

ECOS-TCS

INTERNATIONAL CONGRESS

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JUNE 24-25 2024

PARIS JICP

16 RUE JEAN REY 75015

Endotoxin translocation during ischemia-reperfusion (*in cardiogenic shock*):
Is there a role for adsorptive technology?

Maxime Nguyen

Dijon University Hospital

Conflicts of interest

Baxter – Direct payement / Research grant

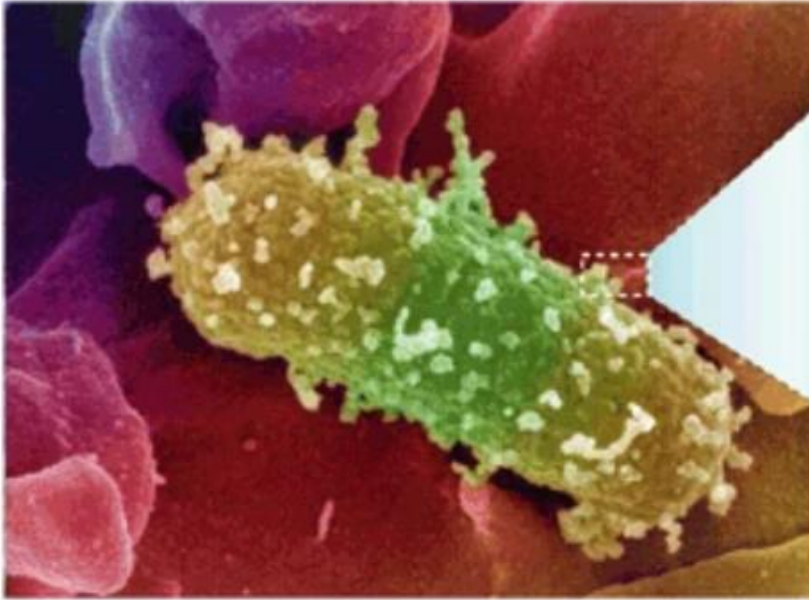
Fresenius – Formation fee

Pfizer – Congres fee

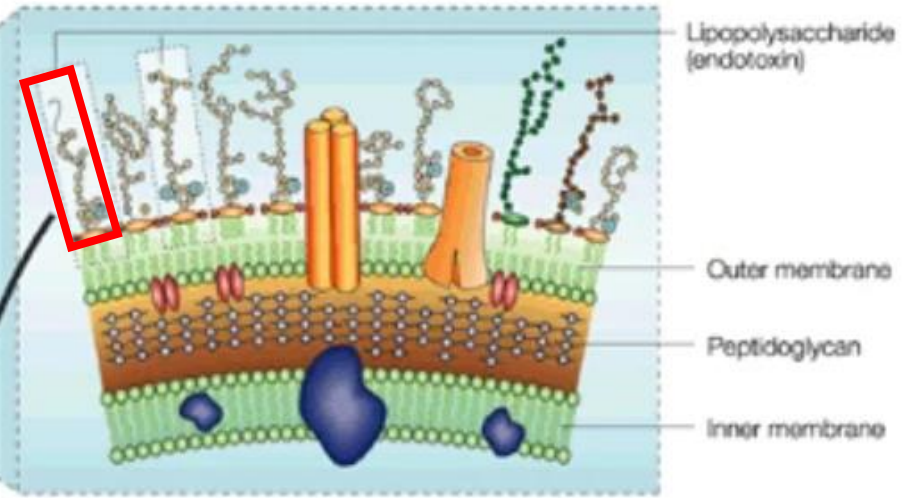
What are translocation and endotoxemia?

Endotoxin, Gram negative bacteria, PAMPs

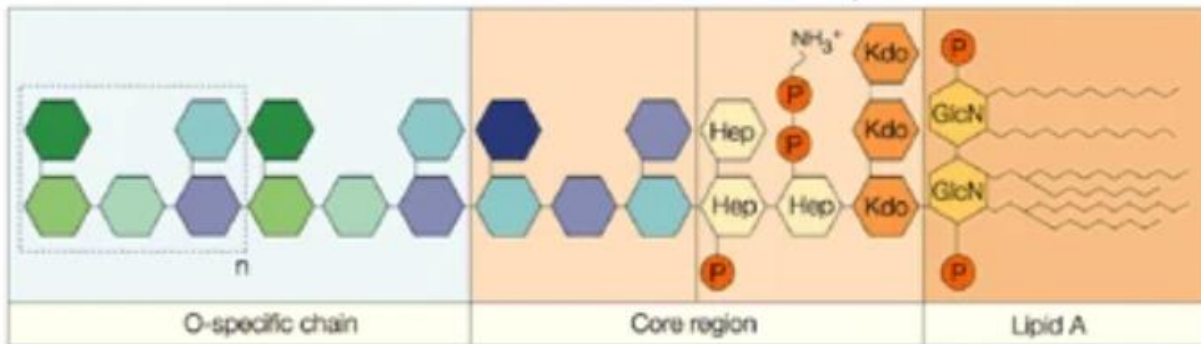
Bacterial cell



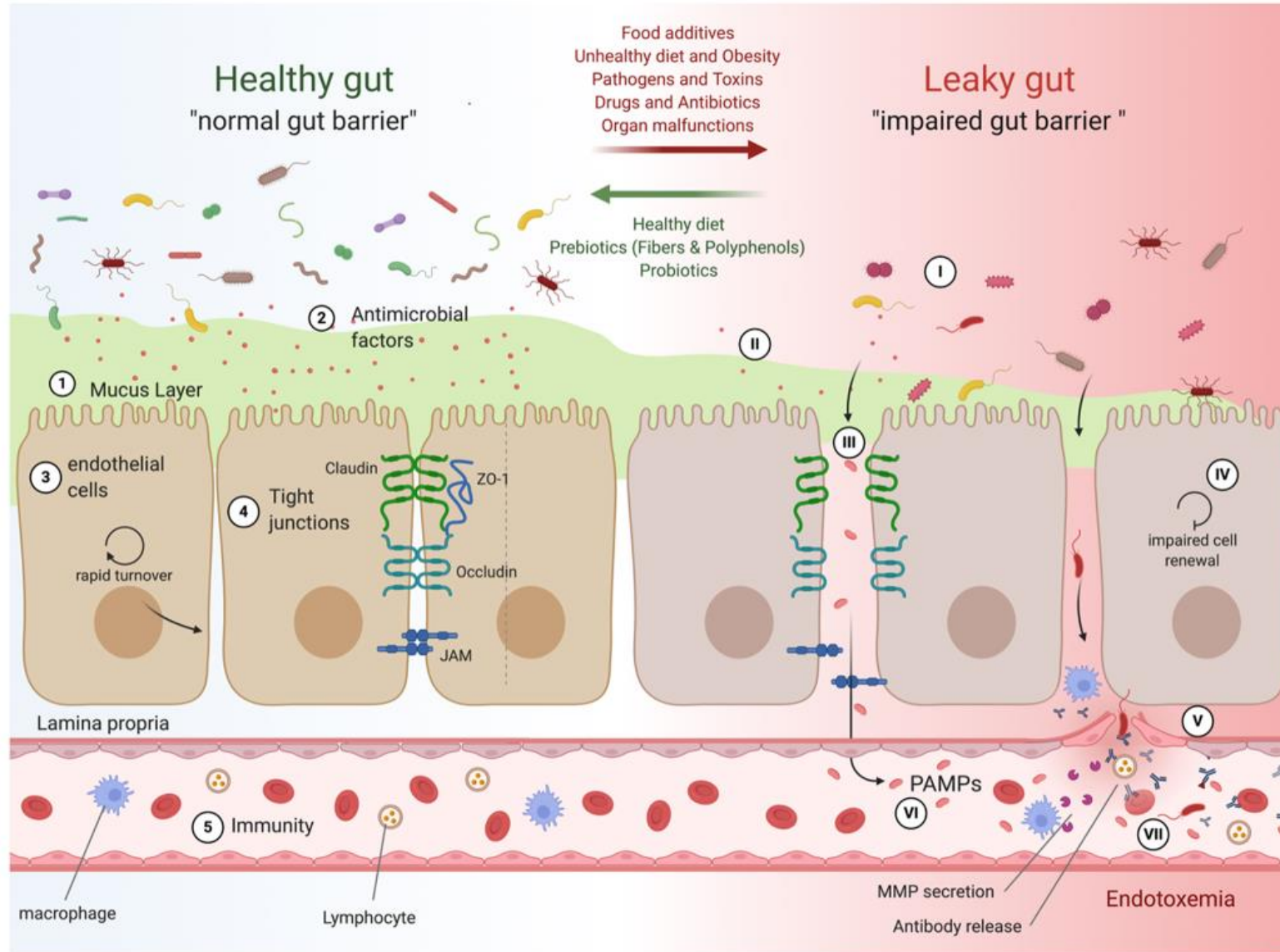
Cell Wall



Lipopolysaccharide, endotoxin

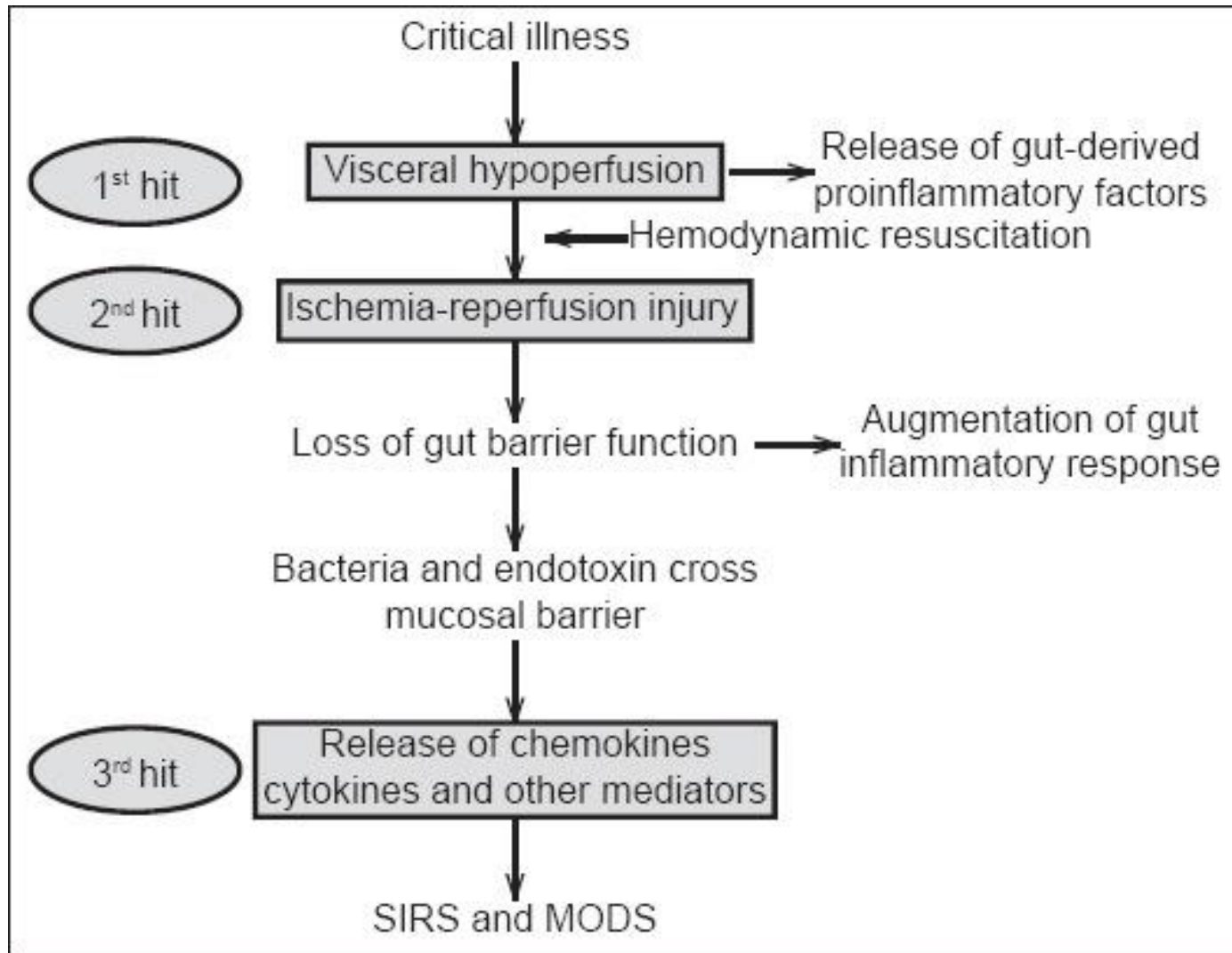


Gut Barrier



Journal of Endocrinology, 248(2), R67-R82.

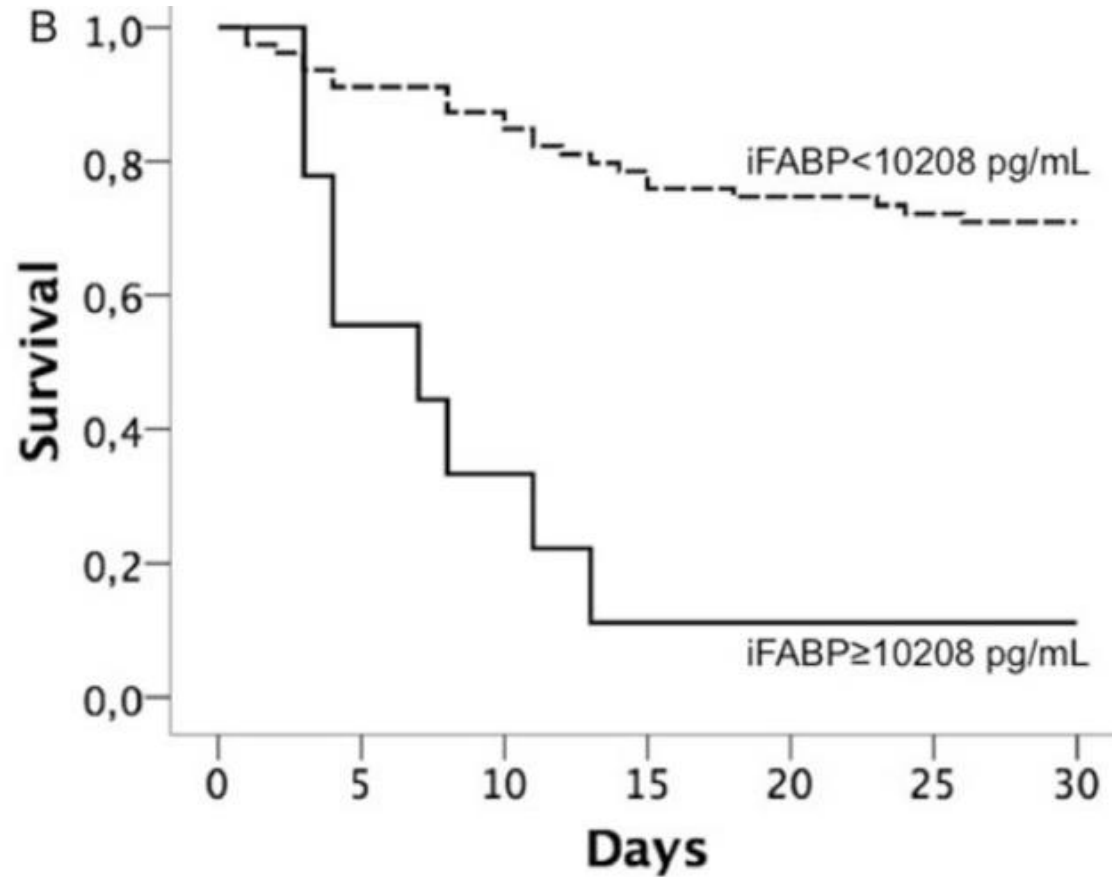
Ischemia reperfusion is a major aggression factor



Annals of Gastroenterology: Quarterly Publication of the Hellenic Society of Gastroenterology, 28(3), 309.

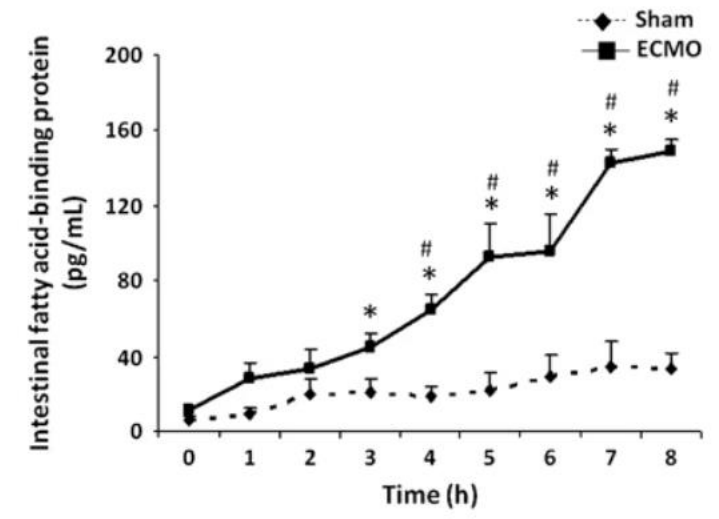
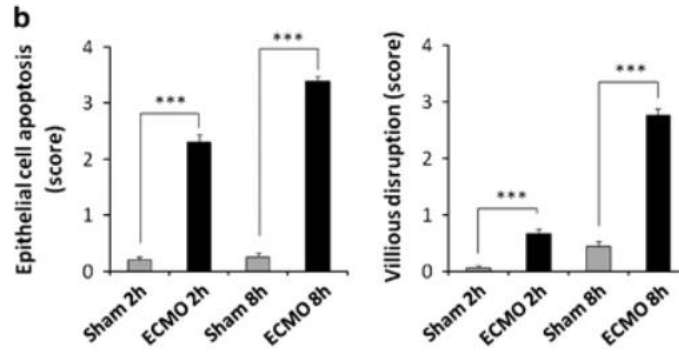
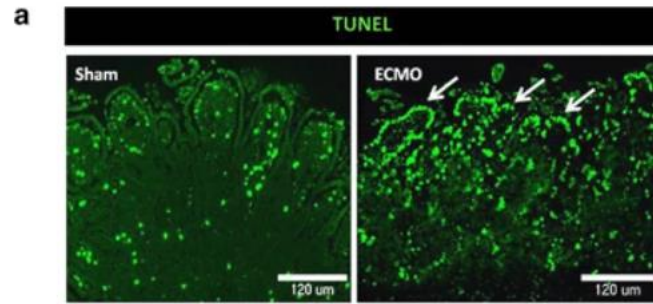
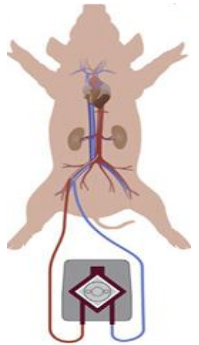
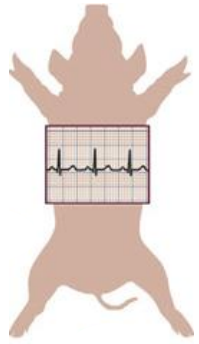
Cardiogenic shock gut injury and mortality

90 patients acute heart failure or cardiogenic shock



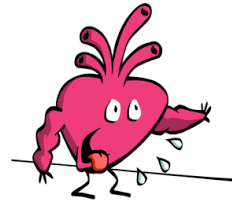
Kastl, S. P., Krychtiuk, K. A., Lenz, M., Distelmaier, K., Goliasch, G., Huber, K., ... & Speidl, W. S. (2019). Intestinal fatty acid binding protein is associated with mortality in patients with acute heart failure or cardiogenic shock. *Shock*, 51(4), 410-415.

Ecmo is associated with gut injury



Why does translocation matters in cardiogenic shock?

Inflammation is central in the pathogenesis of cardiogenic shock



Acute cardiac injury

↓ Cardiac Output

Peripheral vasoconstriction

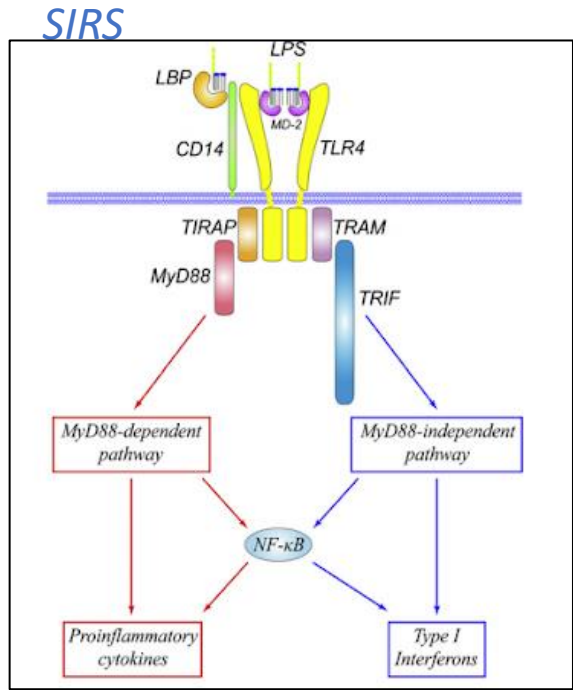
SIRS

Pulmonary congestion

Systemic & cardiac ischaemia

↓↓↓ Cardiac Output

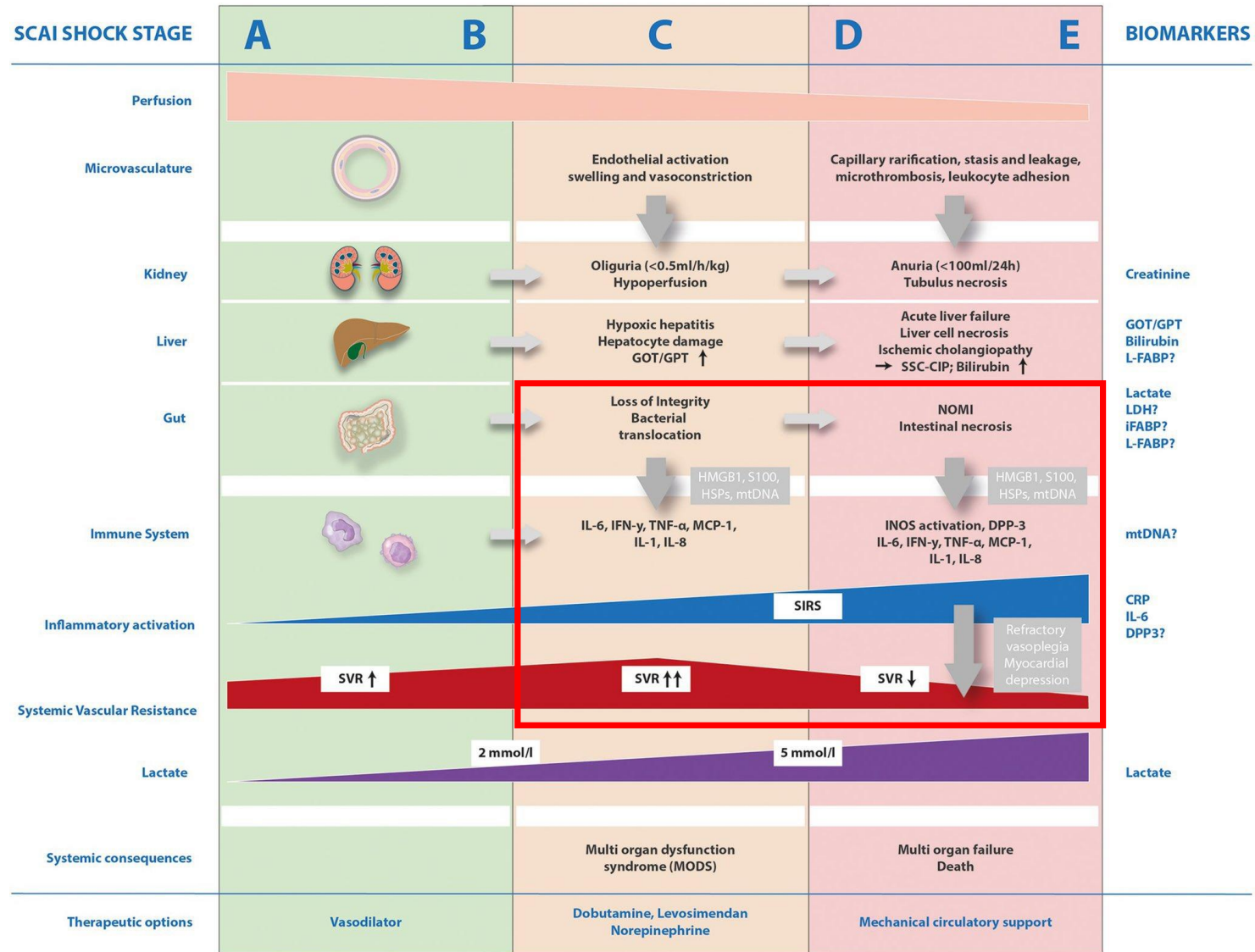
Death



Lu, Y. C., Yeh, W. C., & Ohashi, P. S. (2008). LPS/TLR4 signal transduction pathway. *Cytokine*, 42(2), 145-151.

Jones, T. L., Nakamura, K., & McCabe, J. M. (2019). Cardiogenic shock: evolving definitions and future directions in management. *Open Heart*, 6(1), e000960.

Gut injury leads to translocation in cardiogenic shock

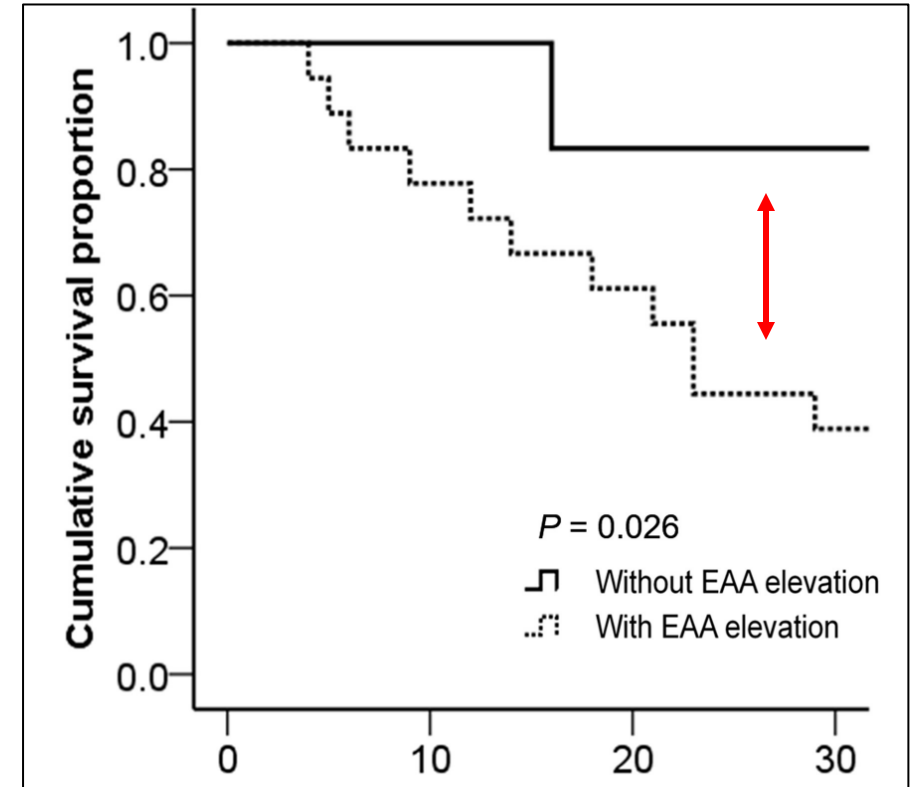


Translocation is associated with higher mortality

Prospective observational study 54 ECMO (VA and VV), evaluation of endotoxin activity

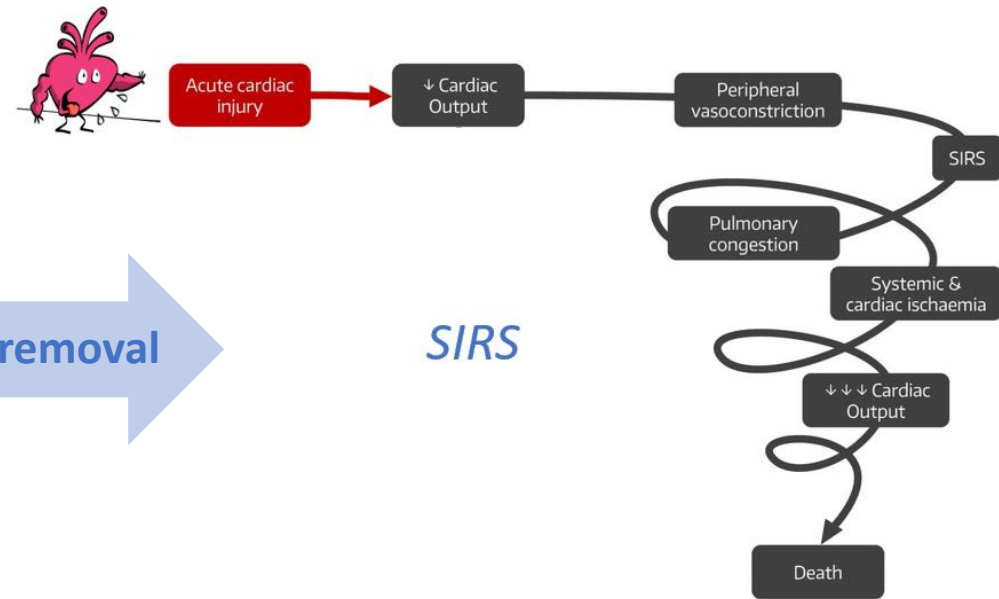
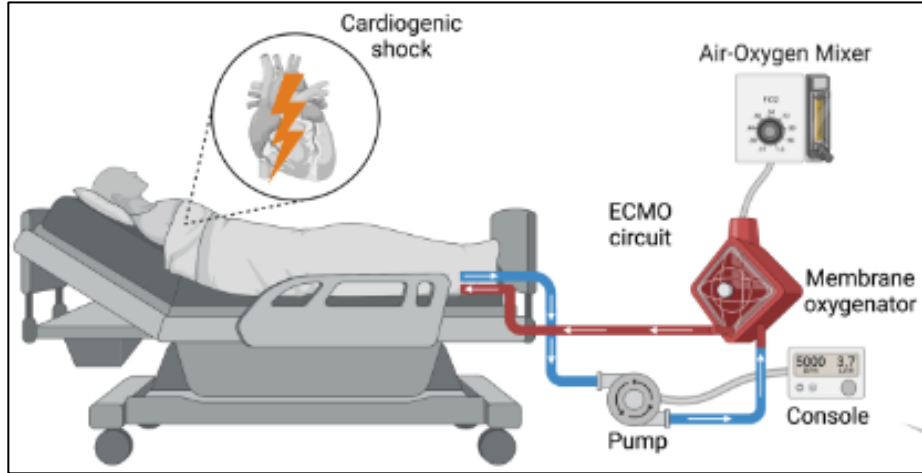
	VV-ECMO (n = 15)	VA-ECMO (n = 39)
ECMO indication		
E-CPR	-	16
Heart failure	-	17
Postcardiotomy	-	4
Septic shock	-	2
ARDS	15	-
EAA level		
T1 median (IQR)	0.44 (0.31–0.71)	0.33 (0.22–0.50)
T2 median (IQR)	0.50 (0.36–0.66)	0.38 (0.28–0.52)
T3 median (IQR)	0.50 (0.33–0.78)	0.40 (0.23–0.57)
T4 median (IQR)	0.49 (0.37–0.59)	0.44 (0.29–0.56)
ECMO free days ^a	0 (0–17)	14 (0–24)
ICU free days ^b	0	0 (0–2)
30-day survival, n (%)	11 (73%)	21 (54%)

High EAA level (≥ 0.6) 9% VA-ECMO



Should we remove endotoxin in cardiogenic shock?

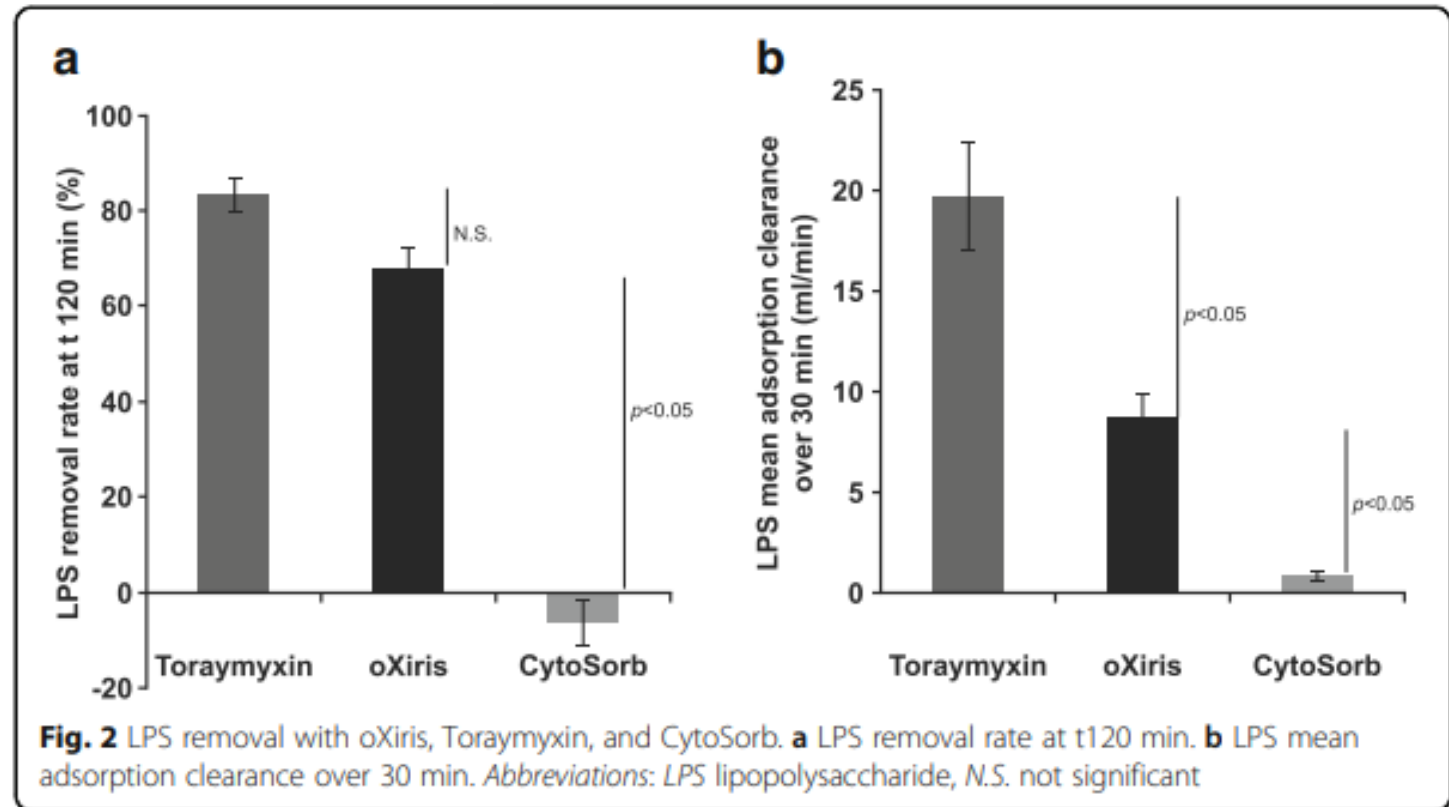
Rational for extracorporeal endotoxin removal





In vitro comparison of the adsorption of inflammatory mediators by blood purification devices

Benjamin Malard^{1*}, Corine Lambert¹ and John A. Kellum²



Early use of polymyxin B hemoperfusion in patients with septic shock due to peritonitis: a multicenter randomized control trial

Early Use of Polymyxin B Hemoperfusion in Abdominal Septic Shock

The EUPHAS Randomized Controlled Trial

Effect of Targeted Polymyxin B Hemoperfusion on 28-Day Mortality in Patients With Septic Shock and Elevated Endotoxin Level

The EUPHRATES Randomized Clinical Trial

Is there a role for adsorptive technology?

Existing rationnal

Little data

=> Need to provide evidence

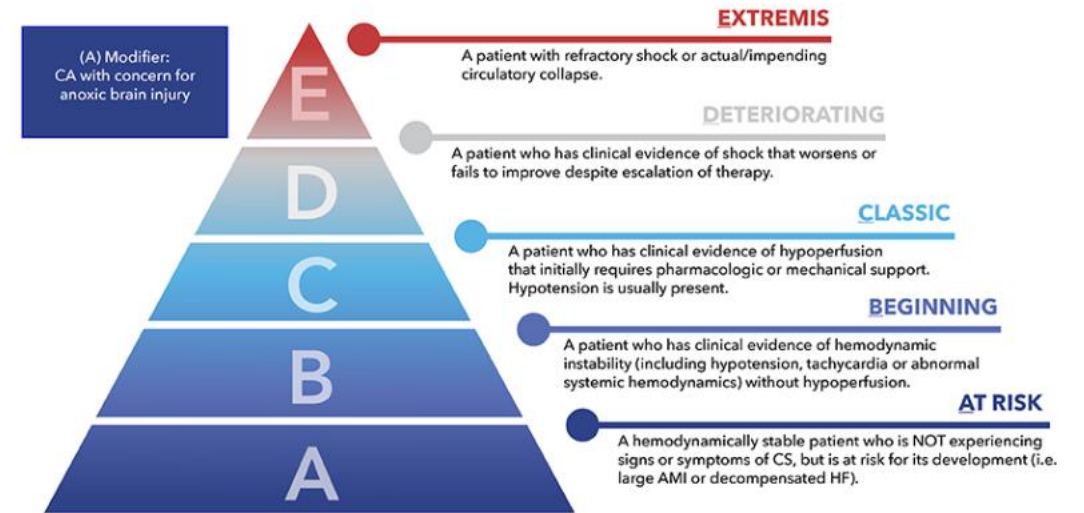
Unanswered questions and challenges

Heterogeneity in cardiogenic shock

Etiology

Severity

Organ injury

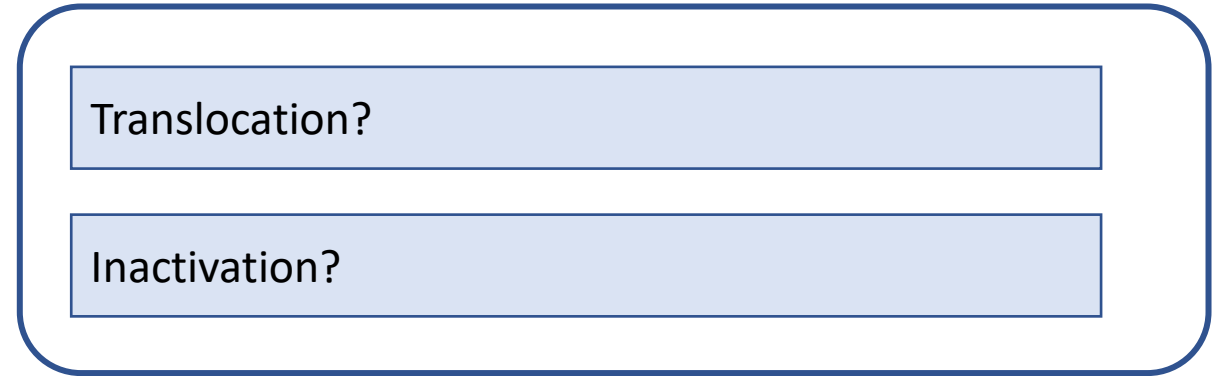


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Translocation is associated with higher mortality

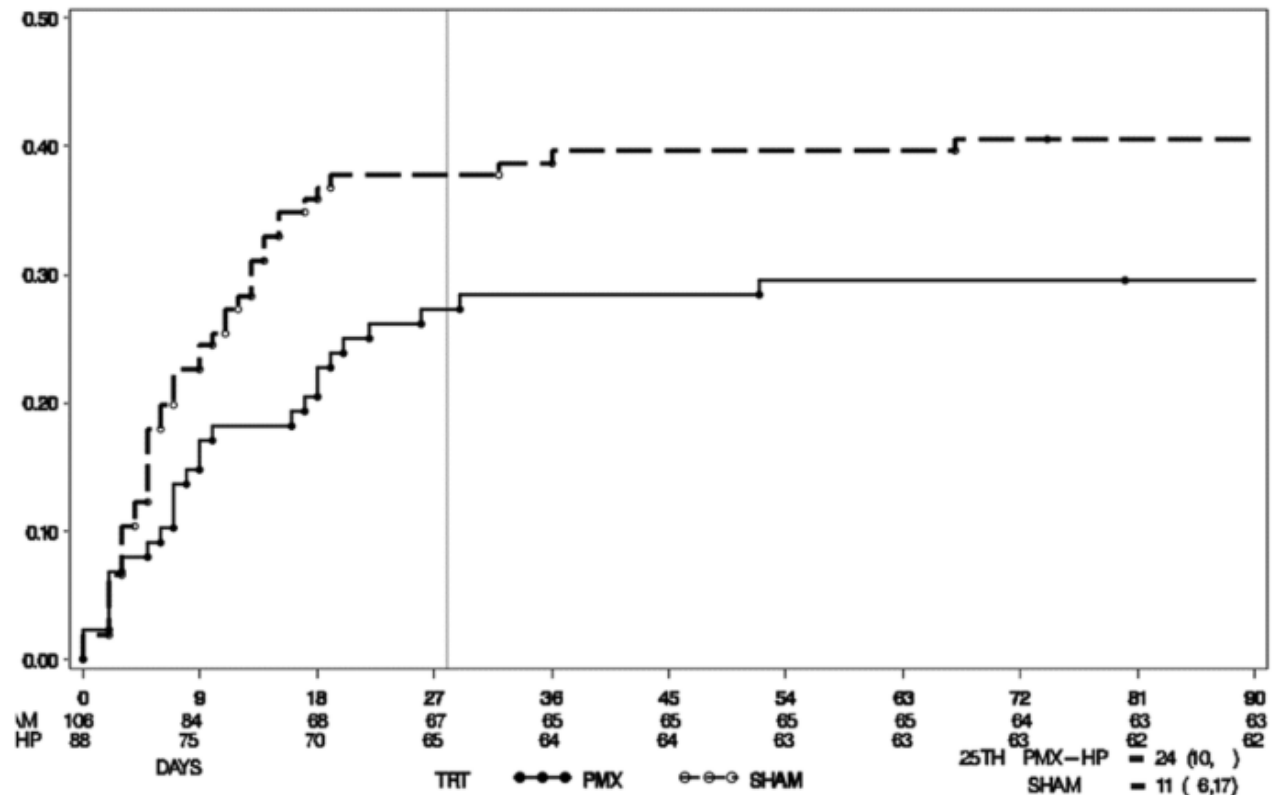
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Polymyxin B hemoperfusion in endotoxemic septic shock patients without extreme endotoxemia: a post hoc analysis of the EUPHRATES trial



Contribution of endotoxin removal to immune homeostasis?

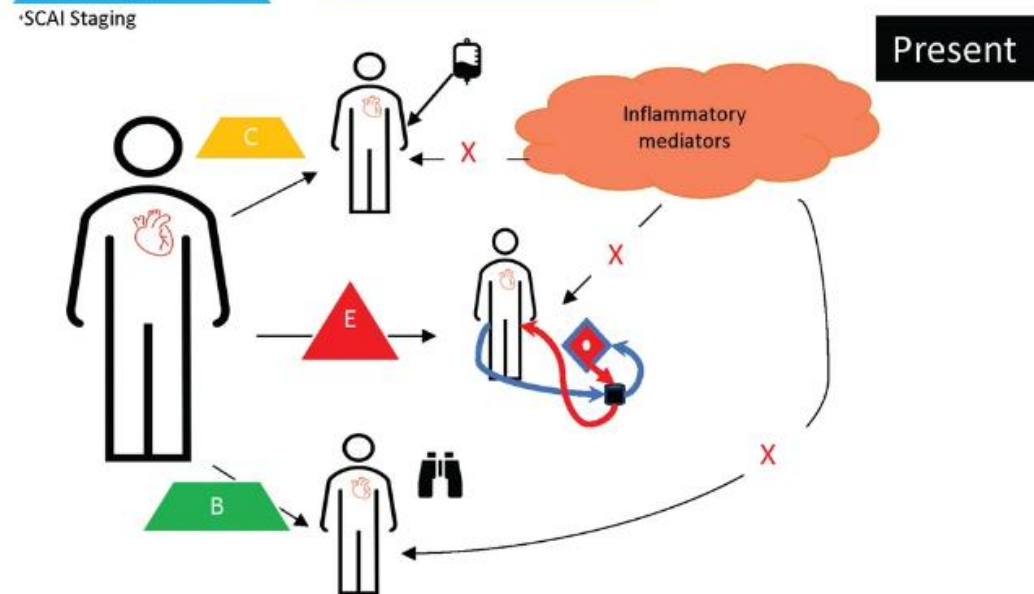
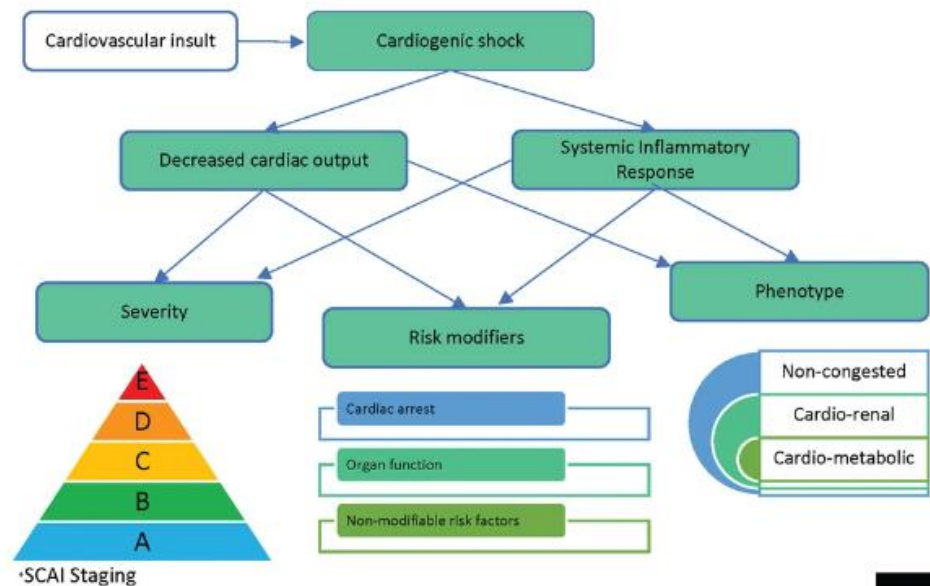
REVIEW

Open Access



Extending the 'host response' paradigm from sepsis to cardiogenic shock: evidence, limitations and opportunities

Marie Buckel^{1†}, Patrick Maclean^{2†}, Julian C. Knight^{2,3}, Patrick R. Lawler^{4,5} and Alastair G. Proudfoot^{1,6*}



Need for precision medicine?

1/ Identify population

Endotoxemia (#target)

Timing / dose

Competition with endogenous systems

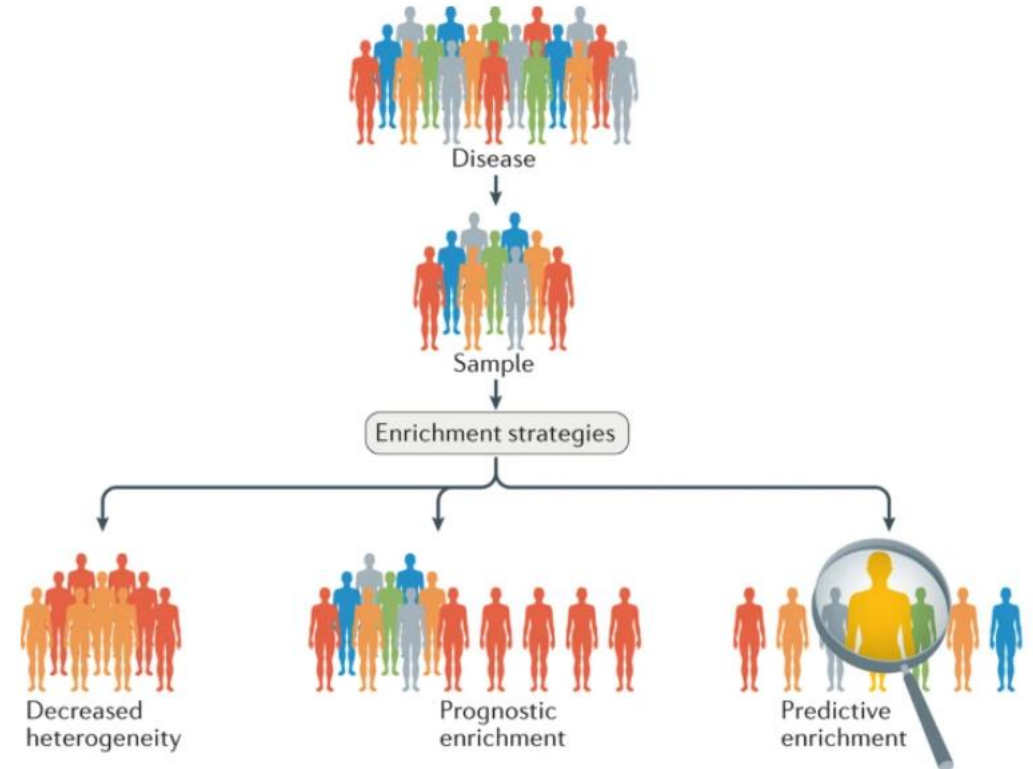
Significant contribution to SIRS

Immunity (#endotypes?)

2/ Develop enrichment strategies

3/ Implement the intervention

4/ Monitor the intervention



« One does not fit them all »

Antman, E. M., & Loscalzo, J. (2016). Precision medicine in cardiology. *Nature Reviews Cardiology*, 13(10), 591-602.