Infusions as dosage forms

Institute of Pharmaceutical Technology and Biopharmacy

Outline of the lecture

- Definition of infusions
  - requirements
  - examinations
- Therapeutic classification
  - classification
    (Total Parenteral Nutrition (TPN), Cytostatic preparations, requirements of preparation, documentation and application)
  - Basic preparations

Infusions (Ph.Hg.VIII.)

Requirements:

Sterile, water based solutions or o/w emulsions

Emulsions: phase separation is not allowed

Usually: isotonic property

Applied in large volume

Infusions do not contain any added microbial preservative.

- Concentrated solutions for injections or infusions
  - Sterile solutions, dilutable
- Powders for injections or infusions
  - Applied after dissolution or suspension
  - It may be freeze-dried products

Differences between infusions and injections

Aspects	Injections	**Infusions**
purpose	parenteral drug application	**water and ions replacement, parenteral nutrition, praenteral drug therapy**
equipment	syringe with needle	**infusion bags, cannulas…**
applyed amount	Max. 20-50 ml	**measured in liters**
application time	Max. 15-20 min.	**more hours**
solvent	water, ethanole, glicerol, propylenglicole, oils, etyl-oleate …	**water**
Isohydration	not required	**required**
Isotonicitation	not required	**required**
Isoionisation	-	**recommended**
Colloid osmotic pressure	-	**recommended by plasma replacements**
container	ampoula	**infusion bags**
Pyrogens	not required	**required**
Physico-chemical properties	it may be a suspension	**solution or o/w emulsion**
application area	anywhere	**subcutaneuous**

Infusions: sterile liquids:

- **solution**
- **colloidal solution**
- **emulsion**
- **powders, that are dissolved before use**

Requirements:

In all cases:

- sterility
- drug content
- stability
- particle free

not always possible:

- isotonicity
- isohydric-
- isoionic property

Advantages of parenteral route

1. Rapid action
2. The *inactivation effect* of gastrointestinal tract is not present
3. No *absorption problems*
4. The drug *plasma level is more controllable* than other cases

   There is no need for patient cooperation.

   (*baby*, *unconscious*, *vomiting*, *diarrhea*)
5. Volume replacement or nutrition is possible
6. In specific cases may also be appropriate: local anesthesia, depot effect

   (with proper dosage form and with proper application)

Disadvantages of parenteral route

1. Hazardous (invasive)
2. It is not removable (side effect, overdose)
3. Expensive therapy (preparation process, examinations, requirements)
4. Difficult to use (patient alone vs. qualified person)
5. Discomfort, pain at the injection (patient compliance)

Manufacture process and examinations of infusions

- Generally manufactured the same as the injections
  - Differences:
    - **Concentration of any substance has to be given in mmol/l (injection – mg/l)**
    - Most frequently used ***glass or plastic containers*** to store
    - Large manufacturable amount, therefore the Pharmacopoeias give a unit (1000 ml)
- Examinations
  - Same as injections
  - Sterile, uninjured (intact) with perfect closure
  - At most 3% of API can be the difference between the declared and real

Therapeutic classification of infusions

1. Liquid- and electrolyte-therapy
2. Blood- and volume replacement, volume expanders
3. Infusion mixtures
    a) i.v. additives
    b) Cytostatics
    c) Total Parenteral Nutrition (TPN)
4. Solutions for osmotherapy
5. Solutions for dialysis

1. Liquid- and electrolyte-therapy

1. Liquid- and electrolyte-therapy

1.1. Water supply

They contain „physiological free water”

Electrolyte free:

(basic solutions)

- Inf. Glucosi 5% Isodex
- Fructosol 5

isotonic
Its osmolarity equals with plasma (300±10 mOsm/l)

With electrolyte:

(starter-solutions)

- Rindex 5
  Rindex 10
- Saletanol D5
  Saletanol D10
- ½ Ringer
- Inf. Natr.chlor.0,45%

Half-isotonic

Infusio glucosi Ph. Hg. VII.

Glucosum anhydricum	50,00 g
Acidum chloratum	5,00 g
Aqua ad iniectabilia	ad 1000,0 ml (ad 1020 g)

1. Liquid- and electrolyte-therapy

1.2. isotonic electrolyte inf.

Its osmolarity equals with plasma (300±10 mOsm/l)

Isotonic, but not isoionic → Inf. Natr.chlor.0,9% Salsol A

Isotonic and nearly isoionic → Inf. Glucosi salina; Inf. Salina Ringer; Ringer-lactate

They do **not contain „physiological free water”,** because the ions are in dissociated form in the solution.

Application: isotonic dehydration (great loss of gastro-intestinal secretion, case of burning…)

Infusio salina Ph. Hg. VII.

Kalium chloratum		0,30 g
Calcium chloratum ($CaCl_2 \cdot 6H_2O$)		0,50 g
Natrium chloratum		8,60 g
Aqua ad iniectabilia	ad 1000,0 ml (ad	1004,0 g)

Infusio glucosi salina Ph. Hg. VII.

Kalium chloratum		0,15 g
Calcium chloratum ($CaCl_2 \cdot 6H_2O$)		0,25 g
Natrium chloratum		4,30 g
Glucosum anhydricum		25,00 g
Acidum chloratum 0,1n		5,00 g
Aqua ad iniectabilia	ad 1000,0 ml (ad	1010,0 g)

1. Liquid- and electrolyte-therapy

1.3. supplementary inf.

Metabolic acidosis: pH<7,36

$H_2CO_3 \longleftrightarrow HCO_3^-$

Fast (rapid)

Inf. Natr.hydrogencarb.”4,2%”
Alkaligen (1,4%)

Inf. Natr.lact.
Inf. Natr.lact.c.kalio
Inf. Natr.lact.salina

Slow (long)

Inf.Trometamoli
Tris-buffer

Fast (rapid)

Metabolism of lactate
H^+-consumption

„trometamol” can absorb and eliminate H^+ trought the kidney

Indirect $NaHCO_3$ intake:
From H_2CO_3 ➔ H^+ to rbc.
→a HCO_3^- conc. rises→ pH rises

1. Liquid- and electrolyte-therapy

1.3. supplementary inf.

Methabolic alkalosis: pH>7,45

Hipokalaemia: conc. <3,5 mmol/l

diarrhea

vomiting

Cl^--intake

1 n NaCl + 0,1 n HCl

Inj.KCl 10%
Inj.KCl 7,4%

Acidigen
(NH_4Cl infusion)
/ **arginin-hydrochloride**

Loss of acid: → Cl^- intake is required

Loss of alkaline: → total electrolytes replacement + $NaHCO_3$

Infusio natrii lactici Ph. Hg. VII.

Natrium lacticum solutum 20% pro infusione	86,00 g
Aqua ad iniectabilia	ad 1000,0 ml (ad 1005 g)

Infusio natrii lactici cum kalio Ph. Hg. VII.

Kalium chloratum	3,80 g
Natrium lacticum solutum 20% pro infusione	56,00 g
Aqua ad iniectabilia	ad 1000,0 ml (ad 1005 g)

Infusio natrii lactici salina Ph. Hg. VII.

Kalium chloratum	0,30 g
Calcium chloratum	0,50 g
Natrium chloratum	6,00 g
Natrium lacticum solutum 20% pro infusione	24,00 g
Aqua ad iniectabilia	ad 1000,0 ml (ad 1005 g)

1. Liquid- and electrolyte-therapy

1.4. balancing solution (basic solution)

water + 30-50% electrolites of the physiologic amount + carbohydrates

It is applied before the application of TPN.

Balansol S5

2. Blood- and volume replacement, volume expanders

2. Blood- and volume replacement, volume expanders

1. natural „body's own" volume replacements

Holosanguis humanus conservatus (preserved total human blood)

Preservation:	ACD	21 days
	CPD	28 days

Storage: +4 °C (±2°C)

Solutio anticoagulans „ACD”

Acidum citricum ($C_6H_8O_7 \cdot H_2O$)		5,10 g (24,30 mmol/l)
Trinatrium citricum ($C_6H_5Na_3O_7 \cdot 2H_2O$)		20,0 g (68,0 mmol/l)
Glucosum anhydricum		27,0 g (149,86 mmol/l)
Aqua ad iniectabilia	ad	1000,0 ml (=1023 g)

Solutio anticoagulans „CPD”

Trinatrium citricum ($C_6H_5Na_3O_7 \cdot 2H_2O$)		26,30 g (89,42 mmol/l)
Acidum citricum ($C_6H_8O_7 \cdot H_2O$)		3,27 g (15,56 mmol/l)
Glucosum anhydricum		34,47 g (191,32 mmol/l)
Natrium dihydrogenphosphoricum ($NaH_2PO_4 \cdot 2H_2O$)		2,22 g (14,23 mmol/l)
Aqua ad iniectabilia	ad	1000,0 ml

2. Blood- and volume replacement, volume expanders

Requirements:

- The colloidal substances should be suitable for volume replacement
- Water binding capability (such as: blood plasma proteins)
- Same osmotic pressure as blood
- The rheological properties of the preparations may be equal to the blood.
- Should not accumulate in the body (liver, kidney)
- The solutions must not be toxic, not contain pyrogens, not cause allergy.
- Constant chemical composition
- Do not affect the coagulation process
- Remain fluent in a large temperature range

2. Blood- and volume replacement, volume expanders

2. Artificial

Solution of the macromolecules.

- **40 000- 450 000 Dalton** (1 u ≈ 1,6605402 · 10^{-27} kg $^{1}/_{12}$ C^{12})
- Because of their molecular size is larger than the pores of the healthy (intact) blood vessel they remain intravascular with their osmotically bound water too.
- Because they are macromolecules:
  - Slowly eliminated
  - May have allergic effect (anaphylaxis)
- Indication : volume replacement (without the administration of other person's blood)
- The **volume expanders:** it is hyperosmotic solution, that can be eliminate the water from the interstitial area → decreasing edema

2. Blood- and volume replacement, volume expanders

a. Albumine

•Physiological protein, normal value 34-47 g/l, produced by the liver

•575 amino acid→ **65 000 dalton**, it responsible for 85% of the colloid osmotic pressure.

•**transport function:** fatty acids, bilirubin, Ca^{+}, steroid hormons, vitamins, medications.

•**Binding oxygen free radicals** ➔ antioxidant effect.

Application

• 5% solution: acute volume replacement
•20-25%solution: volume expander, if the synthetic colloids are contraindicated.

• pregnant, breastfeeding mother, infant
• if the albumin concentration is < 25-30 g/l
• for burning lesions
• therapeutic plasma replacement

Preparations

5%, 15%, 20%, 25%

It is wrong!!!

•for acute volume replacement (**routine**)
•for parenteral nutrition

2. Blood- and volume replacement, volume expanders

b. Gelatine

1. **It is a mixture**: Purified protein obtained either by partial acid hydrolysis (type A), partial alkaline hydrolysis (type B) or enzymatic hydrolysis of collagen from animals (including fish and poultry).
2. **35 000 dalton**.
3. It may cause allergy (anaphylaxis)
4. Its colloid osmotic pressure equals with blood ➔ it is not suitable as volume expander
5. It eliminates rapidly from the circulation system (less than 50 000 Da➔kidney) Does not cause kidney damages.
6. **Accumulation does not occur**
7. Duration: 1-2 hour(s).
8. Decrease the blood viscosity, **antithrombotic effect.**

Preparations

Gelofusine, Gelifundol
(3-5% gelatin + electrolites)

2. Blood- and volume replacement, volume expanders

c. Dextrin

1. Glycogen-like, mixture of polysaccharides, principally of the α-1,6-glucan type**.**
2. It is produced by fermentation (*Leuconostoc mesenteroides*), than fractionized, → **average molecular mass: 40 000, 60 000 Dalton**.
3. The volume increasing capacity (180-200%), is increasing with**:**
   - Increasing of the concentration,
   - Reduction of the molecular mass,
   - Increasing of water binding capability per gram.
4. **Duration of action:**
   - Excretion: through the kidney if the molecule is less than 50 000 Da
   - Metabolisms: enzymatic degradation (kidney, liver, spleen)
5. Duration of action: 3-4 hours
6. Haemodilution → decreasing of viscosity → improvement of circulation

2. Blood- and volume replacement, volume expanders

c. Dextrin

7. The dextrin can alter the coagulation parameters:
   - The macromolecules can coat the thrombocytes/ platlet → decreasing of aggregation
   - Fibrins and clots can be dissolved easier.
8. **Disturb the blood group determination**
9. **Increasing the viscosity of urine** → damage the renal tubules prevention
10. **Allergy,** anaphylaxis **: therefore: PROMIT inj. (1000 Dalton)**

Preparations

Macrodex 6% + NaCl Macrodex 6% + glucose 60-70 kD replacement	Rheomacrodex 10% + NaCl Rheomacrodex 10% + glucose 40 kD, plasmaexpanders

2. Blood- and volume replacement, volume expanders

d. Hydroxyethyl starch (HES)

1. Preparation: hydrolyzed corn starch

   - **Molecular mass**: 450 000, 200 000, 40 000 Da

     Substitution of glucose molecule (on C_2 or C_6) with hydroxyethyl groups→ water solubility increases, results in slower degradation by serum amylase.

     Substitution index= substituted /non substituted (0.5, 0.62, 0.7)

The duration of the action depends on:

a./ molecular mass

b./ substitution index

c./ C_2/C_6 ratio

2. Blood- and volume replacement, volume expanders

d. Hydroxyethyl starch (HES)

2. **Elimination:** mainly kidney,
3. **Accumulate:** hepatocytes, glands, spleen, renal tubular cells, skin

   → Contraindicated in renal insufficiency!
4. **Rarely allergy**
5. **Delaying effect to coagulation >** 450 000 Da

Preparations

Isohes 6%
Haes-steril 6%
replacement

Expahes 10%
Haes-steril 10%
plasmaexpander

Osmohes 10%
plasmaexpander

life-threatening, acute hypovolaemia:
7.2% NaCl + colloids

Decreasing of edema
Decreasing of peripheral vessel resistance

Acut hypovolaemia

The absence of circulating blood volume	Colloids	Blood
<25 %	1	0
25-50 %	1	1
>50%	1	2

3. Infusion mixtures

1. Intravenous additives: preparations, that are diluted with solvents and administered parenterally as infusions

1. **Individual drug preparations**
2. **Ensure the compatibility**:
   - Compatible with infusion,
   - Simple
   - Miscible
   - pH compatible (equal to the administered preparation)
3. **Aseptic formulation**
4. **Stability, storage** (room temperature, cool place, protected from light…).
5. **Labelling and documentation**

3. Infusion mixtures

2. Cytostatics

Labour hygiene (Guidance on Health and Standards)

Double protection is needed:

1. Protection of the preparation
2. Protection of the pharmacist (from the cytostatics)

Aseptic work area + **Vertical airflow Laminair-box Cytoflow 915**

3. Infusion mixtures

2. Cytostatics

Personal conditions

job specifications:

qualified: specialist, who knows the risks what can increase the **destructiveness of health**

Healthy:

reproductive-aged women's consent!

Must not be employed:: young, pregnant, breast-feeding women

Contraindicated (diseases): CNS, liver, heart, lung, kidney, hematopoietic (blood-forming), endocrine or immunology

Monitoring of the workers:

beginning → qualification (suitability),

periodic → annually,

extraordinary → complaint, symptom, after contamination

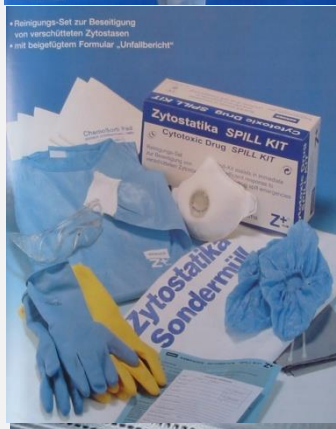
final examination → retire or withdraw

3. Infusion mixtures

2. Cytostatics

Compounding and dispensing

1. Aseptic work area:
   equipment, room, person, substance
2. Hygienic hand disinfection, protective clothing :
   steril coat with tight cuff
   special steril latex gloves (single used)
   Protective cap, face mask (single used)
3. Equipments (steril, single used):
   Syringe, needle,
   absorbent tissues
4. Waste disposal:
   separated from the others, with a different mark



3. Infusion mixtures

2. Cytostatics

Constructional safety regulations:

1. Protective equipment and protective clothing
2. Checking of Cytoflow 915

   direction of air flow, microfilters, differences of pressure (manometer)
3. Microbiology: room and the cytoflow
4. Exposition: (Hungary) max 6 hours per day (6 hours contact with the cytostatic active ingredients, documentation is an other thing) [6/1981.(VII.24.) regulation].
5. Contamination

Decontamination → rinse with a neutralizing solution, removal of contaminated cloths

Record book → substance, person, applied protocol.

3. Infusion mixtures

2. Cytostatics

Documentation:

1. Patient data:

name, birth date, body height, body weight, body surface area (BSA), disease

2. Medication data:

doctor's name, **protocol**, which treatment in the cycle

3. Preparation composition data:

active ingredient, name of drug, amount of the drug, batch number, storage, expiry date, name of the Galenic infusion, its amount, its batch number, its expiry date

3. Infusion mixtures

2. Cytostatics

Documentation:

4. Preparation data:

S.No., date (year, month, day, hour), name of the pharmacist

5. Storage date:

temperature, Is it necessary to protect the preparation from light?

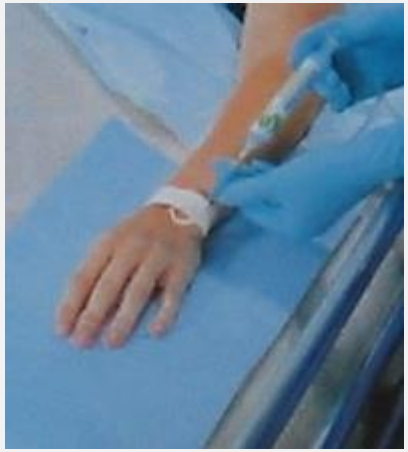
6. Labelling:

primary colored- Background colored, (patient name, bed number; name of cytostatic medicine, amount; storage temperature, protection from light; expiry date; batch number)

3. Infusion mixtures

2. Cytostatics

Administration



1.

- separated hospital room (ward).
- tight cuff sterile coat with sterile latex gloves (injection or infusion)
- sterile latex gloves (at dispensing tablets contaning cytostatics)

3. Infusion mixtures

2. Cytostatics

Administration

2.

- Patient's direct environment should be protected with rubber- or plastic bed-sheet.
- If decontamination is happened

5% Hypo must be applied for 24 hours

3. Infusion mixtures

2. Cytostatics

Administration

3.

- Every equipment (and sputum, stool…), what are any contact with the patient, must be single used.
- Have to be handled as hazardous waste!

3. Infusion mixtures

3. TPN

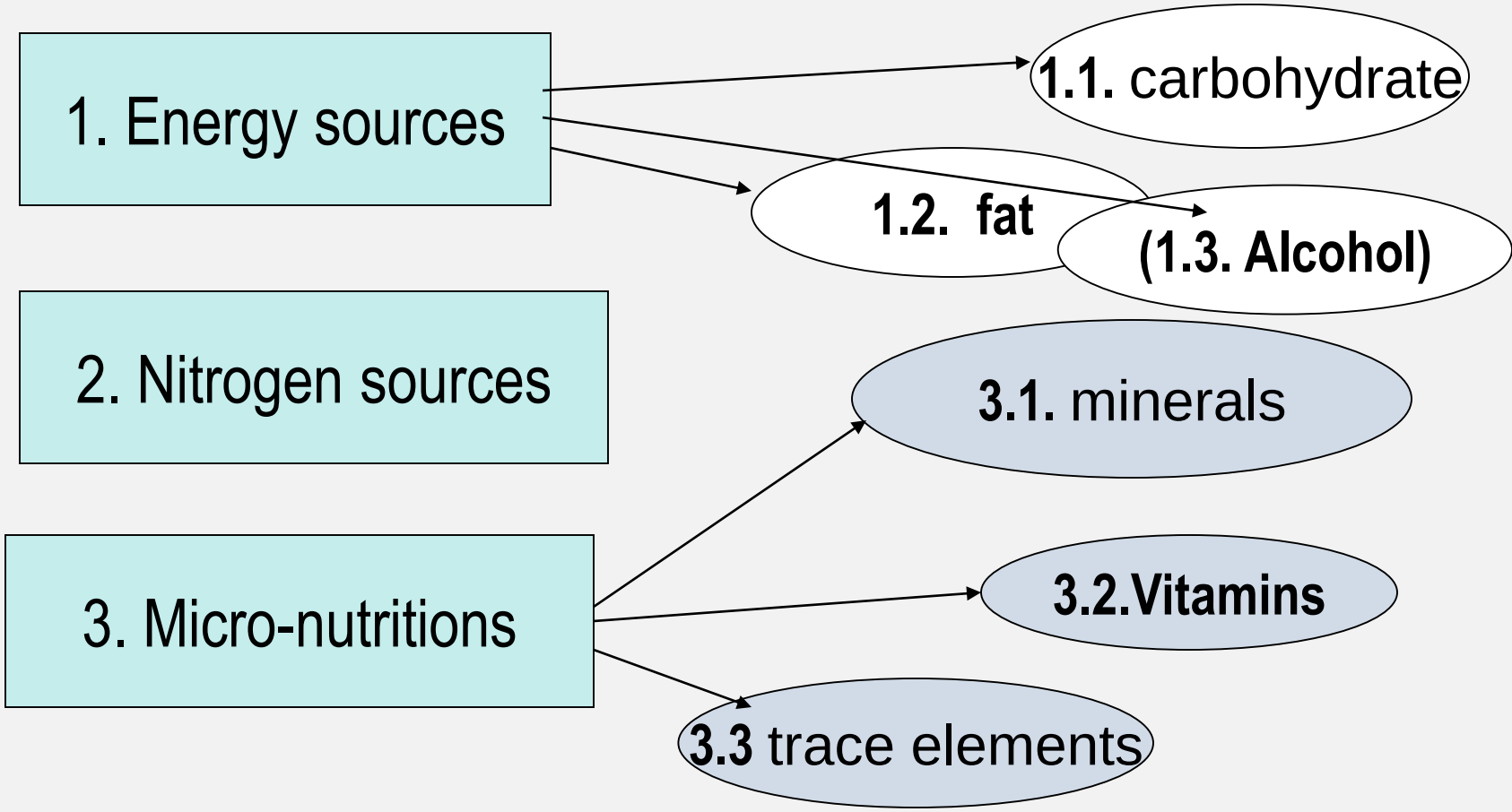
3. Total Parenteral Nutrition

1. Sterility, pyrogens (!)
2. The nutrients are contained in the form of monomers.
3. I.v. administration is possible
4. Include all the necessary nutrients.
5. The ratio of nutrients meet with the patient's need.
6. Stabile (chemical, microbial)

Causes of application of parenteral nutrition

- If enteral/peroral nutrition giving is not possible (1 week) (polytrauma)
- The patient cannot eat (GI obstruction, malabsorption)
- The patient must not eat (operation, inflammatory bowel syndrome, pancreatitis)
- The patient does not want to eat (nausea, loss of appetite)

Nutritions


1. Energy sources
1.1. carbohydrate
1.2. fat
(1.3. Alcohol)
2. Nitrogen sources
3. Micro-nutritions
3.1. minerals
3.2.Vitamins
3.3 trace elements

1. Energy sources

1.1. Carbohydrate

glucose

Daily need:150 g - 350 g

Fructose

(2 g - 5 g / kg of body mass / day)

Invertose

Sorbitol

Xylitol

1.2. Fats

triglycerides

Daily need: 80 g - 100 g
(1 g - 1,5 g / kg / day)

The length of fatty acid chain

- LCT
- MCT
- SCT

Its consumption is faster
Essential fatty acids are not included

Saturation of fatty acids:

- Saturated
- Mono-unsaturated
- Poly-unsaturated

Immune protection, inflammatory reactions thrombolysis

Essential fatty acids: ω-3, ω-6, ω-9
Linoleic acid, ω-linolenic acid, arachidonic acid

2. Nitrogen sources

Aminoacids

Daily needs: 60 g -140 g (0,8 g – 2,0 g / kg / day)

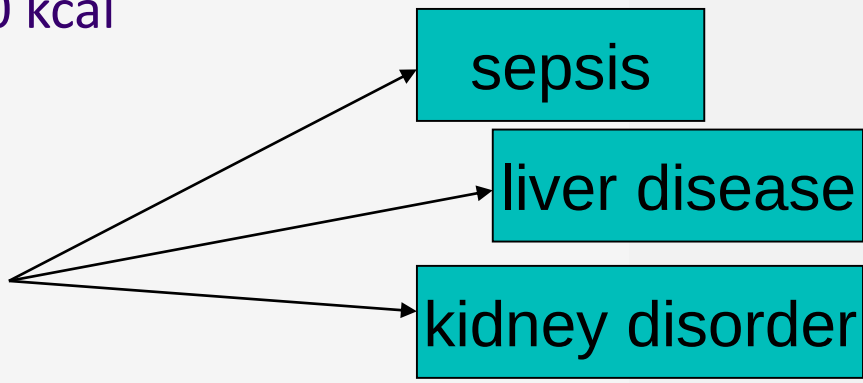
At the same time: calorie intake!

1g non-proteins N needs 100-150 kcal

Amino acid composition :

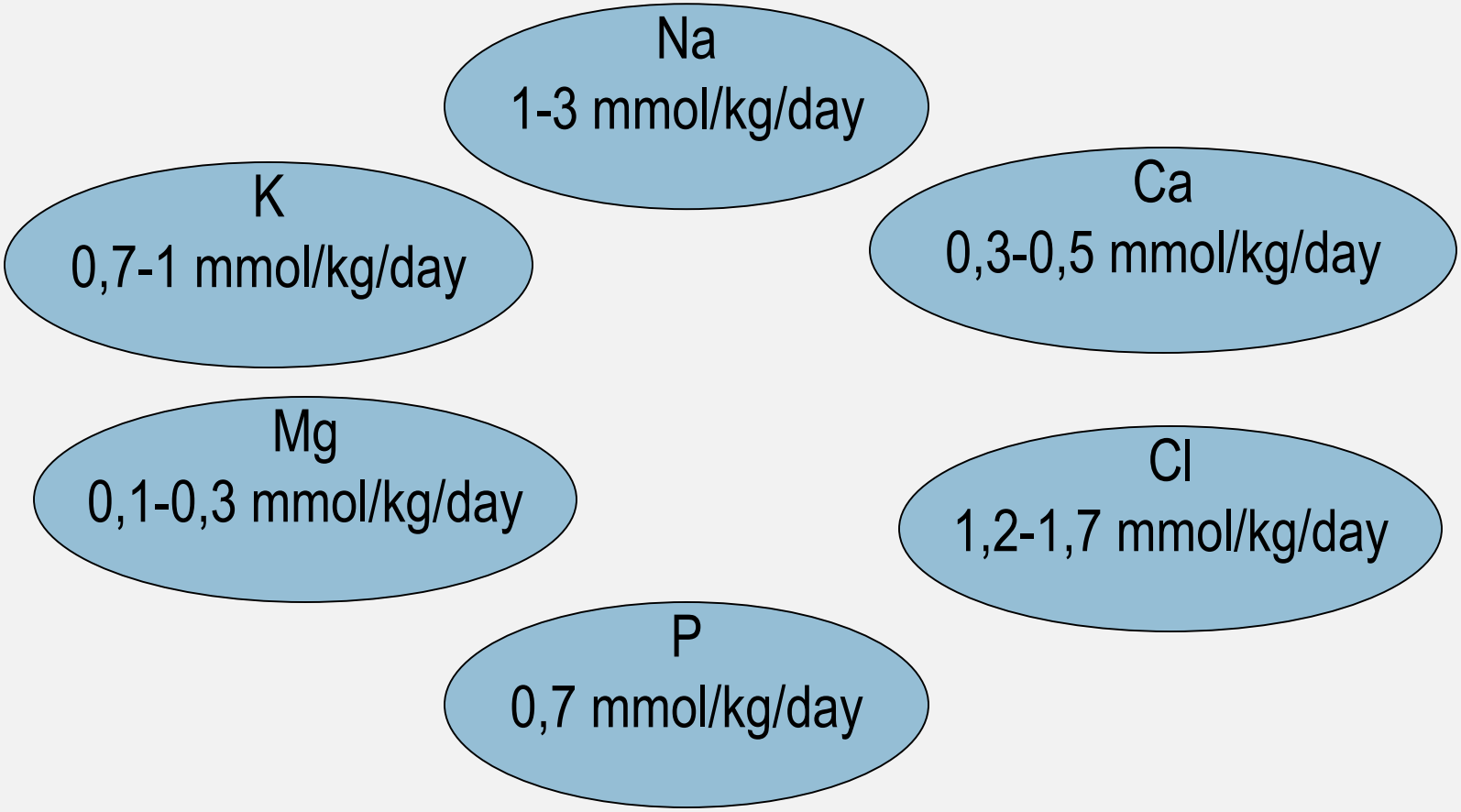
Nutriment (food preparation)

special amino acid composition



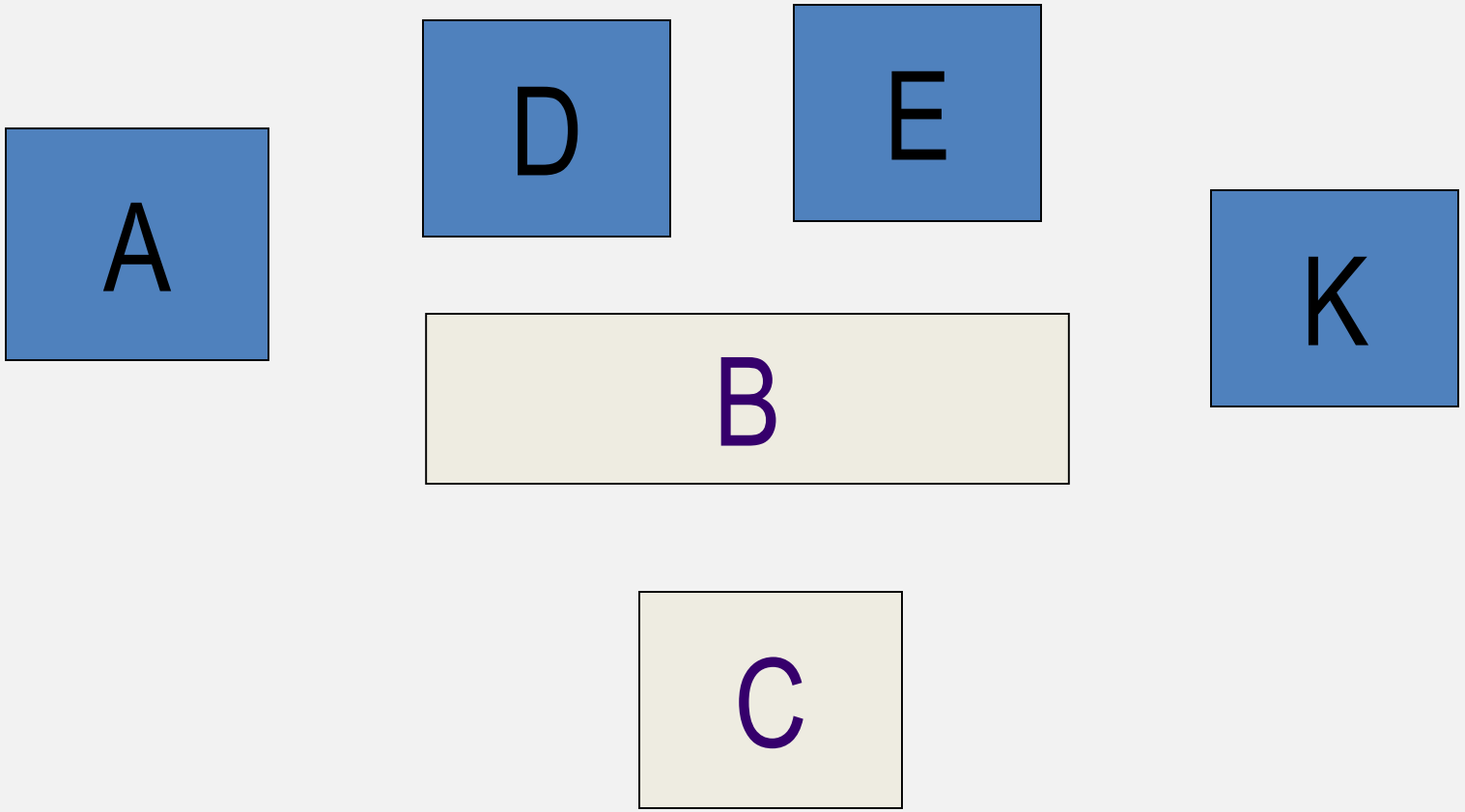
3. micro-nutritions

3.1. minerals



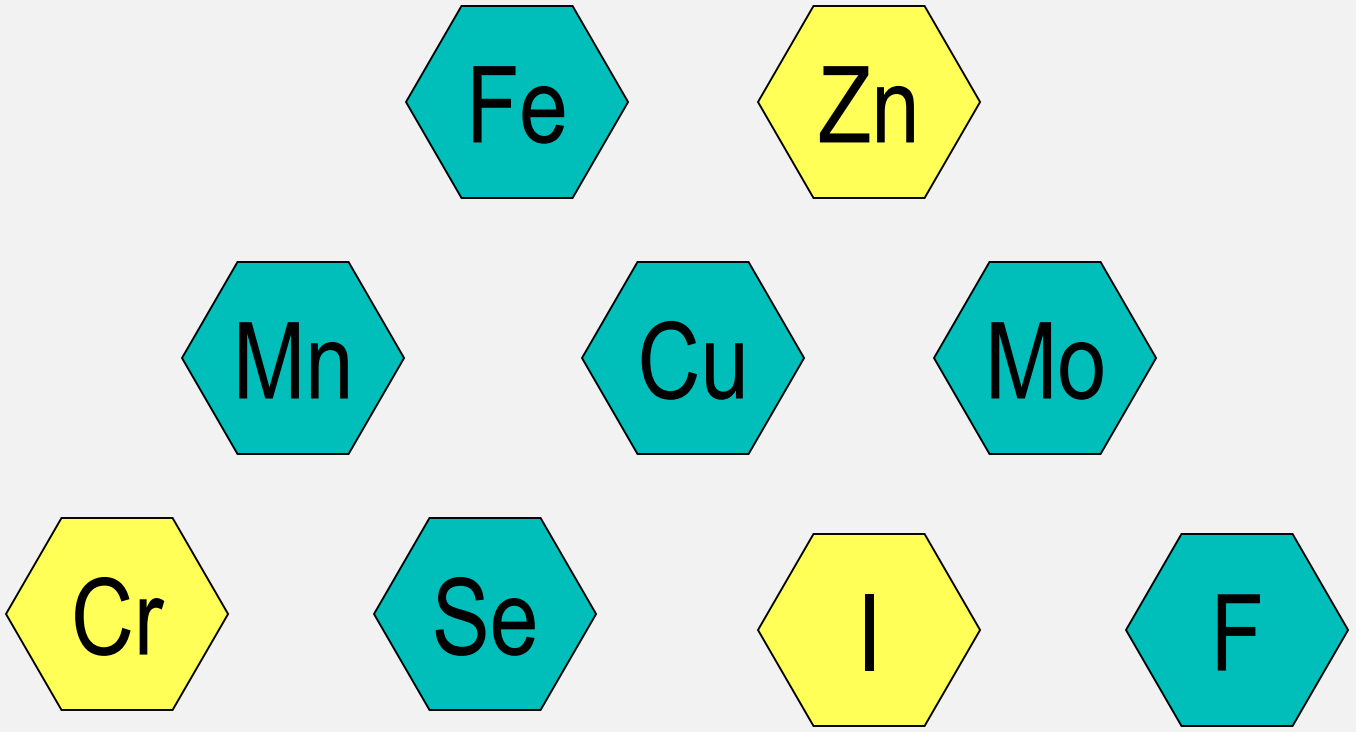
3. micro-nutritions

3.2. Vitamines



3. micro-nutritions

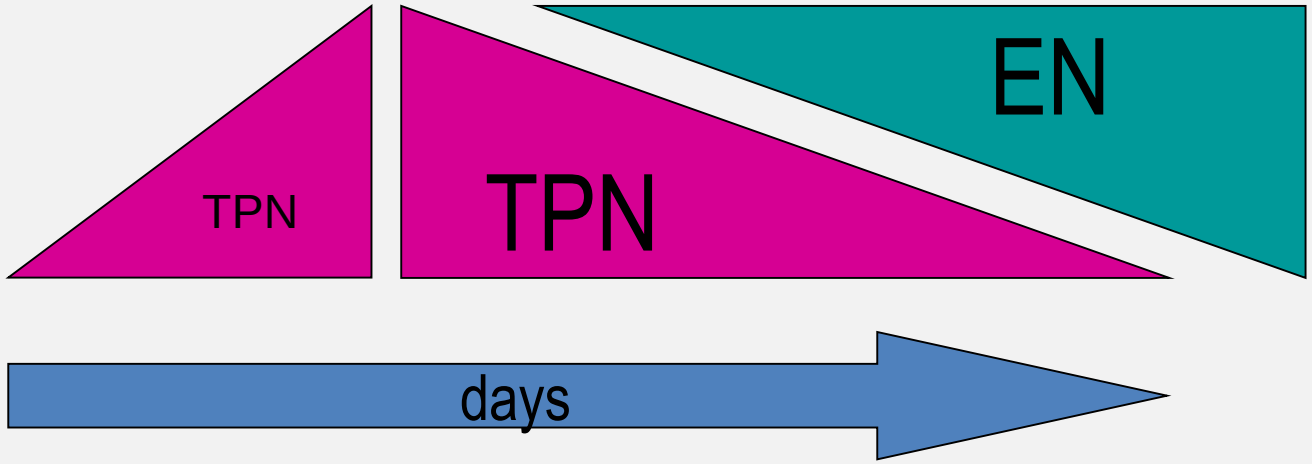
3.3. trace elements



The nutrition

If it possible: enteral nutrition (EN) is used!

TPN➔EN:



The nutrition

1. Parenteral:

peripheral or central

1.1. fractional-parenteral nutrition

AA + G | **AA + G + V** | **AA + G + FA**

1.2. Total parenteral nutrition (TPN)

AA + G + FA + V + TE

AA=amino acids
G=glucose
V=vitamines
FA=fatty acids
TE=trace elements

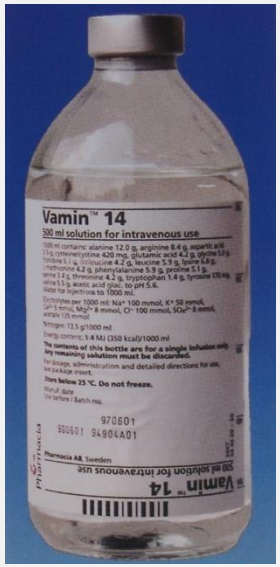
Parenteral nutriments:

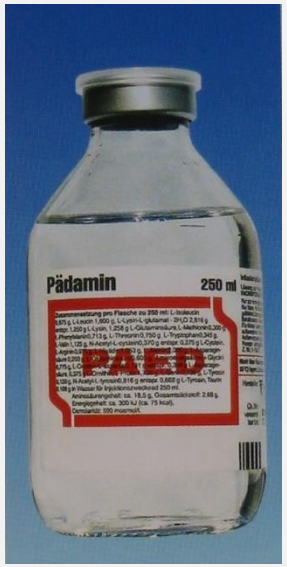
1. *One component systems*

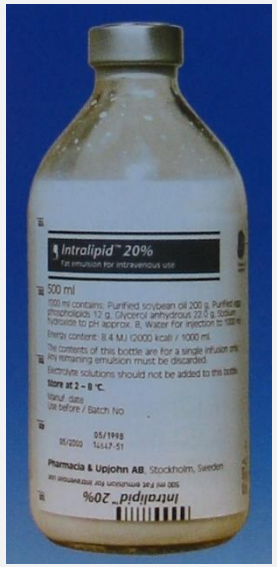
1.1. aminoacids: Vamin 14, Aminosteril KE, Pedamin, Aminoven 15%

1.2. carbohydrate: Glucosum 20%, Glucosum 40%

1.3. fats: Intralipid 10% és 20%, Lipovenös 10% PLR, Lipofundin MCT







Parenteral nutriments:

2. **Incomplete mixtures:**

Aminomix 1, 2, 3,

Nutriflex peri, basal, plus, special

3. **Complete mixtures:**

Clinomel N4, N5, N6, N7, Kabiven, Kabiven peripheral
„All in one”

Parenteral nutriment-supplements:

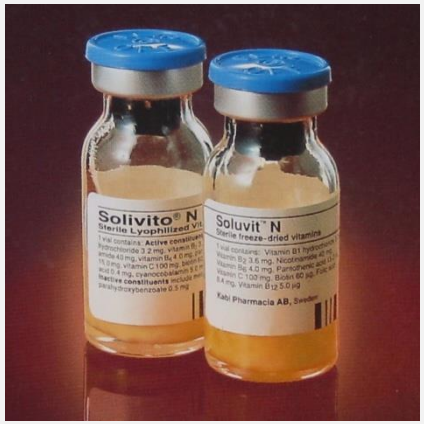
1. Vitamins

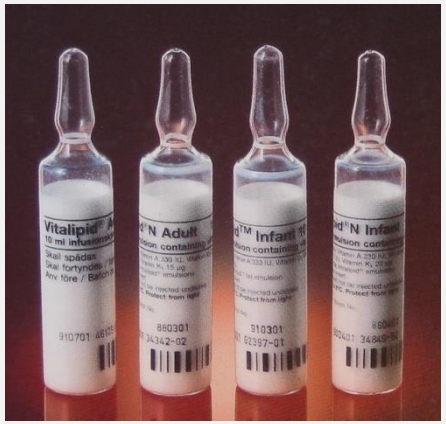
Soluvit,

Vitalipid N infant,

Vitalipid N adult

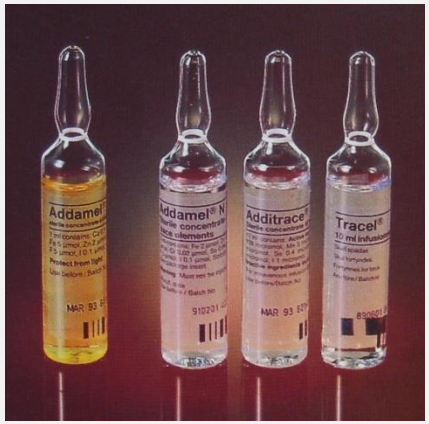
Cernevit





2. Trace elements:

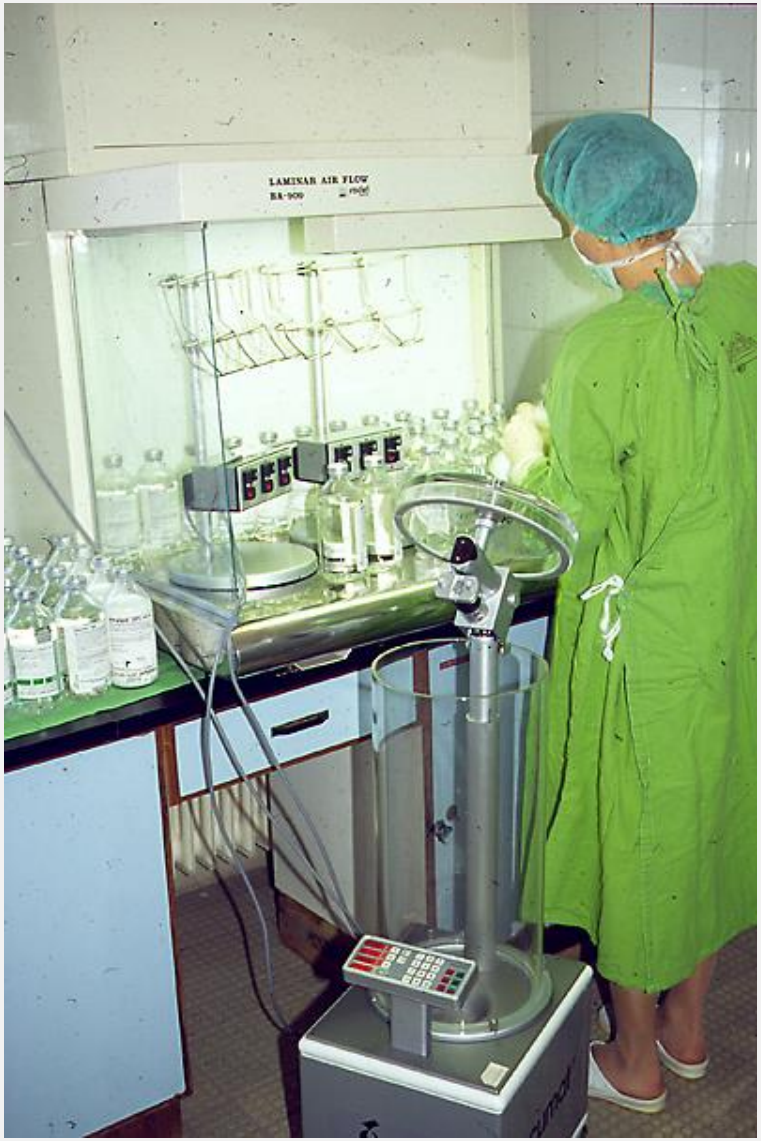
Addamel N,
Tracutil,
Tracitrans



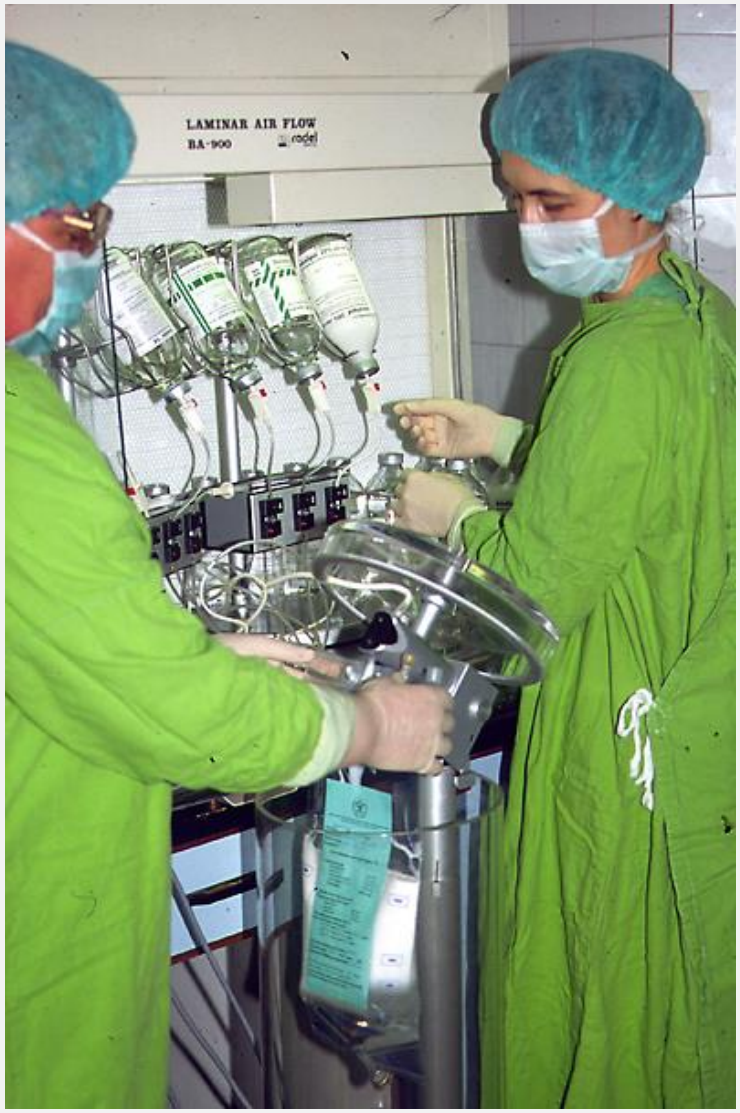
3. Glutamine:

Dipeptiven

Preparation of TPNs



Preparation of TPNs



4. Osmotherapy

They are applied as osmotic parenteral diuretics to decrease edemas.

Requirements:

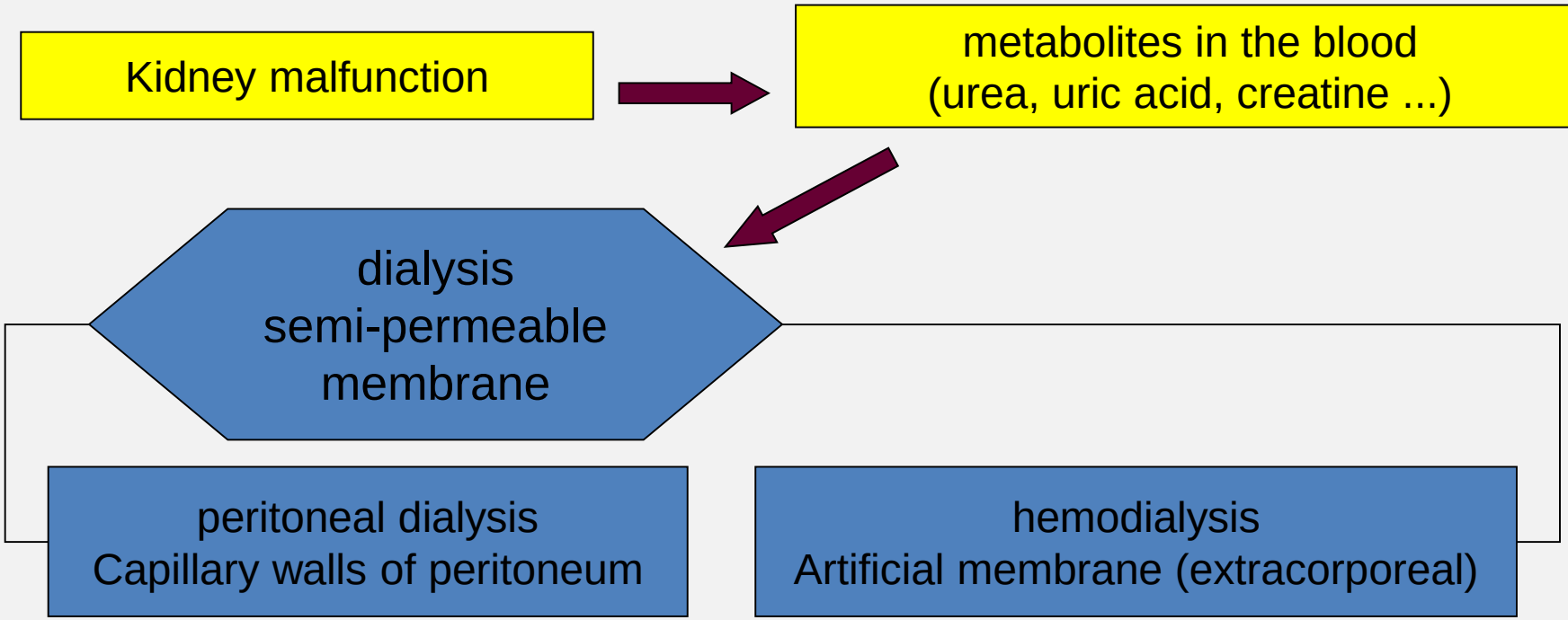
1. **Osmotically active ingredients**
2. **If it is possible: elimination trough the kidney in same form**
3. **Water soluble**
4. **Easy to prepare and sterile**
5. **It not cause tissue damage or laboratory abnormalities**

Preparations:

- Inf. Manniti 10%
  Inf. Manniti 20%
  Mannisol A, Mannisol B
- Glycerin 10% + NaCl
- Inf. Sorbiti 40%
  Onkovertin (dextrin)

Metabolism in the liver

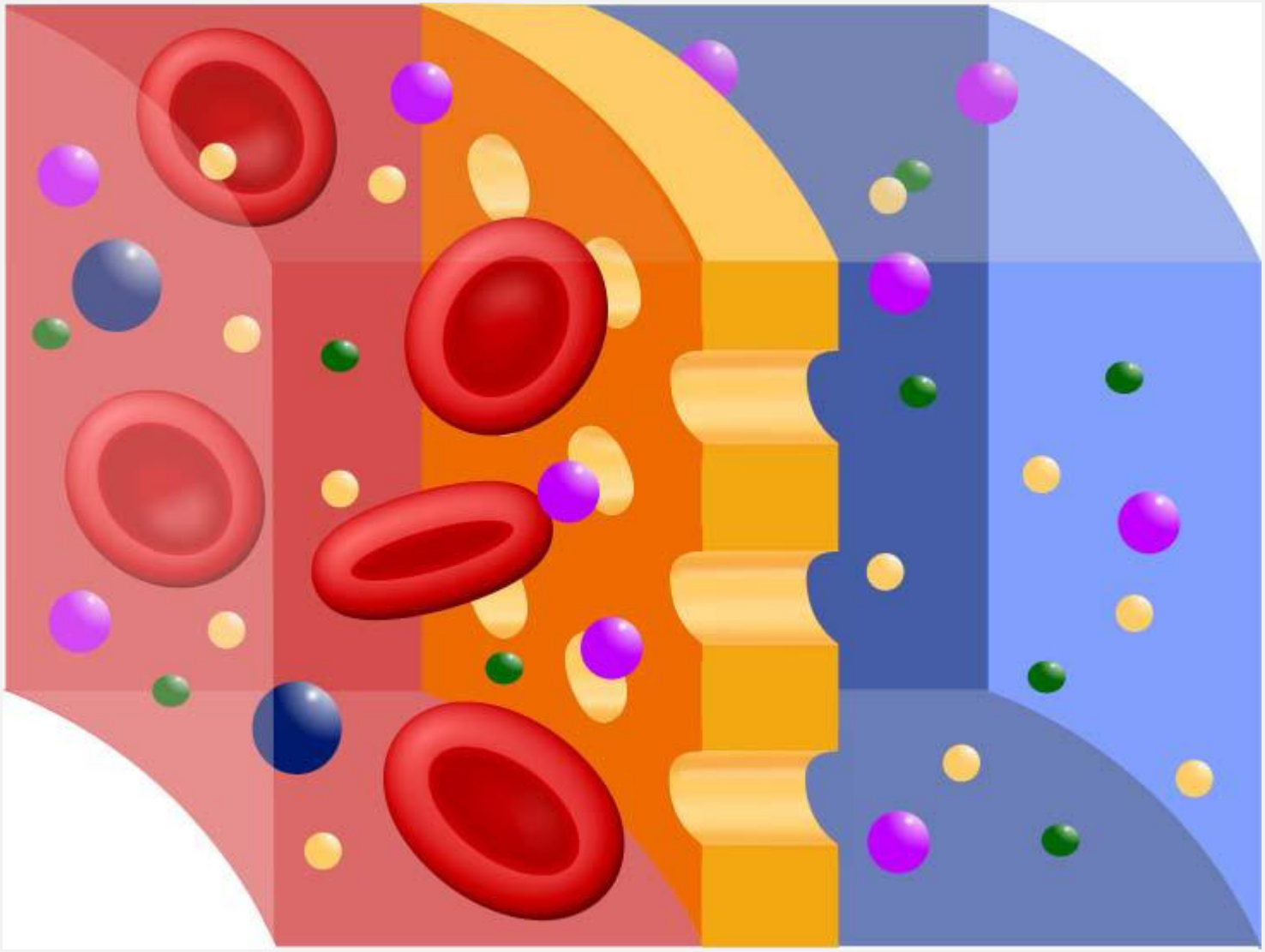
5. Solutions for dialysis



Solutions for dialysis:

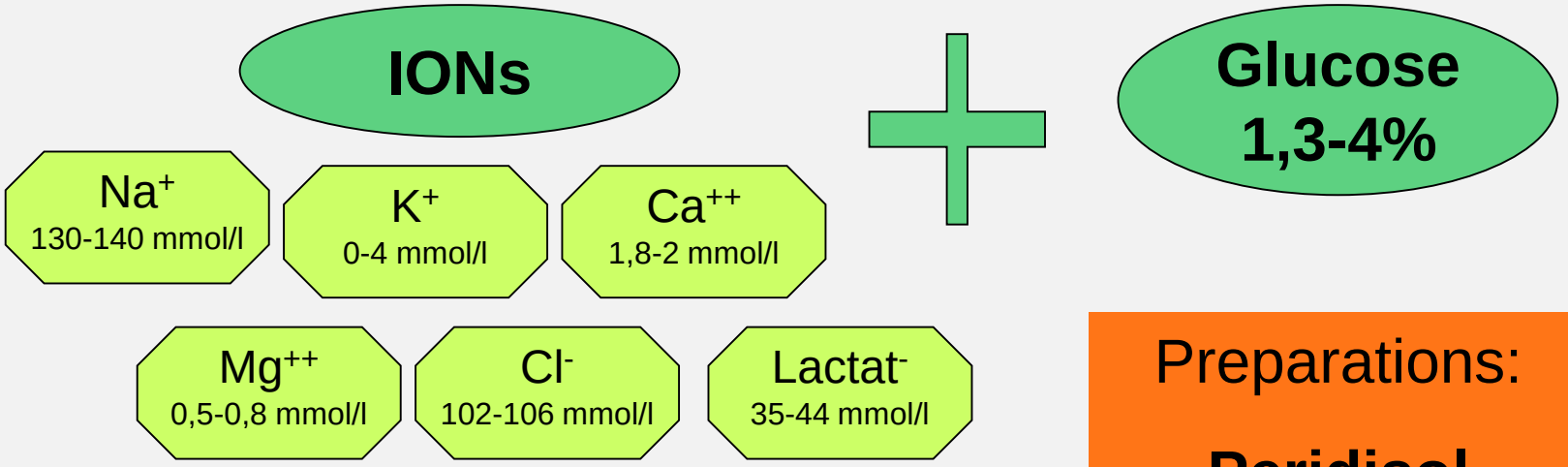
The „washing liquid” of the hemodialysis must have the same quality as infusions.

5. Solutions for dialysis



1996, Caruaru (Brasil) ***1996, Curacao (Netherland Antilles)***

5. Solutions for dialysis



Osmolarity: 350-680 mosm/l

Applied volume**: in liters**!

Preparations:

Peridisol

CAPD

Dianeal

Gambrosol

5. Solutions for dialysis

	mmol/l						
	Na^+	K^+	Ca^{2+}	Mg^{2+}	Cl^-	$Lactate^-$	Glucose
Peridisol 1-D	140	-	2	0,75	102	43,5	83
Peridisol 1-DK	140	4	2	0,75	106	43,5	83
Peridisol 2-D	140	-	2	0,75	102	43,5	389
CAPD 2	134	-	1,75	0,5	103,5	35	83
Dianeal PD1	132	-	1,75	0,75	102	35	75

Examples

Solutio pro dialysi peritoneale I.	**Ph. Hg.VII.**	
Magnesium chloratum ($MgCl_2 \cdot 6H_2O$)		0,152 g
Calcium chloratum ($CaCl_2 \cdot 6H_2O$)		0,438 g
Natrium chloratum		5,64 g
Natrium lacticum solutum 20% pro infusione		24,50 g
Glucosum anhydricum		13,50 g
Aqua ad iniectabilia	ad	1000,0 ml

Solutio pro dialysi peritoneale II.	**Ph. Hg. VII.**	
Magnesium chloratum ($MgCl_2 \cdot 6H_2O$)		0,152 g
Calcium chloratum ($CaCl_2 \cdot 6H_2O$)		0,438 g
Kalium chloratum (KCl)		0,298 g
Natrium chloratum (NaCl)		5,64 g
Natrium lacticum solutum 20% pro infusione		24,50 g
Sorbitum ($C_6H_{12}O_6$)		70,0 g
Aqua ad iniectabilia	ad	1000,0 ml

Hepatoprotective infusions

Infusio glutaspari

L – Acidum asparaginicum		5,00 g
Magnesium oxydatum		0,20 g
Kalium carbonicum		1,00 g
L – Acidum glutaminicum		5,00 g
Natrium hydrocarbonicum		4,00 g
Natrium chloratum		2,25 g
Sorbitum		25,00 g
Aqua ad iniectabilia	ad	500,00 ml

Cardiostop I.

Natrium chloratum		0,877 g
Kalium chloratum		0,745 g
Magnesium chloratum solutum 50%		0,608 g
Glucosum anhydricum		3,00 g
Mannitum		41,31 g
Aqua ad iniectabilia	ad	1000,0 ml

Therapeutic classification of infusions

1. Liquid- and electrolyte-therapy
2. Blood- and volume replacement, volume expanders
3. Infusion mixtures
    a) I.v. additives
    b) Cytostatics
    c) Total Parenteral Nutrition (TPN)
4. Solutions for osmotherapy
5. Solutions for dialysis

Thank you for your attention!