

### The crystalloid-colloid controversy

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## Fluid is important



## Fluid improves outcome

The New England Journal of Medicine

#### EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

EMANUEL RIVERS, M.D., M.P.H., BRYANT NGUYEN, M.D., SUZANNE HAVSTAD, M.A., JULIE RESSLER, B.S., ALEXANDRIA MUZZIN, B.S., BERNHARD KNOBLICH, M.D., EDWARD PETERSON, PH.D., AND MICHAEL TOMLANOVICH, M.D., FOR THE EARLY GOAL-DIRECTED THERAPY COLLABORATIVE GROUP\* 2001;345:1368-77.-

| TREATMENT         | Hours           | AFTER THE START O | OF THERAPY       |
|-------------------|-----------------|-------------------|------------------|
|                   | 0-6             | 7-72              | 0-72             |
| Total fluids (ml) |                 |                   |                  |
| Standard therapy  | $3499 \pm 2438$ | $10,602\pm6,216$  | $13,358\pm7,729$ |
| EGDT              | $4981 \pm 2984$ | $8,625\pm 5,162$  | $13,443\pm6,390$ |
| P value           | < 0.001         | 0.01              | 0.73             |

#### Mortality: 46.5 vs. 30.5% (p=0.009)



## Maybe harmful: SOAP study

Vincent JL, et al. Crit Care Med 2006; 34: 344–353

Table 7. Multivariate, forward stepwise logistic regression analysis in sepsis patients (n = 1177), with intensive care unit mortality as the dependent factor

|  | OR (95% CI)  | p Value |
|--|--------------|---------|
| SAPS II score <sup>a</sup> (per point increase)            | 1.0(1.0-1.1) | <.001   |
| Cumulative fluid balance <sup>b</sup> (per liter increase) | 1.1(1.0-1.1) | .001    |
| Age (per year increase)                                    | 1.0(1.0-1.0) | .001    |
| Initial SOFA score (per point increase)                    | 1.1(1.0-1.1) | .002    |
| Blood stream infection                                     | 1.7(1.2-2.4) | .004    |
| Cirrhosis  | 2.4(1.3-4.5) | .008    |
| Pseudomonas infection                                      | 1.6(1.1-2.4) | .017    |
| Medical admission  | 1.4(1.0-1.8) | .049    |
| Female gender  | 1.4(1.0-1.8) | .044    |

OR, odds ratio; CI, confidence interval; SAPA, Simplified Acute Physiology Score; SOFA, Sequential Organ Failure Assessment.

<sup>a</sup>At admission; <sup>b</sup>within the first 72 hrs of onset of sepsis.



### Give as much as needed

#### Bungaard-Nielsen M, et al. ACTA Anaesthesiol Scand 2009; 53: 843-51





# Crystalloid *vs*. Colloid Which is the killer?





## Meta-analysis on mortality

#### Choi PT et al. Crit Care Med 1999; 27: 200





SAFE

| Table 3. Primary and Secondary Outcome                              | S. <sup>ŵ</sup> |                 |                           |                                 |         |
|---|-----------------|-----------------|---------------------------|---------------------------------|---------|
| Outcome   | Albumin Group   | Saline Group    | Relative Risk<br>(95% Cl) | Absolute Difference<br>(95% CI) | P Value |
| Status at 28 days — no./total no. (%)                               |                 |                 |                           |                                 |         |
| Dead  | 726/3473 (20.9) | 729/3460 (21.1) | 0.99 (0.91 to 1.09)       |                                 | 0.87    |
| Alive in ICU  | 111/3475 (3.2)  | 87/3460 (2.5)   | 1.27 (0.96 to 1.68)       |                                 | 0.09    |
| Alive in hospital†  | 793/ 473 (22.8) | 848/3460 (24.5) | 0.93 (0.86 to 1.01)       |                                 | 0.10    |
| Length of stay in ICU — days  | 6.5±6.6         | 6.2±6.2         |                           | 0.24 (-0.06 to 0.54)            | 0.44    |
| Length of stay in hospital — days†                                  | 15.3±9.6        | 15.6±9.6        |                           | -0.24 (-0.70 to 0.21)           | 0.30    |
| Duration of mechanical ventilation –<br>days                        | 4.5±6.1         | 4.3±5.7         |                           | 0.19 (-0.08 to 0.47)            | 0.74    |
| Duration of renal-replacement<br>— days                             | 0.48±2.28       | 0.39±2.0        |                           | 0.09 (-0.0 to 0.19)             | 0.41    |
| New organ 5   |                 |                 |                           |                                 | 0.855   |
|   | 1397 (52.7)     | 1424 (53.3)     |                           |                                 |         |
|   | 795 (30.0)      | 796 (29.8)      | 21                        | 10/                             |         |
| 20.970  | 369 (13.9)      | 361 (13.5)      |                           | •1 /0                           |         |
| 3 01  | 68 (2.6)        | 75 (2.8)        |                           |                                 |         |
| 4 organs  | 18 (0.7)        | 17 (0.6)        |                           |                                 |         |
| 5 organs  | 2 (0.1)         | 0               |                           |                                 |         |
| Death within 28 days according to sub-<br>group — no./total no. (%) |                 |                 |                           |                                 |         |
| Patients with trauma  | 81/596 (13.6)   | 59/590 (10.0)   | 1.36 (0.99 to 1.86)       |                                 | 0.06    |
| Patients with severe sepsis   | 185/603 (30.7)  | 217/615 (35.3)  | 0.87 (0.74 to 1.02)       |                                 | 0.09    |
| Patients with acute respiratory dis-<br>tress syndrome              | 24/61 (39.3)    | 28/66 (42.4)    | 0.93 (0.61 to 1.41)       |                                 | 0.72    |

\* Plus-minus values are means ±SD. CI denotes confidence interval, and ICU intensive care unit.

† The data include the numbers of patients in the ICU or the length of stay in the ICU.

Data were available for 2649 patients in the albumin group and 2673 patients in the saline group. New organ failure was defined as a Sequential Organ-Failure Assessment score<sup>13</sup> of 0, 1, or 2 in any individual organ system at baseline, followed by an increase in the score to 3 or 4 in the same system.

§ The P value pertains to the comparison between the albumin and saline groups in the numbers of patients who had no new organ failure or new failure of one, two, three, four, or five organs.

Finfer S et al. SAFE study. N Eng J Med 2004; 350: 2247



#### ORIGINAL ARTICLE

#### Intensive Insulin Therapy and Pentastarch Resuscitation in Severe Sepsis

Frank M. Brunkhorst, M.D., Christoph Engel, M.D., Frank Bloos, M.D., Ph.D.,

N Engl J Med 2008;358:125-39.



Acute Renal Failure: HES-34.9% vs RL-22.8%, p=0.002



• Patients with severe sepsis assigned to fluid resuscitation with HES 130/0.4 had an increased risk of death at day 90 and were more likely to require renal-replacement therapy, as compared with those receiving Ringer's acetate.

| The NEW ENGLAND JOURNAL of MEDICINE     |   |
|---|---|
| ORIGINAL ARTICLE                        | ] |
| Hydroxyethyl Starch or Saline for Fluid |   |
| Resuscitation in Intensive Care         |   |

Myburh JA et al. 2012; DOI: 10.1056/NEJMoa1209759

• In patients in the ICU, there was no significant difference in 90-day mortality between patients resuscitated with 6% HES (130/0.4) or saline. However, more patients who received resuscitation with HES were treated with renal-replacement therapy.



## Verdict on HES in 2012

Dellinger RP et al. Intensive Care Med 39. doi: 10.1007/s00134-012-2769-8

#### TABLE 6. Recommendations: Hemodynamic Support and Adjunctive Therapy

#### G. Fluid Therapy of Severe Sepsis

- 1. Crystalloids as the initial fluid of choice in the resuscitation of severe sepsis and septic shock (grade 1B).
- 2. Against the use of hydroxyethyl starches for fluid resuscitation of severe sepsis and septic shock (grade 1B),
- 3. Albumin the fluid resuscitation of severe sepsis and septic shock when patients require substantial amounts of crystalloids (grade 2C).
- 4. Initial fluid challenge in patients with sepsis-induced tissue hypoperfusion with suspicion of hypovolemia to achieve a minimum of 30 mL/kg of crystalloids (a portion of this may be albumin equivalent). More rapid administration and greater amounts of fluid may be needed in some patients (grade 1C).
- Fluid challenge techi based on dynamic (e

# End of the synthetic colloid story?

namic improvement either eart rate) variables (UG).



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#### EDITORIAL

#### Do no harm: use starches?

K. TÁNCZOS <sup>1</sup>, Z. MOLNÁR <sup>2</sup>



# There is only one reason why you give fluid...



## ...to avoid oxygen debt

- $DO_2 = (SV \cdot P) \cdot (Hb \cdot 1.39 \cdot SaO_2 + 0.003 \cdot PaO_2) \sim 1000 \text{m}/\text{m}(SaO_2 = 100\%)$ CO CaO<sub>2</sub>
- $VO_2 = CO \cdot (CaO_2 CvO_2) \sim 250 \text{ ml/min} (ScvO_2 \sim 70-75\%)$









## Oxygen debt and mortality

#### Rixen D, et al. Shock 2001, 16:239-244





## What shall we give?



## Milestones

- Crystalloids:
  - Robert Lewins 1832
    - INJECTION OF SALINE SOLUTIONS IN EXTRAORDINARY QUANTITIES II THE VEINS IN CASES OF MALIGN CHOLERA

THE

LAXCET.

- Sydney Ringer 1885
- Alexis Hartmann (1898-1964)
- Albumin
  - Pearl Harbor 1941



## The semipermeable membranes

ON THE ABSORPTION OF FLUIDS FROM THE CONNECTIVE TISSUE SPACES. BY ERNEST H. STARLING. (Two Figures in Text.)

(From the Physiological Laboratory, Guy's Hospital.)

J Physiol May 5, 1896 19 (4) 312-326







# How does physiology work in critically ill patients?

RIT



#### **SAFE**

| Variable  | Albumi   | n Group  | Saline   | Group  | P Value  |
|---|--|--|--|--|--|
|   | No. of Patients  | Value  | No. of Patients  | Value  |  |
| Study fluid (ml)  |  |  |  |  |  |
| Day 1   | 3410   | 1183.9±973.6   | 3418   | 1565.3±1536.1  | <0.001   |
| Day 2   | 3059   | 602.7±892.7  | 3068   | 9 <mark>4.0±1484.4</mark>  | <0.001   |
| Day 3   | 2210   | 268.0±554.5  | 2202   | 3.3±753.5  | 0.03   |
| Day 4   | 1686   | 192.3±427.0  | 1664   | 22 6±642.6   | 0.57   |
| Nonstudy fluid (ml)   |  |  |  |  |  |
| Day 1   | 3392   | 1459.4±1183.2  | 3405   | 150 1254.3   | 0.30   |
| Day 2   | 3  | 2615.9±1372.5  | 3057   | 270 .435.7   | 0.009  |
| Day 3   |  | 2618.5±1346.5  | 2191   | 266 319.3  | 0.15   |
| Day 4   | 80   | 2691.5±1228.7  | 1656   | 2707 55.4  | 0.36   |
| Packed red cells (ml)   |  |  |  |  |  |
| Day1  | 3411   | 97.8±360.7   | 3415   | 71 8   | <0.001   |
| Day 2   | 3066   | 106.5±321.4  | 3074   | 61.  | < 0.001  |
| Day 3   | 2217   | 59.8±225.5   | 2210   | 49   | 0.30   |
| Day 4   | 1692   | 43.6±167.5   | 1668   |  |  |
| Net Alb•  |  |  |  | Salin  | <b>A</b> •   |
| AIU.  | 3  |  | 832  | Sam  |  |
| 1101  | 4(   | 25%  | )0.  |  | _  |
| <b>1184 m</b>   | 90   |  | 218  | 1565   | ml   |
| Day III III   | 16/1   |  | 1649   | 1000   |  |
| Mean arterial present (1967)  |  |  |  |  |  |
| Day 1   | 3406   | 81.4±14.4  | 3408   | 80.9±14.5  | 0.14   |
| Day 2   | 3068   | 84.4±15.1  | 3075   | 84.2±15.7  | 0.49   |
| Day 3   | 2215   | 87.2±15.3  | 2209   | 86.9±16.1  | 0.62   |
| Day 4   | 1688   | 88.3±15.9  | 1666   | 88.4±16.3  | 0.87   |
| Heart rate (beats/min)  |  |  |  |  |  |
| Day 1   | 3398   | 88.0±20.2  | 3406   | 89.7±20.8  | < 0.001  |
| Day 3   | 3071   | 88.5±19.5  | 3075   | 89.5±19.2  | 0.06   |
|   |  |  |  |  |  |
| Day 3   | 2216   | 88.8±19.1  | 2213   | 89.7±18.8  | 0.10   |
| Day 3<br>Day 4  | 2216<br>1691   | 88.8±19.1<br>89.5±18.9   | 2213<br>1668   | 89.7±18.8<br>89.9±18.5   | 0.10   |
| Day 3<br>Day 4<br>Central venous pressure (mm Hg)   | 2216<br>1691   | 88.8±19.1<br>89.5±18.9   | 2213<br>1668   | 89.7±18.8<br>89.9±18.5   | 0.10<br>0.52   |
| Day 3<br>Day 4<br>Central venous pressure (mm Hg)<br>Day 1  | 2216<br>1691<br>2204   | 88.8±19.1<br>89.5±18.9<br>11.2±4.8   | 2213<br>1668<br>2270   | 89.7±18.8<br>89.9±18.5<br>10.0±4.5   | 0.10<br>0.52<br><0.001   |
| Day 3<br>Day 4<br>Central venous pressure (mm Hg)<br>Day 1<br>Day 2   | 2216<br>1691<br>2204<br>2095   | 88.8±19.1<br>89.5±18.9<br>11.2±4.8<br>11.6±4.9   | 2213<br>1668<br>2270<br>2135   | 89.7±18.8<br>89.9±18.5<br>10.0±4.5<br>10.4±4.3   | 0.10<br>0.52<br><0.001<br><0.001   |
| Day 3<br>Day 4<br>Central venous pressure (mm Hg)<br>Day 1<br>Day 2<br>Day 3  | 2216<br>1691<br>2204<br>2095<br>1531                                 | 88.8±19.1<br>89.5±18.9<br>11.2±4.8<br>11.6±4.9<br>11.4±4.8   | 2213<br>1668<br>2270<br>2135<br>1589                                 | 89./±18.8<br>89.9±18.5<br>10.0±4.5<br>10.4±4.3<br>10.7±4.4   | 0.10<br>0.52<br><0.001<br><0.001<br><0.001   |
| Day 3<br>Day 4<br>Central venous pressure (mm Hg)<br>Day 1<br>Day 2<br>Day 3<br>Day 4   | 2216<br>1691<br>2204<br>2095<br>1531<br>1221                         | 88.8±19.1<br>89.5±18.9<br>11.2±4.8<br>11.6±4.9<br>11.4±4.8<br>11.1±4.8                                     | 2213<br>1668<br>2270<br>2135<br>1589<br>1230                         | 89.7±18.8<br>89.9±18.5<br>10.4±4.5<br>10.4±4.3<br>10.7±4.4<br>10.5±4.4                                     | 0.10<br>0.52<br><0.001<br><0.001<br><0.001<br><0.001                               |
| Day 3<br>Day 4<br>Central venous pressure (mm Hg)<br>Day 1<br>Day 2<br>Day 3<br>Day 4<br>Serum albumin (g/liter)                            | 2216<br>1691<br>2204<br>2095<br>1531<br>1221                         | 88.8±19.1<br>89.5±18.9<br>11.2±4.8<br>11.6±4.9<br>11.4±4.8<br>11.1±4.8                                     | 2213<br>1668<br>2270<br>2135<br>1589<br>1230                         | 89.7±18.8<br>89.9±18.5<br>10.4±4.5<br>10.4±4.3<br>10.7±4.4<br>10.5±4.4                                     | 0.10<br>0.52<br><0.001<br><0.001<br><0.001<br><0.001                               |
| Day 3<br>Day 4<br>Central venous pressure (mm Hg)<br>Day 1<br>Day 2<br>Day 3<br>Day 4<br>Serum albumin (g/liter)<br>Day 1                   | 2216<br>1691<br>2204<br>2095<br>1531<br>1221<br>2081                 | 88.8±19.1<br>89.5±18.9<br>11.2±4.8<br>11.6±4.9<br>11.4±4.8<br>11.1±4.8<br>28.7±7.0                         | 2213<br>1668<br>2270<br>2135<br>1589<br>1230<br>2061                 | 89.7±18.8<br>89.9±18.5<br>10.4±4.5<br>10.4±4.3<br>10.7±4.4<br>10.5±4.4<br>24.7±6.5                         | 0.10<br>0.52<br><0.001<br><0.001<br><0.001<br><0.001<br><0.001                     |
| Day 3<br>Day 4<br>Central venous pressure (mm Hg)<br>Day 1<br>Day 2<br>Day 3<br>Day 4<br>Serum albumin (g/liter)<br>Day 1<br>Day 2          | 2216<br>1691<br>2204<br>2095<br>1531<br>1221<br>2081<br>2708         | 88.8±19.1<br>89.5±18.9<br>11.2±4.8<br>11.6±4.9<br>11.4±4.8<br>11.1±4.8<br>28.7±7.0<br>30.8±6.4             | 2213<br>1668<br>2270<br>2135<br>1589<br>1230<br>2061<br>2703         | 89.7±18.8<br>89.9±18.5<br>10.4±4.5<br>10.4±4.3<br>10.7±4.4<br>10.5±4.4<br>24.7±6.5<br>24.5±5.9             | 0.10<br>0.52<br><0.001<br><0.001<br><0.001<br><0.001<br><0.001<br><0.001           |
| Day 3<br>Day 4<br>Central venous pressure (mm Hg)<br>Day 1<br>Day 2<br>Day 3<br>Day 4<br>Serum albumin (g/liter)<br>Day 1<br>Day 2<br>Day 3 | 2216<br>1691<br>2204<br>2095<br>1531<br>1221<br>2081<br>2708<br>1921 | 88.8±19.1<br>89.5±18.9<br>11.2±4.8<br>11.6±4.9<br>11.4±4.8<br>11.1±4.8<br>28.7±7.0<br>30.8±6.4<br>30.0±6.4 | 2213<br>1668<br>2270<br>2135<br>1589<br>1230<br>2061<br>2703<br>1905 | 89.7±18.8<br>89.9±18.5<br>10.4±4.5<br>10.4±4.3<br>10.7±4.4<br>10.5±4.4<br>24.7±6.5<br>24.5±5.9<br>23.6±5.6 | 0.10<br>0.52<br><0.001<br><0.001<br><0.001<br><0.001<br><0.001<br><0.001<br><0.001 |

Finfer S et al. SAFE study. N Eng J Med 2004; 350: 2247

\* Plus-minus values are means ±SD.  $\dot{\gamma}$  P values are for the comparison between the two means for each variable at each time point.



ORIGINAL ARTICLE

Hydroxyethyl Starch 130/0.4 versus Ringer's Acetate in Severe Sepsis Perner A et al. 2012; DOI: 10.1056/NEJMoa1204242









## Is physiology wrong?



## Central venous oxygen saturation is a good indicator of altered oxygen balance in isovolemic anemia

S. Kocsi<sup>1</sup>, G. Demeter<sup>1</sup>, J. Fogas<sup>1</sup>, D. Érces<sup>2</sup>, J. Kaszaki<sup>2</sup> and Z. Molnár<sup>1</sup>

Acta Anaesthesiol Scand 2012; 56: 291–297

| Hemodynamic effe   | ects of isovolemic  | anemia.   |  |  |  |   |
|--|---|---|--|--|--|---|
|  | To  | T <sub>1</sub>  | T <sub>2</sub>                                       | T₃   | T <sub>4</sub>   | T₅  |
| Hb (g/l)   | 125 <u>(113–134)</u>  | 102 (90-109)*†  | 79 (73–93)*†   | 68 (60-76)*†   | 59 (53-67)*†   | 49 (43–55)*†  |
| (mmol/l)<br>HR (beats/min)   | 7.<br>125   |   | Decrease by (  | 60%  |  | 3.0 (2.6–3.4)<br>47 (131–177)*  |
| MAP (mm Hg)<br>CVP (mm Hg)   | 91 (79–105)<br>6 (5–8)  | 89 (79–101)<br>8 (5–9)                                  | 83 (75–98)*<br>7 (4–9)                               | 82 (68–90)*<br>7 (5–9)                                 | 72 (59–85)*<br>7 (5–9)   | 72 (63–86)*<br>7 (3–10)   |
| GEDI (ml/m <sup>2</sup> )  | 270 (243-284)   | 271 (245-320)   | 276 (248-298)  | 274 (236–305)  | 268 (227-302)  | 261 (232-298)   |
| ITBI (ml/m <sup>2</sup> )<br>ELWI (ml/kg)<br>SVI (ml/m <sup>2</sup> )<br>SVV (%)<br>dPmx (mm Hg/s) | 335 (307–352)<br>9 (9–10)<br>21 (18–29)<br>17 (14–21)<br>540 (485–790 | 335 (305–400)<br>10 (10–10)<br>26 (23–31)<br>15 (12–21) | 343 (303–373)<br>9 (9–10)<br>27 (24–31)<br>19 (9–21) | 342 (295–383)<br>10 (9–10)<br>28 (25–31)<br>15 (11–20) | 334 (282–375)<br>10 (9–10)<br>25 (21–33)<br>19 (11–25)<br>60)* | 333 (285–375)<br>10 (9–11)<br>28 (22–31)<br>14 (11–27)<br>975 (562–1275)* |
|  |   | Blee  | ding: 150 ±  | 33  ml/event   | t  |   |
|  |   |   | blood:HES  | <b>b</b> = 1.1   |  |   |



Effect of volume loading with 1 liter intravenous infusions of 0.9% saline, 4% succinulated gelatine (Gelofusine) and 6% hydroxyethyl starch (Voluven) on blood volume and endocrine responses: A randomized, three-way crossover study in healthy volunteers

Dileep N. Lobo, DM, FRCS; Zeno Stanga, MD; Mark M. Aloysius, MRCS; Catherine Wicks, BMedSci, BM, BS; Quentin M. Nunes, MRCS; Katharine L. Ingram, FRCA; Lorenz Risch, MD, MPH; Simon P. Allison, MD, FRCP

Crit Care Med. 2010 58(2):1-7

#### 10 healthy adults 1000 ml fluid/60 min









Intensive Care Med (2004) 30:1356–1360 DOI 10.1007/s00134-004-2278-5

#### ORIGINAL

Zsolt Molnár András Mikor Tamás Leiner Tamás Szakmány

## Fluid resuscitation with colloids of different molecular weight in septic shock

|  | tb  | t <sub>ep</sub> | t <sub>30</sub>                      | t60  |
|--|---|-----------------|--------------------------------------|--|
| ITBVIurs (ml/m <sup>2</sup> )  | 798±37  | 956±53*         | $904 \pm 70^{*}$                     | 854±116*   |
| ITBVIGEL   | 791±52  | 967±71*         | 897±96*                              | $905 \pm 92^*$   |
| CI <sub>HES</sub> (1-min-m <sup>2</sup> )  | 3.84±0.96   | 5.06±1.19*      | 4.69±1.14*                           | 4.04±1.09  |
| CIGEL  | $3.82 \pm 0.88$                                       | 4.88±0.85*      | 4.69±0.77*                           | 4.58±1.25  |
| Hb <sub>HES</sub> (g/l)  | 99±14   | 97±15           | 97±18                                | 96±16  |
| HbGEL  | 95±21   | 95±22           | 93±22                                | 94±22  |
| DO <sub>2</sub> I <sub>HES</sub> (ml·min·m <sup>2</sup> )  | 477±99  | 630±183         | 598±126                              | $527 \pm 109$  |
| DO <sub>2</sub> I <sub>GEL</sub>   | 457+101   | 615+186         | 560+163                              | 550±178  |
| EVLW <sub>HE</sub>   |   | $\sim$ C 11     | · 1.                                 | ±6   |
| EVLWGE   |   |                 | O1O                                  | ±3   |
| - GE   |   |                 |                                      |  |
| MAPHES   | Conord  |                 | 010.                                 | ±10  |
| MAP <sub>HES</sub><br>MAP <sub>GEL</sub>   | Size do   | asn't ma        | ottor                                | ±10<br>±13   |
| MAP <sub>HES</sub><br>MAP <sub>GEL</sub><br>CVP <sub>HES</sub> (   | Size do   | esn't ma        | itter                                | ±10<br>±13<br>±6   |
| MAP <sub>HES</sub><br>MAP <sub>GEL</sub><br>CVP <sub>HES</sub> (<br>CVP <sub>GEL</sub>   | Size do   | esn't ma        | itter                                | ±10<br>±13<br>±6<br>±8   |
| MAP <sub>HES</sub><br>MAP <sub>GEL</sub><br>CVP <sub>HES</sub> (<br>CVP <sub>GEL</sub><br>HR <sub>HES</sub> (beats/min)  | Size do   | esn't ma        | 103±12                               | ±10<br>±13<br>±6<br>±8<br>104±10                               |
| MAP <sub>HES</sub><br>MAP <sub>GEL</sub><br>CVP <sub>HES</sub> (<br>CVP <sub>GEL</sub><br>HR <sub>HES</sub> (beats/min)<br>HR <sub>GEL</sub>   | Size do   | esn't ma        | 103±12<br>108±26                     | ±10<br>±13<br>±6<br>±8<br>104±10<br>110±28                     |
| MAP <sub>HES</sub><br>MAP <sub>GEL</sub><br>CVP <sub>HES</sub><br>CVP <sub>GEL</sub><br>HR <sub>HES</sub> (beats/min)<br>HR <sub>GEL</sub><br>PaO <sub>2</sub> /FiO <sub>2HES</sub> (mmHg)                                     | Size do   | esn't ma        | 103±12<br>108±26<br>189±52           | ±10<br>±13<br>±6<br>±8<br>104±10<br>110±28<br>189±78           |
| MAP <sub>HES</sub><br>MAP <sub>GEL</sub><br>CVP <sub>HES</sub><br>CVP <sub>GEL</sub><br>HR <sub>HES</sub> (beats/min)<br>HR <sub>GEL</sub><br>PaO <sub>2</sub> /FiO <sub>2HES</sub> (mmHg)                                     | Size do<br>107±9<br>116±30<br>207±114<br>182±85       | esn't ma        | 103±12<br>108±26<br>189±52<br>180±87 | 104±10<br>110±28<br>189±78                                     |
| MAP <sub>HES</sub><br>MAP <sub>GEL</sub><br>CVP <sub>HES</sub><br>CVP <sub>GEL</sub><br>HR <sub>HES</sub> (beats/min)<br>HR <sub>GEL</sub><br>PaO <sub>2</sub> /FiO <sub>2HES</sub> (mmHg)<br>PaO /EiO                         | Size do<br>107±9<br>116±30<br>207±114<br>182±85<br>ES | esn't ma        | 103±12<br>108±26<br>189±52<br>180±87 | ±10<br>±13<br>±6<br>±8<br>104±10<br>110±28<br>189±78<br>182±85 |
| MAP <sub>HES</sub><br>MAP <sub>GEL</sub><br>CVP <sub>HES</sub><br>CVP <sub>GEL</sub><br>HR <sub>HES</sub> (beats/min)<br>HR <sub>GEL</sub><br>PaO <sub>2</sub> /FiO <sub>2HES</sub> (mmHg)<br>PaO/FiO<br>V/100 ml <sub>H</sub> | Size do<br>107±9<br>116±30<br>207±114<br>182±85<br>ES | esn't ma        | 103±12<br>108±26<br>189±52<br>180±87 | ±10<br>±13<br>±6<br>±8<br>104±10<br>110±28<br>189±78<br>182±85 |



## Facts and fiction

- 1. Fluid therapy is life saving in acute hypovolemia
- 2. Less colloid is needed for the same change in CI
- 3. V/R ratio (Cryst/Coll) may be 4:1 in healthy but~2:1 or even less in critically ill
- 4. Is there any point dealing with colloids at all?



## Microcirculation



## Part 1: Sepsis



Journal of Critical Care (2010) 25, 659.e1-659.e8

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Journal of Critical Care

Comparison of 6% hydroxyethyl starch 130/0.4 and saline solution for resuscitation of the microcirculation during the early goal-directed therapy of septic patients  $\dot{\alpha}, \dot{\alpha}, \dot{\alpha}$ 

Arnaldo Dubin MD<sup>a,b,\*</sup>, Mario O. Pozo MD<sup>c</sup>, Christian A. Casabella MD<sup>a</sup>, Gastón Murias MD<sup>c</sup>, Fernando Pálizas Jr. MD<sup>c</sup>, Miriam C. Moseinco MD<sup>a</sup>, Vanina S. Kanoore Edul MD<sup>a,b</sup>, Fernando Pálizas MD<sup>c</sup>, Elisa Estenssoro MD<sup>d</sup>, Can Ince PhD<sup>e,1</sup>





SHOCK, Vol. 28, No. 3, pp. 300–308, 2007

#### HYDROXYETHYL STARCH NORMALIZES PLATELET AND LEUKOCYTE ADHESION WITHIN PULMONARY MICROCIRCULATION DURING LPS-INDUCED ENDOTOXEMIA

Sebastian Küpper,\* Soeren Torge Mees,\* Peter Gassmann,\* Martin F. Brodde,<sup>†</sup> Beate Kehrel,<sup>†</sup> and Joerg Haier\*



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Colloids prevent LPS caused vasoldilataion and preserve platelet and leukocyte function

NaCl 0.9% (□) thout treatment (■) roxyethyl starch (▲) Ringer lactate (△)







## Part 2: Surgery and bleeding



#### Goal-directed Colloid Administration Improves the Microcirculation of Healthy and Perianastomotic Colon

Oliver Kimberger, M.D.,\* Michael Arnberger, M.D.,\* Sebastian Brandt, M.D.,\* Jan Plock, M.D.,† Gisll H. Sigurdsson, M.D., Ph.D.,‡ Andrea Kurz, M.D.,§ Luzius Hiltebrand, M.D.\*

Colon anastomosis – 240 minutes observatoin

R-RL group:3ml/kg fluidGD-RL group:3ml/kg fluid + 250 ml if  $ScvO_2 < 60\%$ GD-C group:3ml/kg fluid + 250 ml if  $ScvO_2 < 60\%$ 





#### EFFECTS OF COLLOID RESUSCITATION ON PERIPHERAL MICROCIRCULATION, HEMODYNAMICS, AND COLLOIDAL OSMOTIC PRESSURE DURING ACUTE SEVERE HEMORRHAGE IN RABBITS

Makiko Komori,\* Katsumi Takada,\* Yasuko Tomizawa,<sup>†</sup> Shoichi Uezono,\* Keiko Nishiyama,\* and Makoto Ozaki\*





## Physiological background



## The secret: Glycocalyx

#### Reitsma S, et al. J Vasc Res 2011, 48:297-306





## The secret: Glycocalyx

#### Bernard M. et al. Circulation Research. 2003; 92: 592-594





• Patients with severe sepsis assigned to fluid resuscitation with HES 130/0.4 had an increased risk of death at day 90 and were more likely to require renal-

## Had these patients received bolus fluids unnecessarily?

Hydroxyethyl Starch or Saline for Fluid Resuscitation in Intensive Care Myburh JA et al. 2012; DOI: 10.1056/NEJMoa1209759

• In patients in the ICU, there was no significant difference in 90-day mortality between patients resuscitated with 6% HES (130/0.4) or saline. However, more patients who received resuscitation with HES were treated with renal-replacement therapy.



- 1. Glycocalyx is impaired in many critically ill
- 2. Colloids act farster and longer if the glycocalix is intact

3. They improve microcirculation and cause less edema as compared to crystalloids



## My dilemma

## What should we give? *vs.* When should we give?



#### The NEW ENGLAND JOURNAL of MEDICINE

#### **REVIEW ARTICLE**

#### CRITICAL CARE MEDICINE

Simon R. Finfer, M.D., and Jean-Louis Vincent, M.D., Ph.D., Editors

#### **Resuscitation Fluids**

John A. Myburgh, M.B., B.Ch., Ph.D., and Michael G. Mythen, M.D., M.B., B.S.

#### TYPES OF RESUSCITATION FLUID

Globally, there is wide variation in clinical practice with respect to the selection of resuscitation fluid. The choice is determined largely by regional and clinician preferences that are based on institutional protocols, availability, cost, and commercial marketing.<sup>11</sup> Consensus documents about the use of resuscitation fluids have been developed and directed primarily at specific patient populations,<sup>12-14</sup> but such recommendations have been based largely on expert opinion or lowquality clinical evidence. Systematic reviews of



## Solve the hemodynamic puzzle first!

Tánczos K, Németh M, Molnár Z 2014 Ann. Up. in Int. Care and Em. Med. 2014 in press **Annual Update** in Intensive Care and **Emergency** Medicine 2012  $SvO_2$ SVV SV CI ScvO<sub>2</sub> **PVV** DO2 VO2 5 GEDV OER  $dCO_2$ OPS lactate ( NIRS **Tissue perfusion** 



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Computers in Biology and Medicine 41 (2011) 1022-1032

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Computers in Biology

R. A

journal homepage: www.elsevier.com/locate/cbm

#### The diagnosis of hypovolemia using advanced statistical methods

Gergely Bárdossy <sup>a,\*</sup>, Gábor Halász <sup>a</sup>, Tibor Gondos<sup>b</sup>

\* Budapest University of Technology and Economics, Department of Hydrodynamic, Systems, 1111 Budapest Müegyetem rkp. 3, Budapest, Hungary <sup>b</sup> Semmelweis University Budapest, Faculty of Health Sciences, 1088 Budapest, Vas u. 17, Hungary









#### Fluid therapy – in just 24 hours!



## The most important lesson



Auguste Rodin: The Thinker





Is physiology wrong?



## No, it's us, who misunderstand the data!



### "Together we win, divided we're slow!"

Jean-Louis VINCENT Daniel De BACKER Alan SUSTIC Ino HUSEDZINOVIC Jan BENES Jean-Louis TEBOUL Xavier MONNET Wolfgang HUBER Daniel REUTER Frank BRUNKHORST Ákos Csomós Béla FÜLESDI János FAZAKAS Lajos BOGÁR Zsolt MOLNÁR Giuseppe CITERIO Andrzej KÜBLER Małgorzata MIKASZEWSKA SOKOLEWICZ Mikhail KIROV Vladimir KULABUKOV Radmilo JANKOVIC Vojislava NESKOVIC Roman ZAHORECZ Matej PODBREGAR Mitja LAINSACK Mervyn SINGER Tamas SZAKMANY Yalim DIKMEN

Belgium Belgium Croatia Croatia Czech Republic France France Germany Germany Germany Hungary Hungary Hungary Hungary Hungary Italy Poland Poland Russia Russia Serbia Serbia Slovakia Slovenia Slovenia United Kingdom United Kingdom Turkey



### FREE for junior doctors!