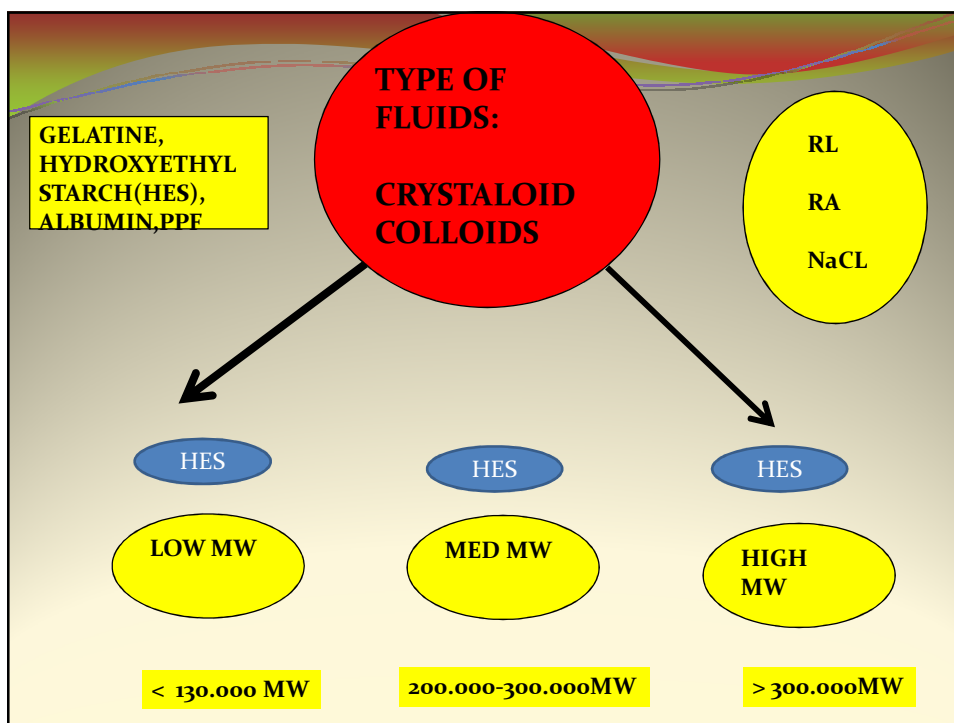
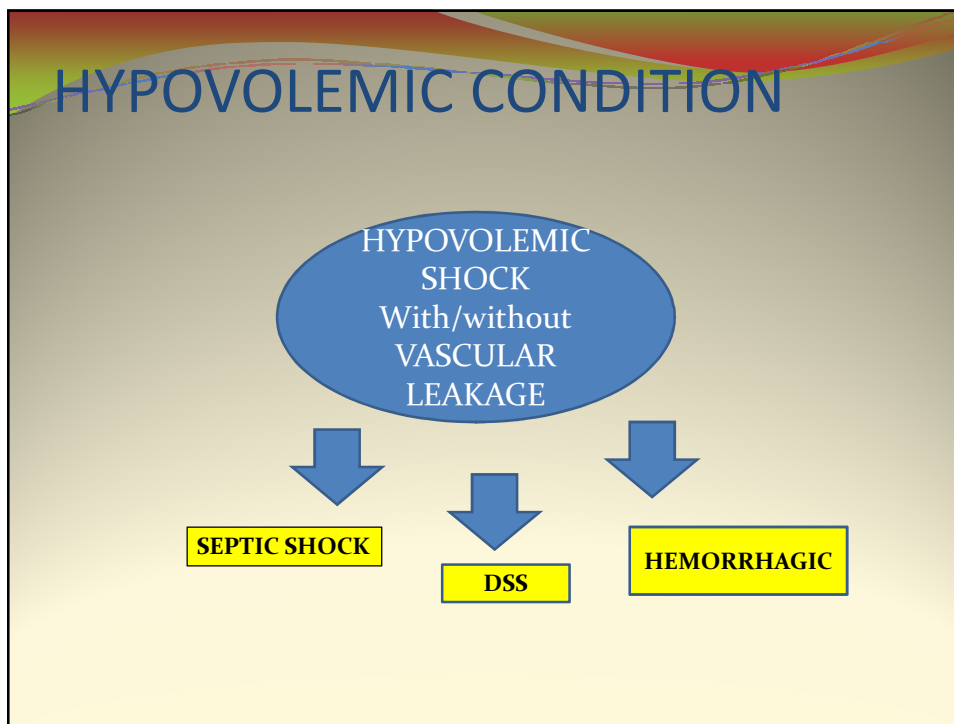
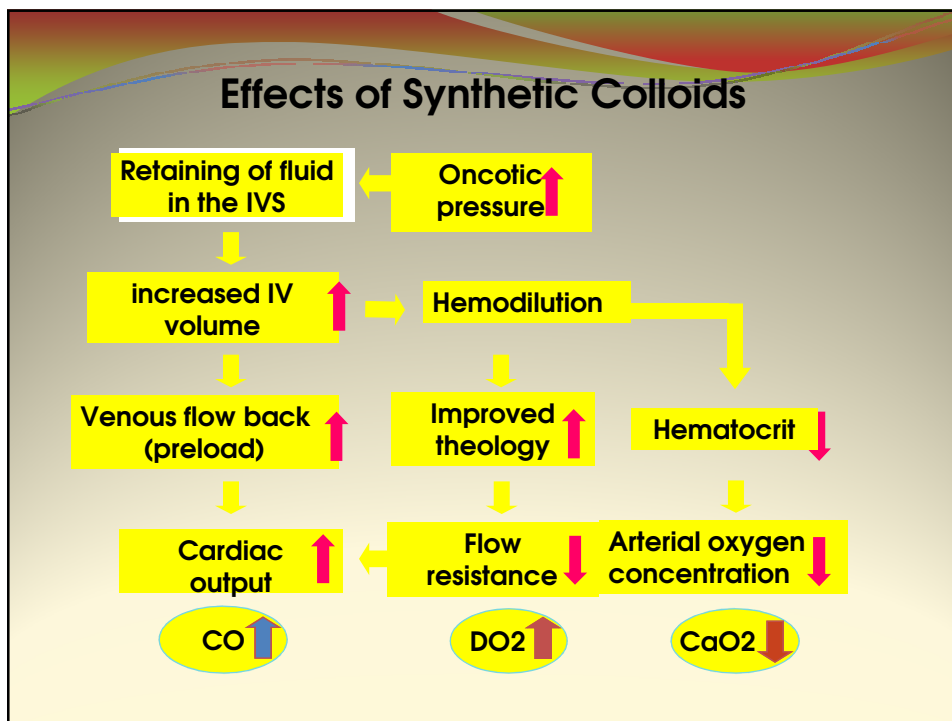


**NEW COLLOID
6% HYDROXYETHYL
STARCH (130/0.4)**

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**CLINICAL USE
OF THIRD
GENERATION
NEW COLLOID
HES 130/0.4**





Ideal Colloid

- Less coagulopathy, hemolysis, red cell hemolysis, cross-match disturbances
- Rapid volume replacement
- Good hemodynamic restoration
- Improvement of Microcirculation
- Improvement of plasma oncotic pressure
- Increase DO₂ and organ function
- Fast metabolism / excretion and good tolerance

DISADVANTAGE EFFECTS OF SYNTHETIC COLLOID

- **Coagulation dilution:** (decrease vWF; platelet adhesion ↓) → Dextran , HMW. HES & high dose/ multiple
- **Renal function:** Dextran, HMW. HES and high DS (450 kD/ 0.7)
- **Tissue Accumulation:** HMW. HES / high DS (RES, skin , nerve)

HES = Hydroxethylstarch (Not all HES are the same!)

1.

(Based on degree of substitution)

Tetrastarch(0.4)
TETRAHES

Pentastarch (0.5)

Hetastarch (0.7)

HES 130 /0.4

HES 200 /0.5

HES 450 /0.7


2.

(Based on Molecular weight)

High molecular weight
HESMedium Molecular weight
HESLow molecular weight
HESHES 450 / 0.7
HES 470 /0.7HES 200 /0.5
HES 200 /0.62HES 40 /0.5
HES 70 /0,5
HES 110 /0,5
HES 130 /0,4Hespan
PlasmasterilHemohes,
Haes-steril
Elohes
Pentaspán

TETRAHES

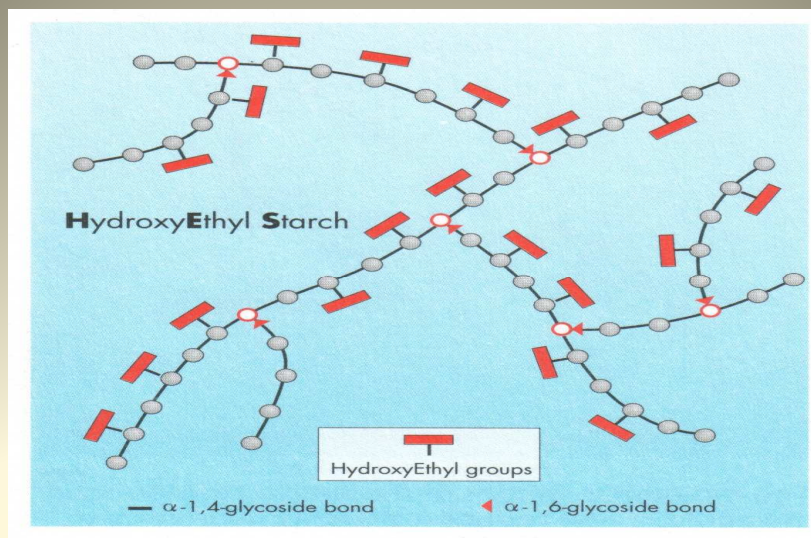
Effects of PVR solutions on haemostasis and coagulation

	Gelatins	HMW. HES	Dextrans
Factor VIII, vWF	No effect	↓	↓
Platelets • Adhesion • Aggregation	No effect	↓	↓
Thrombus formation	No clinical effect	↓	↓
Blood typing	No effect	 In emergency situation blood typing prior to infusion	

Tetrahes structure

- HES → similar to glycogen → consists of:
- D- glucose units linked via linear alpha - 1,4 bonds and branching off from about one in every 17 glucose units via alpha-1.6 bonds
- Hydroxyethyl groups → more resistant to enzymatic degradation and the longer its intravascular residence time

Schematic Representation of HES molecule



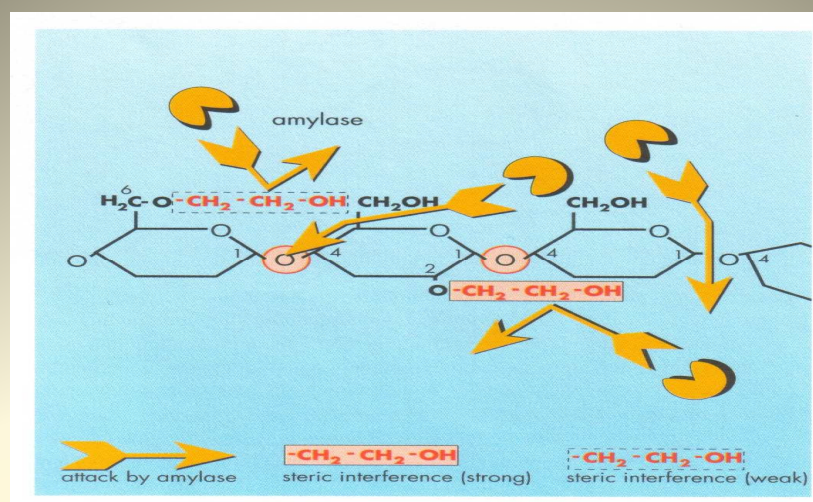
Characteristic of 6% HES 130/0.4

- 6% HES 130/0.4 in 0.9% sodium chloride sol.
- **Mean Molecular Weight** **130.000 ±20.000 Da**
- **Molecular DS** **0.38- 0.45**
- **C₂ / C₆ substitution pattern** **≥ 8**
- **Sealing effect** **positive**
- Water binding capacity 21ml H₂O/g HES
- Colloid Osmotic Pressure 36 mmHg
- Theoretical osmolarity 308 mosm/l
- pH value 4.0-5.5
- Titration acidity < 1.0 mmol/l NaOH

Extent and Duration of Volume expansion (Tetrahes)

- Concentration : 6%
- Degree of mollar substitution (MS): 0.4 →
- 4 hydroxyethyl group per 10 glucose unit
- Sustitution pattern (site of hydroxyethylation) → position 2,3, and 6 of the glucose unit. Ratio C₂/C₆ > 8

Structural formula of HES and mode of steric interference with degradation by amylase



HES 130/0.4 (TETRAHES)

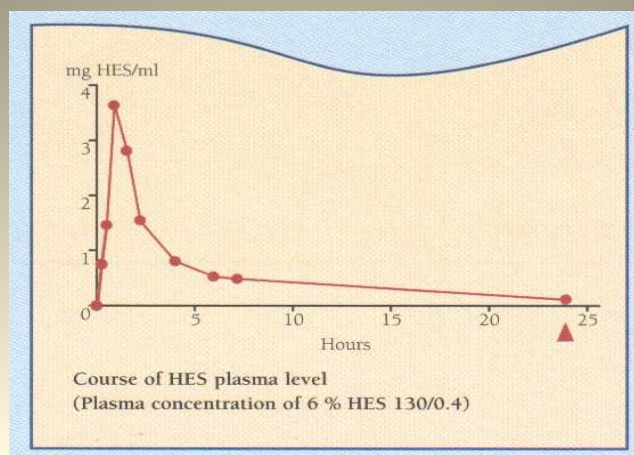
- HES 130/0.4 → 130.000 MW, DS 0.4 and improved C₂/C₆ ratio (> 8)
- **Advantages**
 - No tissue storage; Quickly excreted;
 - Improve safety profil (hemostasis);
 - Comparable macro/microcirculatory efficacy
 - Initial volume efficacy
 - Good hemorrheology
 - Complete elimination
 - Maximal Dose** : 50 ml/kg/day

Pharmacodynamic Studies On Volume Effect

- **12 Volunteers**: 500 ml blood letting 30 ' ; single inf.500 ml HES 130/0.4 15 ' . Results: Reduction in Ht, Increase in plasma volume/ blood volume; Volume effect 100%; Plateau effect 4 hours; Volume effect 6 hours
- **RCT of HES 130/0.4** in variety of clinical situation → HES 130/0.4 is a comparable in efficacy to HES 200/0.5 (Kapsler, Boldt, Langeron, Huet, Vogt)

Volume Therapy With HES 130/0.4

- The extent & Duration of the Volume Effect → Vital for macro & microcirculation
- A fast & effective replacement of the intravascular volume → optimize capillary perfusion; improve blood rheology & its O₂ transport capacity → prevent excessive release of mediators & MOF (Bold, 1998)



Influence On Macro and Microcirculation

- Effective volume replacement → improved acute and chronic macro & microcirculation disturbances
- ↑ perfusion pressure and ↓ blood / plasma viscosity improve rheological properties → improvement in the microcirculation

Stimulation of Pro-inflammatory Process

- No cytokines release in vitro
- No affecting on various surface antigens
- No affecting on adhesion molecules on monocytes and endothelial cells
(Dietrich et al 1998)
- Slightly reduce plasma concentration of adhesion molecules (Boldt et al, 1998)

Problems in Colloid Therapy

- “We are just giving colloid to the patient!”
 - What should happen?”

Possible side effects amongst others can be:

- ⌘ Influence on Renal Function
- ⌘ Influence on coagulation
- ⌘ Anaphylaxis reaction
- ⌘ Tissue accumulation
- ⌘ Acid base balance disturbances

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Safety Profile Of HES 130/0.4

- **Influenced on Hemostasis**
 - ❖ Fast & complete elimination → minimal influence on coagulation
 - ❖ Evidence showed that after HES 130/0.4 → faster recovery of the vWF and Ristocetin co-factor compared to HES 200/0.5 (Vogt et al 1998, Bepperling et al 1999, Jungheinrich C et al 2004)

Anaphylactoid Reactions

- The lowest rate of allergic reaction of all colloids (0.06%)
- Major anaphylactoid reaction (gr III & IV) are seldom during HES therapy (Ring and Mezmer, 1997 ; Laxenaire et al, 1994)


No Influenced on The Normal Kidney

- No affect on the healthy kidney, if the dosage instructions are not exceeded
- After long-term HES therapy could be caused by reduced diuresis as a result of hyperviscosity of renal tubular
- **Evidenced showed:** HES 130/0.4 safely administered to patients with severe renal impairment as long as urine flow is preserved (Jungheinrich, et al 2002)

Relevance of Mol Weight, Molar Substitution and $C_2:C_6$ - ratio

- Influence on Kidney function and coagulation depend on MS, $C_2:C_6$ than MW

- $MS \gg C_2 : C_6 > MW$

 **130/0.4/9:1** **MW/MS/C2:C6**

130/0.42/6:1

200/0.5/ 5:1

25

TETRAHES
(6% HES
130/0.4)



GOOD INTRAVASCULAR VOLUME EFFECT

IMPROVEMENT OF MACRO & MICROCIRCULATION

MINIMAL SIDE EFFECT (COAGULATION, RENAL,

ANAPHYLACTOID RX, TISSUE ACCUMULATION)

