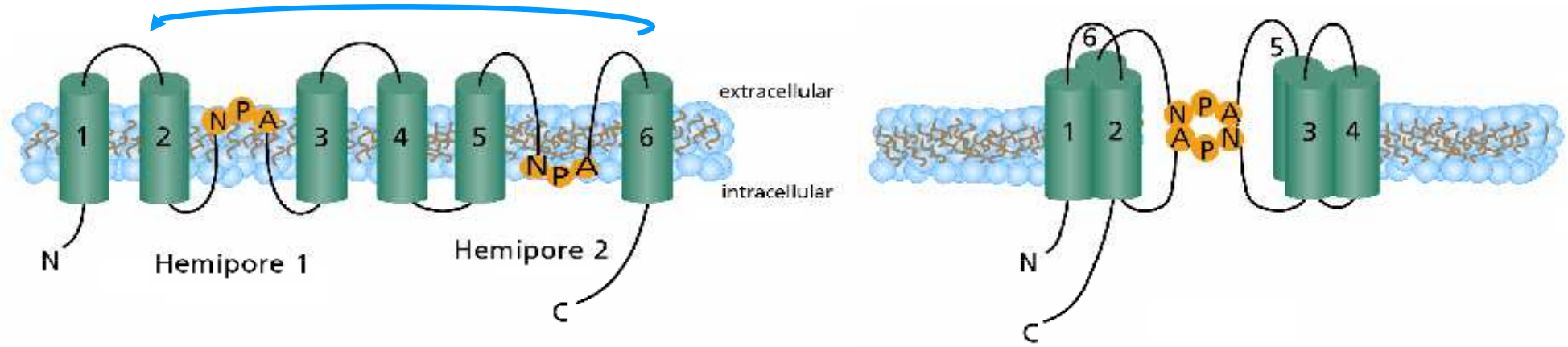
In most clinical considerations the volume of transcellular fluids is not taken into account, but it must be considered, when ascites or other large exsudates might be awaited.

The movement of ions and polar neutral molecules across cell membranes is due to the existence of specific transport proteins (including ion pumps).

Diffusion of water molecules is possible, but it is slow and not efficient.

Aquaporins are membrane proteins that form water channels and account for the nearly free and rapid two-way moving of water molecules across most cell membranes (about 3×10^9 molecules per second).

Aquaporin channel structure



Aquaporins consist of six membrane-spanning segmenst arranged in two hemi-pores, which fold together to form the "hourglass-shaped" channel.

The highly conserved NPA motifs (Asn-Pro-Ala) may form a size-exclusion pore, giving the channel its high specifity.

In membranes, some of aquaporin types exist as homotetramers, or form regular square arrays.

Aquaporins are controlled by means of gene expression, externalization of silenced channels in the cytoplasmic vesicles, and also by the changes in intracellular pH values (e.g., increase in proton production inhibits water transport through AQP-2 and increases the permeability of AQP-6).

More than 12 isoforms of aquaporins were identified in humans, 7 of which are located in the kidney.

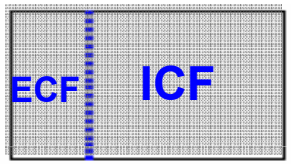
Examples:

AQP1 (aquaporin-1), opened permanently, is localized in red blood cells, endothelial and epithelial cells, in the proximal renal tubules and the thin descendent limb of the loop of Henry.

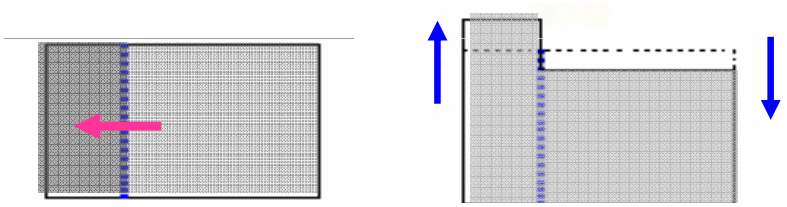
AQP2 is the main water channel in the renal collecting ducts. It increases tubule wall permeability to water under the control of ADH: If ADH binds onto the V_2 receptors located in the basolateral membrane, AQP2 in the membranes of cytoplasmic vesicles is phosphorylated and exposed in the apical plasma membrane. Reabsorbed water leaves cells through **AQP3** and **AQP4** in the basolateral plasma membrane.

The movement of water across cell membranes is controlled by osmolality

Examples of four simplified causes of water movements:
(Any other solute can substitute sodium salt in the examples.)

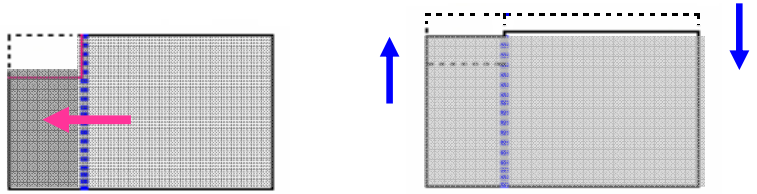


Sodium salt retention or overload



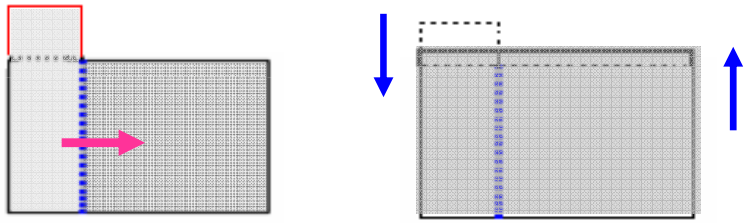
Hypernatraemia (hyperosmolality of ECF) → hyperosmolar expansion of ECF, decrease in ICF volume (cellular dehydration).

Significant loss of solute-free water



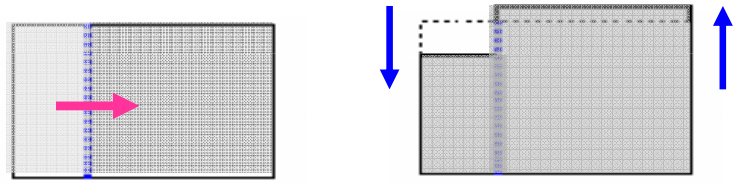
Hypernatraemia (hyperosmolality of ECF) by dehydration → cellular dehydration

Solute-free water excess



Hyponatraemia by dilution (a decrease in ECF osmolality) → expansion of ICF volume, oedema

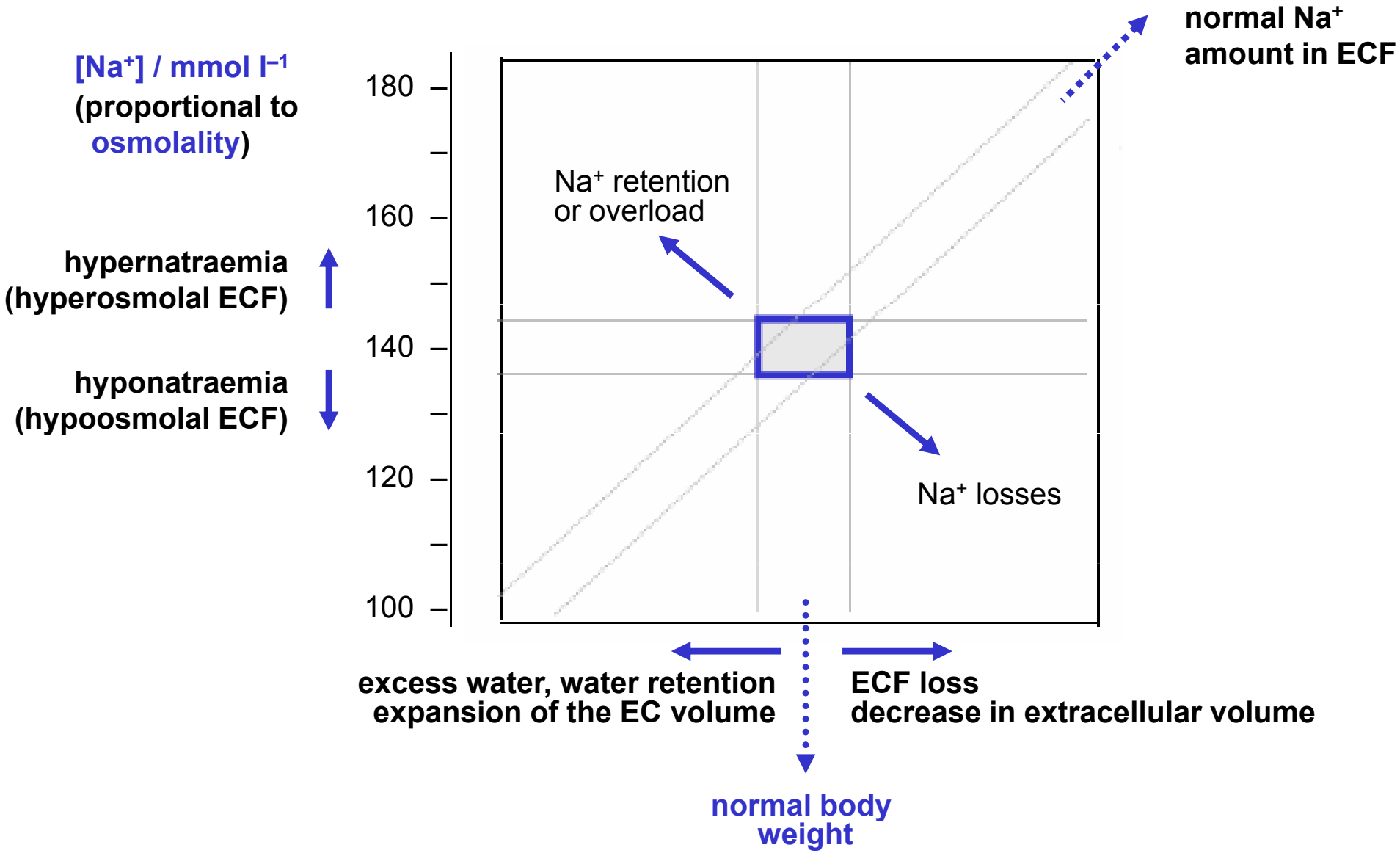
"Pure" sodium salt loss



Hyponatraemia (hypoosmolal ECF) → decrease in ECF volume, expansion of the cell volume.

Expansion of ICF →increase in intracranial pressure, imminent danger of cerebral oedema.

Na^+ concentration (as well as osmolality) depends on changes in both ECF volume and amount of Na^+ in ECF:



The **approximate calculation of Na^+ ion deficit**
in patients with hypovolaemic hyponatraemia:

$$\textbf{Na}^+ \textbf{ deficit} = (140 - [\textbf{Na}^+]) \times \textbf{0.6} \times \text{kg } \textbf{b.w.} \quad \text{(in millimoles)}$$

The **approximate calculation of water deficit** in patients with hypernatraemia:

$$\textbf{water deficit} = \frac{[\textbf{Na}^+] - 140}{[\textbf{Na}^+]} \times \textbf{0.6} \times \text{kg } \textbf{b.w.} \quad \text{(in litres)}$$

The daily water intake and loss in an adult person

Water intake at least **2000** ml/d

drink	> 1200 ml
food	500 ml
metabolism	300 ml
1 g saccharide →	0.55 ml
1 g protein →	0.41 ml
1 g fat →	1.07 ml

Water loss at least **2000** ml/d

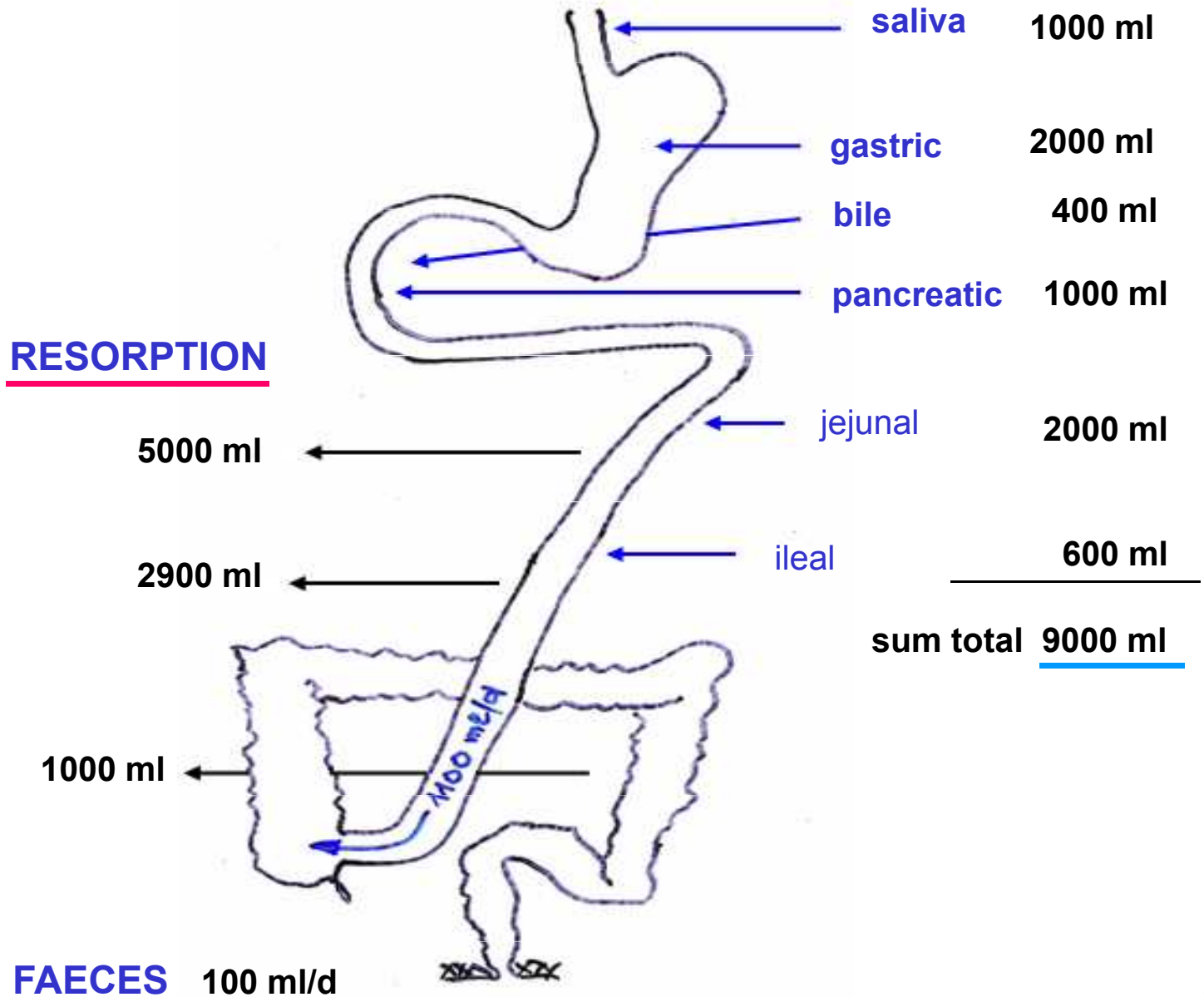
urine	> 1200 ml
expired air	300 ml
sweat and perspiration	500 ml
(profuse sweating up to litres /d)	
faeces	100 ml

Attention should be paid to the water intake in the childhood and namely in the elders (the feeling of thirst is impaired or lacking)

Intestinal fluid balance

Per day: **FOOD / FLUIDS** oral intake 2000 ml

SECRETION



Osmolality of blood plasma

men	**290 ± 10 mmol / kg H_2O**
women	**285 ± 10 mmol / kg H_2O**

Osmolality of biological fluids is measured by means of osmometers that are based mostly on the cryoscopic principle.

Osmolality of blood plasma depends predominantly on the concentrations of Na+, K+, glucose, and urea.

Even if the osmolality of a sample is known (it has been measured), it is useful to compare the value with the approximate assessment:

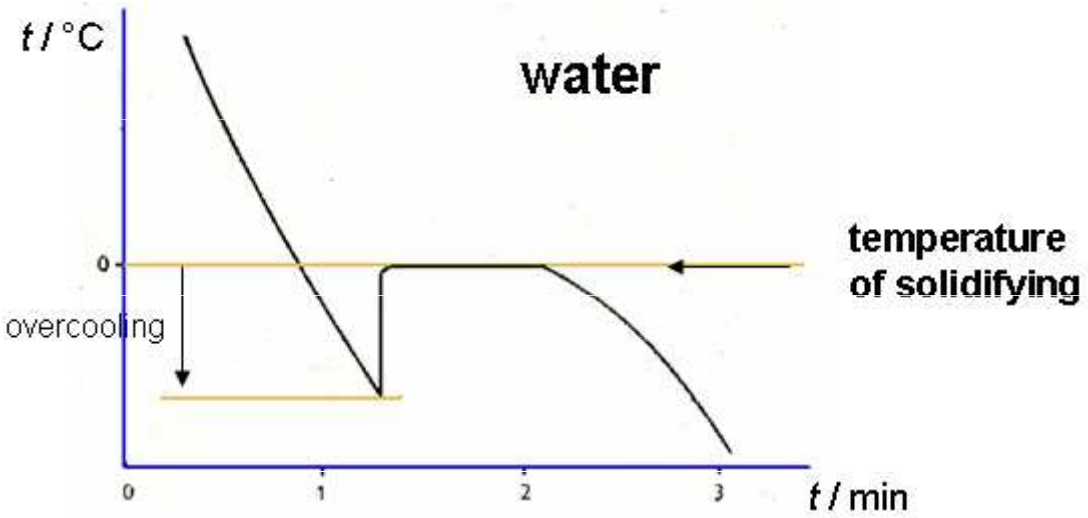
osmolality (in mmol / kg H_2O) $\approx$ 2 [**Na^+**] + [**glucose**] + [**urea**] (in mmol l^{-1}).

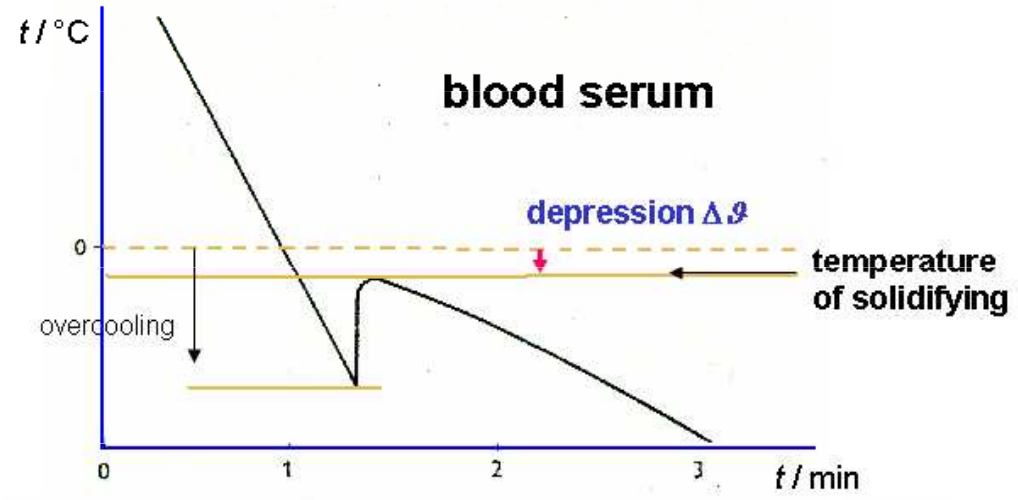
An **osmotic gap** can be perceived in this way. The measured value is higher than the calculated rough estimate, if there is a high concentration of an **unionized compound** in the sample (e.g. alcohol, ethylene glycol, acetone).

One gram of ethanol per litre will increase the osmolality by about 22 mmol / kg H_2O.

Osmometers – cryoscopic principle:

Depression of the temperature of solidifying is one of the colligative properties that depends only on the activity of solutes in solutions. Thermistors able to measure temperature differences less than 0.01 °C are required.





Cryoscopic constant

K'(water) = 1.85 K kg mol^{-1}

- i.e. Increase in osmolality

+ 10 mmol / kg H_2O will depress the temperature of solidifying by – 0.0185 °C.

Osmolality in mol / kg H_2O equals $\Delta\vartheta$ / K'**(water).**

Oncotic pressure – colloid osmotic pressure (COP)

Within the extracellular fluid, the **distribution of water** between blood **plasma and interstitial fluid** depends on the plasma protein concentration.

The capillary wall, which separates plasma from the interstitial fluid, is freely permeable to water and electrolytes, but restricts the flow of proteins.

Oncotic pressure is a small fraction of the osmotic pressure that is induced by plasma proteins.

ρ (plasma proteins) = 62 – 82 g / l $c \approx 1 – 1.3$ mmol / l

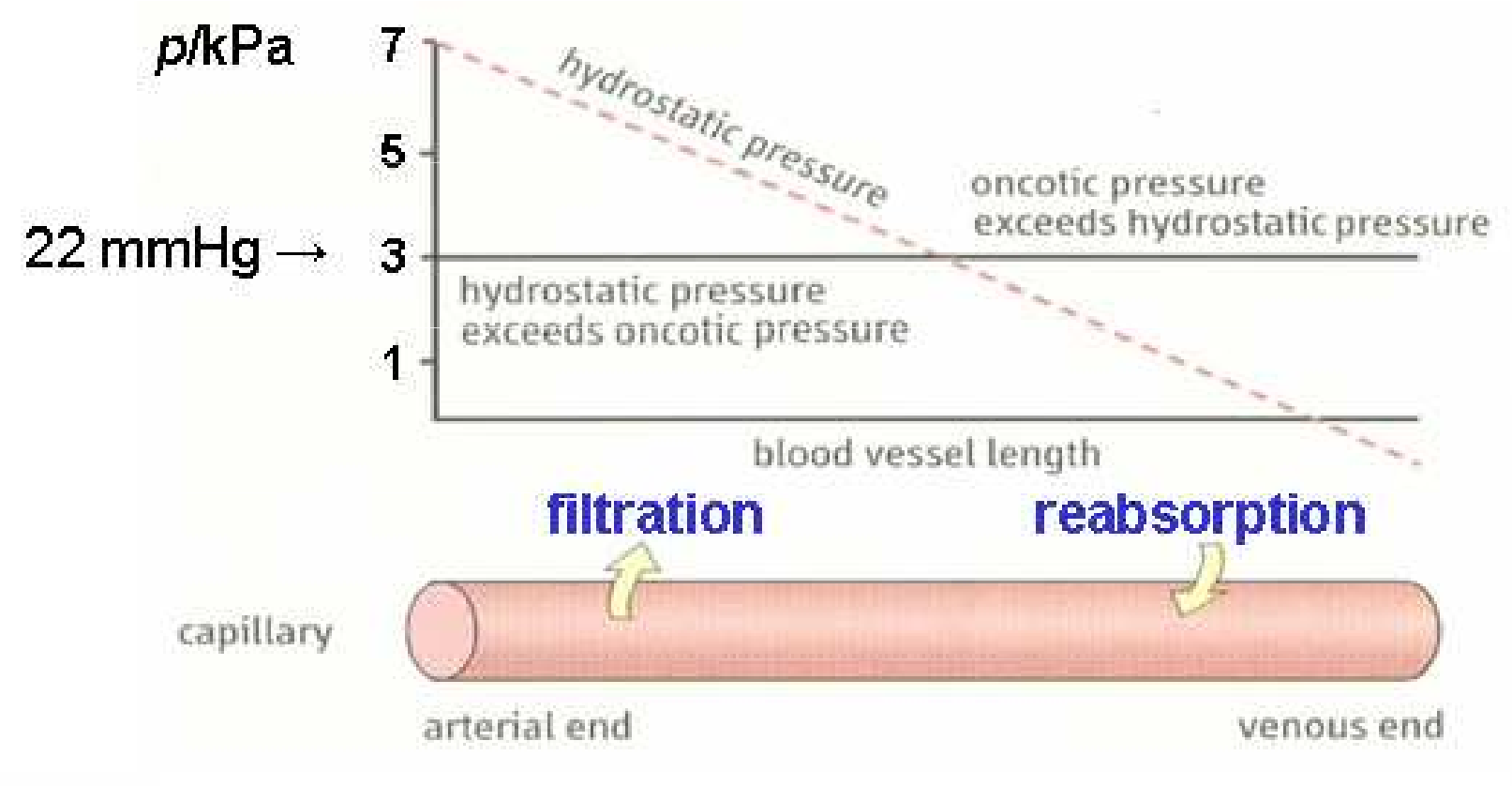
ρ (plasma albumin) = 35 – 50 g / l $c = 0.52 – 0.75$ mmol / l

(albumin – about 80 % of oncotic pressure)

Oncotic pressure of blood plasma equals approx. **3 kPa** (2.7 – 3.3 KPa).

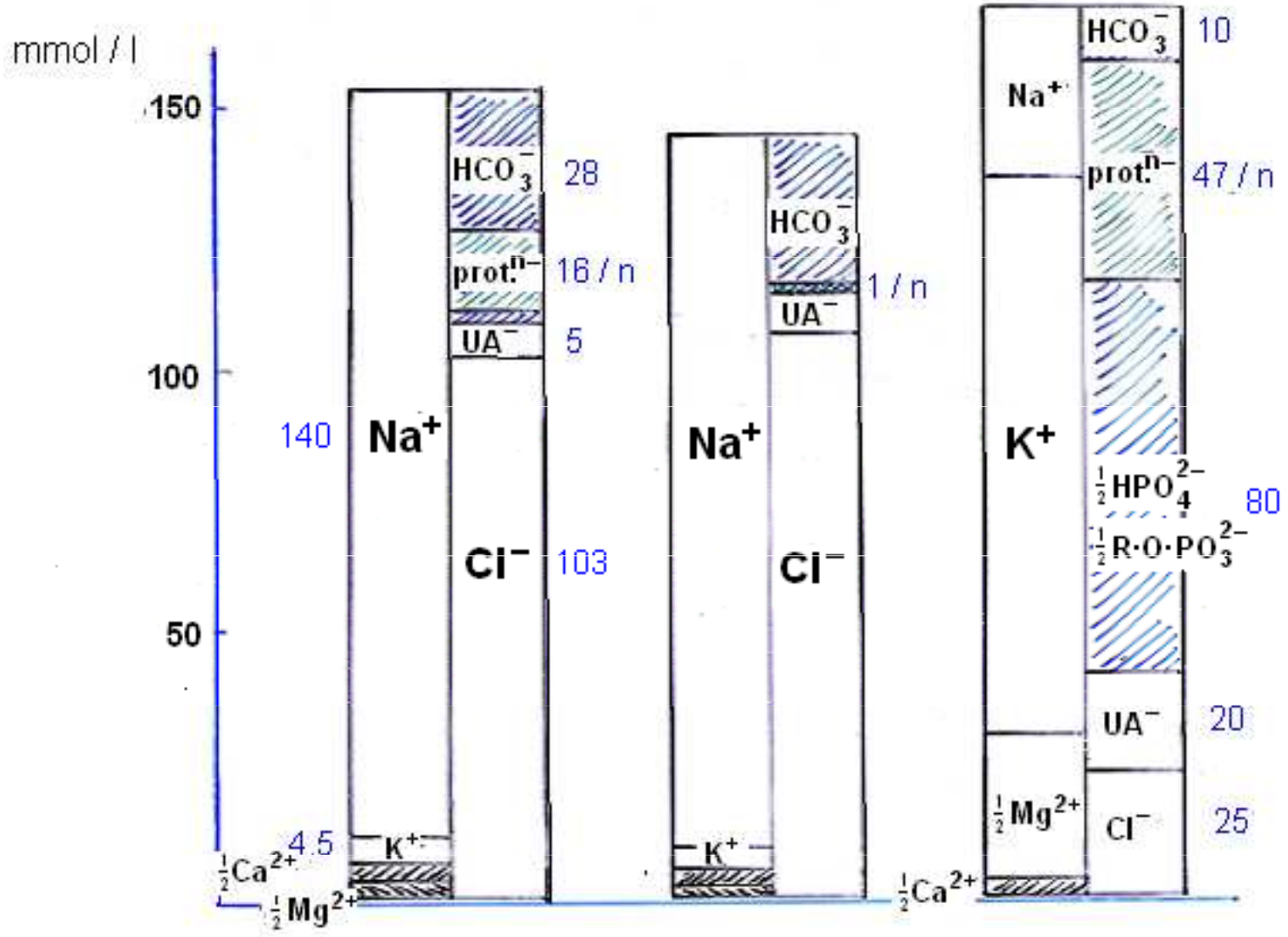
Values 2.7 – 1.4 kPa - sizable oedemas, imminent danger of pulmonary oedema;
< 1.4 kPa – unless albumin is given i.v., survival is hardly possible.

The movement of fluid between plasma and interstitial fluid

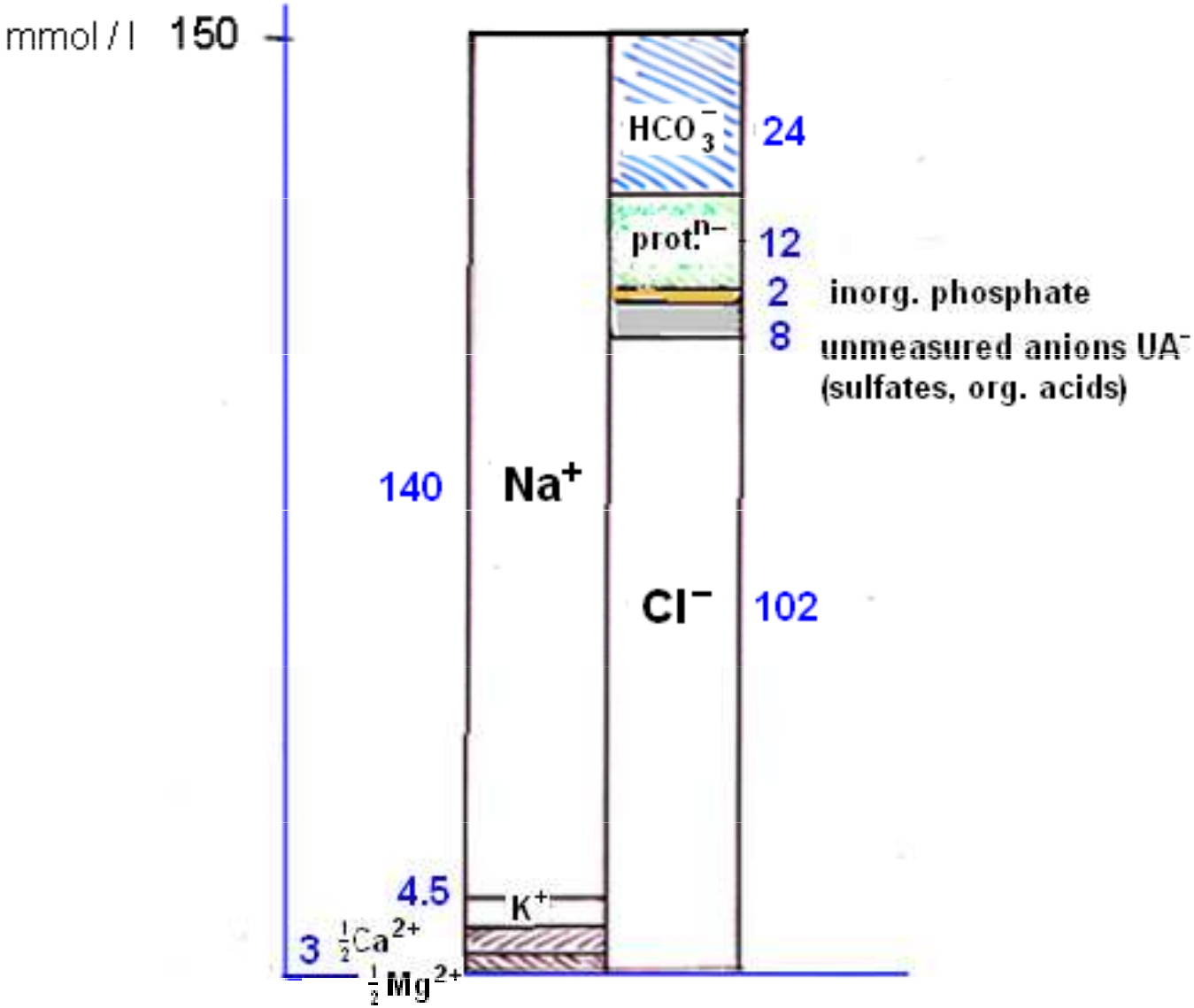


Oncotic pressure can be measured by means of colloid osmometers.

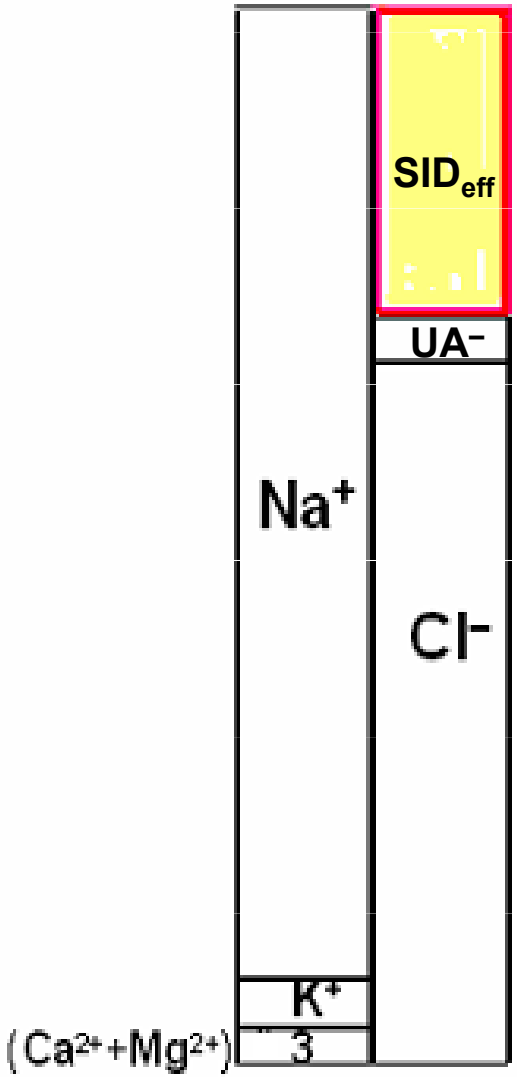
Ions in body fluids



Ions in blood plasma / serum



Effective "strong ion difference" (SID_{eff})



$$SID_{eff} = [Na^+] + [K^+] + 3 - [Cl^-] - [UA^-]$$

The value SID_{eff} determinates the concentration of plasma buffer bases BB_p.

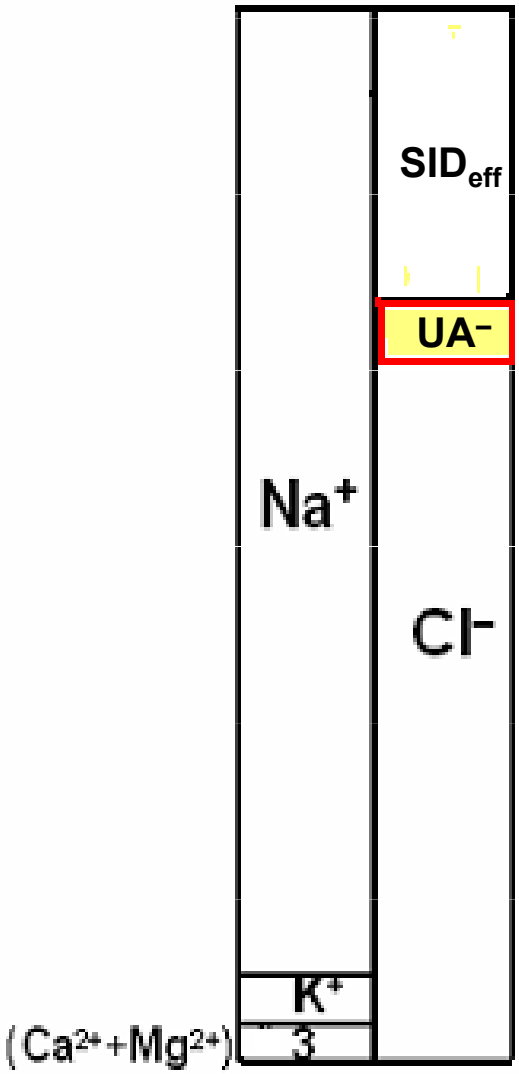
Normal range = 42 ± 3 mmol / l)

SID_{eff} then can be calculated from measurable concentrations of plasma buffer bases::

$$SID_{eff} = [HCO_3^-] + 0.28\ \mathbf{Alb}(g/l) + 1.8\ [P_i]$$

Strong ion **ratio** $[Na^+]+[K^+] / [Cl^-]$ (normal value 1.35 – 1.43) is occasionally used as another sign of strong ion imbalance that is typical for hyperchloridaemic acidosis or hypochloridaemic alkalosis).

Unmeasured anions (UA^-)



$$[UA^-] = [Na^+] + [K^+] + 3 - [Cl^-] - SID_{eff}$$

Normal range **8 ± 2 mmol / l**

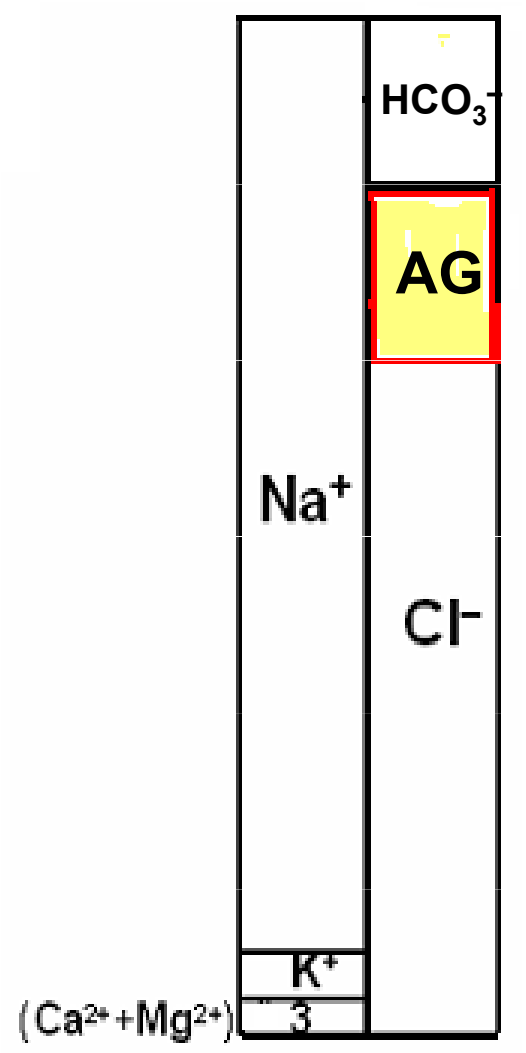
Components: **sulfate**
lactate
acidic ketone bodies
the other carboxylic acids

Corrected value for water content:

$$[UA^-]_{corr} = [UA^-] \times 140 / [Na^+]_{measured}$$

Anion gap (AG) – a simple accessory parameter

that may call an attention to the **possible increase in UA^-:**



$$AG = [Na^+] + [K^+] + 3 - [Cl^-] - [HCO_3^-]$$

Usual values 19 ± 2 mmol/l.

AG represents the "space" filled in by
unmeasured anions,
proteins, and
phosphates.

In hypoproteinaemia, AG value should be corrected:

$$AG_{corr} = AG_{observed} + 0.25 \times (Alb_{ref} - Alb_{measured})$$

(decrease in albumin by 1 g/l enables an increase in HCO_3^- by 1 mmol/l)

Water and osmolality control

Antidiuretic hormone (ADH, Arg-vasopressin, AVP)

released from the nerve terminals in posterior pituitary

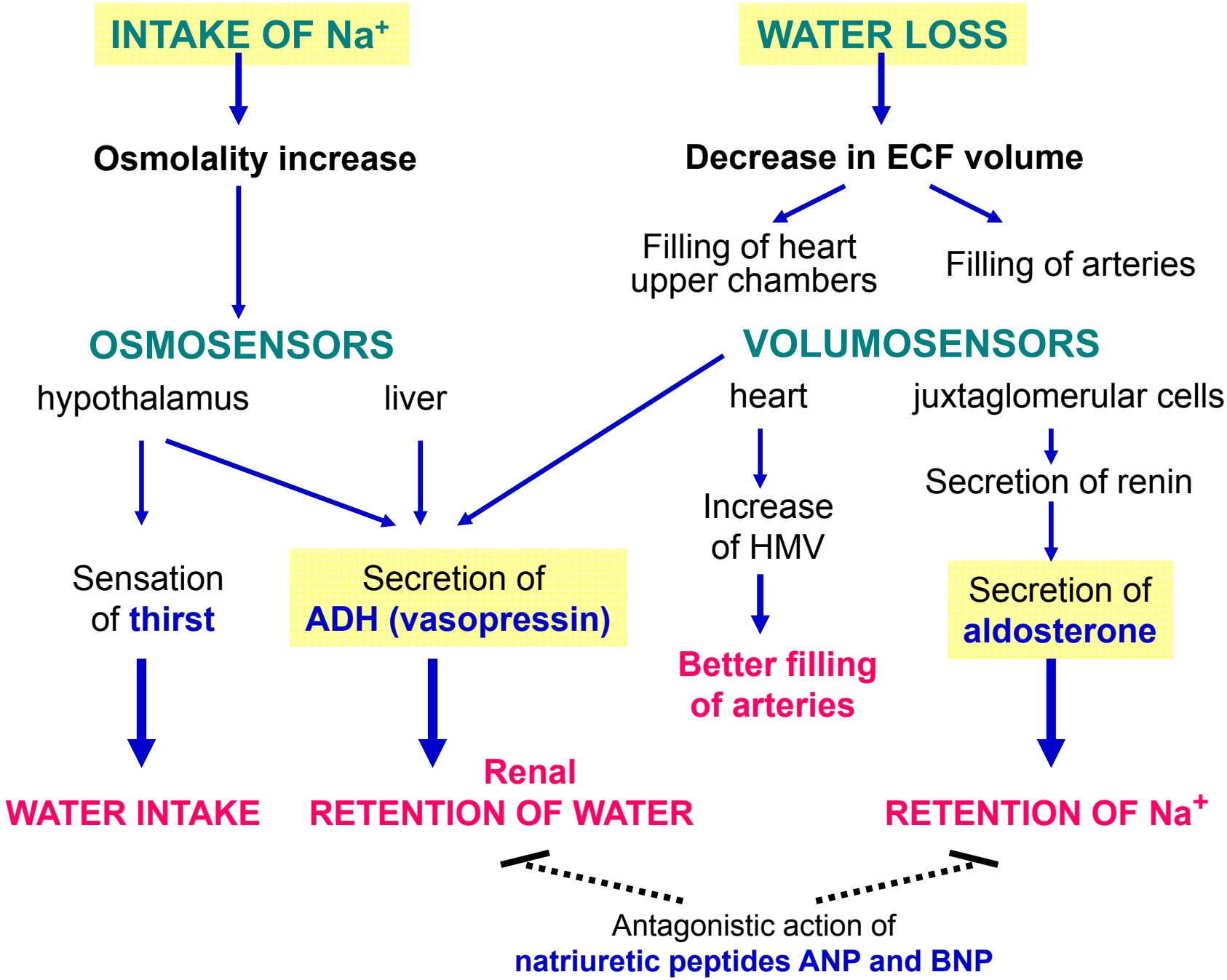
Aldosterone

secreted from the zona glomerulosa of adrenal cortex after activation of the renin-angiotensin system (RAS)

Natriuretic peptides ANP and BNP

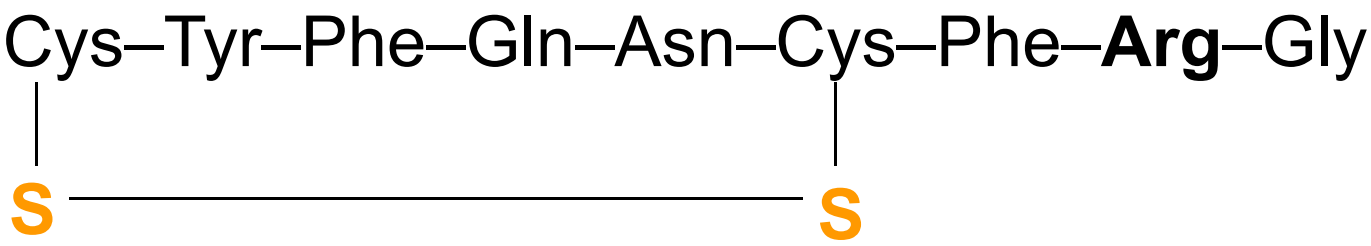
secreted from some kinds of cardiomyocytes in heart atria and chambers

Water and osmolality control



Antidiuretic hormone (ADH, Arg-vasopressin, AVP)

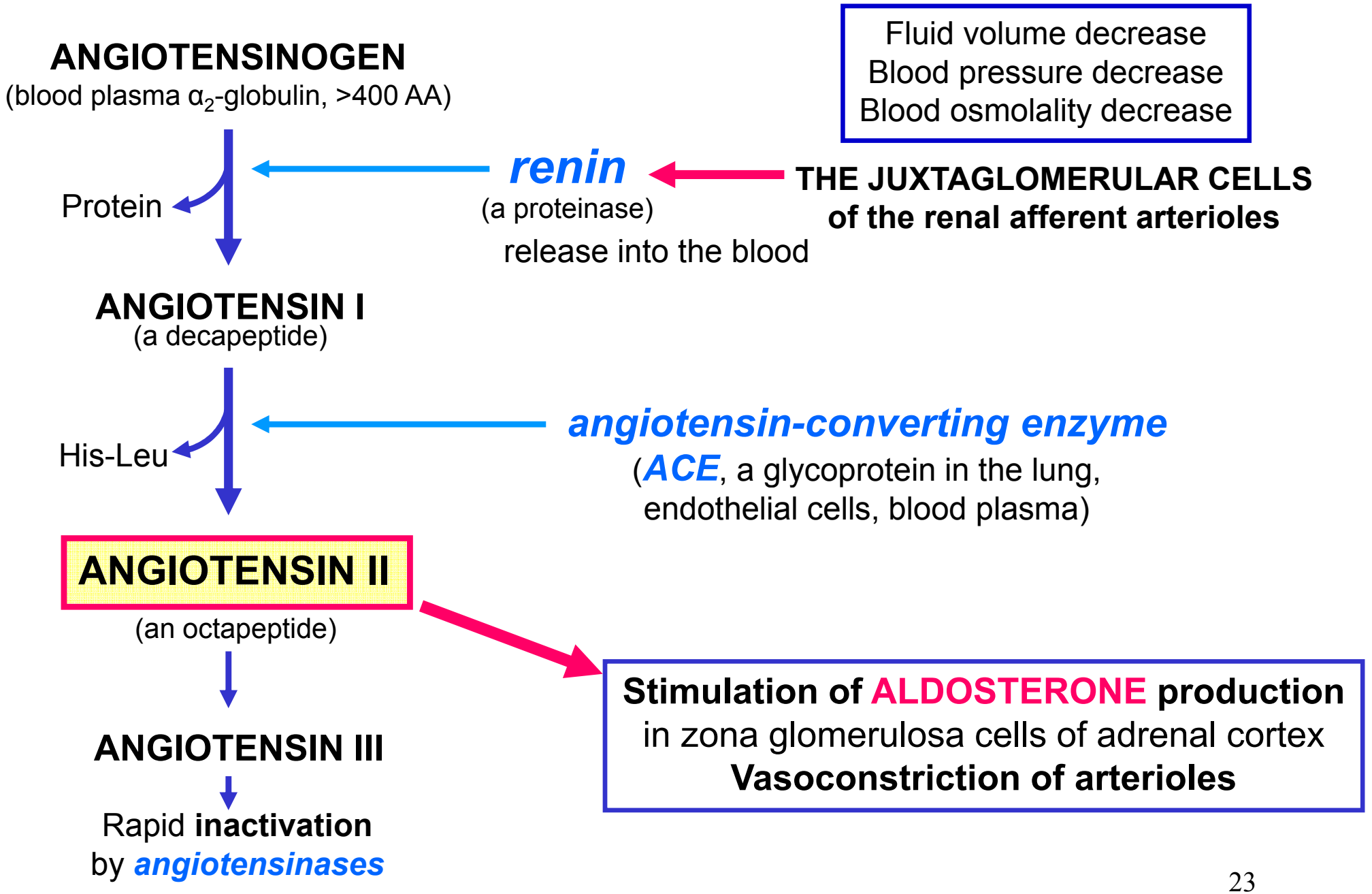
is a nine amino acid cyclic peptide:



Vasopressin receptors V_2 are in the basolateral membranes of cells renal of **renal collecting ducts** (see picture 5).

Vasopressin receptors V_1 are responsible for the vasoconstriction.

The renin-angiotensin system (RAS)



Angiotensin II and III

N-Terminal sequence of the plasma α_2-globulin **angiotensinogen:**

NH_2–Asp–Arg–Val–Tyr–Ile–His-Pro–Phe–His–Leu–Leu–Val–Tyr ⟶

renin

Decapeptide **angiotensin I:**

NH_2–**Asp–Arg–Val–Tyr–Ile–His-Pro–Phe–His–Leu**

angiotensin converting enzyme (***ACE***)

Octapeptide **angiotensin II:**

NH_2–**Asp–Arg–Val–Tyr–Ile–His-Pro–Phe**

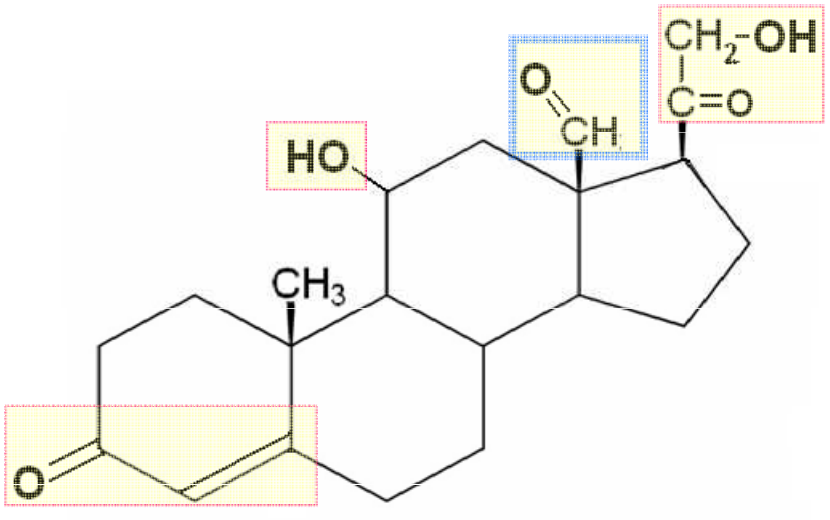
aminopeptidase

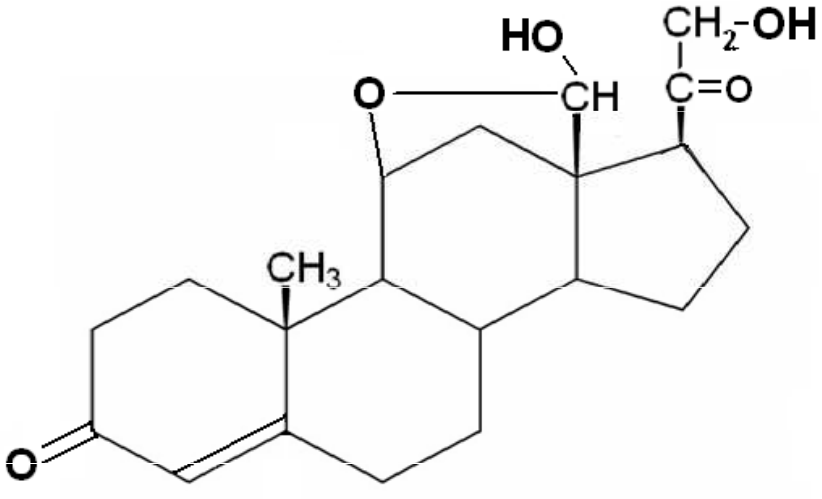
Heptapeptide **angiotensin III:**

Arg–Val–Tyr–Ile–His-Pro–Phe

inactivating *angiotensinases*

Aldosterone

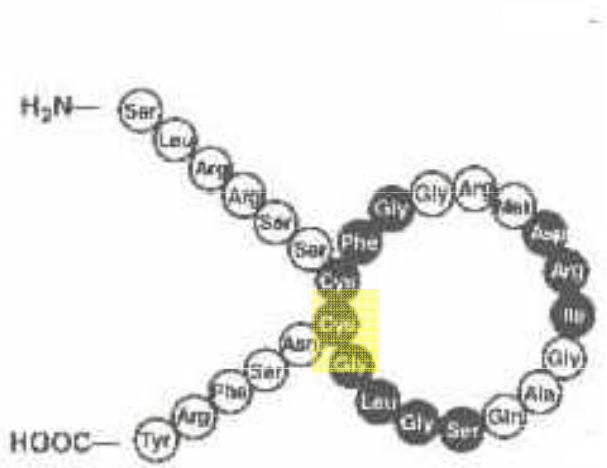


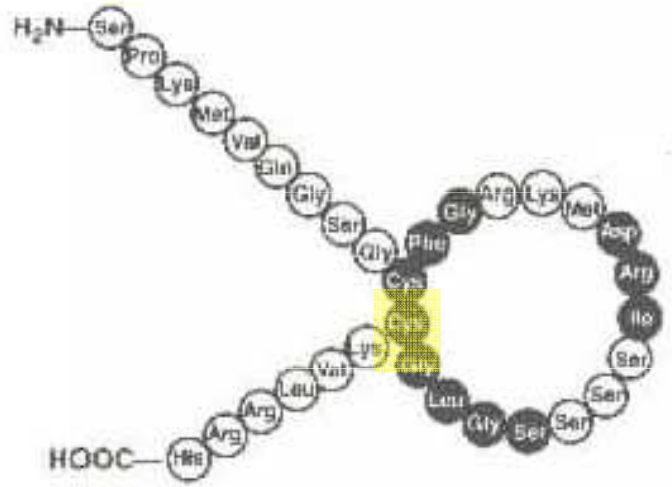


(hemiacetal form)

(11β,21-dihydroxy-3,20-dioxo-4-pregnen-18-al)

Natriuretic peptides





Atrial natriuretic peptide (ANP)

Brain natriuretic peptide (BNP) which, despite its name, is largely of cardiac ventricular origin.

Both peptides have a cyclic sequence (17 amino acyl residues) closed by a disulfide bond; ANP consists of 28 residues, BNP of 32.

They originate from C-ends of their precursors (126 and 108 residues) by hydrolytic splitting and have short biological half-lives. Released N-terminal sequences are inactive, but because they are long-lived, they determination is useful.

Both ANP and BNP have been shown

- to have **diuretic and natriuretic effects**,
- to **induce peripheral vasodilatation**, and
- to **inhibit the release of renin** from the kidneys and **aldosterone** from the adrenal cortex.

These peptides are viewed as protectors against volume overload and as inhibitors of vasoconstriction (e.g. during a high dietary sodium intake).

Membrane receptors for natriuretic peptides are of unique kind – they exhibit **intrinsic guanylate cyclase activity**; binding of NPs onto receptors increases intracellular concentration of cGMP.