

# Journal club

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Critical Care

RESEARCH

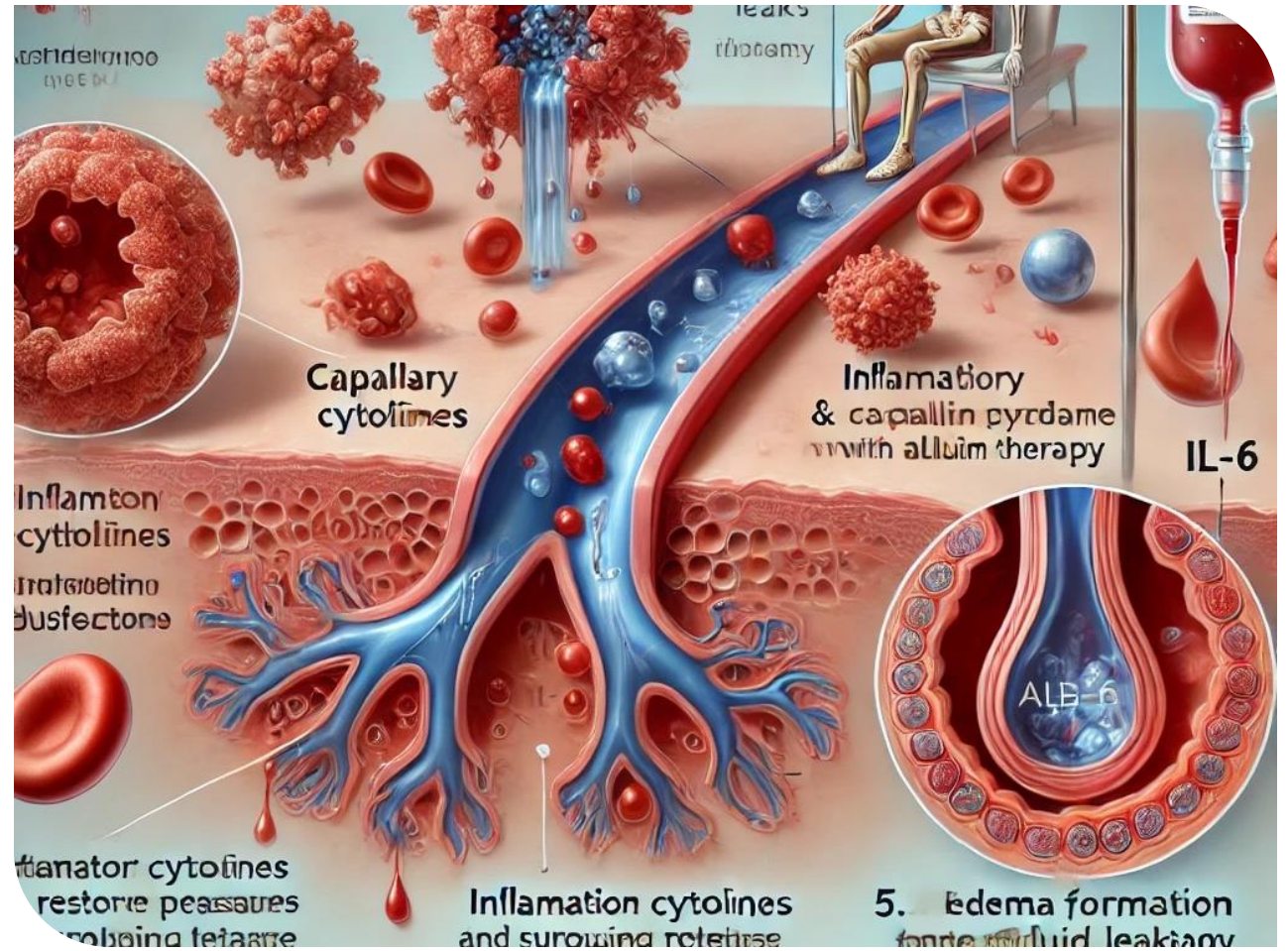
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## Net albumin leakage in patients in the ICU with suspected sepsis. A prospective analysis using mass balance calculations

Dag Seldén<sup>1\*</sup>, Nicolas Tardif<sup>2</sup>, Jan Wernerman<sup>1,2</sup>, Olav Rooyackers<sup>1,2</sup> and Åke Norberg<sup>1,2</sup>



Door Erik Koomen



10 maart 2025

# Journal club

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Introductie

02

Artikel

03

Impact op werk op  
PICU

# Principle thoughts about capillary leak and sepsis



Kidney International  
Volume 92, Issue 1, July 2017, Pages 37-46

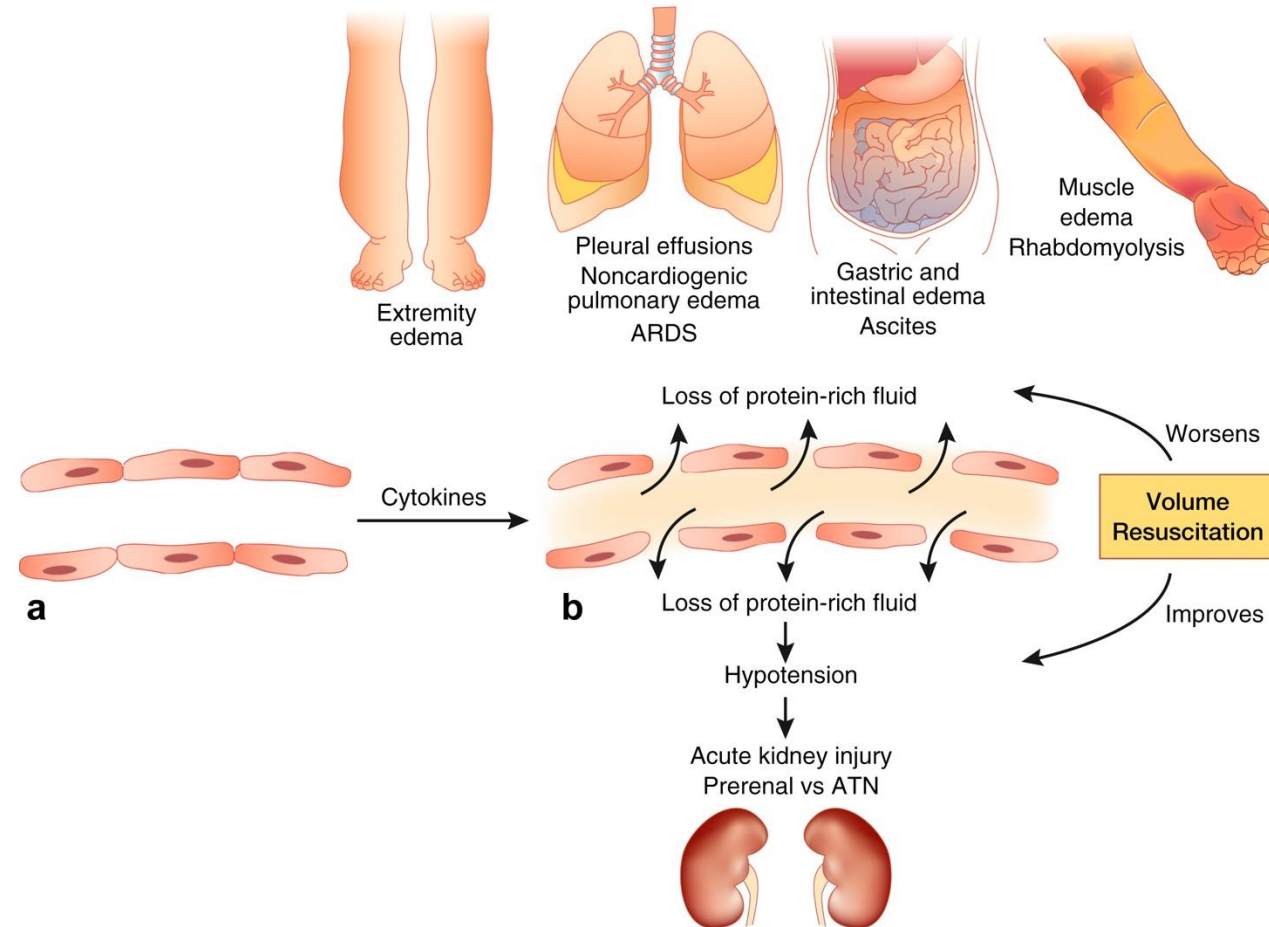


Review

## Capillary leak syndrome: etiologies, pathophysiology, and management

Eric Siddall<sup>1</sup>, Minesh Khatri<sup>2</sup>, Jai Radhakrishnan<sup>1</sup> ✉

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# Net albumin leakage in patients in the ICU with suspected sepsis. A prospective analysis using mass balance calculations

Daan Seldén<sup>1\*</sup>, Nicolas Tardif<sup>2</sup>, Jan Wernerman<sup>1,2</sup>, Olav Roovackers<sup>1,2</sup> and Åke Norberg<sup>1,2</sup>

# Hypothesis

To evaluate NAL (Netto (leakage – lymf return) Albumin Leakeage) in ten ICU patients with suspected sepsis

Hypothese: There is a net positive leakage

Secondary aims included investigating associations between NAL and fluid overload, glycocalyx shedding products, and cytokines, as well as identifying factors associated with it.

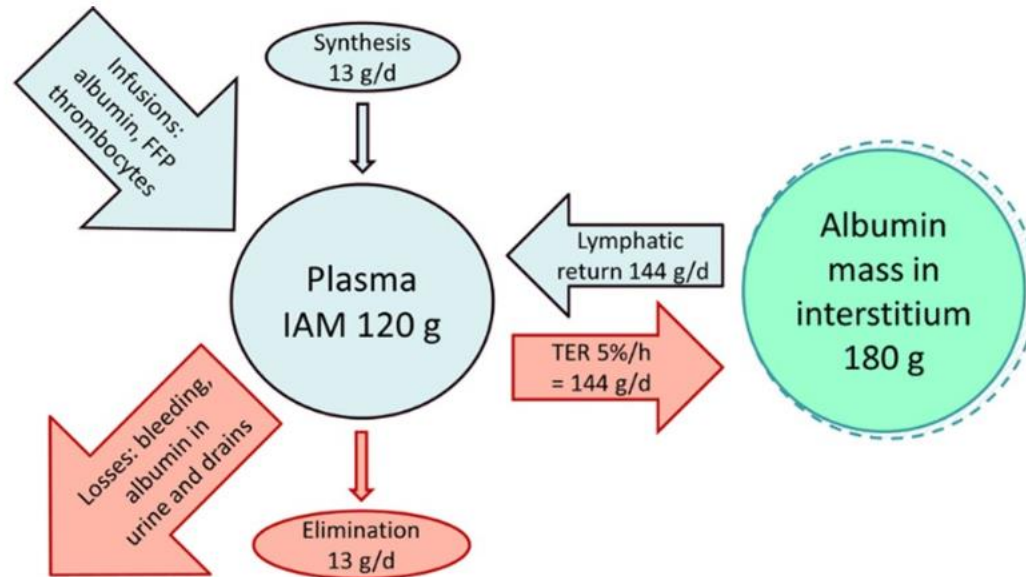
# Methods

## Prospective observational study

**N=10, in de eerste 12 uur verdenking sepsis**

**Albumin, hematocrit, and hemoglobin levels were sampled at 0, 1, 2, 4, 8, and 24 h. NAL was estimated using mass balance calculations, comparing proportional changes in albumin and hemoglobin concentrations over time, adjusted for albumin and hemoglobin infusions and losses.**





**Fig. 1** Albumin turnover and metabolism in a healthy adult. This overview illustrates albumin turnover between the intravascular albumin mass (IAM = 120 g) and the interstitial pool (180 g). Transcapillary escape rate (TER = 144 g/day) is balanced by lymphatic return (144 g/day). Synthesis (13 g/day), elimination (13 g/day), infusions (e.g., albumin, platelets, FFP), and losses (e.g., bleeding, urinary albumin, drains) dynamically influence IAM. Synthesis and elimination are not included in the mass balance calculations but are unlikely to affect results over the 24-h study period. IAM = Intravascular Albumin Mass; MHB = Intravascular Hemoglobin mass; FFP = Fresh Frozen Plasma

# Results

**Table 2** Levels of net albumin leakage, glycocalyx shedding products, cytokines and fluid balance

	Hour 0	Hour 4	Hour 24	p-value	Reference ranges <sup>1</sup>
Net albumin leakage [g]	0	3 ± 8	8 ± 10	0.049 <sup>a</sup>	NA
Syndecan-1 [ng/ml]	410 (140—1122)	155 (112—1208)	445 (165—840)	0.69 <sup>b</sup>	26–439
Hyaluronan [ng/ml]	1081 (418—3294)	815 (527—4234)	524 (95—6932)	0.22 <sup>äa</sup>	5–24
Interleukin-6 [pg/ml]	1114 (132—14,556)	973 (322—12,114)	188 (40—1214)	0.25 <sup>b</sup>	1–2
Interleukin-8 [pg/ml]	155 (38—2432)	171 (37—613)	73 (41—1238)	0.80 <sup>b</sup>	4–10
Tumor necrosis factor-α [pg/ml]	203 (60—3216)	249 (69—1334)	82 (51—615)	0.20 <sup>b</sup>	12–32
Fluid balance [L]	0	1.3 ± 0.8	3.7 ± 3.2	0.0058 <sup>a</sup>	NA

Values are presented as median (range) or mean ± standard deviation, as appropriate. <sup>1</sup> based on analysis of samples from 35 healthy volunteers (24 females, 11 males), aged 39.5 (22–50) years, with a height of 1.68 (1.55–1.90) m, and a body weight of 87.2 (69.6–138.8) kg(22). <sup>a</sup>Anova with the Greenhouse–Geisser correction, <sup>b</sup>Mixed effects model. NA= Not applicable



# Interpretation

- Our cohort of severely ill patients had a lower NAL,  $8 \pm 10$  g, compared to elective patients undergoing major surgery  $24 \pm 17$  g
- We speculate that most of the NAL might have happened before ICU admission
- In our post hoc analysis we correlated albumin levels with NAL and found a positive value but that did not reach statistical significance.
- Post hoc regression analysis revealed that any form of albumin supplementation was associated with an increased NAL

# Strengths and limitations

- **This study provides new data on albumin kinetics in a very sick cohort with sepsis, describing the net effects of capillary leakage counterbalanced by lymphatic return.**
- **The use of mass balance calculations for NAL in septic patients is novel and lacks a defined "time zero" compared to surgical cohorts. Enrolment occurred within 12 h of ICU admission, and patients could be recruited from either the ward or emergency room. Rapid plasma volume changes can occur quickly and likely complicated interpretations of albumin homeostasis preceding enrolment**

# Conclusion

**In a 24-h period, our study observed a NAL of  $8 \pm 10$  g from the circulation, presumably into the interstitium, in 10 patients with suspected sepsis.**

**There was a weak correlation between NAL and pro-inflammatory cytokines during the first 4 h of ICU stay. However, no correlation was found between NAL and either fluid balance or glycocalyx shedding products. The administration of albumin infusions appeared to increase the NAL.**

# Impact op de PICU

**Huidige beleid met terughoudendheid met Albumine in sepsis lijkt gepast, maar spelt zeker ook bij grote abdominale chirurgie**

**Bevestiging huidige beleid**