D.U. THERAPEUTIQUE ANTI-INFECTIEUSE
2026

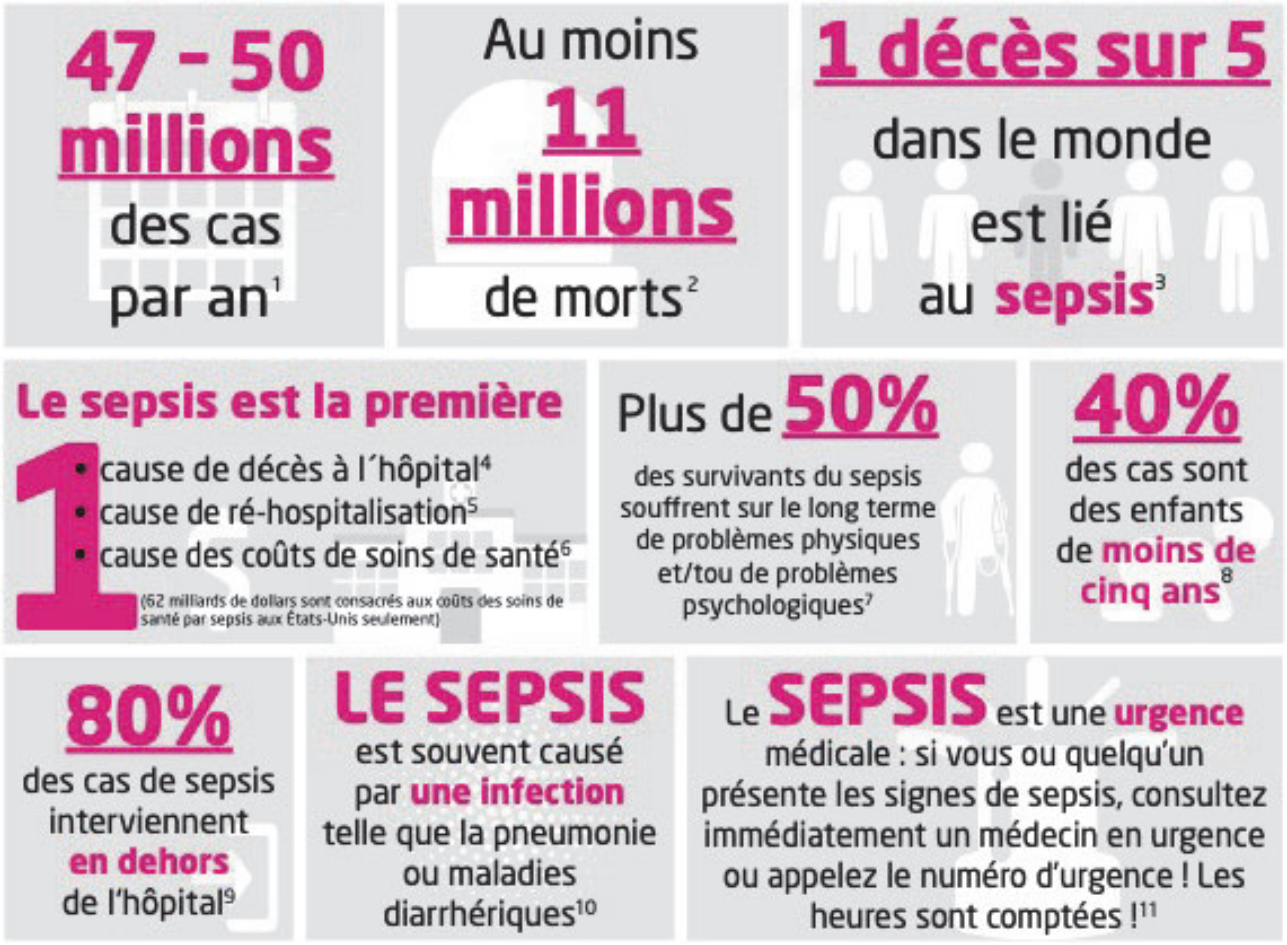
Sepsis

Antoine Dewitte

Service d'Anesthésie-Réanimation Magellan, CHU de Bordeaux

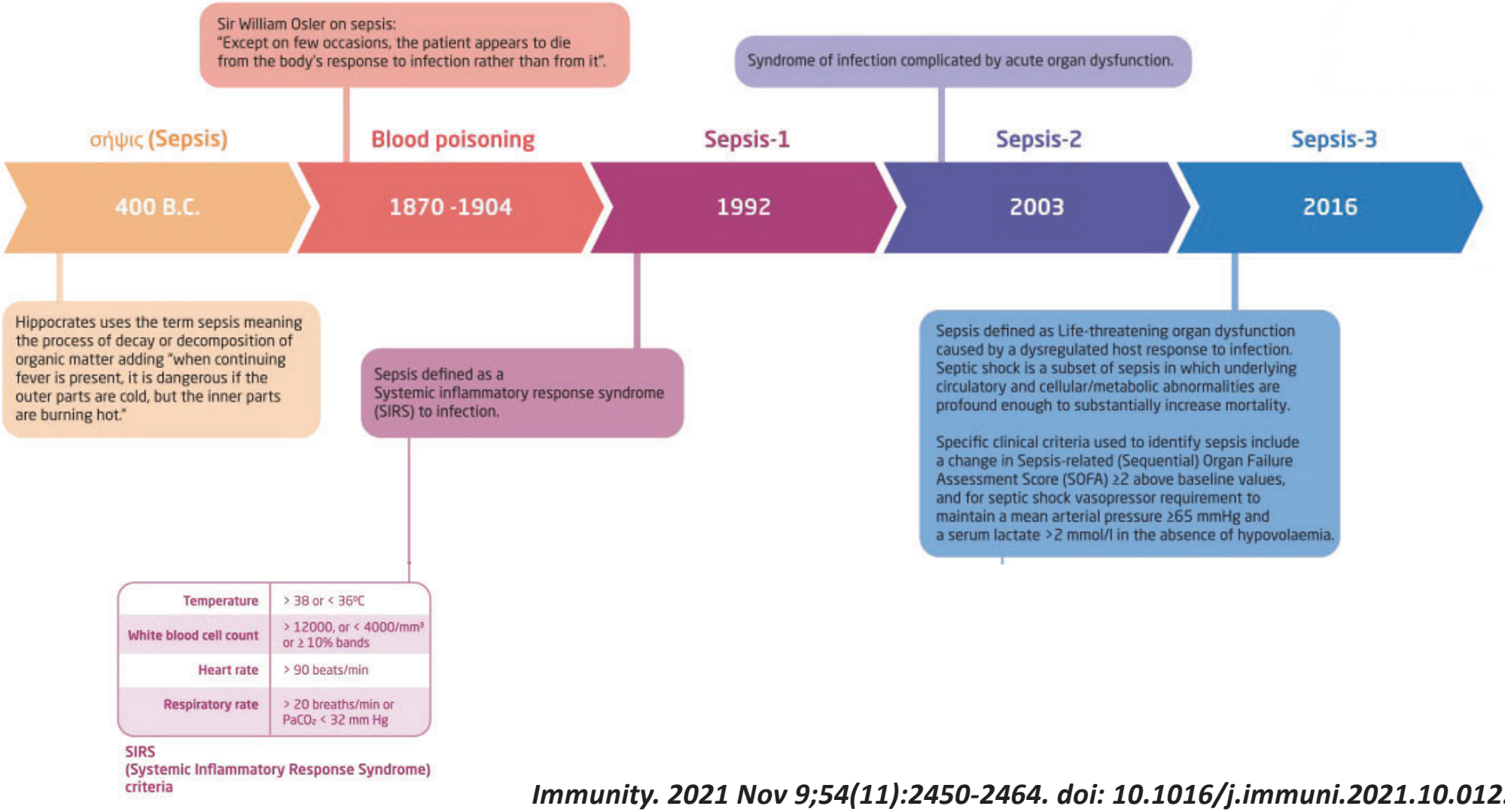
ImmunoConcEpT, Université Bordeaux

2017



N Engl J Med. 2017 Aug 3;377(5):414-417
www.worldsepsisday.org

Définition



Immunity. 2021 Nov 9;54(11):2450-2464. doi: 10.1016/j.immuni.2021.10.012.

Définition

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Mervyn Singer, MD, FRCP; Clifford S. Deutschman, MD, MS; Christopher Warren Seymour, MD, MSc; Manu Shankar-Hari, MSc, MD, FFICM; Djillali Annane, MD, PhD; Michael Bauer, MD; Rinaldo Bellomo, MD; Gordon R. Bernard, MD; Jean-Daniel Chiche, MD, PhD; Craig M. Coopersmith, MD; Richard S. Hotchkiss, MD; Mitchell M. Levy, MD; John C. Marshall, MD; Greg S. Martin, MD, MSc; Steven M. Opal, MD; Gordon D. Rubenfeld, MD, MS; Tom van der Poll, MD, PhD; Jean-Louis Vincent, MD, PhD; Derek C. Angus, MD, MPH

- Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.
- Organ dysfunction can be identified as an acute change in total SOFA score ≥2 points consequent to the infection.

			3	4
Pao_2/Fio_2, mm Hg (kPa)	≥400 (53.3)	<400 (53.3)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
Coagulation					
Platelets, $\times 10^3/\mu L$	≥150	<150	<100	<50	<20
Liver					
Bilirubin, mg/dL (μmol/L)	<1.2 (20)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	>12.0 (204)
Cardiovascular	MAP ≥70 mm Hg	MAP <70 mm Hg	Dopamine <5 or dobutamine (any dose)[b]	Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1[b]	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1[b]
Central nervous system					
Glasgow Coma Scale score[c]	15	13-14	10-12	6-9	<6
Renal					
Creatinine, mg/dL (μmol/L)	<1.2 (110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440)	>5.0 (440)
Urine output, mL/d				<500	<200

JAMA. 2016;315(8):801-810. doi:10.1001/jama.2016.0287

Définition

System	Score				
	0	1	2	3	4
Respiration					
Pao_2/Fio_2, mm Hg (kPa)	≥400 (53.3)	<400 (53.3)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
Coagulation					
Platelets, $\times 10^3/\mu L$	≥150	<150	<100	<50	<20
Liver					
Bilirubin, mg/dL (μmol/L)	<1.2 (20)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	>12.0 (204)
Cardiovascular	MAP ≥70 mm Hg	MAP <70 mm Hg	Dopamine <5 or dobutamine (any dose)[b]	Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1[b]	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1[b]
Central nervous system					
Glasgow Coma Scale score[c]	15	13-14	10-12	6-9	<6
Renal					
Creatinine, mg/dL (μmol/L)	<1.2 (110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440)	>5.0 (440)
Urine output, mL/d				<500	<200

JAMA. 2016;315(8):801-810. doi:10.1001/jama.2016.0287

Définition

Quick SOFA score Criteria

Respiratory rate ≥22/min

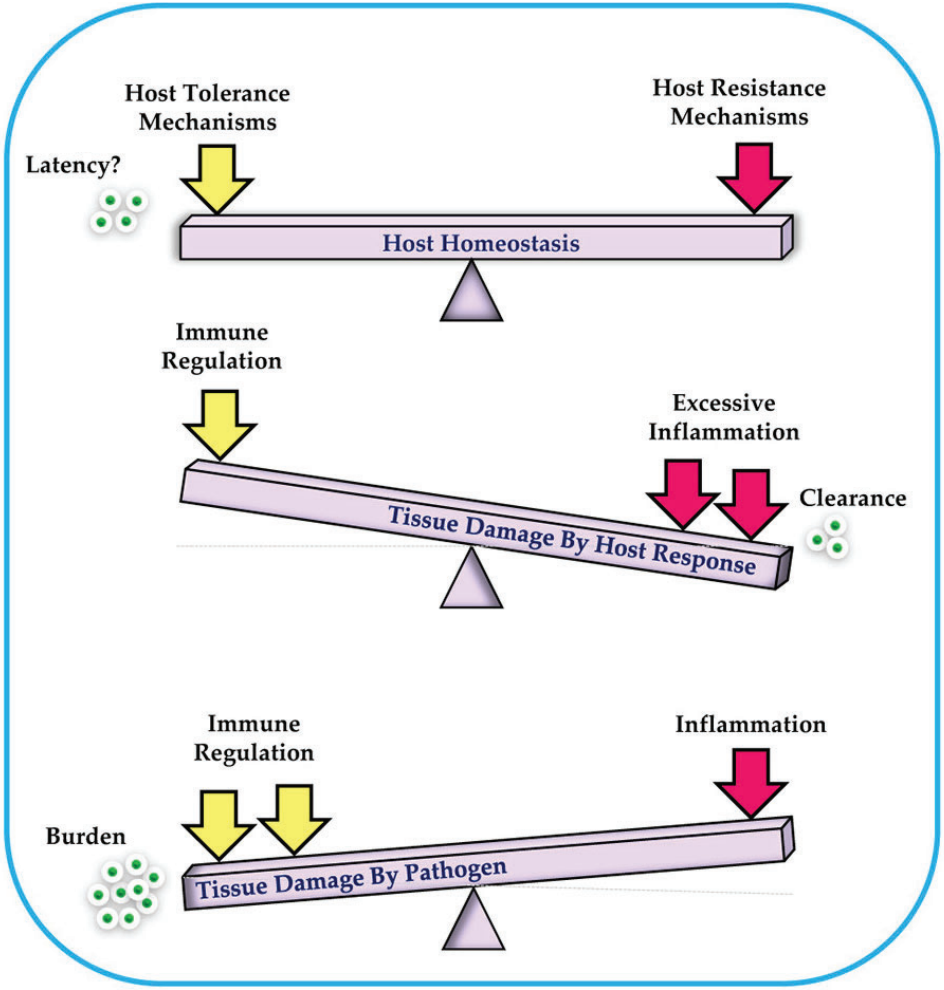
Altered mentation

Systolic blood pressure ≤100 mm Hg

JAMA. 2016;315(8):801-810

Définition **Physiopathologie**

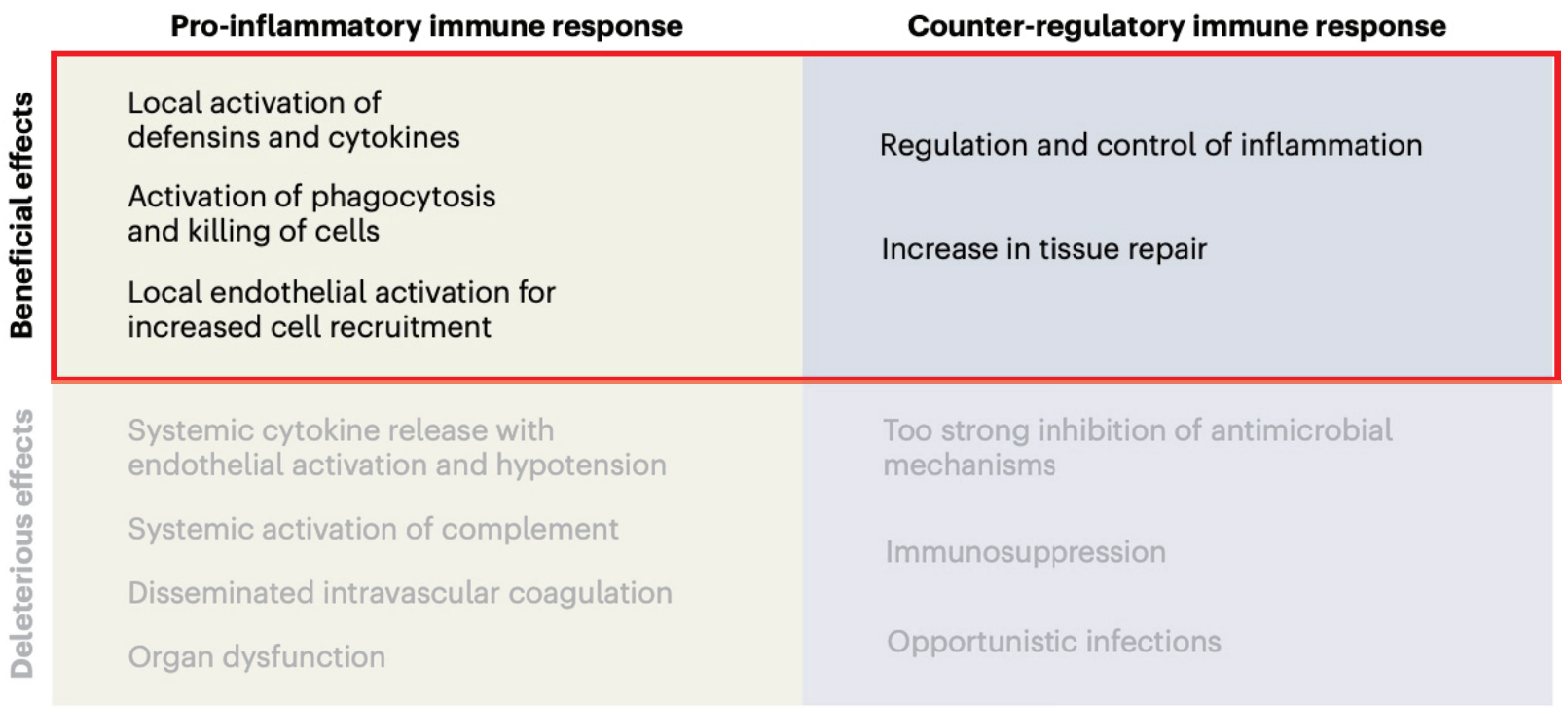
Tolérance



Résistance

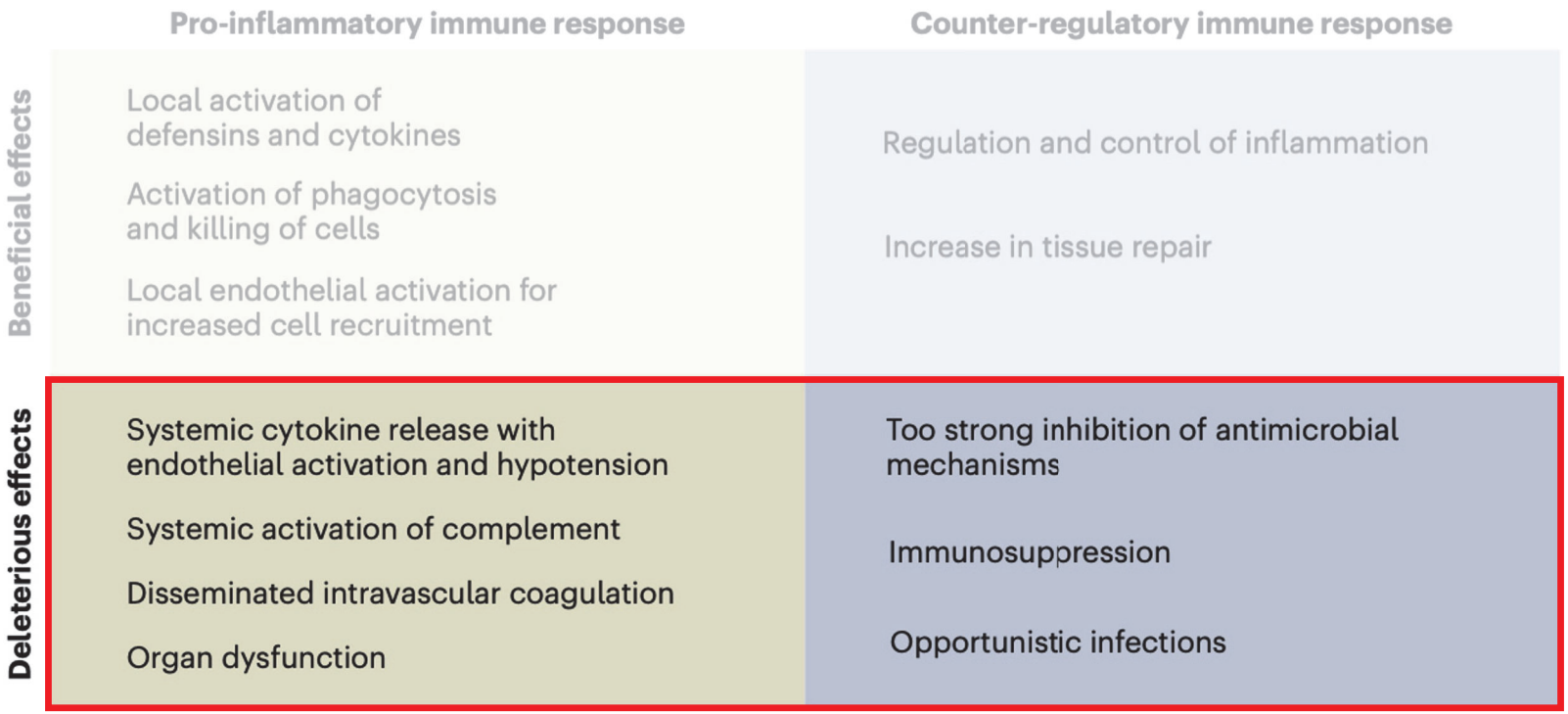
Front Immunol . 2019 Jan 29:10:66. doi: 10.3389/fimmu.2019.00066

Définition **Physiopathologie**



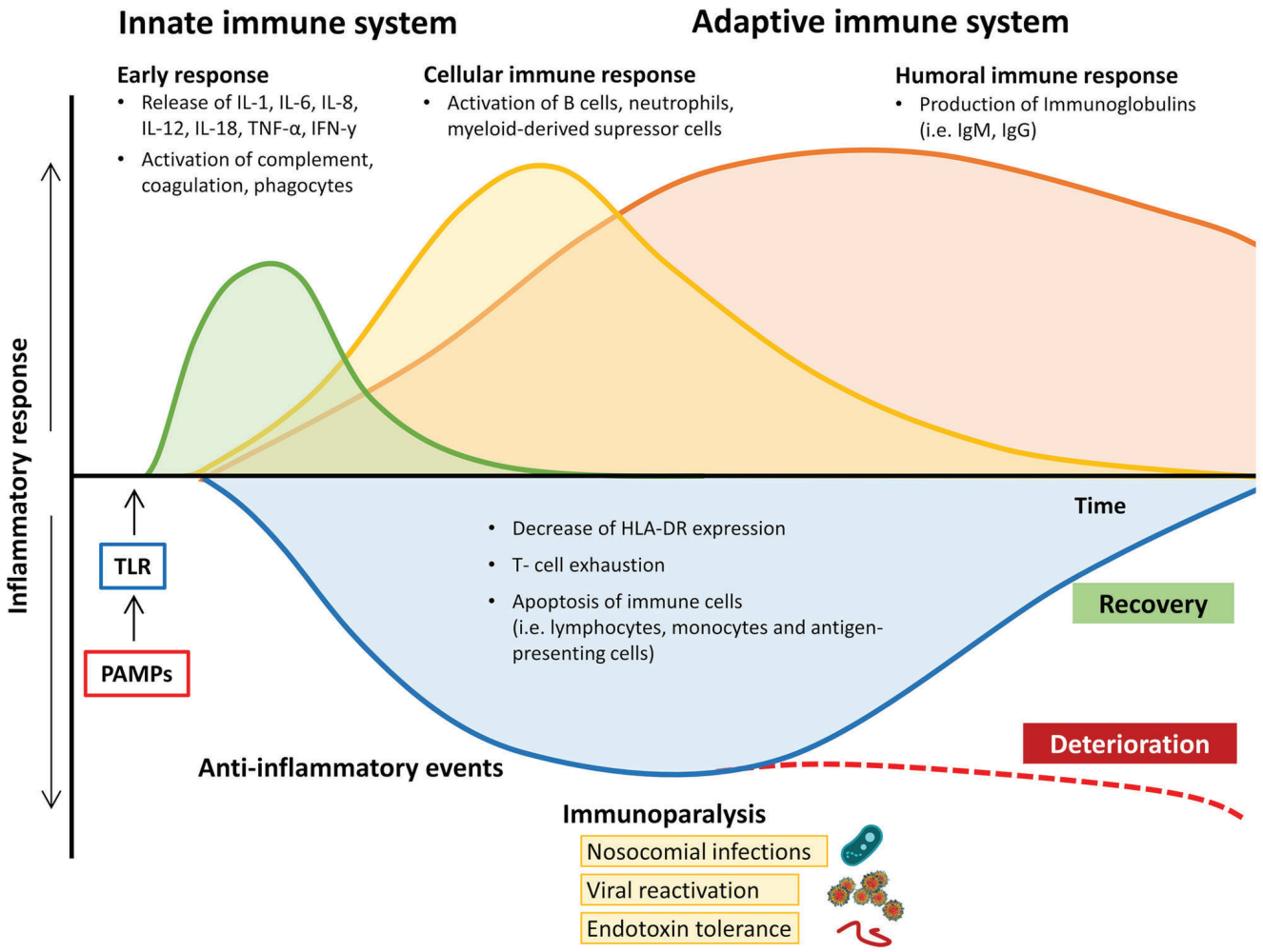
Nature Immunology, Giamarellos-Bourboulis et al, 2024

Définition **Physiopathologie**



Nature Immunology, Giamarellos-Bourboulis et al, 2024

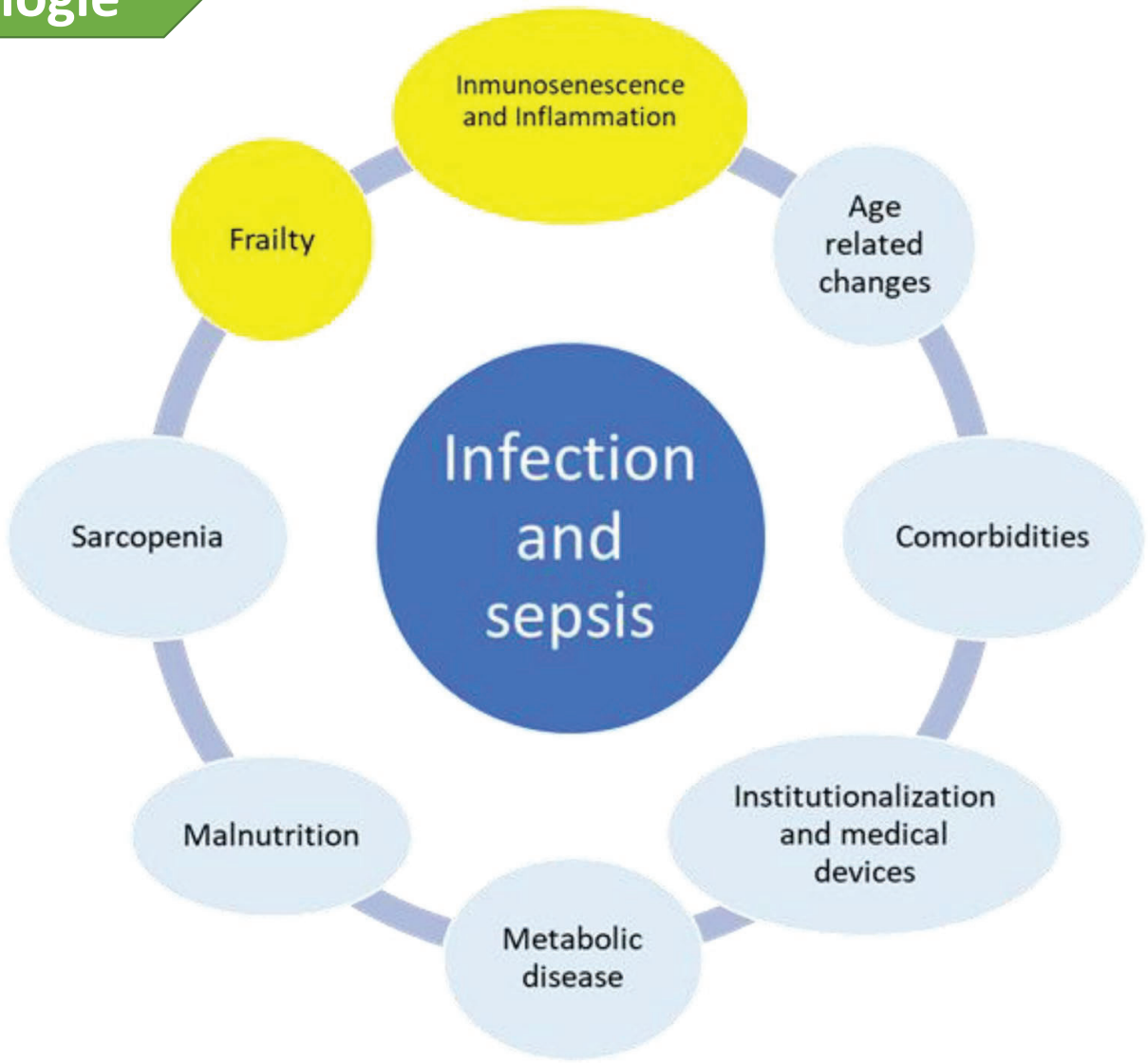
Définition **Physiopathologie**



Front. Med. 8:628302. doi: 10.3389/fmed.2021.628302

Définition **Physiopathologie**

- **Score de fragilité (index de Charlson)**
- **« Inflammaging »**
- **Réduction des réserves physiologiques et métaboliques associée au vieillissement**



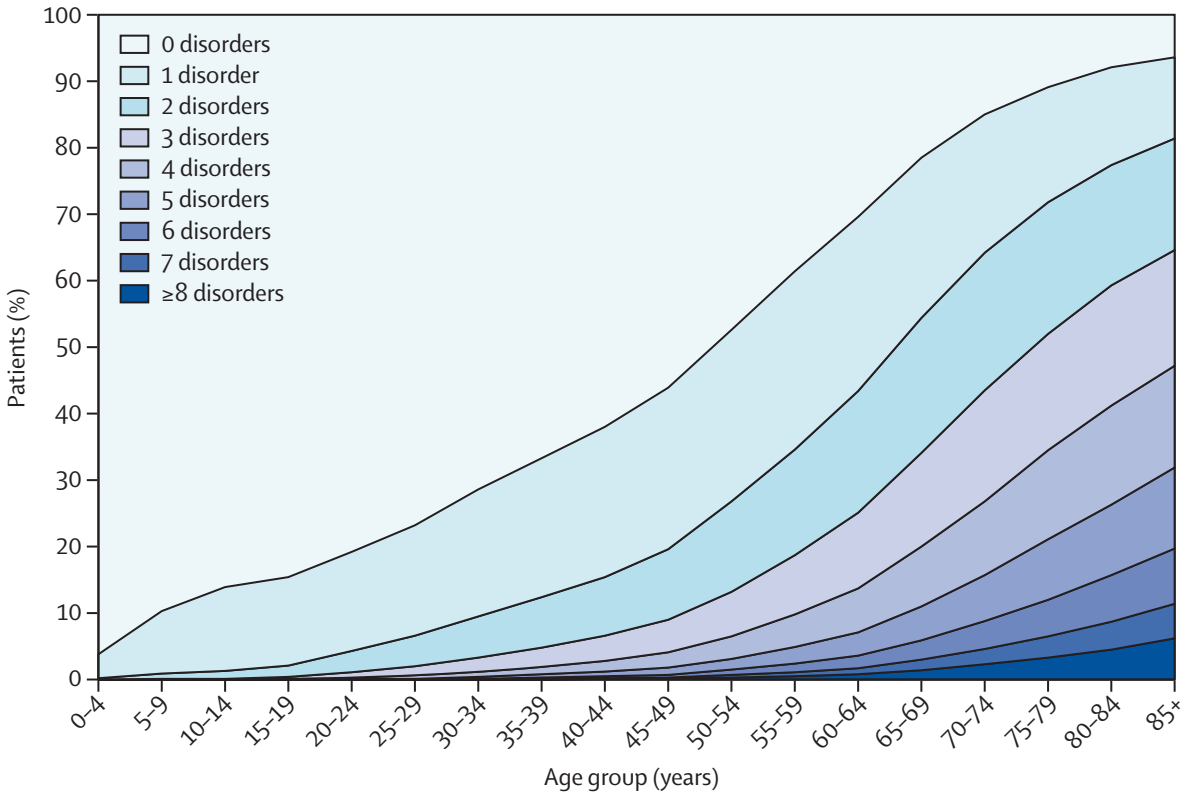
Ann Intensive Care. 2024 Jan 10;14(1):6

Définition **Physiopathologie**

Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study

Karen Barnett, Stewart W Mercer, Michael Norbury, Graham Watt, Sally Wyke, Bruce Guthrie

- **78 % des patients en sepsis présentent au moins une comorbidité**
- **60 % en présentent 3 ou +**
- **Les patients de 65 à 84 ans présentent *2,6 ± 2,2* comorbidités**
- **Ceux âgés de >85 ans en présentent *3,6 ± 2,3***



Lancet . 2012 Jul 7;380(9836):37-43

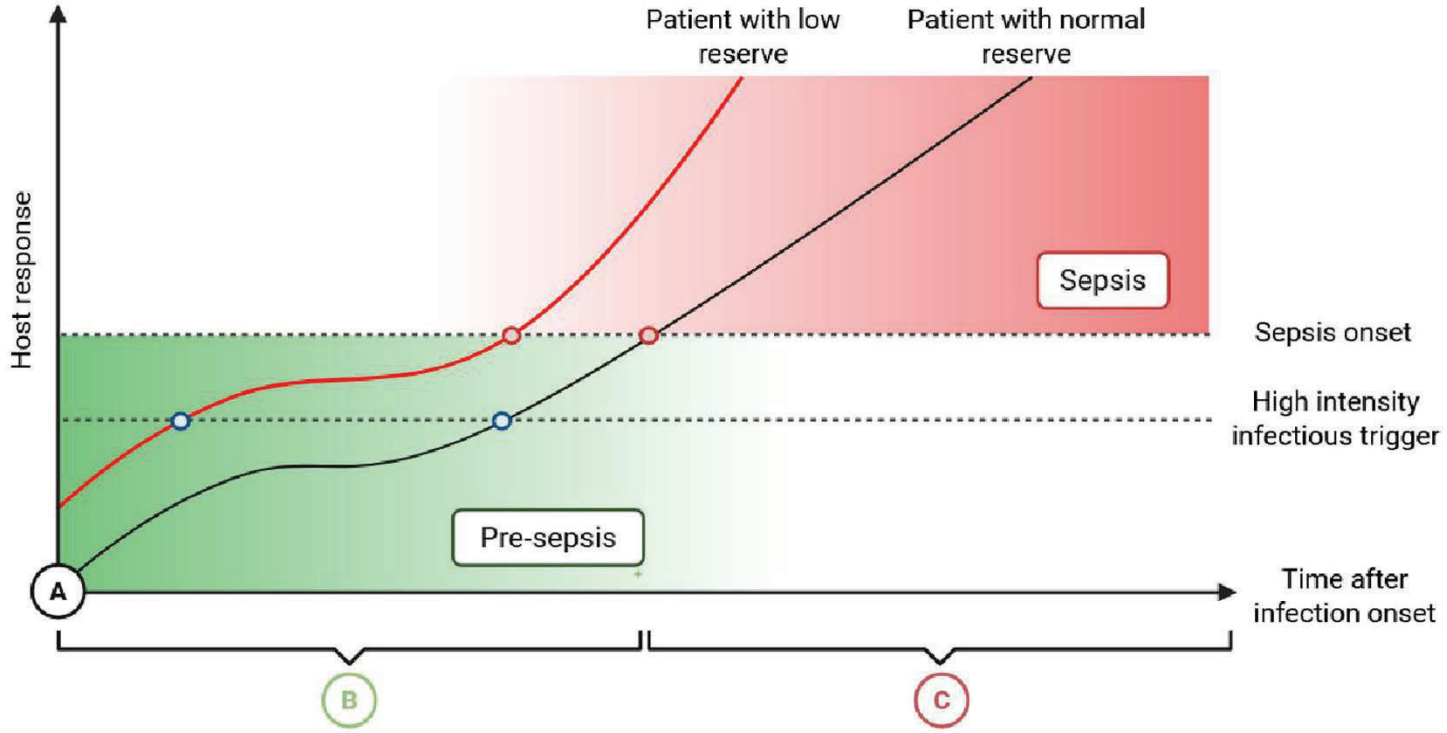
Définition | **Physiopathologie**

PLOS Pathogens

REVIEW

Is "pre-sepsis" the new sepsis? A narrative review

Rémy Gerard[1,2¤*], Antoine Dewitte[2,3], Fridolin Gross[4], Thomas Pradeu[4,5], Maël Lemoine[4], Julien Goret[2,6], Maria Mamani-Matsuda[2]

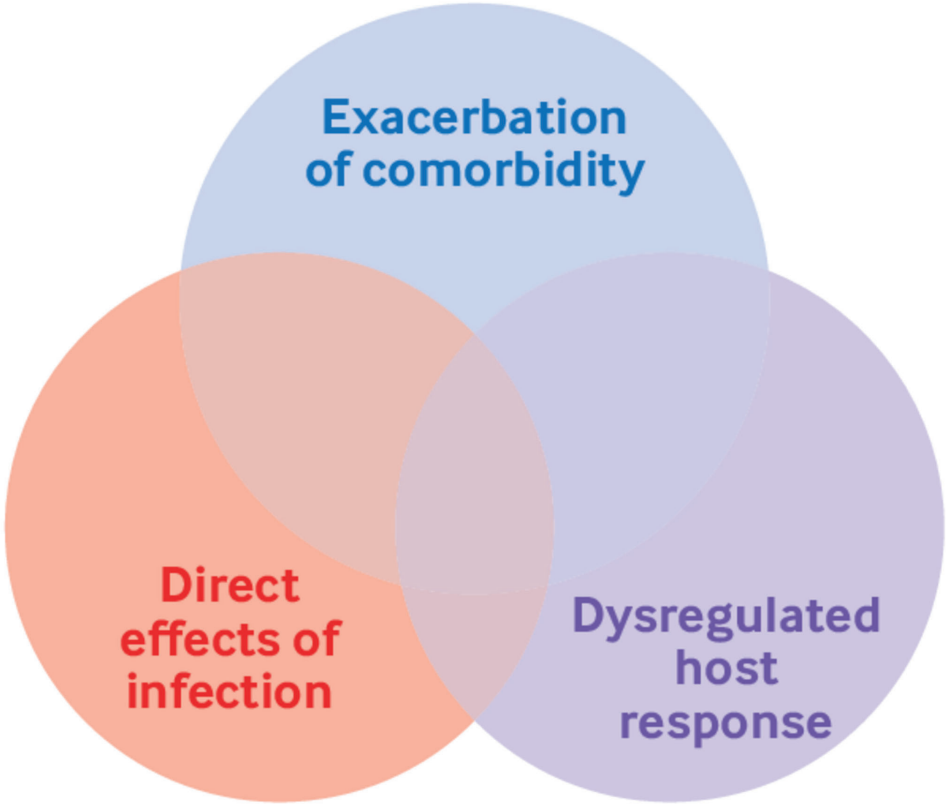


La phase de pré-sepsis correspond à la réponse de l'hôte immédiatement après le contact avec un micro-organisme. L'intensité et la durée de cette réponse varient en fonction de la sensibilité de l'hôte et de l'agent pathogène. Lorsque le point d'équilibre est dépassé, le sepsis se déclare, caractérisée par une défaillance multiviscérale.

Définition **Physiopathologie**

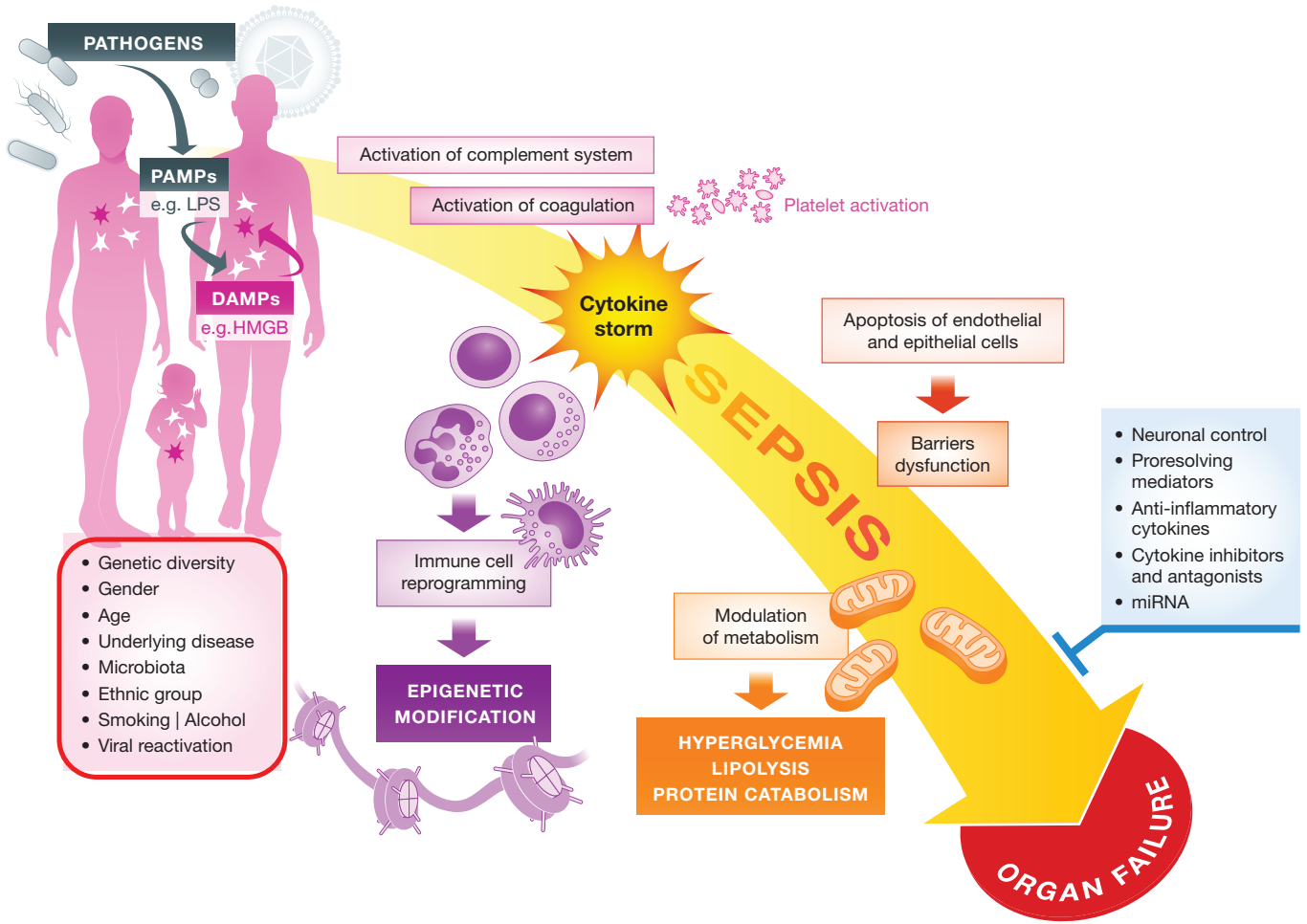
Risque d'identifier des patients présentant un risque de décès :

- secondaire aux comorbidités (potentiellement non connues)
- ou à l'effet direct de l'infection sur l'organe (plutôt qu'à une réponse dérégulée à l'infection)



BMJ 2023;382:e075585

Définition Physiopathologie



EMBO Molecular Medicine 12: e10128 | 2020

Définition **Physiopathologie**

	Origin	PRR
PAMPs		
(Diacyl/triacyl) lipopetides	Gram-positive/Gram-negative bacteria	TLR1,TLR2,TLR6
LTA	Gram-positive bacteria	TLR2
Peptidoglycan	Gram-positive/Gram-negative bacteria	TLR2
dsRNA	Double-stranded RNA virus	TLR3, RIG-1
LPS	Gram-negative bacteria	TLR4
Flagellin	Gram-positive/Gram-negative bacteria	TLR5
ssRNA	Singe-stranded RNA virus	TLR7, TLR8
CpG DNA	Bacteria	TLR9
DAMPs		
HMGB-1	Nucleus, autophagosome	TLR2, TLR4, TLR9, RAGE
Histone	Nucleus	TLR2, TLR4, NLRP3
dsDNA	Cytosol	RIG-1, MDA5, STING
S100A8/A9	Cytosol	TLR4, RAGE
Heat shock proteins	Cytosol, mitochondria, nucleus	TLR2, TLR4, CLR LOX-1
Heparan sulfate	Extracellular matrix component	TLR4
Tenascin-C	Extracellular matrix component	TLR4
Oxidized LPL	Triglycerides	TLR4

Abbreviations: CLR: C-type lectin receptors; DAMPs: damage-associated molecular patterns; HMGB1: high-mobility group protein B1; LOX-1: low-density lipoprotein receptor-1; LTA: lipoteichoic acid; LPL: lipoprotein lipase; LPS: lipopolysaccharide; MDA5: melanoma differentiation-associated protein 5; PAMPs: pathogen-associated molecular patterns; PRR: pattern-recognition receptor; RIG-I: retinoic acid-inducible gene I; STING: stimulator of interferon genes. Of note, only bacterial PAMPs are listed and only the primary PRRs of the indicated PAMPs or DAMPs.

Table 1: **Examples of key PAMPs and DAMPs in sepsis pathophysiology.**

Définition **Physiopathologie**

Prevalence of Antibiotic-Resistant Pathogens in Culture-Proven Sepsis and Outcomes Associated With Inadequate and Broad-Spectrum Empiric Antibiotic Use

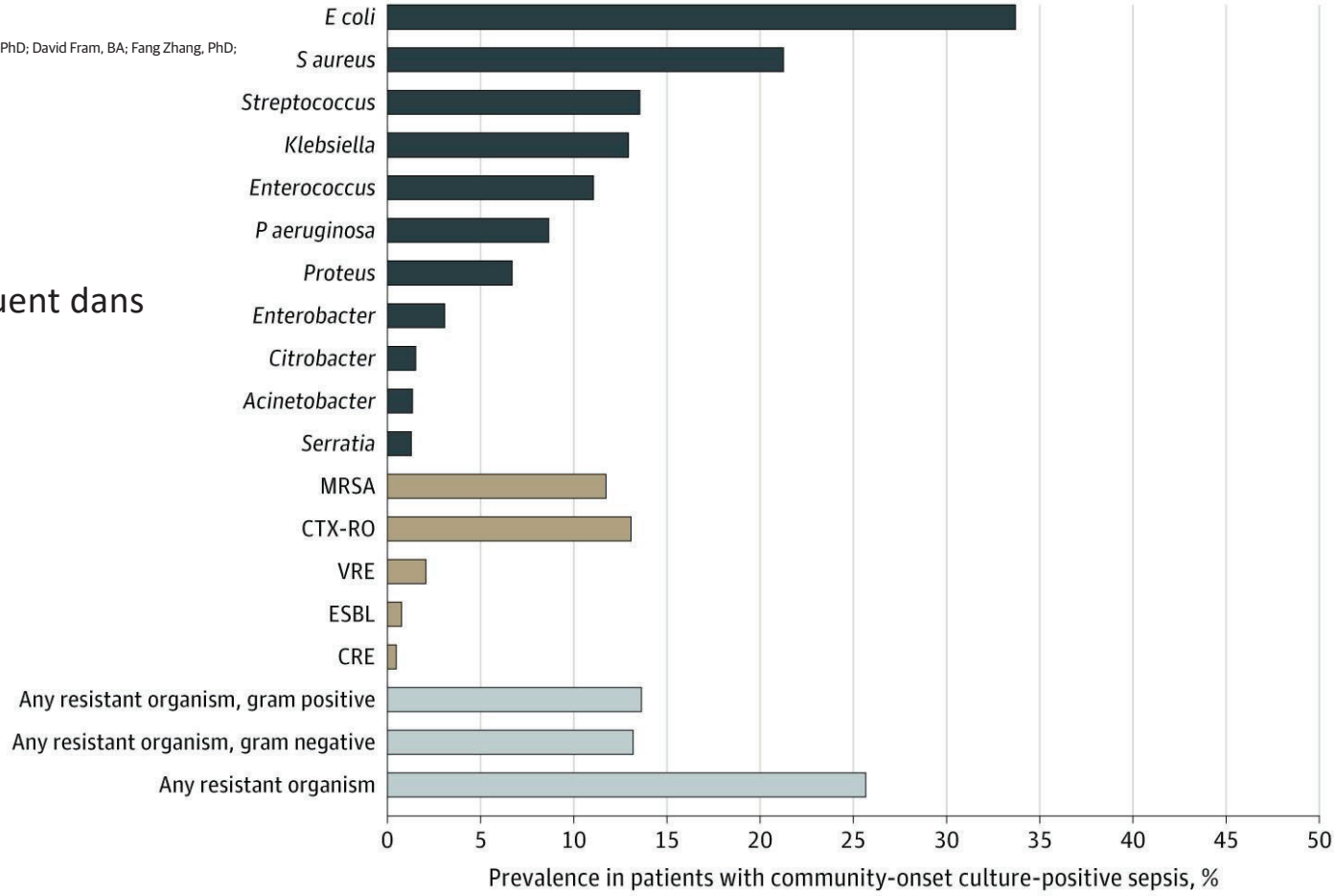
Chanu Rhee, MD, MPH; Sameer S. Kadri, MD, MSc; John P. Dekker, MD, PhD; Robert L. Danner, MD; Huai-Chun Chen, PhD; David Fram, BA; Fang Zhang, PhD; Rui Wang, PhD; Michael Klompas, MD, MPH; for the CDC Prevention Epicenters Program

Bactéries à Gram négatif:

- *Escherichia coli* (pathogène le plus fréquent dans de nombreuses séries)
- *Klebsiella* spp.
- *Pseudomonas aeruginosa*

Bactéries à Gram positif:

- *Staphylococcus aureus* (incluant SARM)
- *Streptococcus pneumoniae*
- *Streptococcus* spp.
- Staphylocoques à coagulase négative



JAMA Network Open. 2020;3(4):e202899.

Définition | **Physiopathologie**

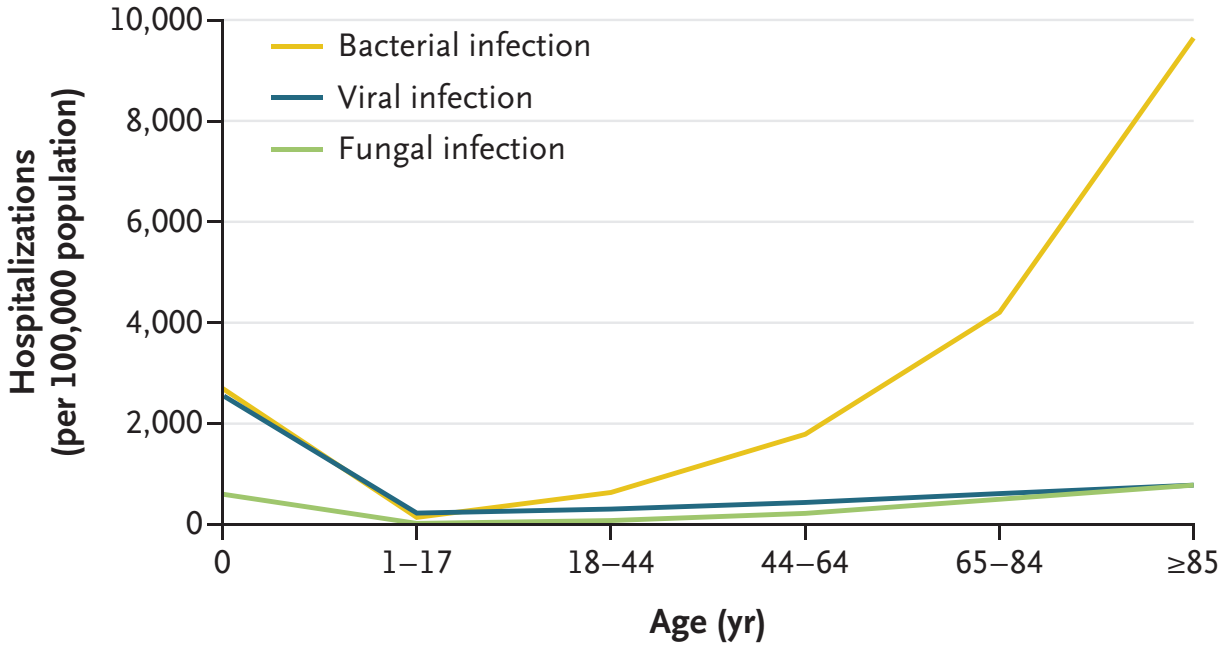
The NEW ENGLAND JOURNAL of MEDICINE

Sepsis and Septic Shock

Nuala J. Meyer, M.D., and Hallie C. Prescott, M.D.

Les **champignons** représentent une proportion croissante des cas de sepsis (4,6% dans certaines séries), avec *Candida* spp. comme troisième type de pathogène le plus fréquent dans les hémocultures aux États-Unis

Les **virus** peuvent également être mis en cause dans un sepsis

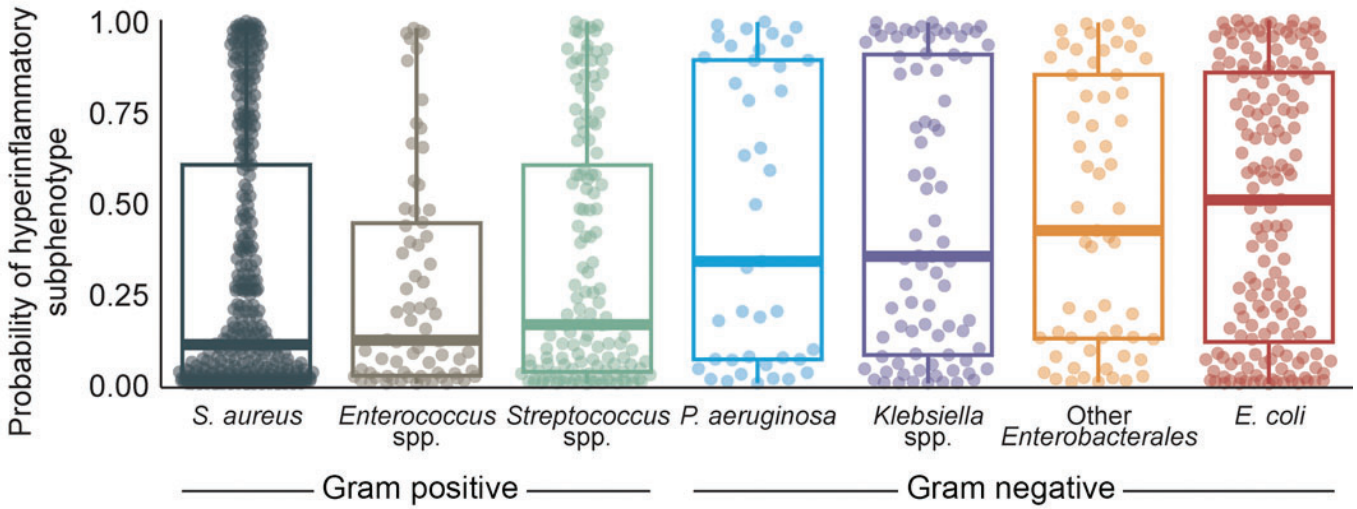


N Engl J Med 2024;391:2133-46.

Définition **Physiopathologie**

Pathogen characteristics are key determinants of distinct host response phenotypes of sepsis

Rishi Chanderraj, Brian Bartek, Kathleen A. Stringer, Mohamad H. Tiba, Michael W. Sjoding, Ying He, Mark Nuppnau, Kale S. Bongers, Mark D. Adame, Sunny S. Lou, V. Eric Kerschberger, Matthew M. Churpek, Carolyn S. Calfee, Sandhya Tripathi, Debra M. Foster, John A. Kellum, Robert P. Dickson, Pratik Sinha



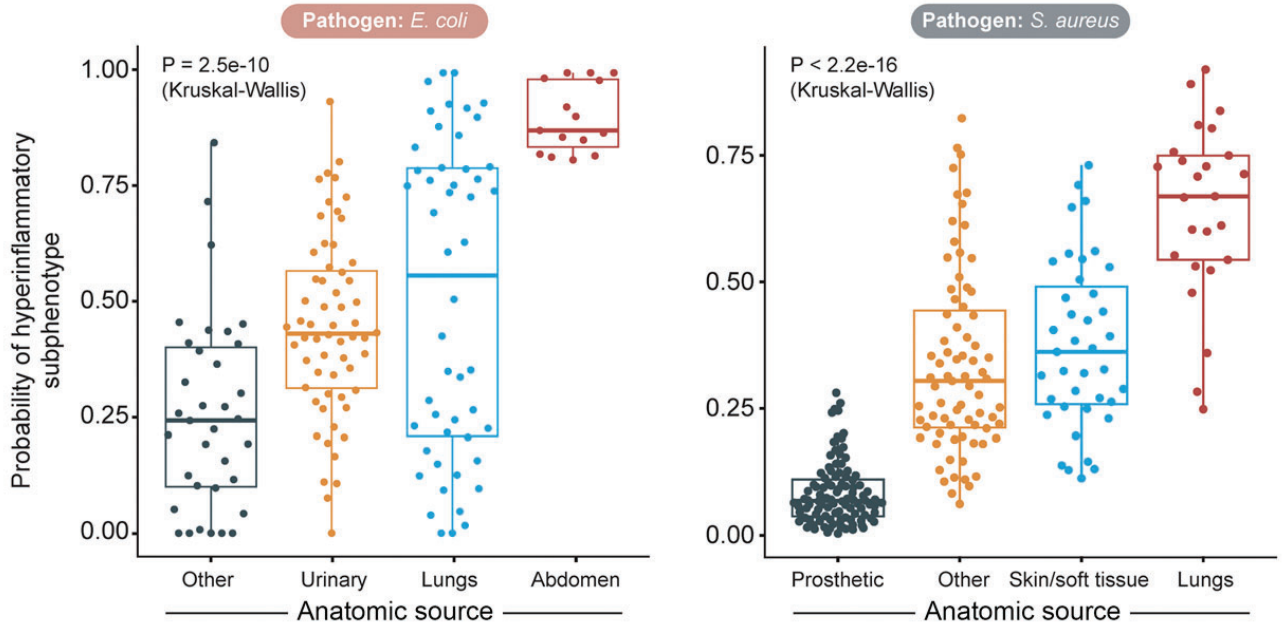
Among 2,108 bacteremic patients with sepsis, the hyperinflammatory subphenotype was strongly predicted by the **identity of the pathogen**, specifically gram-negative members of the Enterobacterales order (E. coli, Klebsiella spp.).

J Clin Invest. 2026;136(6):e197346

Définition **Physiopathologie**

Pathogen characteristics are key determinants of distinct host response phenotypes of sepsis

Rishi Chanderraj, Brian Bartek, Kathleen A. Stringer, Mohamad H. Tiba, Michael W. Sjoding, Ying He, Mark Nuppnau, Kale S. Bongers, Mark D. Adame, Sunny S. Lou, V. Eric Kerschberger, Matthew M. Churpek, Carolyn S. Calfee, Sandhya Tripathi, Debra M. Foster, John A. Kellum, Robert P. Dickson, Pratik Sinha



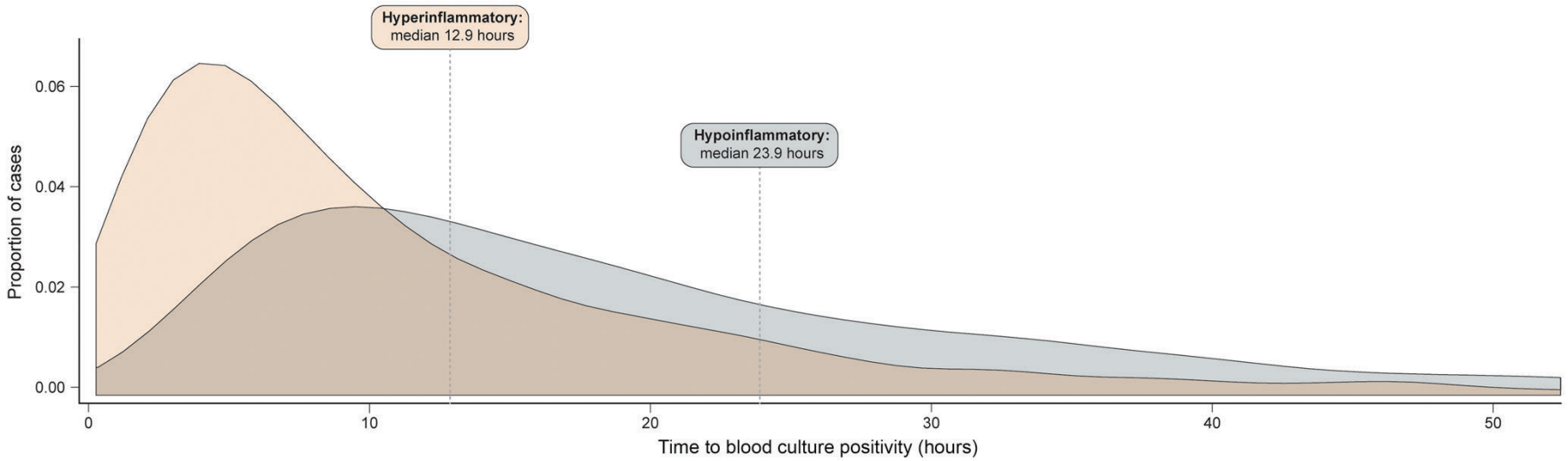
Among patients with the same species of pathogen (E. coli [n = 161], S. aureus [n = 240]), the hyperinflammatory subphenotype was strongly predicted **by anatomic site of initial infection**

J Clin Invest. 2026;136(6):e197346

Définition **Physiopathologie**

Pathogen characteristics are key determinants of distinct host response phenotypes of sepsis

Rishi Chanderraj, Brian Bartek, Kathleen A. Stringer, Mohamad H. Tiba, Michael W. Sjoding, Ying He, Mark Nuppnau, Kale S. Bongers, Mark D. Adame, Sunny S. Lou, V. Eric Kerschberger, Matthew M. Churpek, Carolyn S. Calfee, Sandhya Tripathi, Debra M. Foster, John A. Kellum, Robert P. Dickson, Pratik Sinha



Time to culture positivity, which is inversely correlated with blood bacterial burden, was shorter among patients in the hyperinflammatory subphenotype (n = 2,108).

J Clin Invest. 2026;136(6):e197346

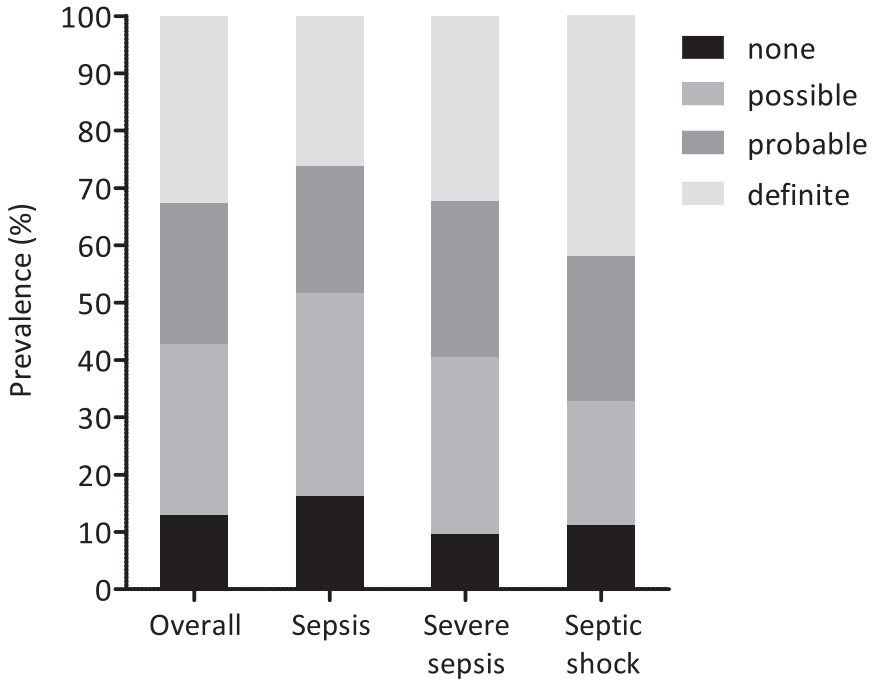
Définition **Physiopathologie**

CRITICAL CARE

Likelihood of infection in patients with presumed sepsis at the time of intensive care unit admission: a cohort study

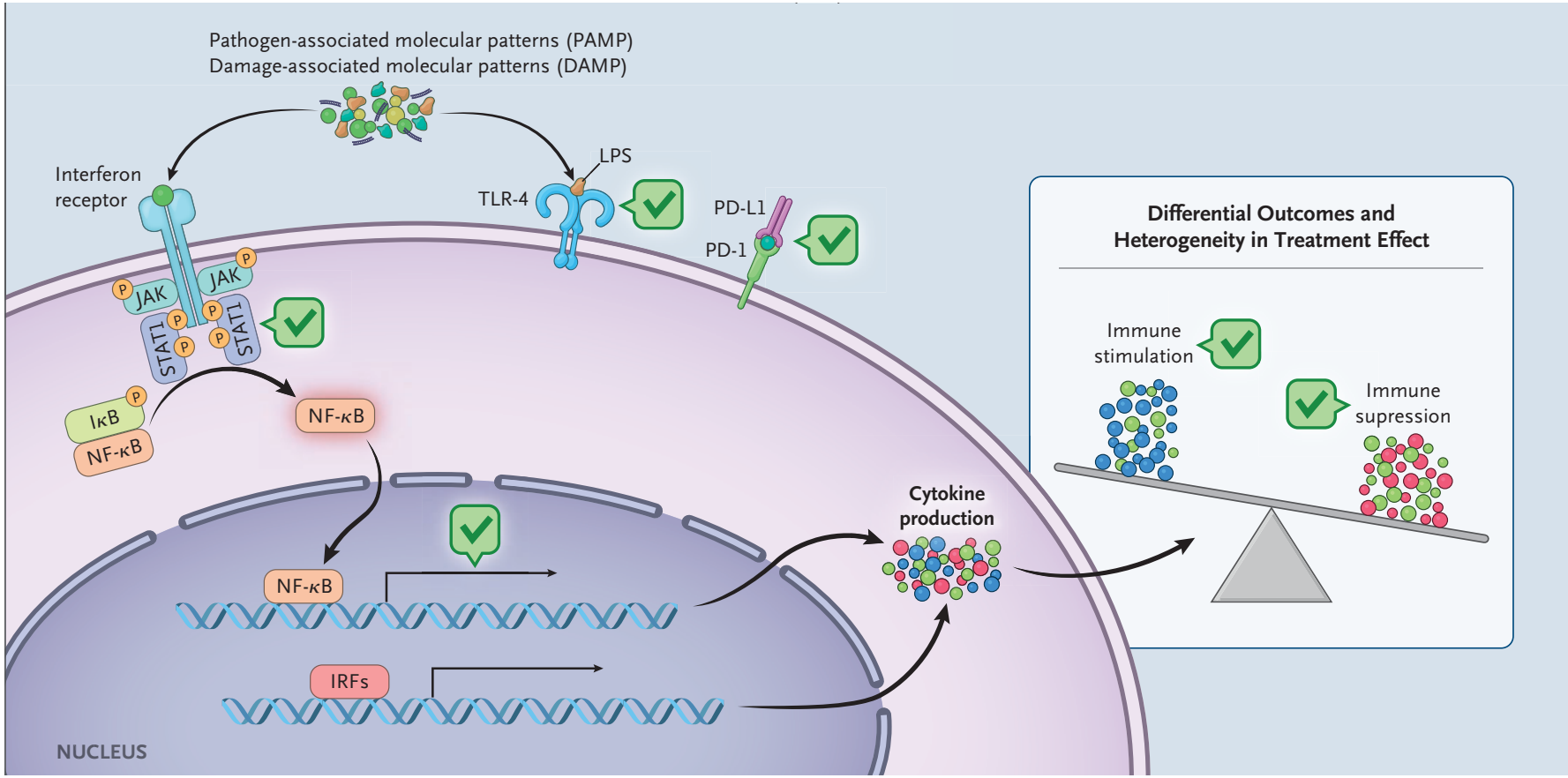
Peter M. C. Klein Klouwenberg[1,2,3*], Olaf L. Cremer[1], Lonneke A. van Vught[4], David S. Y. Ong[1,2,3], Jos F. Frencken[1,3], Marcus J. Schultz[5], Marc J. Bonten[2,3] and Tom van der Poll[4]

Un tiers ou plus des patients diagnostiqués comme sepsis ont en réalité une ou des défaillances d'organe d'origine non infectieuse



Klein Klouwenberg et al. Critical Care (2015) 19:319

Définition **Physiopathologie**



October 25, 2022 NEJM Evid 2022; 1 (11) DOI: https://doi.org/10.1056/EVIDra2200118

Définition **Physiopathologie**

The NEW ENGLAND JOURNAL of MEDICINE

Cytokine Storm

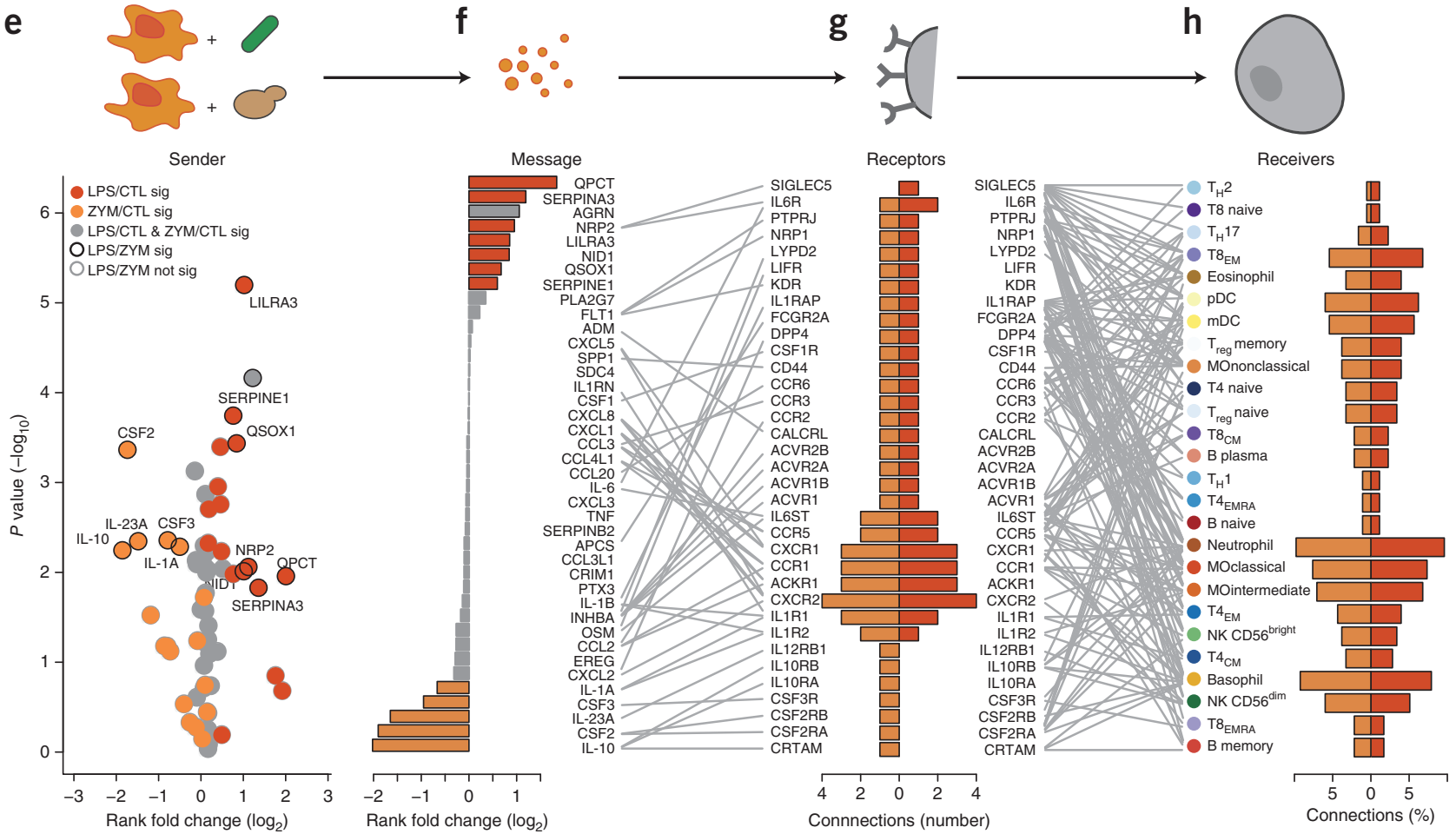
David C. Fajgenbaum, M.D., and Carl H. June, M.D.

Mediator	Main Cell Source	Type and Function
Cytokines and growth factors		
Interleukin-1	Macrophages, epithelial cells; pyroptotic cells	Proinflammatory alarmin cytokine; pyrogenic function, macrophage and Th17 cell activation
Interleukin-2	T cells	Effector T-cell and regulatory T-cell growth factor
Interleukin-6	Macrophages, T cells, endothelial cells	Proinflammatory cytokine; pyrogenic function, increased antibody production, induction of acute-phase reactants
Interleukin-9	Th9 cells	Protection from helminth infections, activation of mast cells, association with type I interferon in Covid-19[26]
Interleukin-10	Regulatory T cells, Th9 cells	Antiinflammatory cytokine; inhibition of Th1 cells and cytokine release
Interleukin-12	Dendritic cells, macrophages	Activation of the Th1 pathway; induction of interferon-γ from Th1 cells, CTLs, and NK cells; acting in synergy with interleukin-18
Interleukin-17	Th17 cells, NK cells, group 3 innate lymphoid cells	Promoting neutrophilic inflammation, protection from bacterial and fungal infections
Interleukin-18	Monocytes, macrophages, dendritic cells	Proinflammatory alarmin cytokine; activation of Th1 pathway, acting in synergy with interleukin-12
Interleukin-33	Macrophages, dendritic cells, mast cells, epithelial cells	Proinflammatory alarmin cytokine; amplification of Th1 and Th2 cells, activation of NK cells, CTLs, and mast cells
Interferon-γ	Th1 cells, CTLs, group 1 innate lymphoid cells, and NK cells	Proinflammatory cytokine; activation of macrophages
Tumor necrosis factor	Macrophages, T cells, NK cells, mast cells	Increasing vascular permeability; pyrogenic function
GM-CSF	Th17 cells	Proinflammatory cytokine
VEGF	Macrophages	Angiogenesis
Chemokines		
Interleukin-8 (CXCL8)	Macrophages, epithelial cells	Recruitment of neutrophils
MIG (CXCL9)	Monocytes, endothelial cells, keratinocytes	Interferon-inducible chemokine; recruitment of Th1 cells, NK cells, plasmacytoid dendritic cells
IP-10 (CXCL10)	Monocytes, endothelial cells, keratinocytes	Interferon-inducible chemokine; recruitment of macrophages, Th1 cells, NK cells
MCP-1 (CCL2)	Macrophages, dendritic cells, cardiac myocytes	Recruitment of Th2 cells, monocytes, dendritic cells, basophils
MIP-1α (CCL3)	Monocytes, neutrophils, dendritic cells, NK cells, mast cells	Recruitment of macrophages, Th1 cells, NK cells, eosinophils, dendritic cells; pyrogenic function
MIP-1β (CCL4)	Macrophages, neutrophils, endothelium	Recruitment of macrophages, Th1 cells, NK cells, dendritic cells
BLC (CXCL13)	B cells, follicular dendritic cells	Recruitment of B cells, CD4 T cells, dendritic cells†
Plasma proteins		
CRP	Hepatocytes	Monomeric CRP increases interleukin-8 and MCP-1 secretion; interleukin-6 increases CRP expression
Complement	Hepatocytes, other cells	Complement activation contributes to tissue damage in cytokine storm; complement inhibition can reduce immunopathologic effects of cytokine storm
Ferritin	Ubiquitous	Primary site of iron storage in cells

Médiateurs solubles dans l'orage cytokinique

N Engl J Med 2020;383:2255-73

Définition **Physiopathologie**

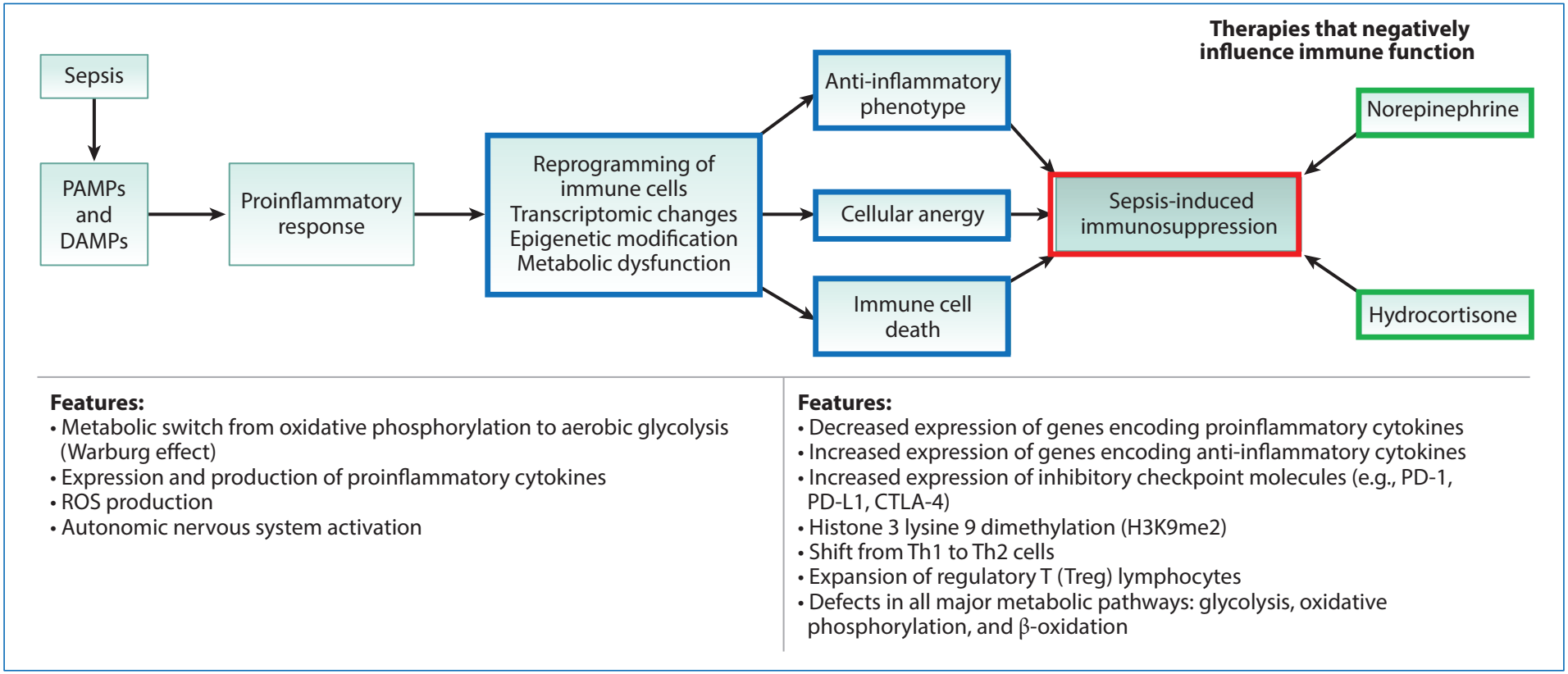


Architecture des réseaux de communication des cellules immunitaires humaines dévoilée (protéomique quantitative)

Nat Immunol. 2017 May;18(5):583-593

Définition **Physiopathologie**

Immunosuppression induite par le sepsis



Annu. Rev. Physiol. 2022. 84:157–81

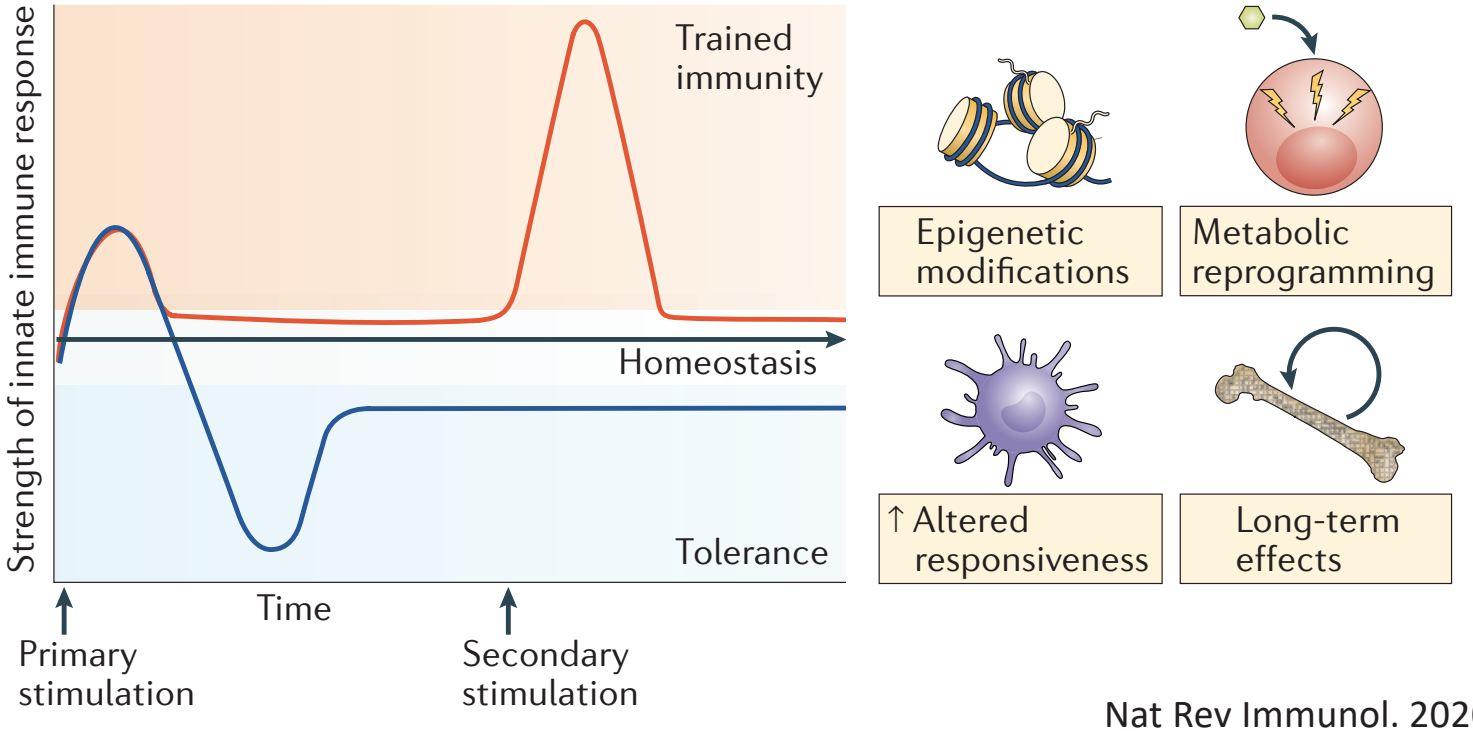
Définition | Physiopathologie

Defining trained immunity and its role in health and disease

Mihai G. Netea[1,2,3]✉, Jorge Domínguez-Andrés[1,2], Luis B. Barreiro[4,5,6], Triantafyllos Chavakis[7,8], Maziar Divangahi[9,10,11], Elaine Fuchs[12], Leo A. B. Joosten[1,2], Jos W. M. van der Meer[1,2], Musa M. Mhlanga[13,14], Willem J. M. Mulder[15,16,17], Niels P. Riksen[1,2], Andreas Schlitzer[18], Joachim L. Schultze[3], Christine Stabell Benn[19], Joseph C. Sun[20,21,22], Ramnik J. Xavier[23,24] and Eicke Latz[25,26,27]✉

- **Etat hyperinflammatoire chronique**
- **Ou état de tolérance immune chronique**

Reprogrammation épigénétique et métabolique des cellules immunitaires innées



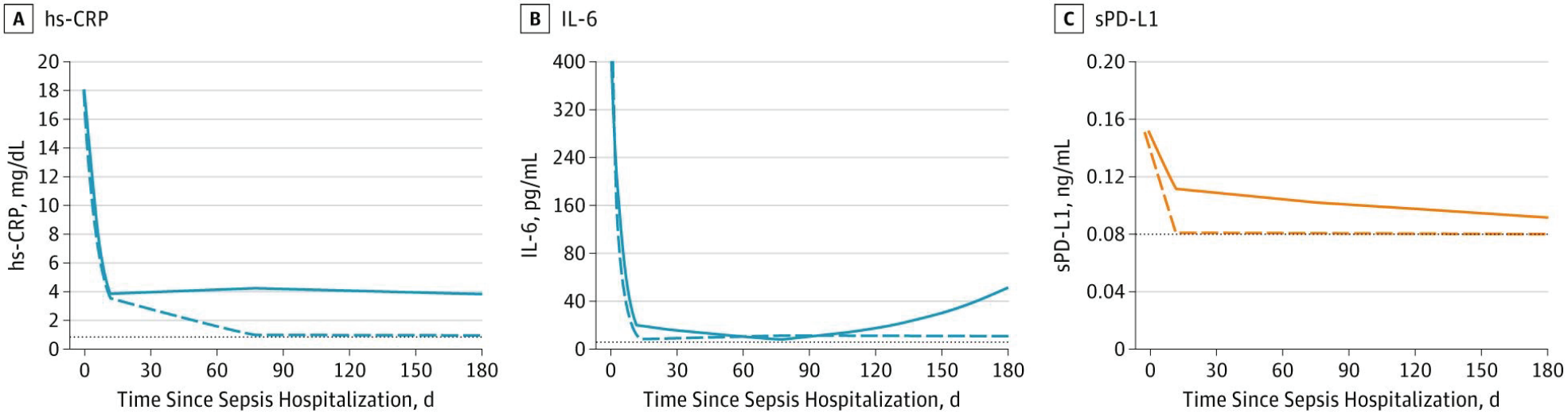
Nat Rev Immunol. 2020 Jun;20(6):375-388

Définition **Physiopathologie**

PICS (Persistent Inflammation, Immunosuppression, and Catabolism Syndrome)

Long-term Host Immune Response Trajectories Among Hospitalized Patients With Sepsis

Sachin Yende, MD, MS; John A. Kellum, MD; Victor B. Talisa, MS; Octavia M. Peck Palmer, PhD; Chung-Chou H. Chang, PhD; Michael R. Filbin, MD, MS; Nathan I. Shapiro, MD, MPH; Peter C. Hou, MD; Arvind Venkat, MD; Frank LoVecchio, MD; Katrina Hawkins, MD; Elliott D. Crouser, MD; Anne B. Newman, MD, MPH; Derek C. Angus, MD, MPH



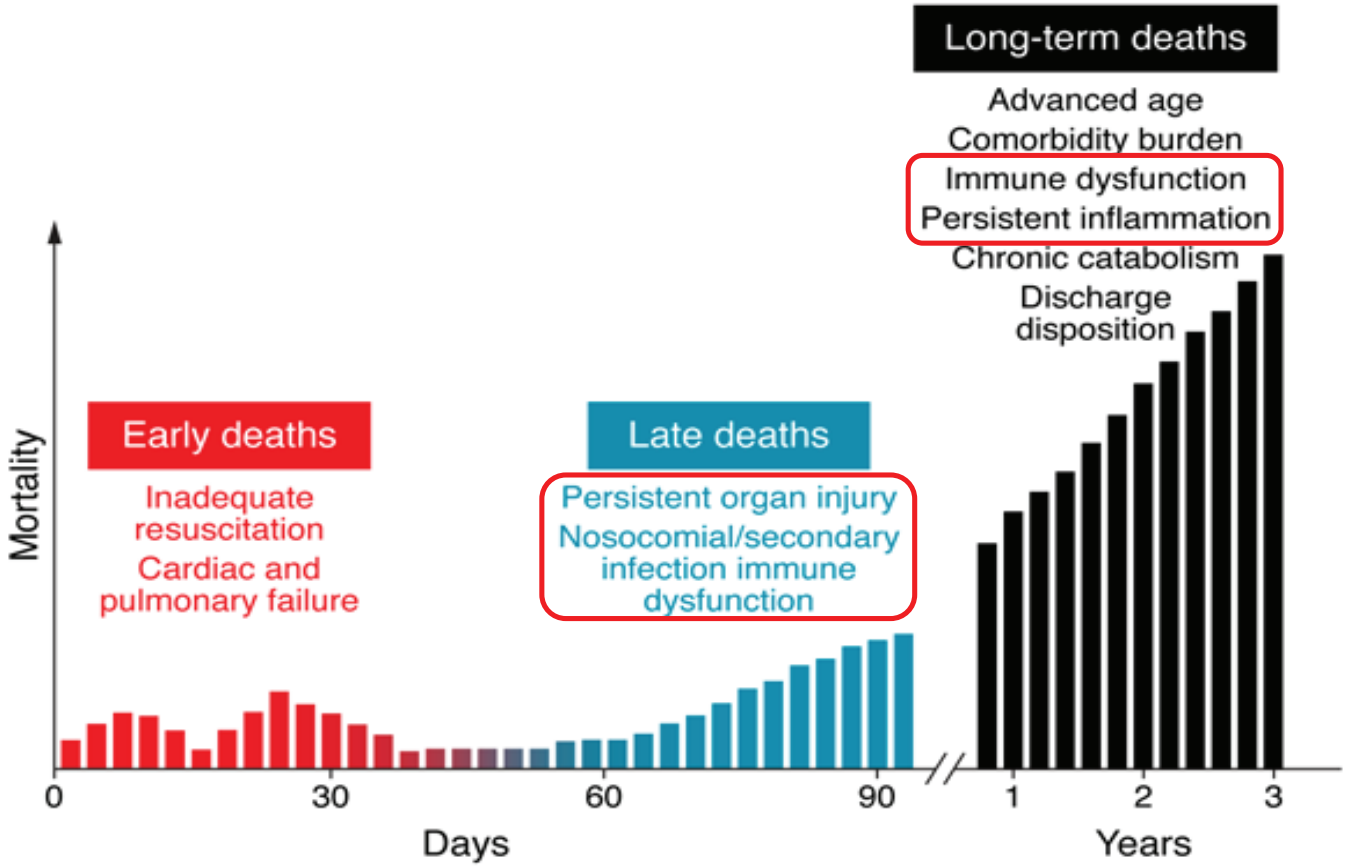
- **Inflammation persistante**: Élévation continue des marqueurs inflammatoires (CRP, IL-6, IL-8)
- **Immunosuppression**: Lymphopénie, dysfonction des LT, expansion des cellules suppressives myéloïdes (MDSC), infections récurrentes
- **Catabolisme**: Perte musculaire progressive (sarcopénie), cachexie, résistance anabolique malgré le support nutritionnel

JAMA Network Open. 2019;2(8):e198686

Définition **Physiopathologie**

Sepsis-induced immune dysfunction: can immune therapies reduce mortality?

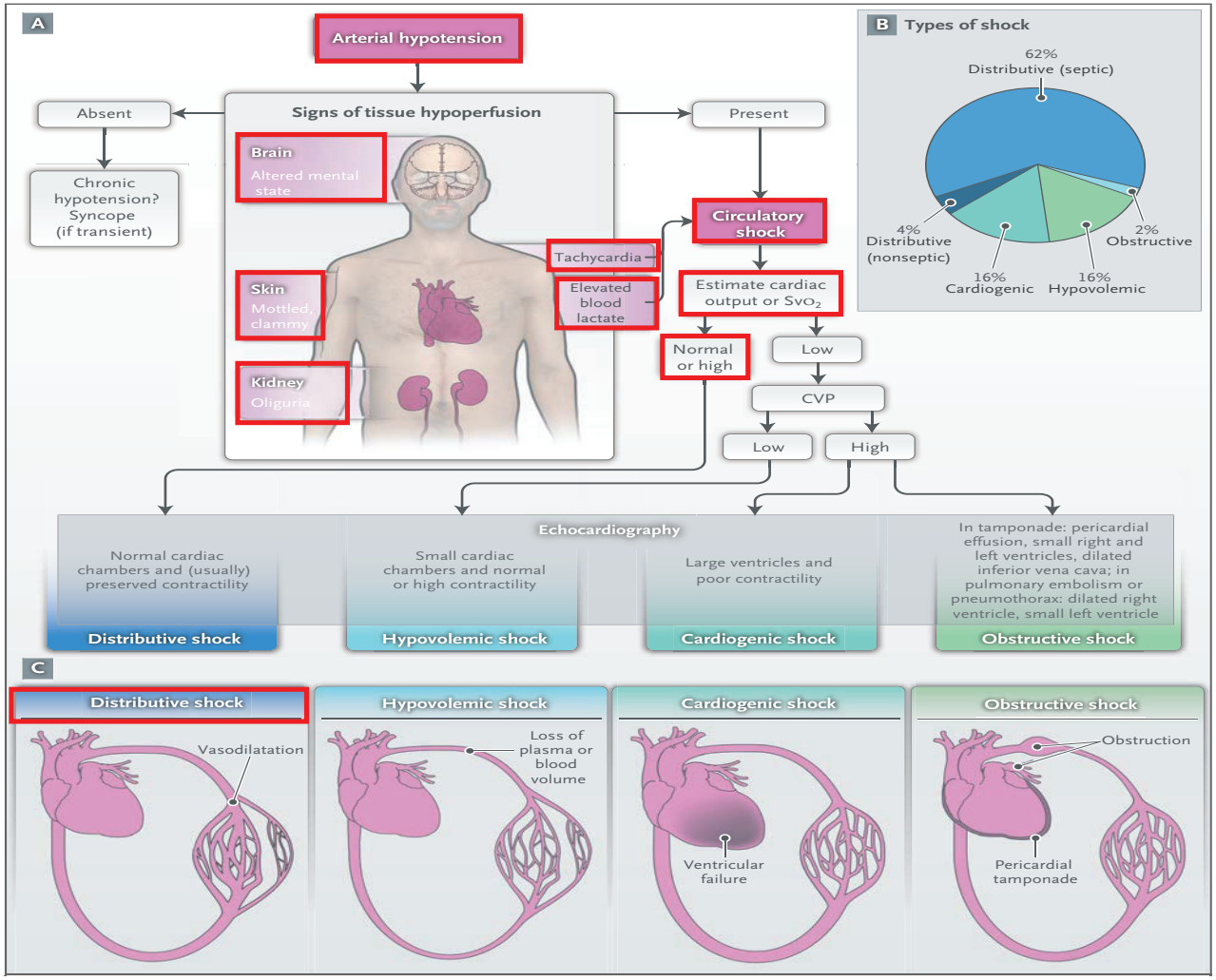
Matthew J. Delano[1] and Peter A. Ward[2]



J Clin Invest. 2016;126(1):23–31

Définition **Physiopathologie**

Dysfonction de l'endothélium vasculaire



N Engl J Med 2013;369:1726-34.

Définition **Physiopathologie**

Personalized Hemodynamic Resuscitation Targeting Capillary Refill Time in Early Septic Shock

The ANDROMEDA-SHOCK-2 Randomized Clinical Trial

JAMA

QUESTION Does a personalized hemodynamic resuscitation strategy targeting capillary refill time improve outcomes in patients with early septic shock vs usual care?

CONCLUSION In patients with early septic shock, a personalized hemodynamic resuscitation protocol targeting capillary refill time (CRT-PHR) was superior to usual care.

POPULATION

831 Men 636 Women

Adults 18 years or older with septic shock

Mean age: 66 years

LOCATIONS

86 Sites in 19 countries

INTERVENTION

1501 Patients randomized
1467 Patients analyzed

720 **CRT-PHR**
Underwent PHR targeted at normalizing CRT over a 6-hour period

747 **Usual care**
Treated according to local protocols or international guidelines over a 6-hour period

PRIMARY OUTCOME

Hierarchical composite outcome: all-cause mortality, duration of vital support, and length of hospital stay at 28 days as an overall win ratio

FINDINGS

Total No. of wins

CRT-PHR	Usual care
131 131 (48.9%)	112 787 (42.1%)

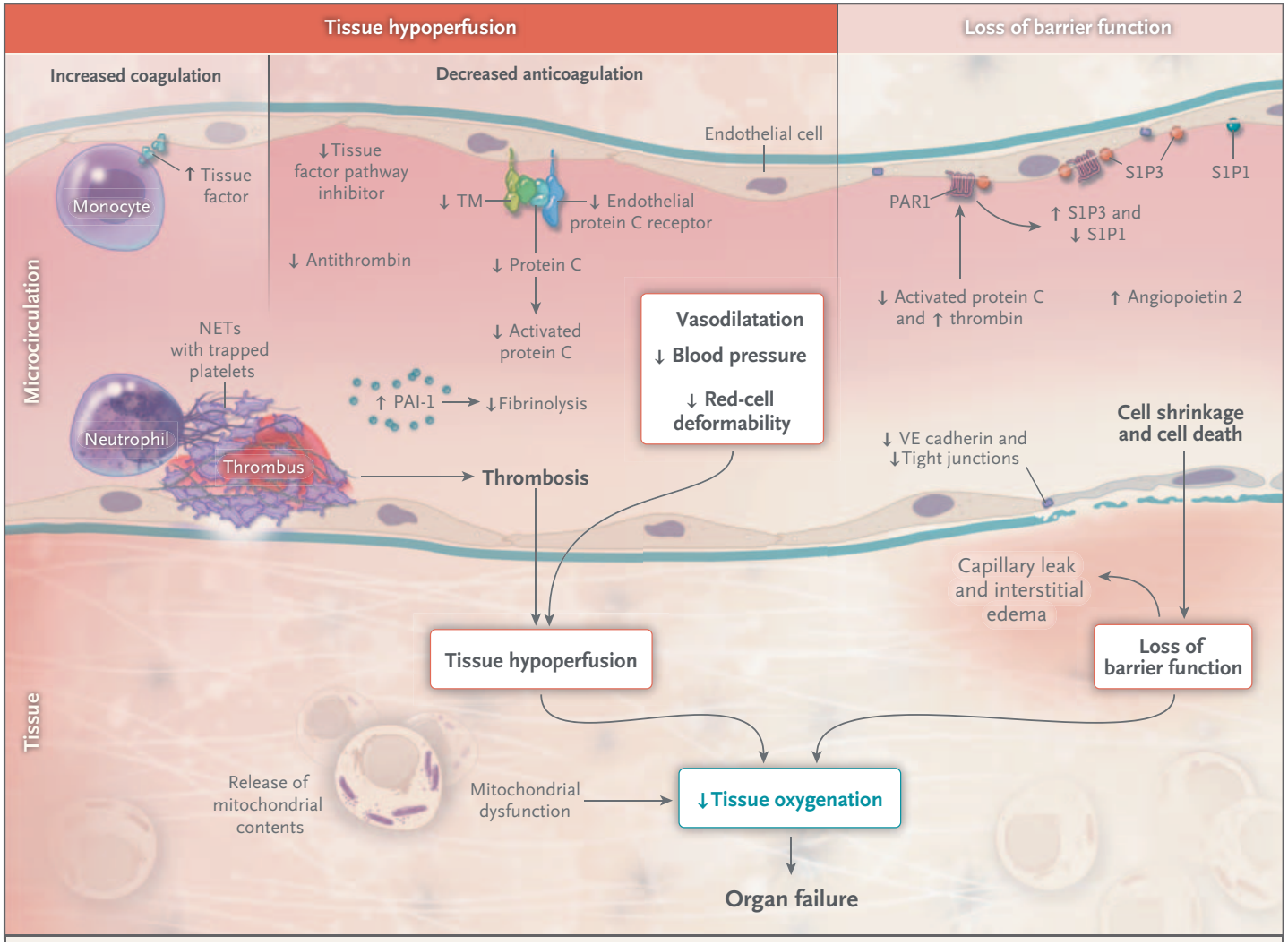
CRT-PHR was superior to usual care:
Win ratio, 1.16
(95% CI, 1.02 to 1.33; *P* = .04)

The ANDROMEDA-SHOCK-2 Investigators. Personalized hemodynamic resuscitation targeting capillary refill time in early septic shock. *JAMA*.
Published online October 29, 2025. doi:10.1001/jama.2025.20402

JAMA.2025;334(22):1988-1999.

Définition **Physiopathologie**

Dysfonction de l'endothélium vasculaire

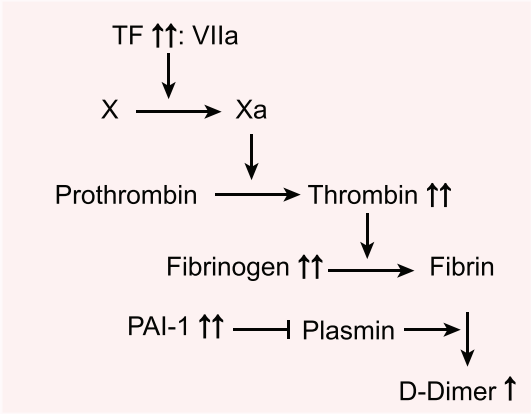


N Engl J Med 2013; 369:840-851

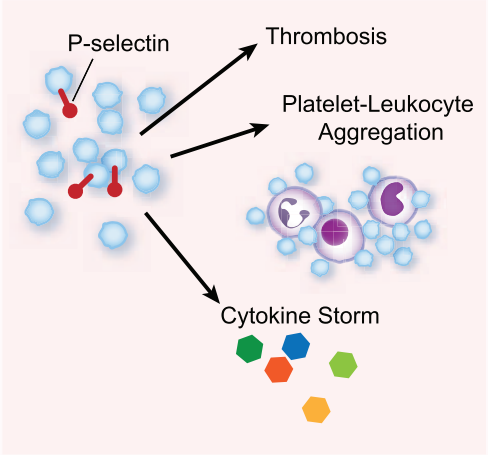
Définition **Physiopathologie**

Atteinte microthrombotique

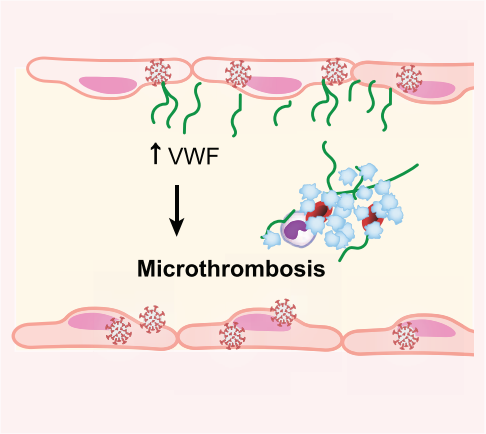
Coagulopathy



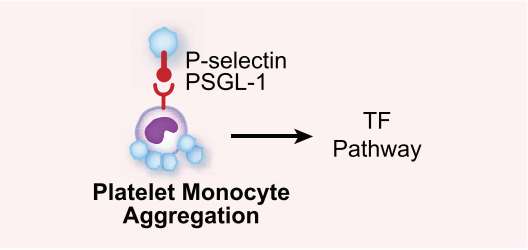
Platelet Hyperreactivity

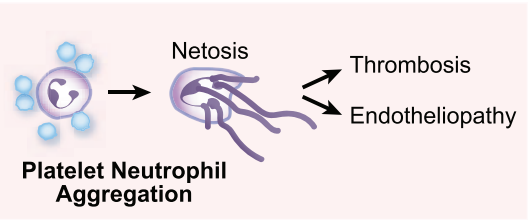


Endotheliopathy



Immunothrombosis

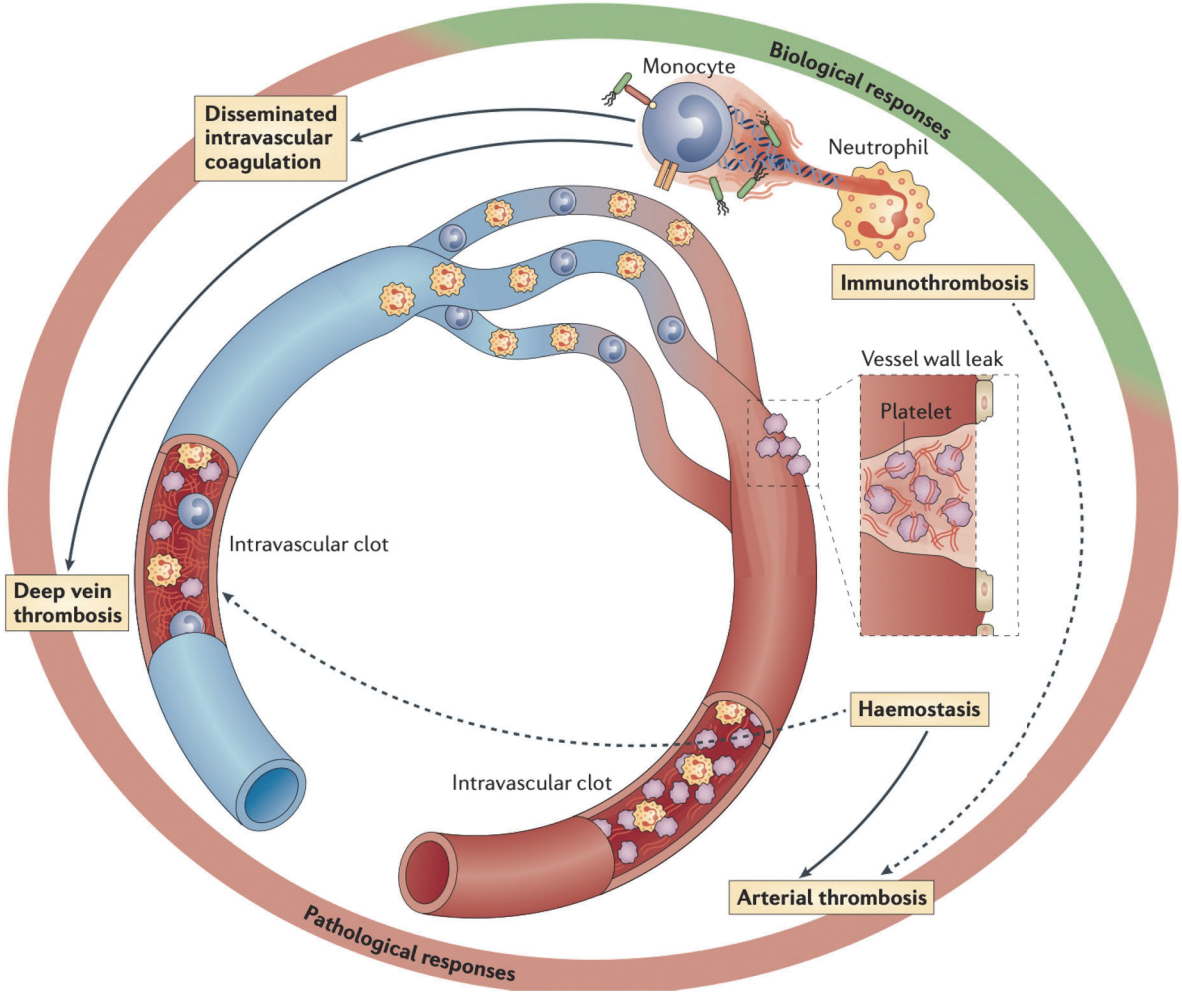




Curr Opin Hematol 2021, 28:445 – 453

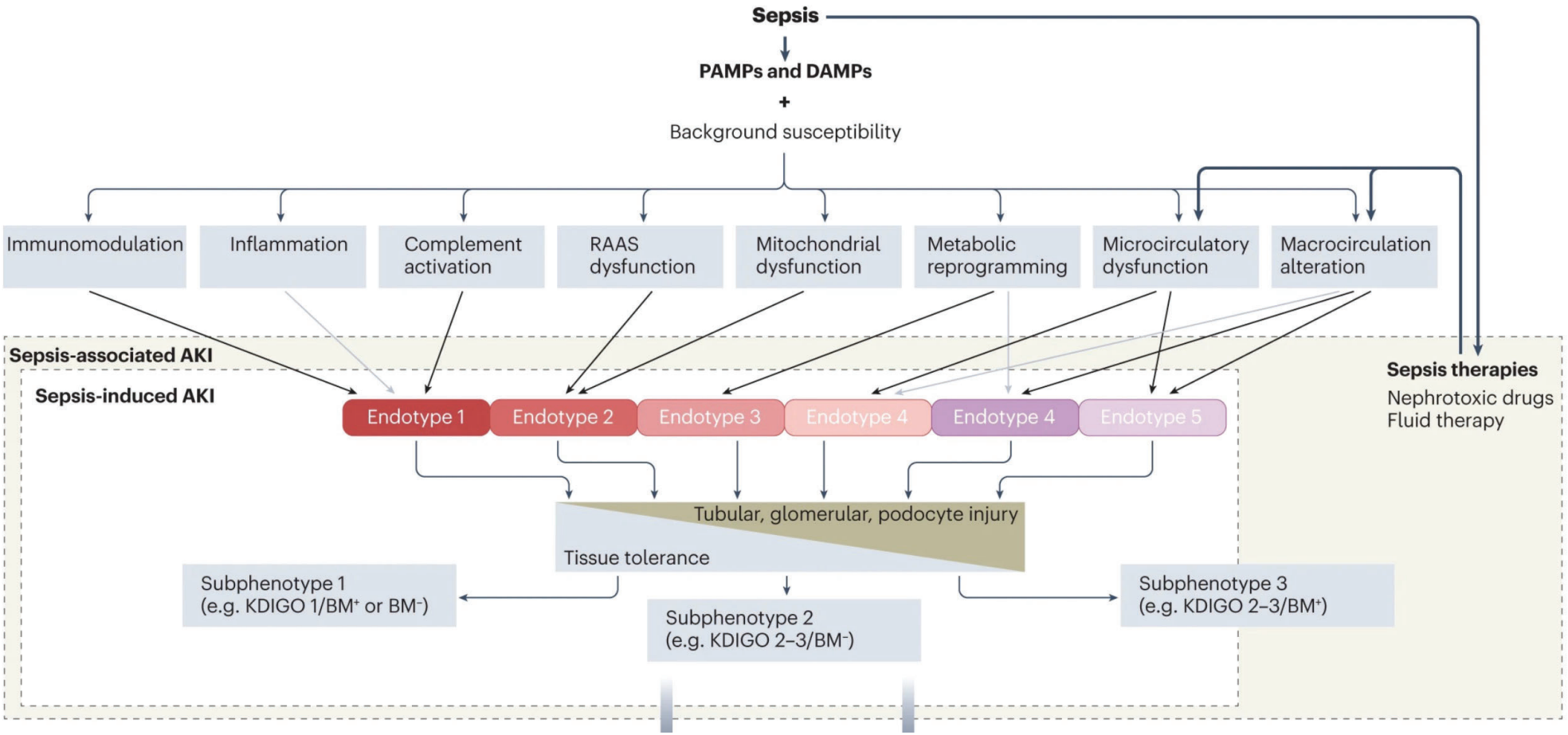
Définition **Physiopathologie**

Immunothrombose et coagulation induite par le sepsis



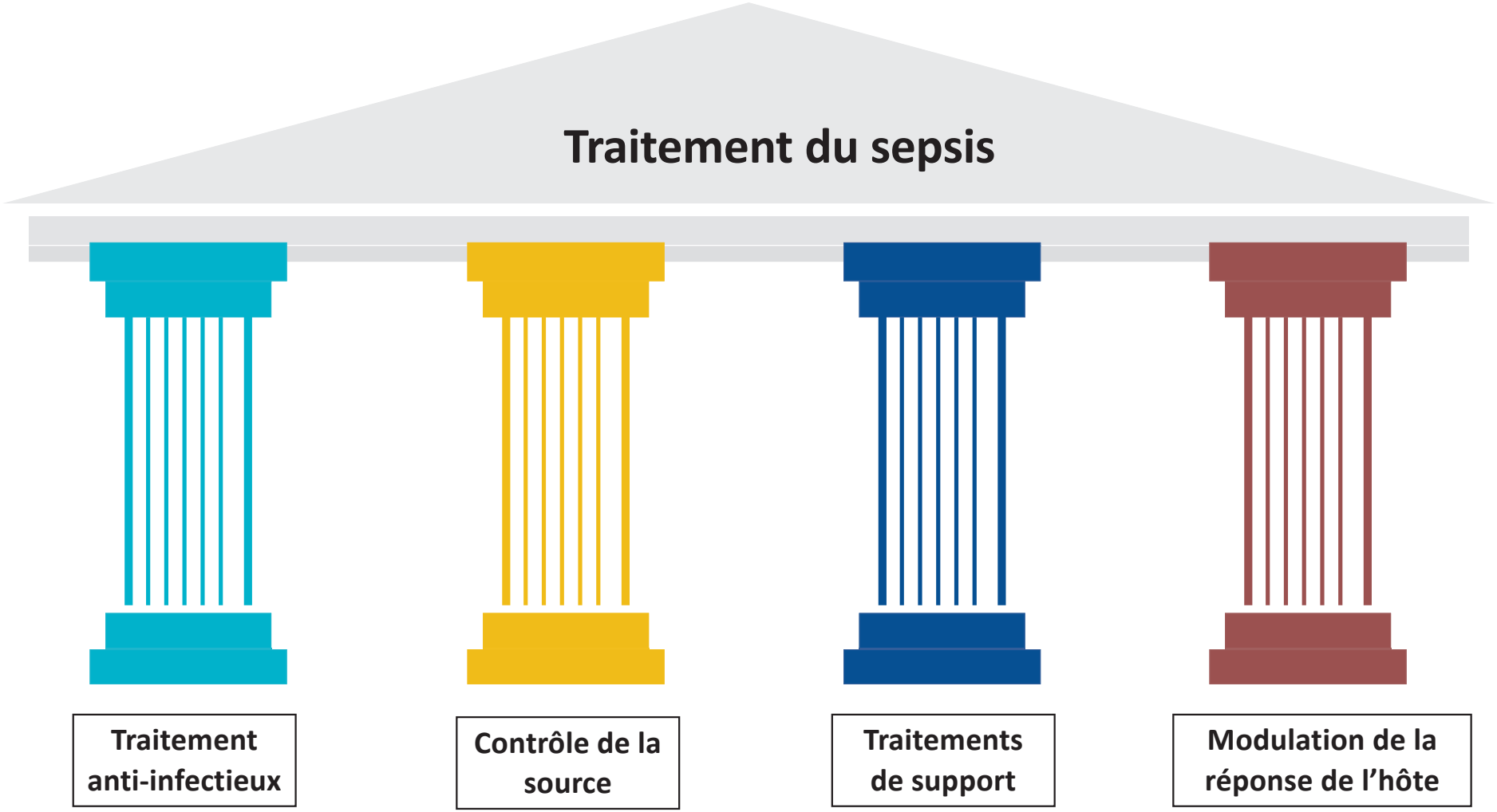
Nat Rev Immunol. 2013 Jan;13(1):34-45

Définition **Physiopathologie**



Nat Rev Nephrol . 2023 Feb 23

Définition | Physiopathologie | Traitement



Définition | Physiopathologie | Traitement

Critical Care Medicine

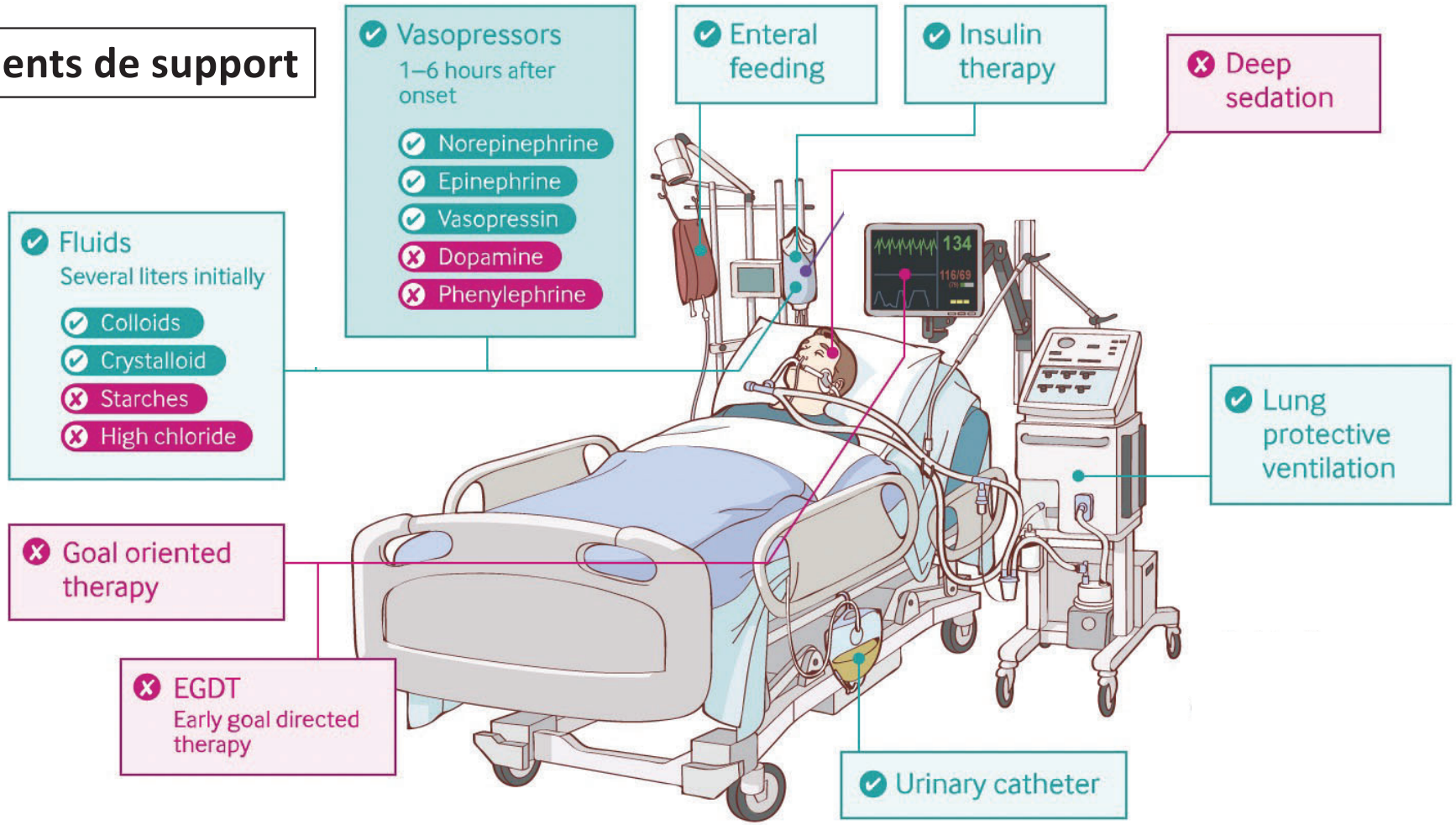
April 2026 • Volume 54 • Number 4 • Pages 725–812

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2026

Crit Care Med. 2026 Apr 1;54(4):725-812

Définition | Physiopathologie | Traitement

Traitements de support



BMJ 2016; 353 doi: https://doi.org/10.1136/bmj.i1585

ORIGINAL ARTICLE

Initiation Strategies for Renal-Replacement Therapy in the Intensive Care Unit

- ***Critères d'inclusion:***
  - AKI compatible with a diagnosis of acute tubular necrosis in the context of ischemic or toxic injury
  - KDIGO stage 3 acute kidney injury
  - Invasive mechanical ventilation or catecholamine infusion
- ***Critères d'exclusion:***
  - Urée > 40 mmol/L
  - Potassium > 6 mmol/L
  - pH <7,15 (acidose métabolique pure ou mixte avec Paco2 > 50 mmHg
  - Acute pulmonary edema due to fluid overload responsible for severe hypoxemia requiring an oxygen flow rate > 5 L/mn or FiO2>50%

N Engl J Med. 2016 Jul 14;375(2):122-33

ORIGINAL ARTICLE

Initiation Strategies for Renal-Replacement Therapy in the Intensive Care Unit

Critères d'initiation de l'EER:

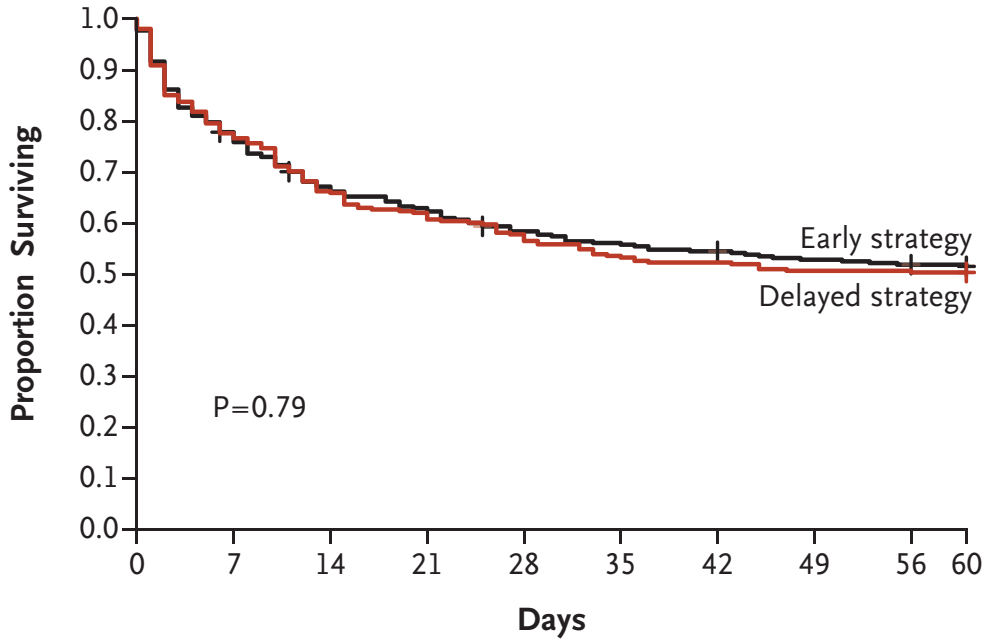
- Une insuffisance rénale KDIGO 3 avec oligurie ou anurie persistante pendant plus de 72 heures ;
- Urée > 40 mmol/L ;
- Potassium > 5,5 mmol/L malgré un traitement médical ;
- pH <7,15 (acidose métabolique pure (PaCO2<30mmHg) ou acidose mixte (Paco2 > 50 mmHg sans possibilité d'améliorer la ventilation alvéolaire) ;
- Œdème pulmonaire aigu secondaire à une surcharge hydrosodée responsable d'une hypoxémie sévère (débit d'oxygène > 5l/min ou FiO2>50% en ventilation mécanique pour maintenir une SaO2>95%) malgré un traitement diurétique.

N Engl J Med. 2016 Jul 14;375(2):122-33

ORIGINAL ARTICLE

Initiation Strategies for Renal-Replacement Therapy in the Intensive Care Unit

A



No. at Risk

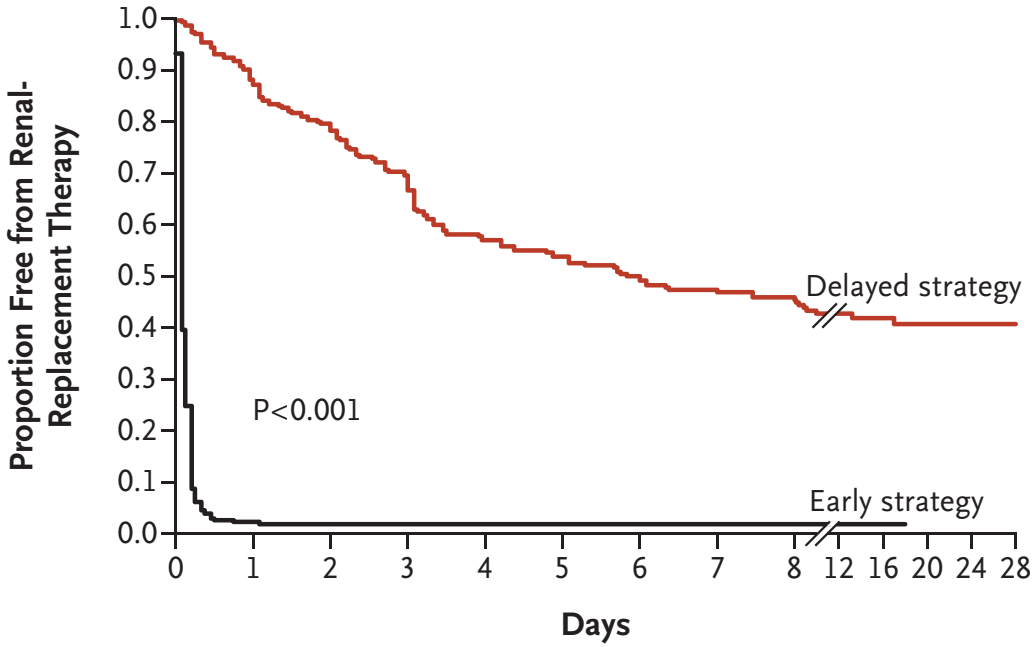
Early strategy	311	241	207	194	179	172	167	161	158 157
Delayed strategy	308	239	204	191	178	165	161	156	156 155

4H vs 57h

N Engl J Med. 2016 Jul 14;375(2):122-33

Initiation Strategies for Renal-Replacement Therapy in the Intensive Care Unit

B



No. at Risk

Early strategy	311	7	4	4	4	4	3	3	3	1	1	0	0	0
Delayed strategy	308	268	229	192	153	135	118	105	92	61	39	28	21	13

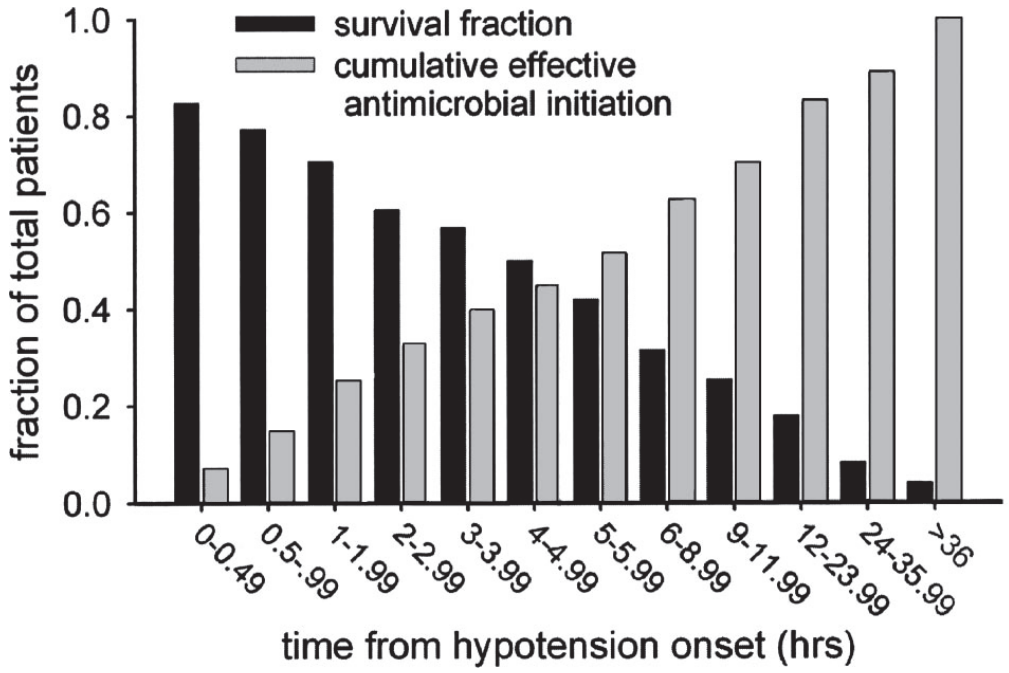
N Engl J Med. 2016 Jul 14;375(2):122-33

Définition | Physiopathologie | Traitement

Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock*

Anand Kumar, MD; Daniel Roberts, MD; Kenneth E. Wood, DO; Bruce Light, MD; Joseph E. Parrillo, MD; Satendra Sharma, MD; Robert Suppes, BSc; Daniel Feinstein, MD; Sergio Zanotti, MD; Leo Taiberg, MD; David Gurka, MD; Aseem Kumar, PhD; Mary Cheang, MSc

Chaque heure de retard est associée à 10% de mortalité en plus



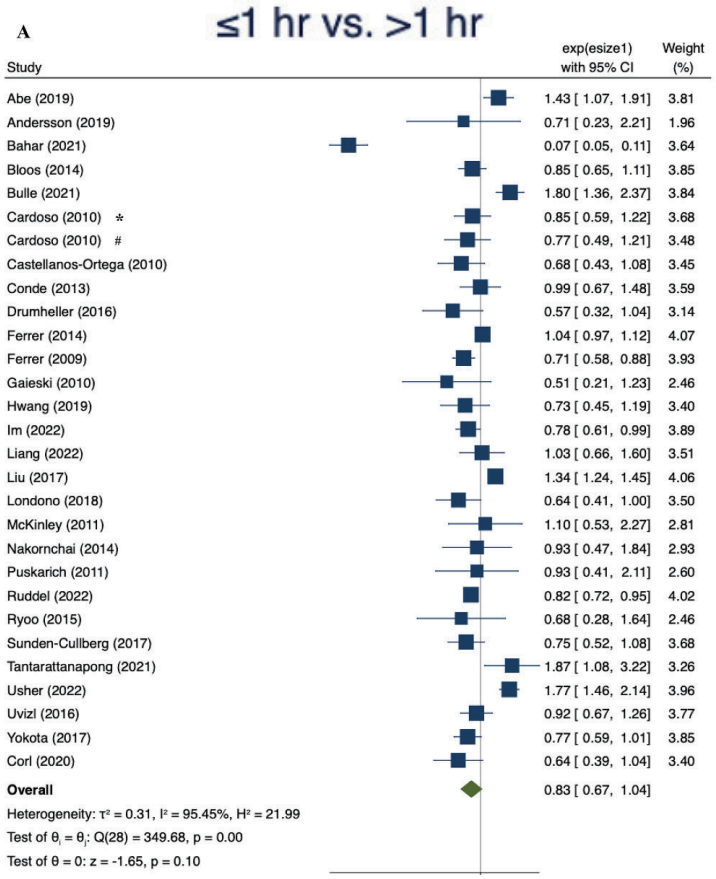
Crit Care Med 2006 Vol. 34, No. 6

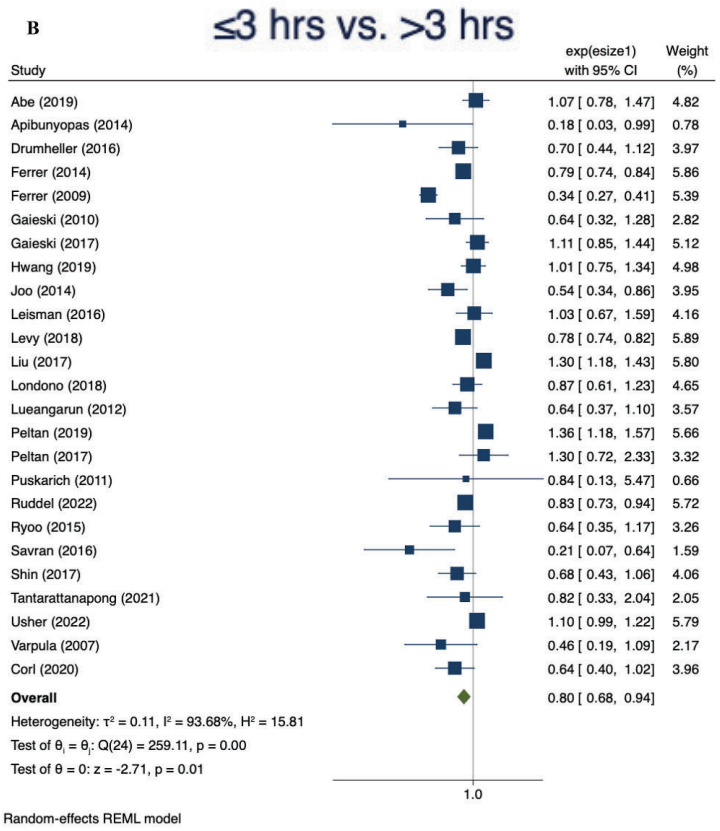
Définition | Physiopathologie | Traitement

Door-to-antibiotic time and mortality in patients with sepsis: Systematic review and meta-analysis☆

Ling Yan Leung [a,1], Hsi-Lan Huang [b,1], Kevin KC Hung [a,1], Chi Yan Leung [b], Cherry CY Lam [a], Ronson SL Lo [a], Chun Yu Yeung [a], Peter Joseph Tsoi [a,c], Michael Lai [a,d], Mikkel Brabrand [e], Joseph H Walline [a], Colin A Graham [a,*]

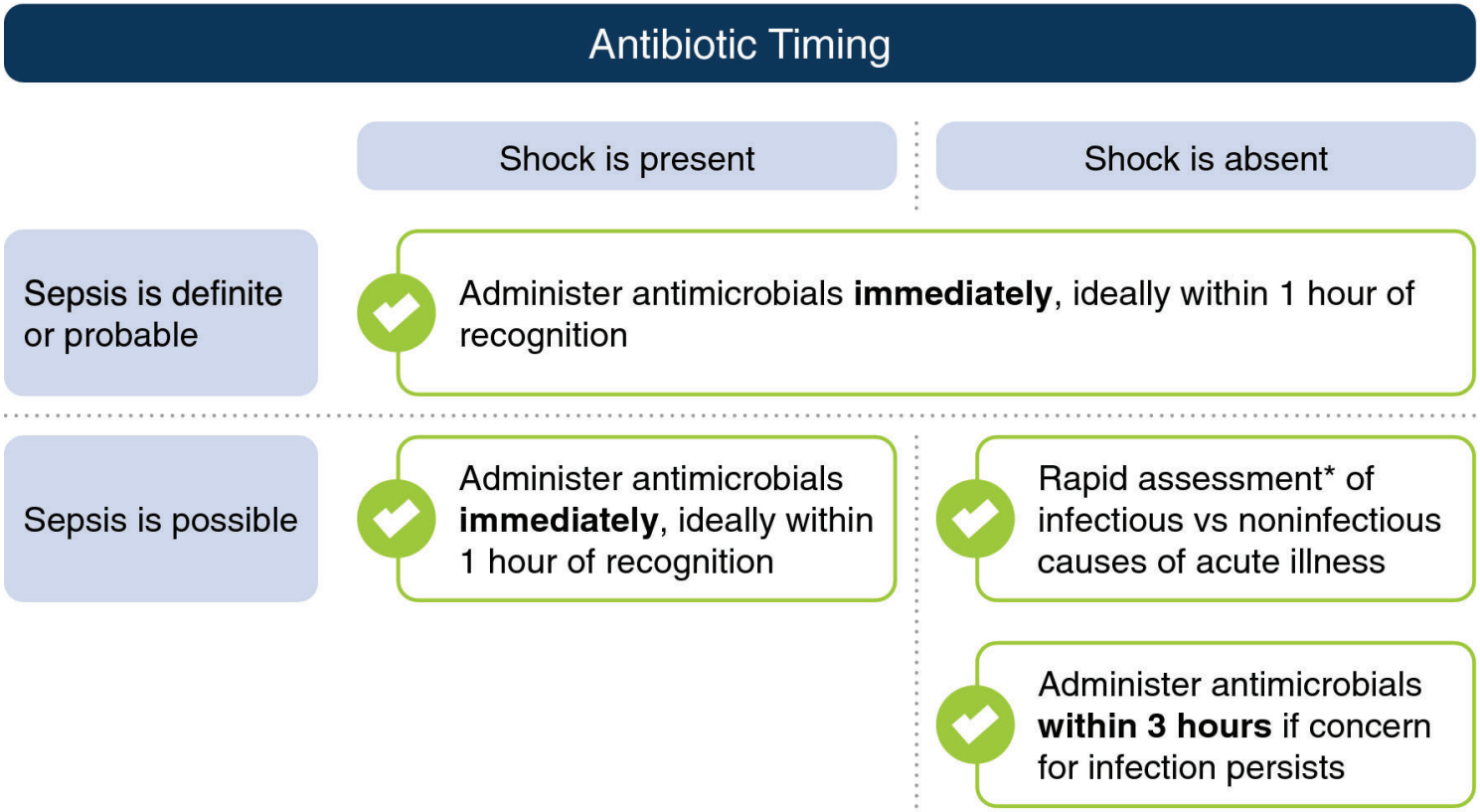
42 études
N= 190 896 patients





European Journal of Internal Medicine 129 (2024) 48–61

Définition | Physiopathologie | Traitement



Crit Care Med. 2026 Apr 1;54(4):725-812

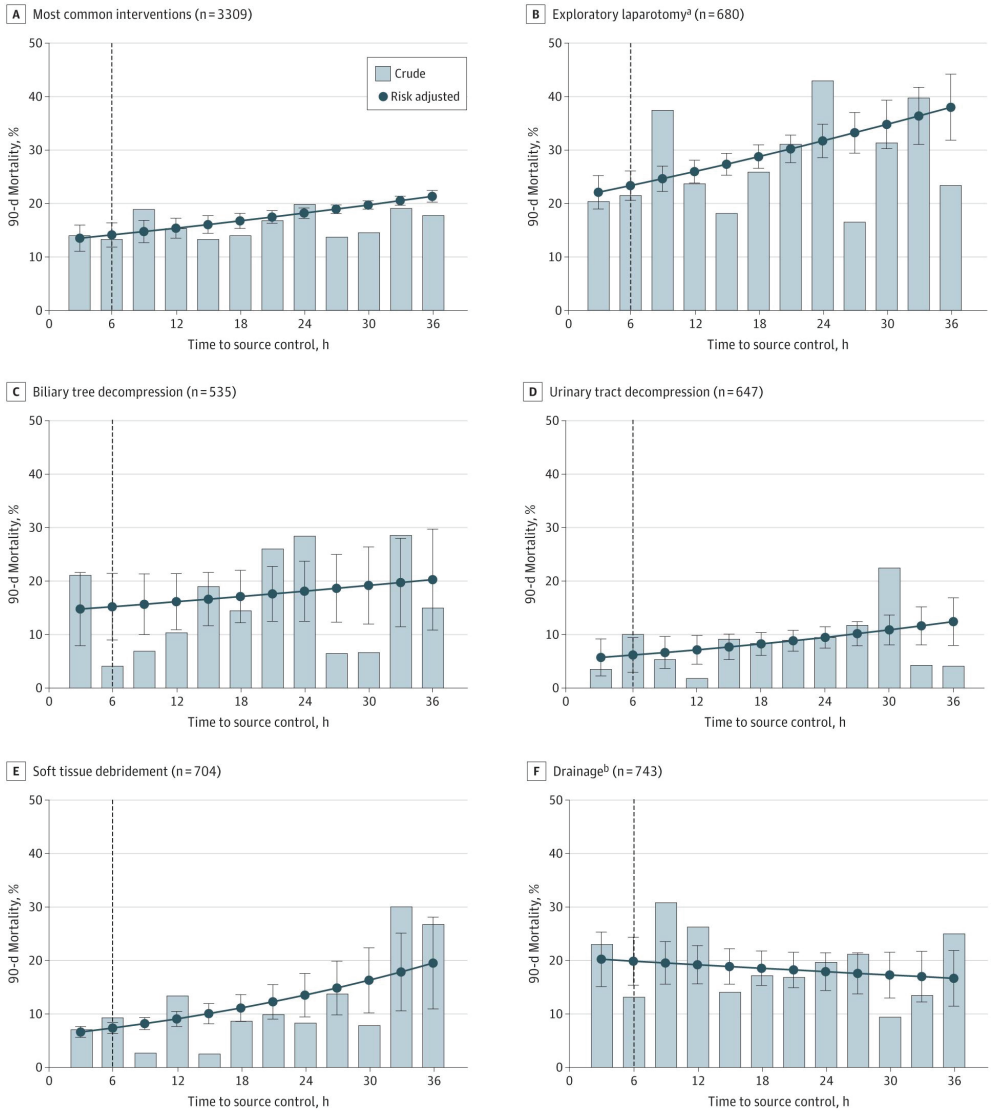
Définition | Physiopathologie | Traitement

Association Between Time to Source Control in Sepsis and 90-Day Mortality

Katherine M. Reitz, MD, MSc; Jason Kennedy, MS; Shimena R. Li, MD; Robert Handzel, MD; Daniel A. Tonetti, MD, MSc; Matthew D. Neal, MD; Brian S. Zuckerbraun, MD; Daniel E. Hall, MD, MDiv, MHSc; Jason L. Sperry, MD, MPH; Derek C. Angus, MD, MPH; Edith Tzeng, MD; Christopher W. Seymour, MD, MSc

Méta-analyse de 11 articles:

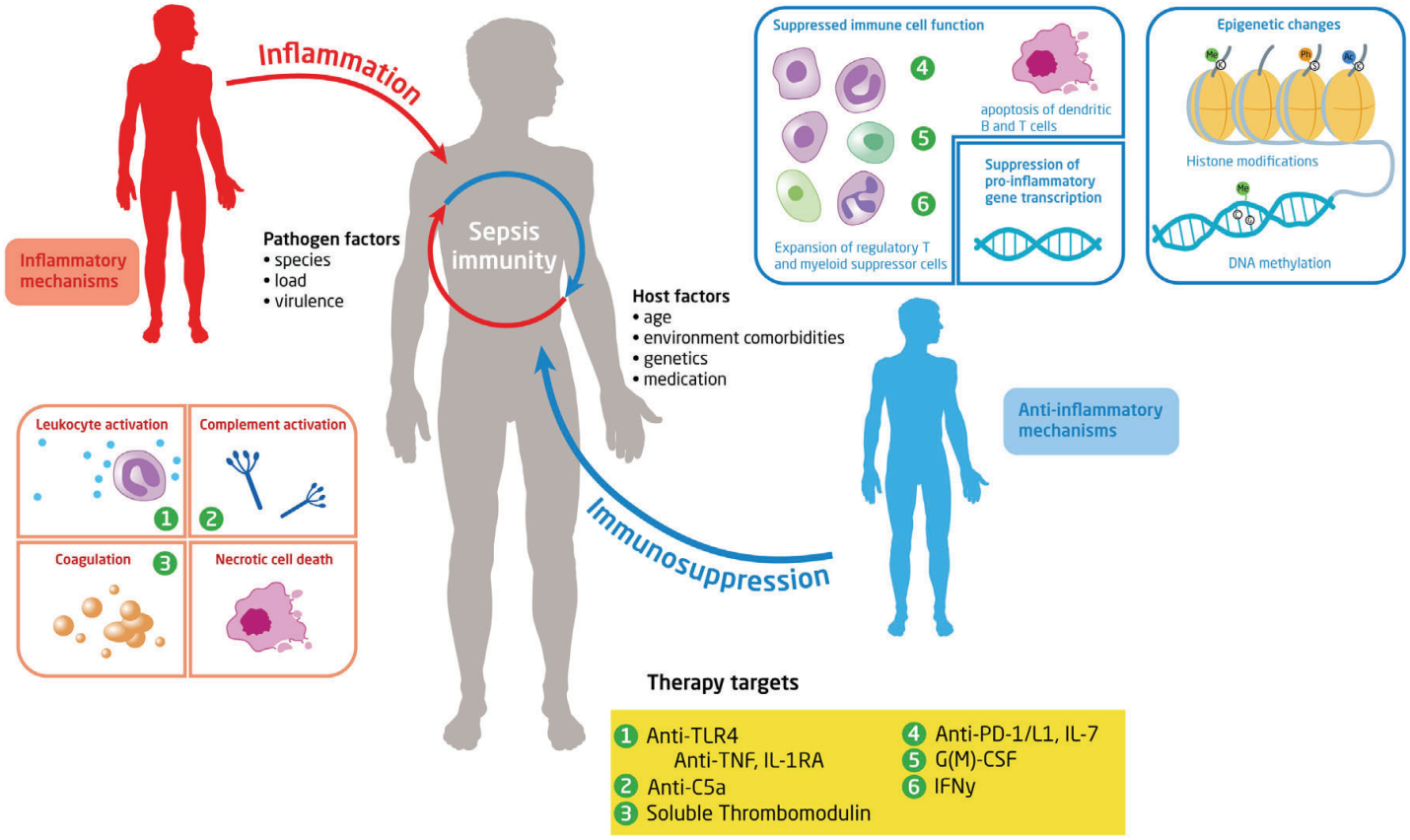
- **Mortalité à court terme** (jusqu'à 90 jours): RR 0,70 (IC 95%, 0,51–0,95, certitude très faible)
- **Mortalité à 1 an**: RR 0,80 (IC 95%, 0,71–0,95, certitude très faible)
- **Durée de séjour en USI**: Différence moyenne de 2,4 jours de moins (IC 95%, 6,3 jours de moins à 1,5 jours de plus, certitude très faible)
- **Durée de séjour hospitalier**: Différence moyenne de 1,1 jour de moins (IC 95%, 8,5 jours de moins à 6,3 jours de plus)



Crit Care Med. 2026 Apr 1;54(4):725-812; JAMASurg. 2022;157(9):817-826

Définition | Physiopathologie | Traitement

Modulation de la réponse de l'hôte



eBioMedicine 2022;86: 104363

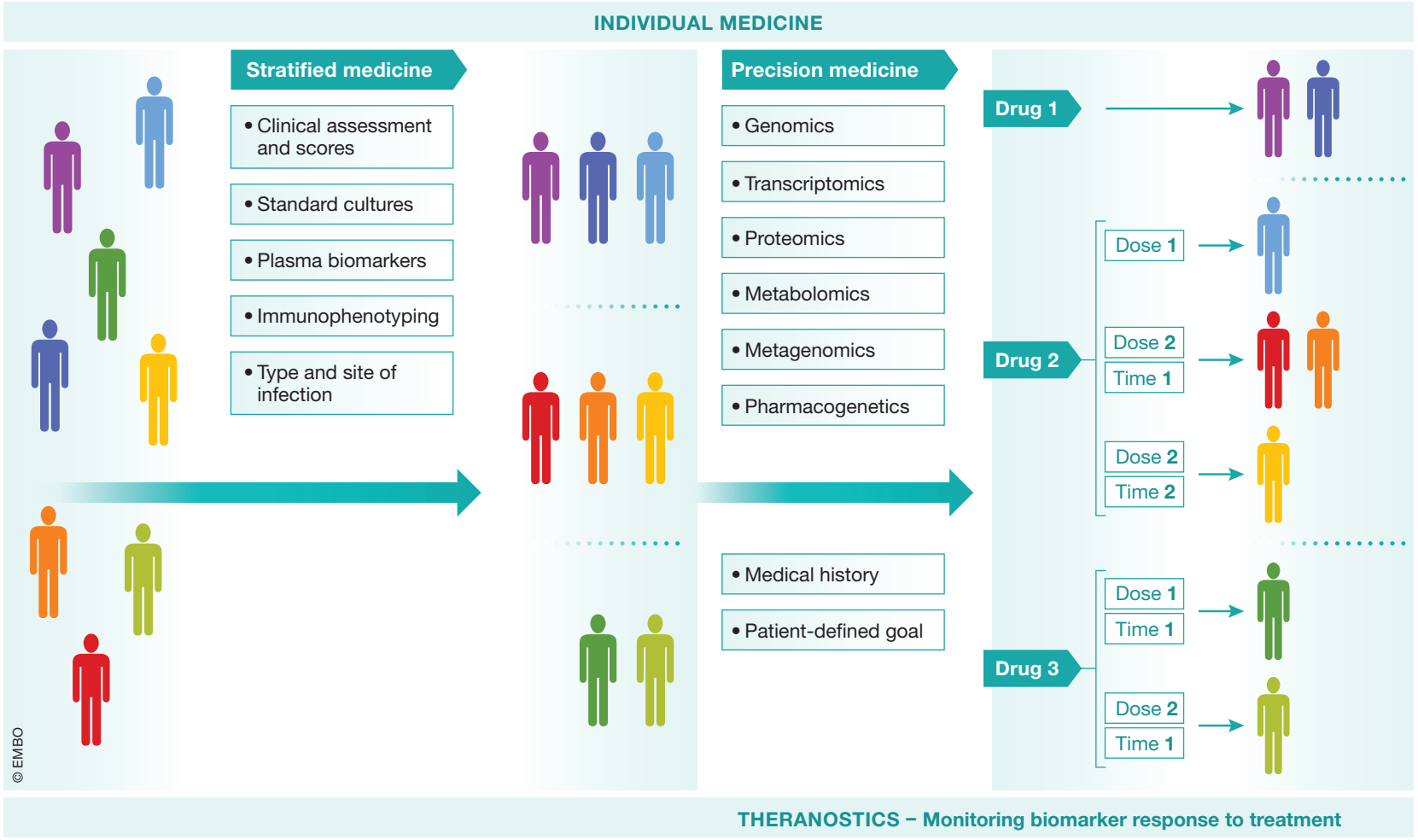
Modulation de la réponse de l'hôte: une longue liste d'échec

Target	Strategy	References
Lps/Endotoxin	HA-1A	Ziegler et al., 1991
	E5531	Bunnell et al., 2000
	Anti-CD14	Reinhart et al., 2004
	Eritoran	Opal et al., 2013
	Polymyxin B conjugate	Payen et al., 2015
Endocrinopathy	Methylprednisolone	Bone et al., 1989
	Vasopressin	Ohsugi et al., 2016
Hypercoagulability /Disseminated Intravascular Coagulation (DIC)	Activated Protein C	Bernard et al., 2001
	Anti-thrombin	Warren et al., 2001
	Heparin	Zhang and Ma, 2006
	Thrombomodulin	Hagiwara et al., 2016
Cytokines	Anti-TNF-α	Tracey et al., 1987
	IL-1 receptor Antagonists	Fisher et al., 1994
	Soluble TNF-α receptor	Borrelli et al., 1996
	Diacerhein	Calisto et al., 2012
Eicosanoids	Ibuprofen	Bernard et al., 1997
Nitric Oxide	L-NMMA	Petros et al., 1994
Oxidat1ve Stress	Statins	Patel et al., 2012
	Selenium	Sakr et al., 2014
Nf-Kb Transcription	Curcumin	Zhong et al., 2016
Apoptosis	Caspase inhibitors	Weber et al., 2009

Most, if not all, were targeting inflammation including caspase inhibitors. Caspases do have a central role in inflammation (Mandal et al., 2018).

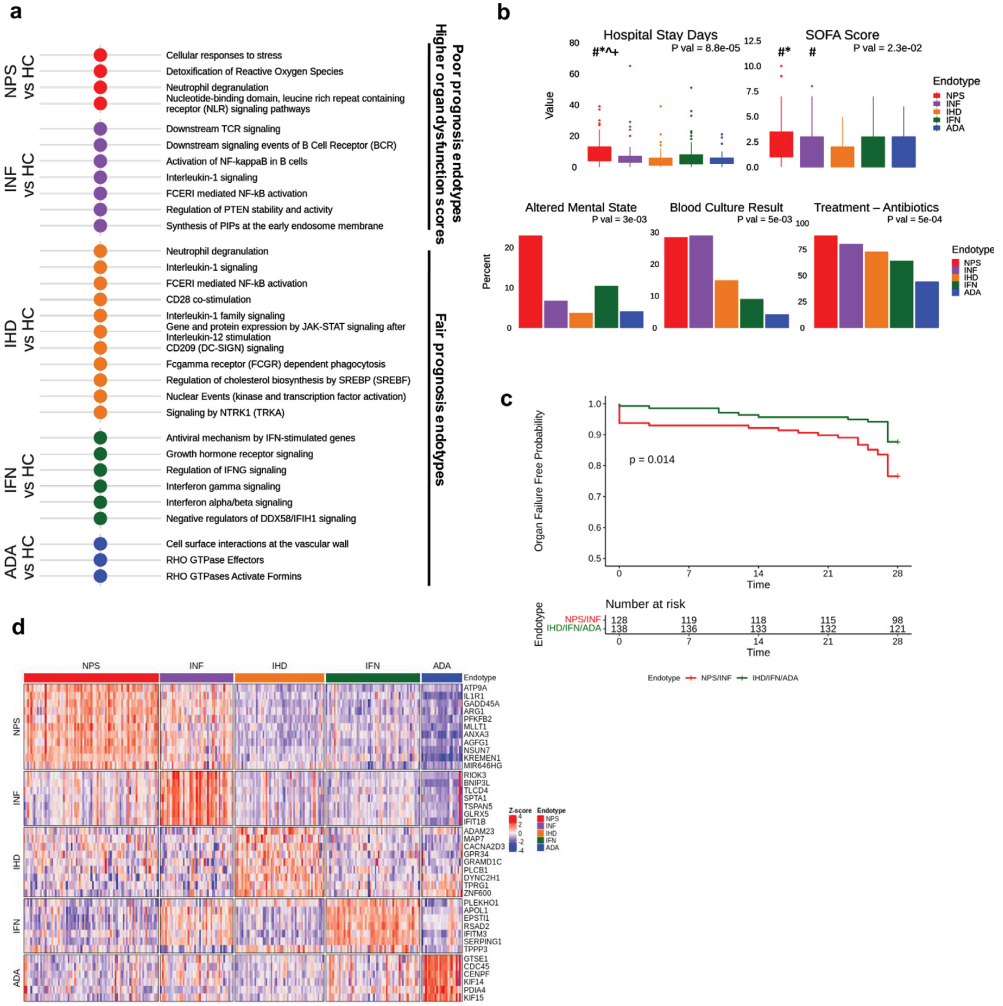
Front. Cell Dev. Biol. 7:108.

Définition | Physiopathologie | Traitement



EMBO Molecular Medicine 12: e10128 | 2020

Définition → Physiopathologie → Traitement



5 endotypes:

- « **neutrophilic-suppressive** » (associated with neutrophil activation and immune suppression)
- « **inflammatory** » (increased proinflammatory response)
- « **innate host defense** » (interleukin signaling)
- « **interferon** » (increased IFNα, IFNβ, and IFNγ)
- « **adaptive** » (increased adaptive immunity

EBioMedicine . 2022 Jan:75:103776.

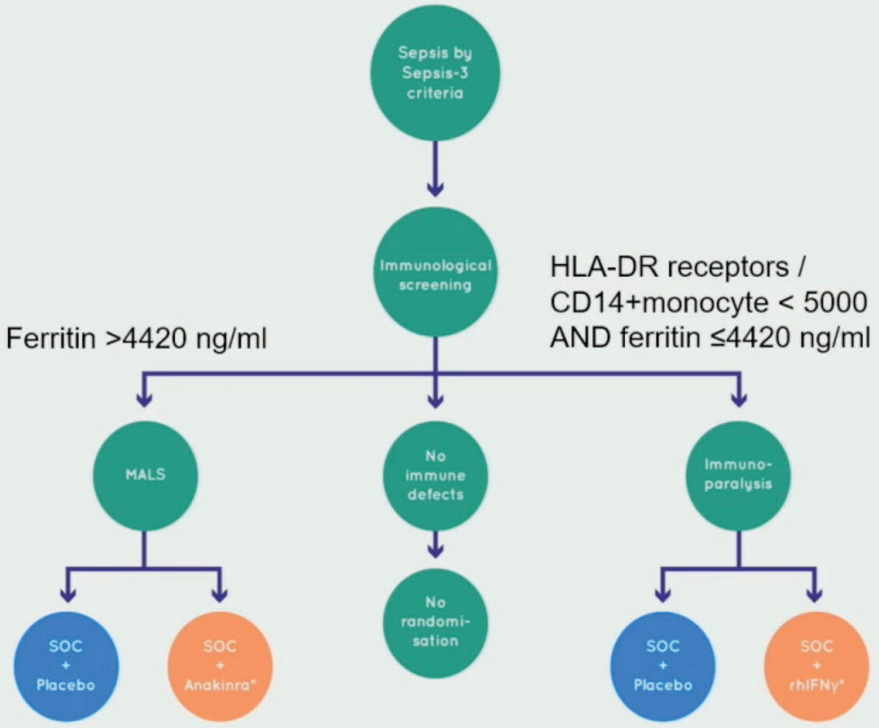
Définition | Physiopathologie | Traitement

Targeting both: The IMMUNOSEP trial

Phase 2b, 6 countries, 33 sites
N= 280 patients with sepsis
pneumonia or primary bacteremia

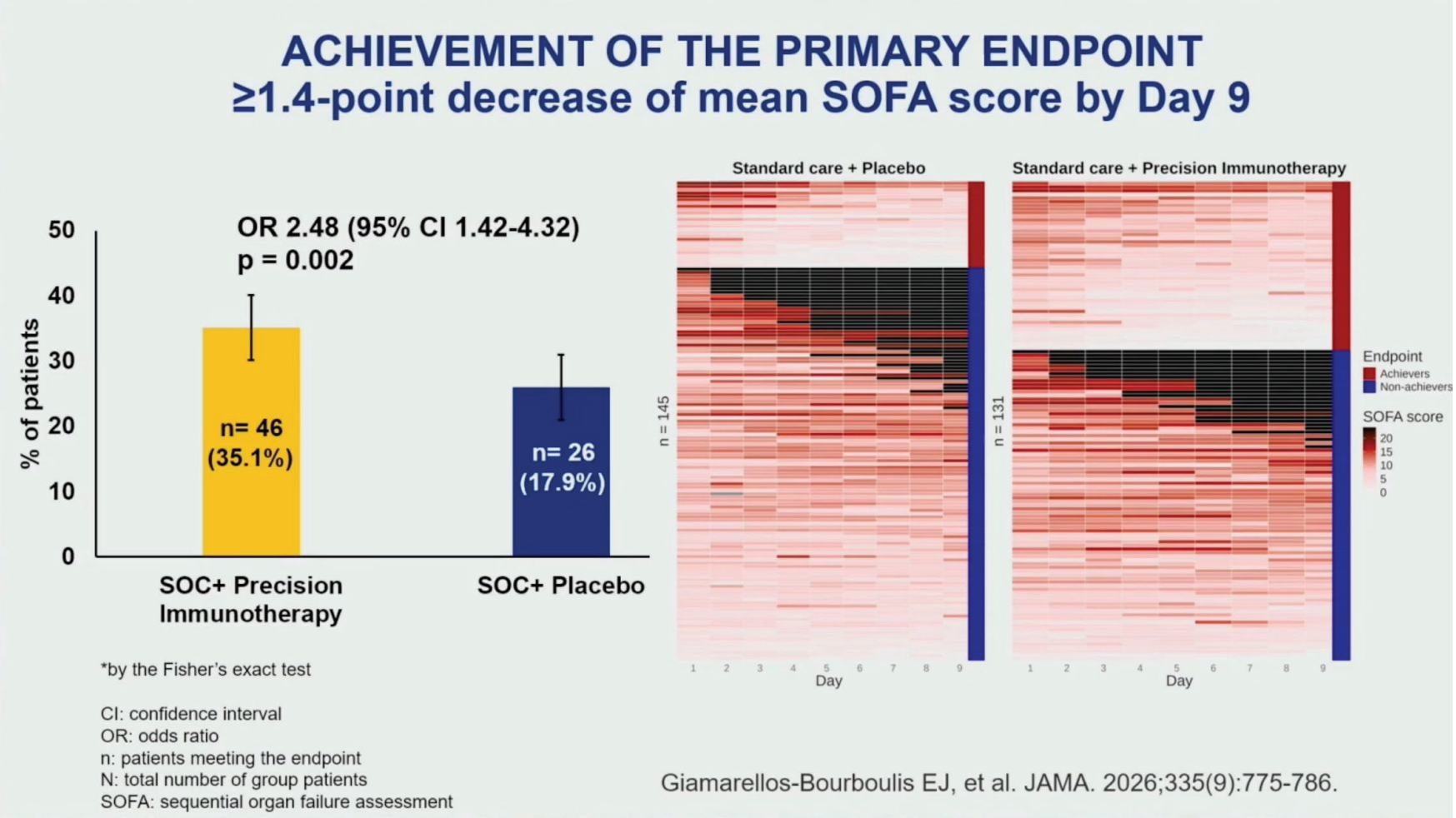
Primary outcome: decrease in mean SOFA score (days 2-9 compared to day 1) by ≥ 1.4

Secondary endpoints:
28-day mortality
90-day mortality
Decrease of mean SOFA score (days 2-15 compared to day 1) by ≥ 1.4
Reversal of immune dysfunction
Ferritin decrease by ≥15% in MALS
HLA-DR increase > 8000 AB/c in immunoparalysis
Infection resolution



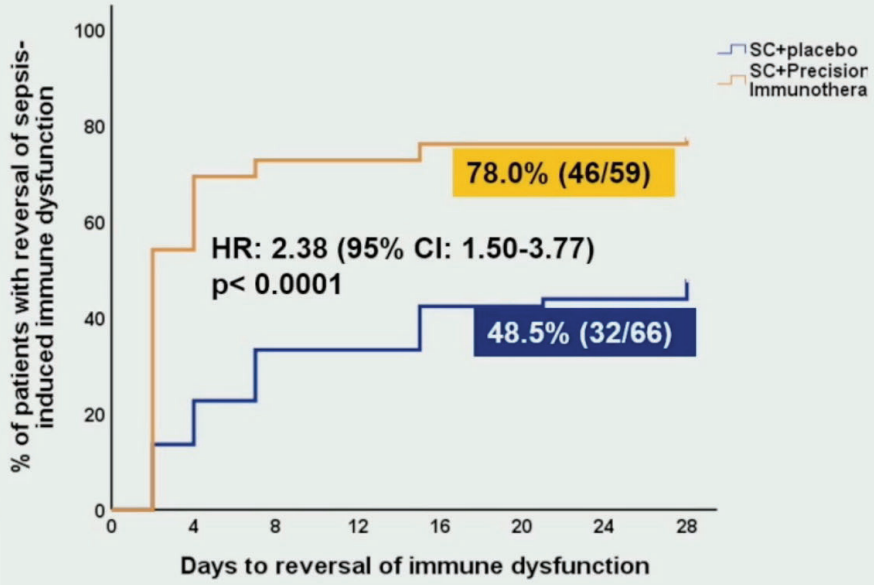
Kotsaki A, et al. BMJ Open 2022; 12: e067251.

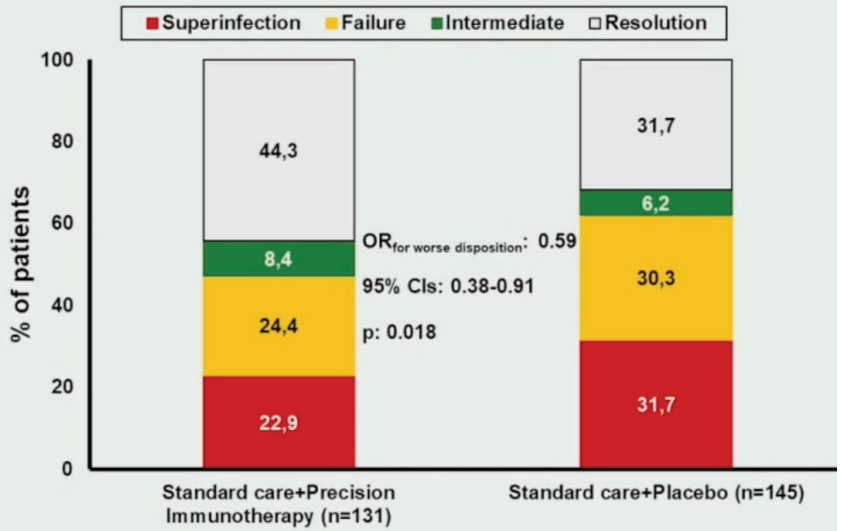
Définition | Physiopathologie | Traitement



Définition | Physiopathologie | Traitement

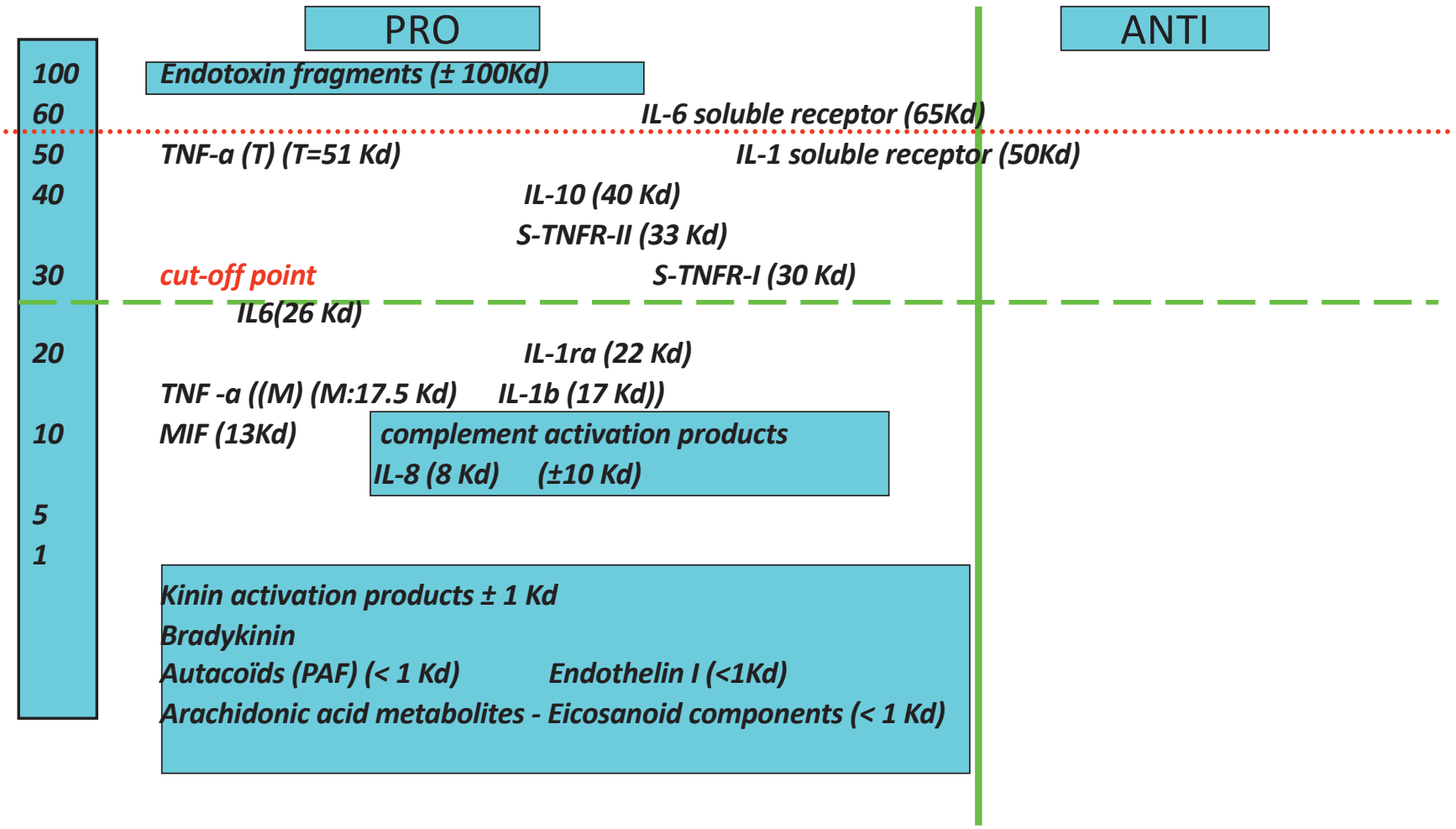
SECONDARY ENDPOINT: Improvement of immune dysfunction and infection resolution





CI: confidence interval
HR: hazard ratio
MALS: macrophage activation-like syndrome
SC: standard care
SII: sepsis-induced immunoparalysis

Filtration des cytokines

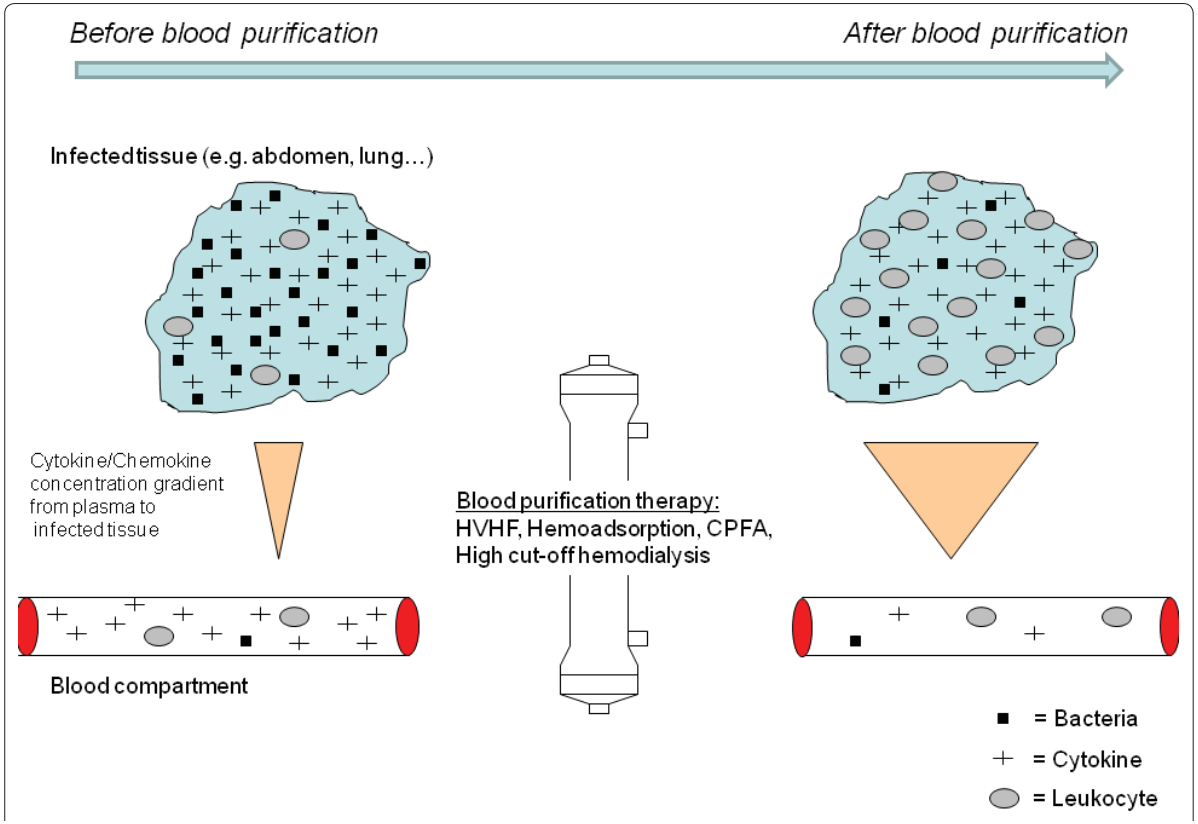


CRITICAL CARE

Modulation of chemokine gradients by apheresis redirects leukocyte trafficking to different compartments during sepsis, studies in a rat model

Zhi-Yong Peng[1,2], Jeffery V Bishop[2], Xiao-Yan Wen[1,2], Michele M Elder[1,2], Feihu Zhou[1,2], Anan Chuasuwan[1,2], Melinda J Carter[2], Jason E Devlin[3], A Murat Kaynar[1,2], Kai Singbartl[1,2], Francis Pike[1,2], Robert S Parker[1,2,5,6], Gilles Clermont[1,2,5,6], William J Federspiel[1,2,4,6] and John A Kellum[1,2,4,6,7*]

2014



High-volume versus standard-volume haemofiltration for septic shock patients with acute kidney injury (IVOIRE study): a multicentre randomized controlled trial

Olivier Joannes-Boyau
Patrick M. Honoré
Paul Perez
Sean M. Bagshaw
Hubert Grand
Jean-Luc Canivet
Antoine Dewitte

2013

137 patients en choc septique et Insuffisance rénale

Dose catécholamine (Nad) Ou > 5µg/kg/m de Dopamine

- Oligurie < 0.5 ml/kg/h
- créatinine X 2

RIFLE Injury

Randomisation sous 24h (choc septique précoce)

35 ml/kg/h

70 ml/kg/h

Mortalité

D28

D90

High-volume versus standard-volume haemofiltration for septic shock patients with acute kidney injury (IVOIRE study): a multicentre randomized controlled trial

Olivier Joannes-Boyau
Patrick M. Honoré
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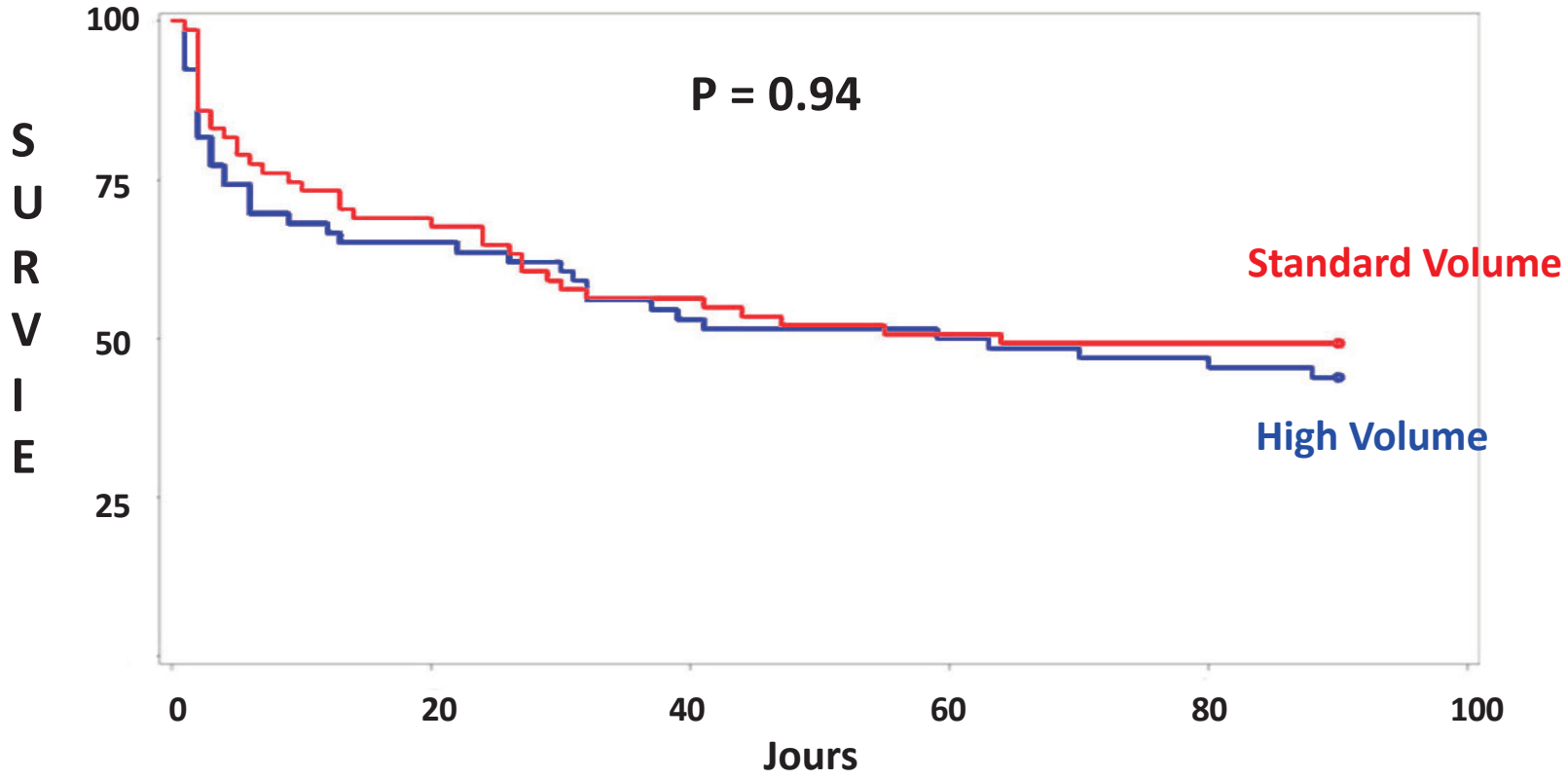
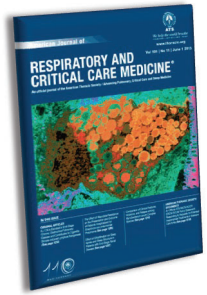
Hubert Grand
Jean-Luc Canivet
Antoine Dewitte

2013





Early High-Volume Hemofiltration versus Standard Care for Post–Cardiac Surgery Shock

The HEROICS Study

Alain Combes[1], Nicolas Bréchot[1], Julien Amour[2], Nathalie Cozic[3], Guillaume Lebreton[4], Catherine Guidon[5], Elie Zogheib[6], Jean-Claude Thiranos[7], Jean-Christophe Rigal[8], Olivier Bastien[9], Hamina Benhaoua[10], Bernard Abry[11], Alexandre Ouattara[12], Jean-Louis Trouillet[1], Alain Mallet[3], Jean Chastre[1], Pascal Leprince[4], and Charles-Edouard Luyt[1]

2015

360 patients en post-chirurgie cardiaque

Dose catécholamine
Nad ou Adre

Randomisation sous 24h

35 ml/kg/h

80 ml/kg/h

Mortality

D28

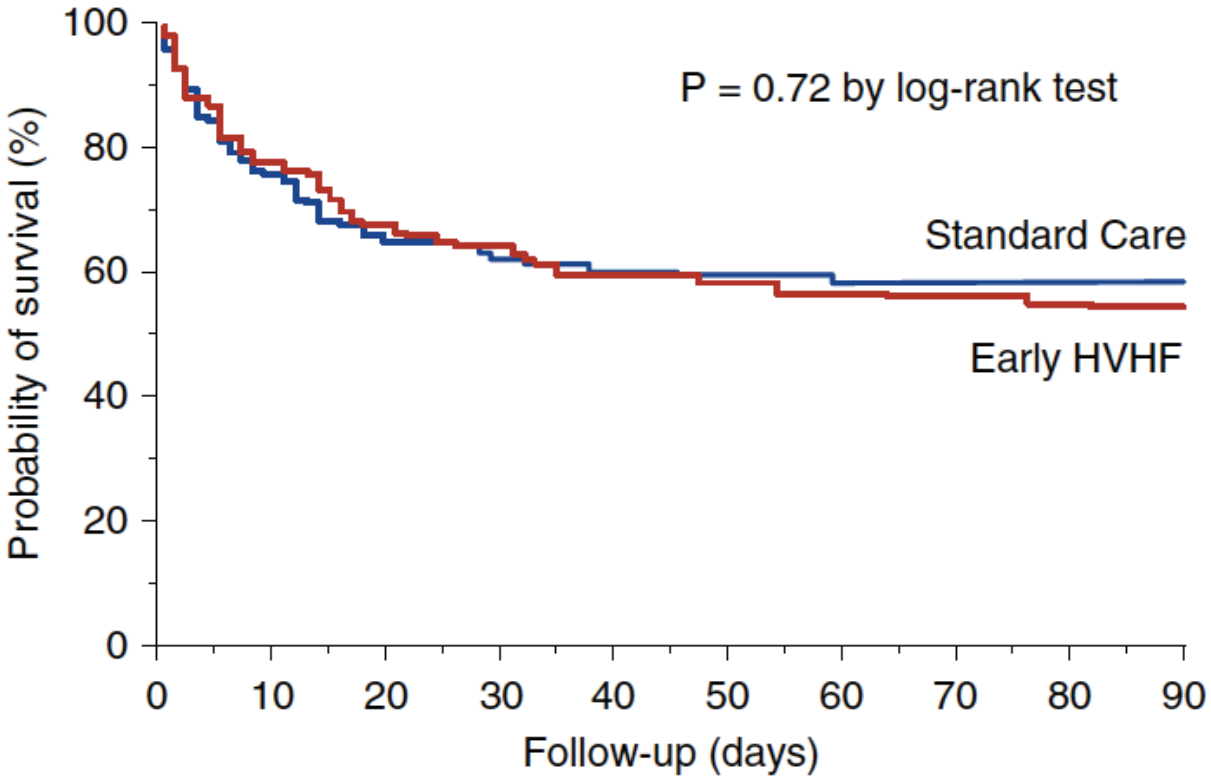
D90

Early High-Volume Hemofiltration versus Standard Care for Post–Cardiac Surgery Shock

The HEROICS Study

Alain Combes[1], Nicolas Bréchot[1], Julien Amour[2], Nathalie Cozic[3], Guillaume Lebreton[4], Catherine Guidon[5], Elie Zogheib[6], Jean-Claude Thiranos[7], Jean-Christophe Rigal[8], Olivier Bastien[9], Hamina Benhaoua[10], Bernard Abry[11], Alexandre Ouattara[12], Jean-Louis Trouillet[1], Alain Mallet[3], Jean Chastre[1], Pascal Leprince[4], and Charles-Edouard Luyt[1]

2015



High-volume hemofiltration for septic acute kidney injury: a systematic review and meta-analysis

Edward Clark[1,2], Amber O Molnar[1,2], Olivier Joannes-Boyau[3], Patrick M Honoré[4], Lindsey Sikora[5] and Sean M Bagshaw[6*]

2014

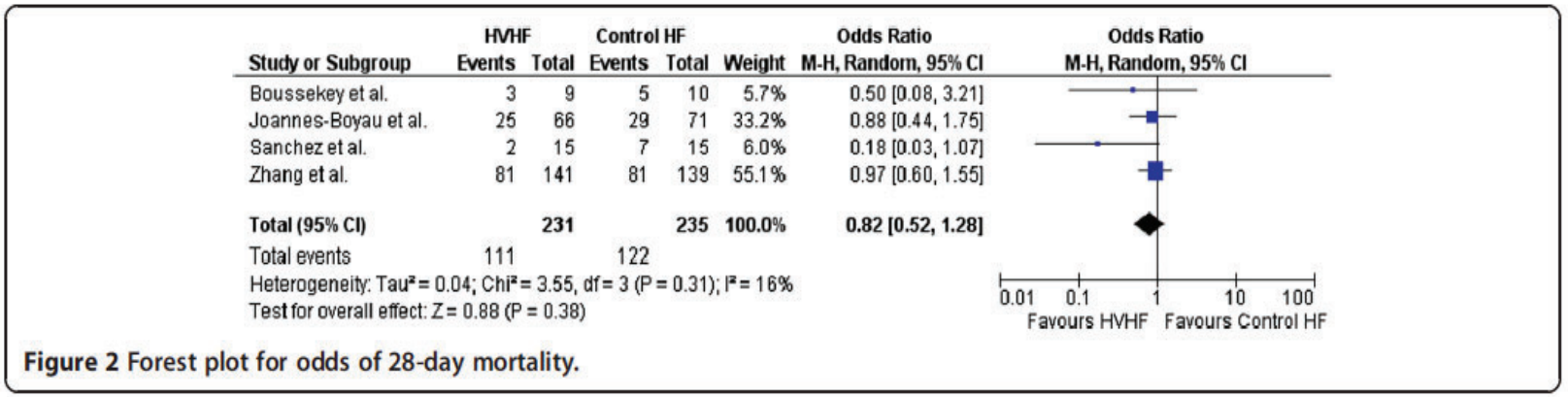
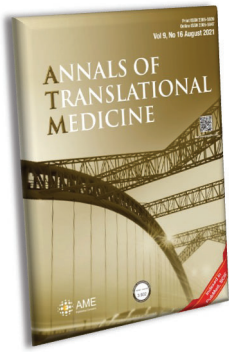


Figure 2 Forest plot for odds of 28-day mortality.



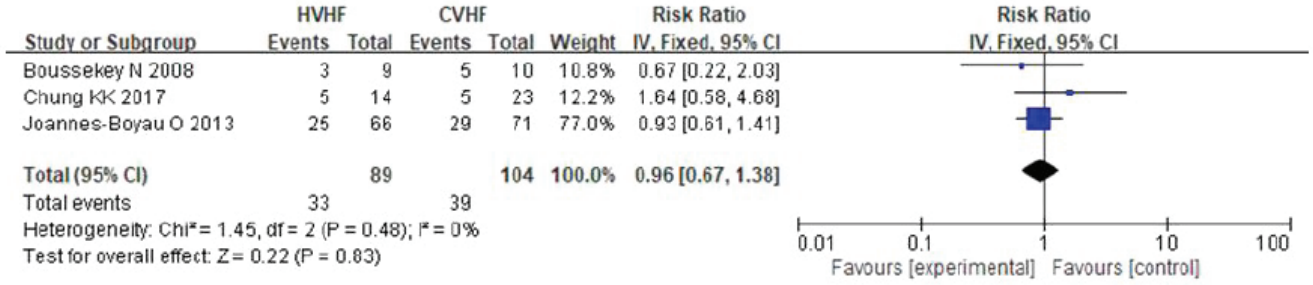
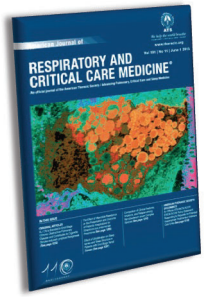


Figure 4 Forest plot of comparison in relative risk of mortality.



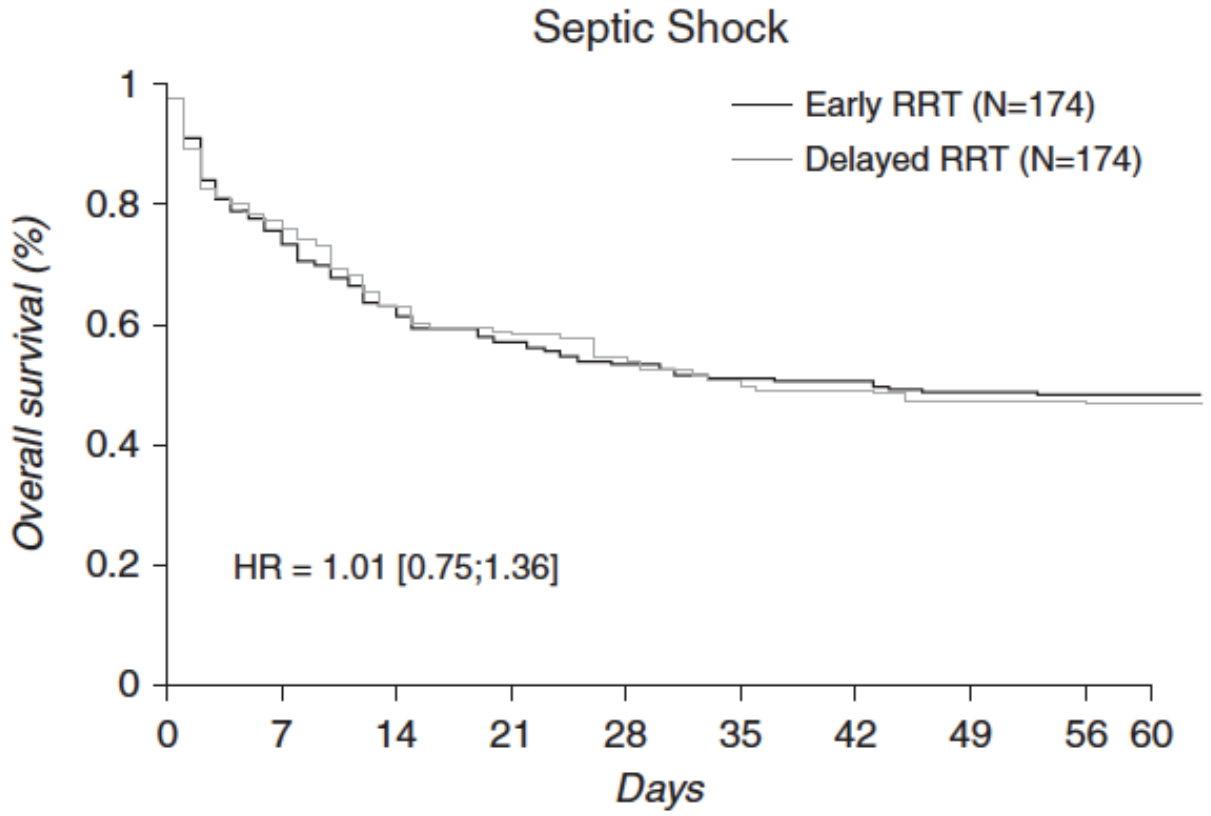
Timing of Renal Support and Outcome of Septic Shock and Acute Respiratory Distress Syndrome

2018

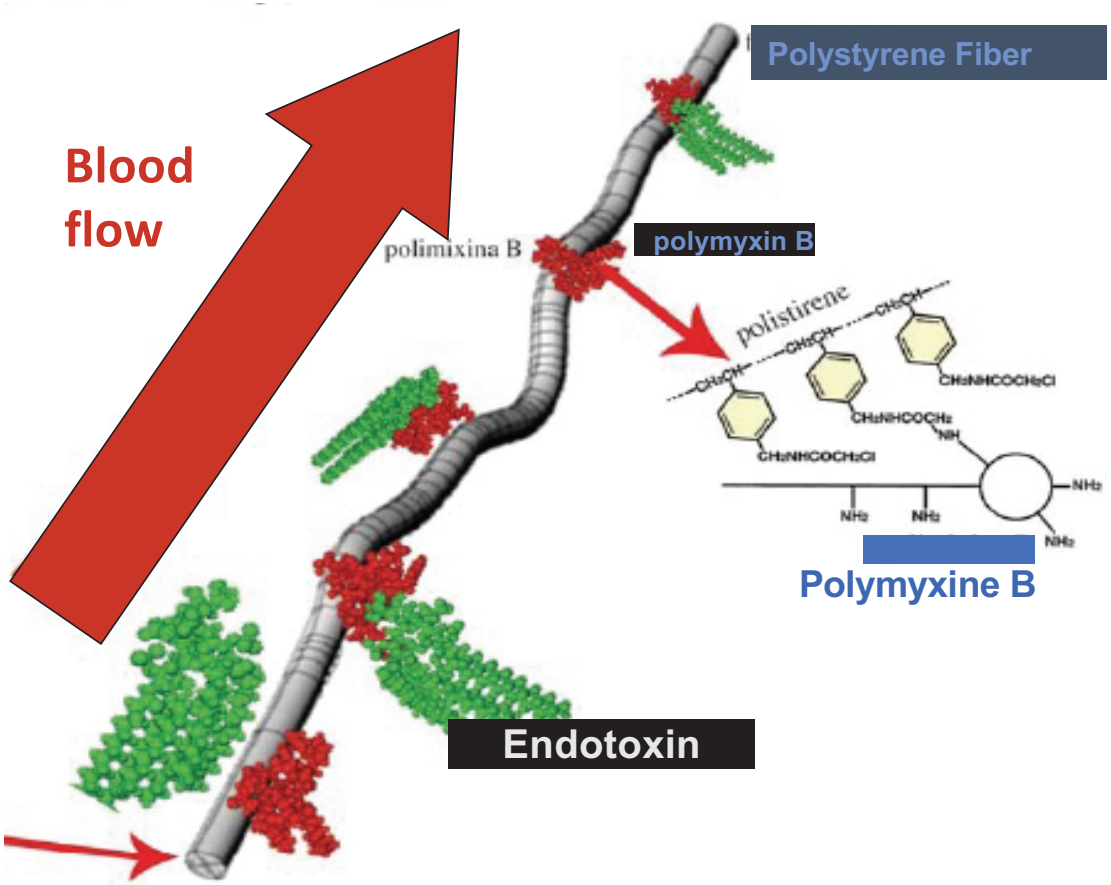
A *Post Hoc* Analysis of the AKIKI Randomized Clinical Trial

Stéphane Gaudry[1,2], David Hajage[3,4,5], Frédérique Schortgen[6], Laurent Martin-Lefevre[7], Charles Verney[1], Bertrand Pons[8,9], Eric Boulet[10], Alexandre Boyer[11], Guillaume Chevrel[12], Nicolas Lerolle[13], Dorothée Carpentier[14],

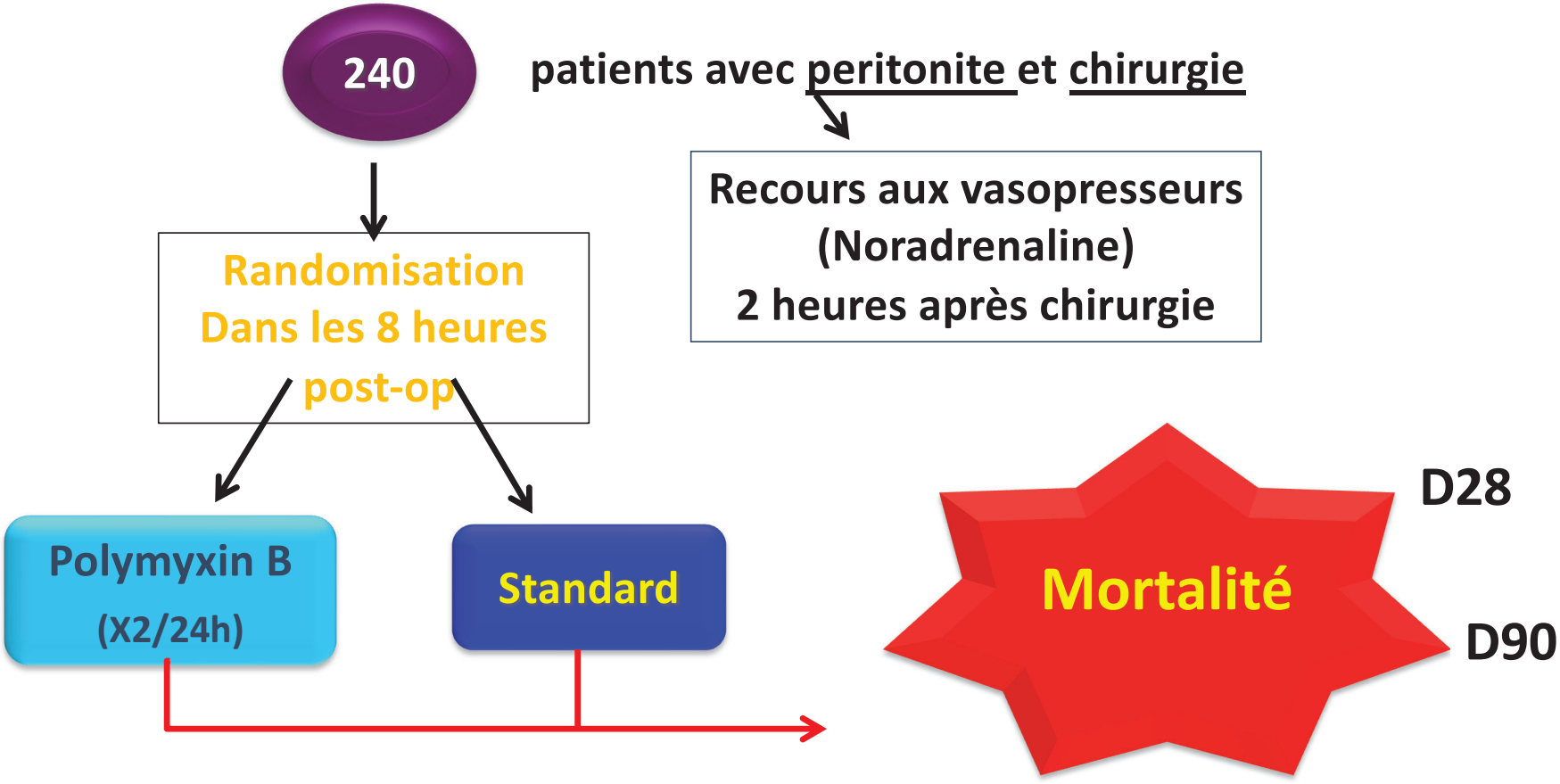
A



Polymyxin B membrane



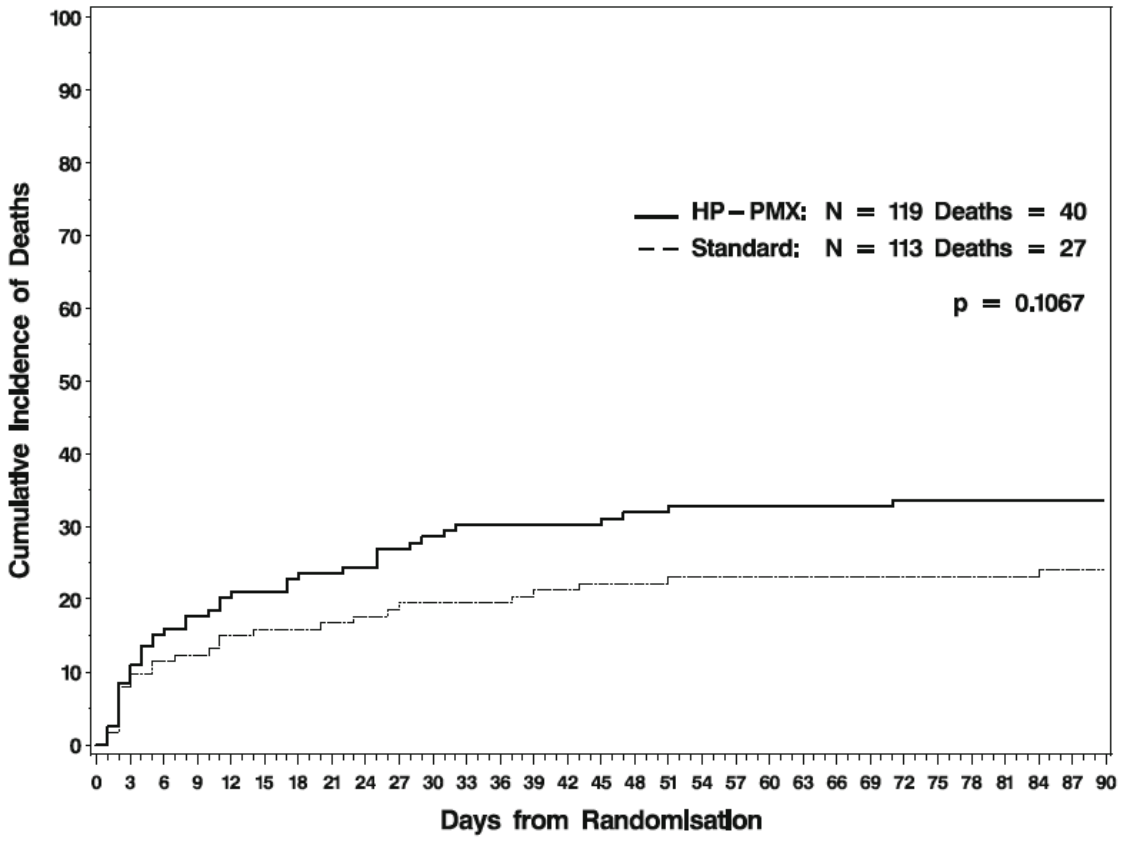
« ABDO-MIX study »



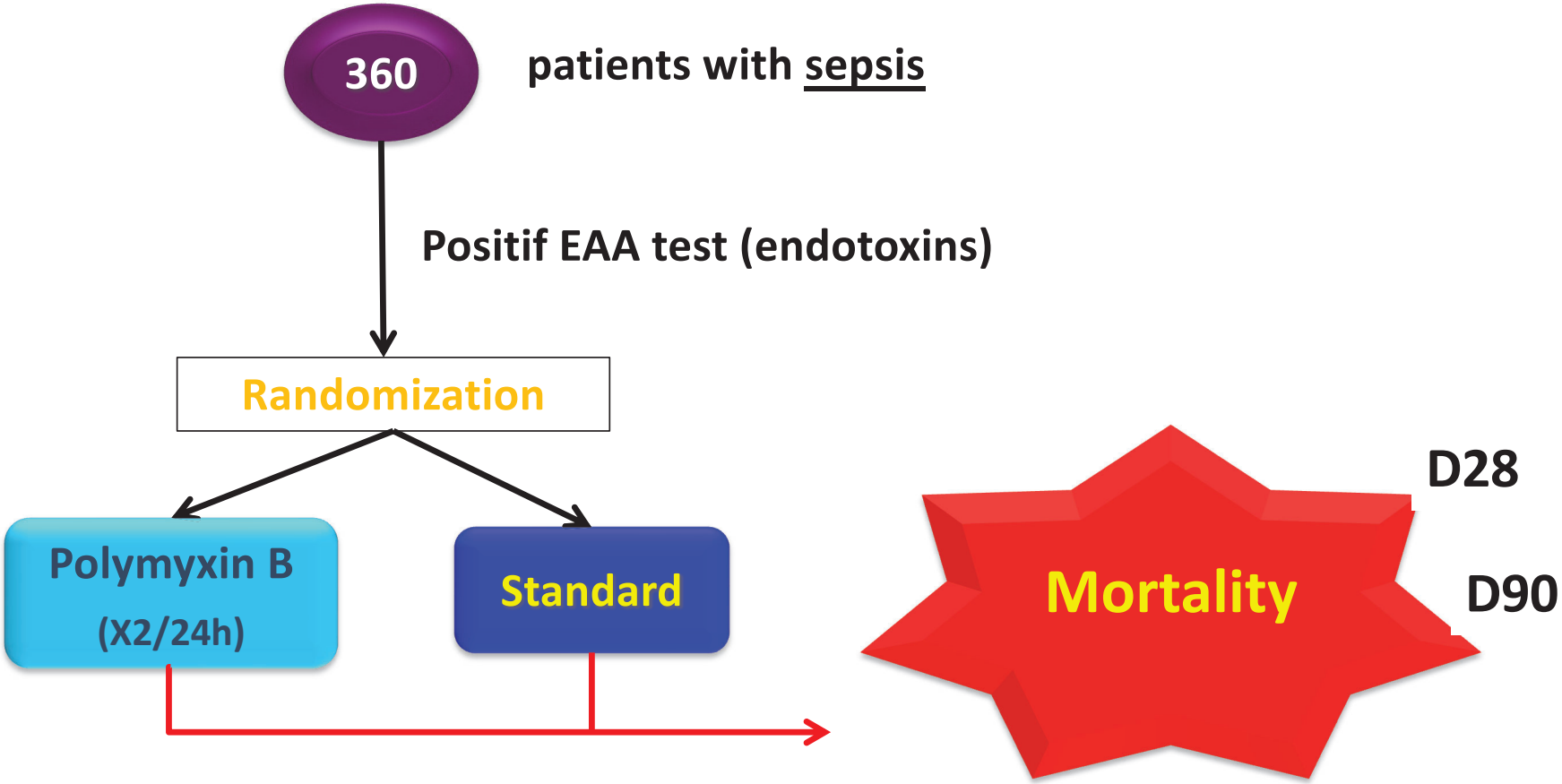
Early use of polymyxin B hemoperfusion in patients with septic shock due to peritonitis: a multicenter randomized control trial

Didier M. Payen
Joelle Guilhot
Yoann Launey
Anne Claire Lukaszewicz
Mahmoud Kaaki
Benoit Veber
Julien Pottecher
Olivier Joannes-Boyau
Laurent Martin-Lefevre

2015



« EUPHRATES study »



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

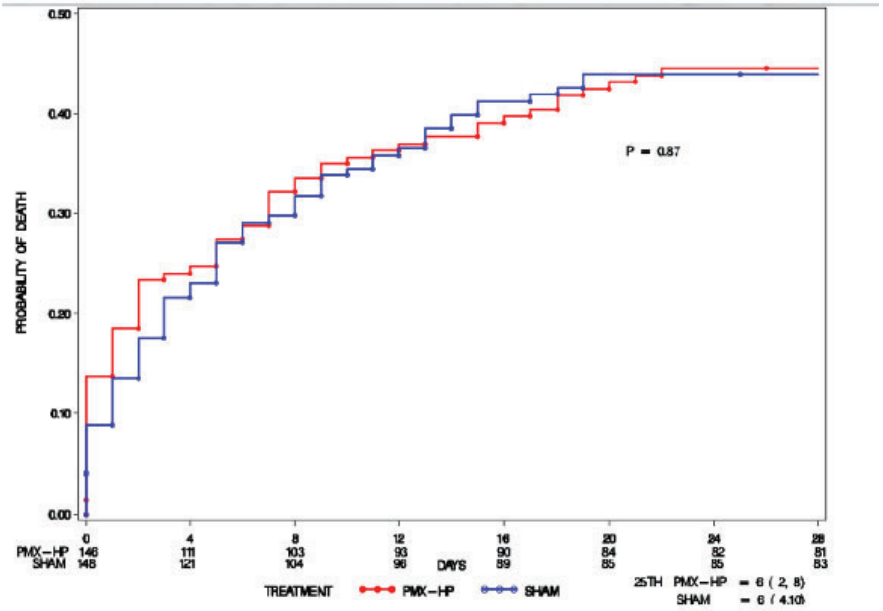
The EUPHRATES Randomized Clinical Trial

2018

R. Phillip Dellinger, MD, MSc; Sean M. Bagshaw, MD, MSc; Massimo Antonelli, MD; Debra M. Foster, BSc; David J. Klein, MD, MBA; John C. Marshall, MD; Paul M. Palevsky, MD; Lawrence S. Weisberg, MD; Christa A. Schorr, DNP, MSN, RN; Stephen Trzeciak, MD, MPH; Paul M. Walker, MD, PhD; for the EUPHRATES Trial Investigators

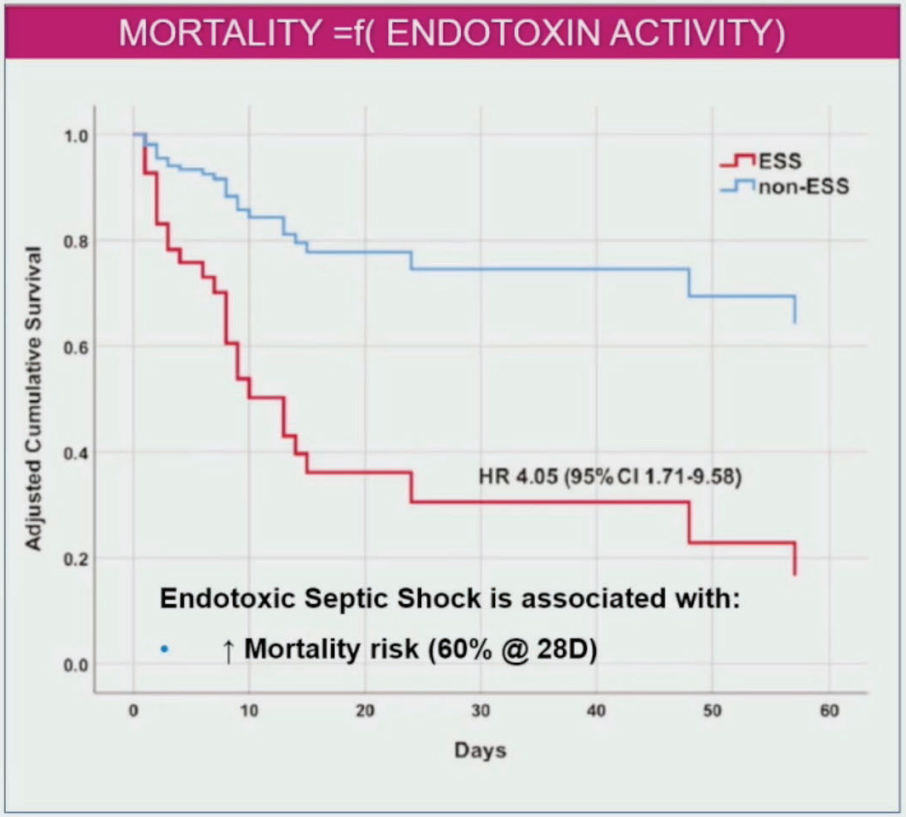
Table 2. Summary of the Primary End Point of 28-Day Mortality for All Participants and for Patients With MODS of More Than 9

	No./Total (%)		(95% CI)		
	Polymyxin-B Hemoperfusion	Sham	Risk Difference	Risk Ratio	*P* Value[a]
All Participants	84/223 (37.7)	78/226 (34.5)	3.15 (−5.73 to 12.04)	1.09 (0.85 to 1.39)	.49
>9 MODS[b]	65/146 (44.5)	65/148 (43.9)	0.60 (−10.75 to 11.97)	1.01 (0.78 to 1.31)	.92

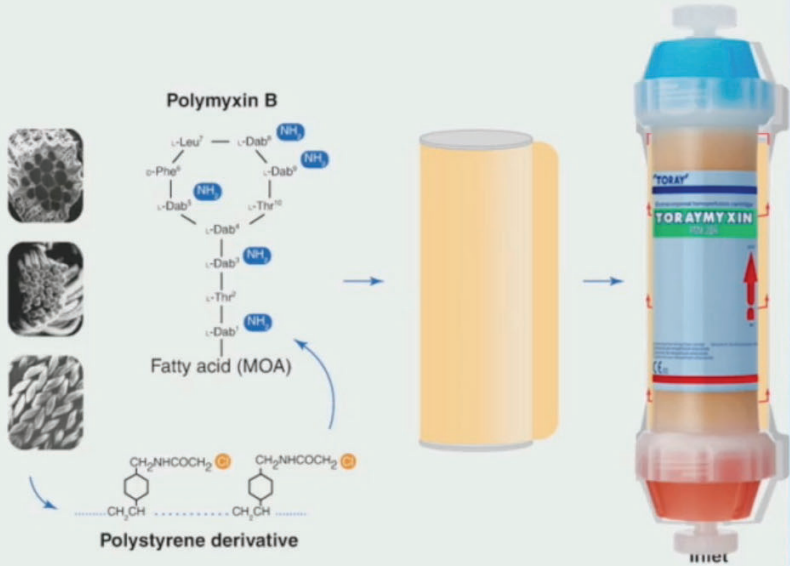


Définition | Physiopathologie | Traitement

Endotoxic Septic Shock



- **POLYMYXIN Based Endotoxin Adsorption**



Définition | Physiopathologie | Traitement

Polymyxin B haemoadsorption in endotoxic septic shock (Tigris): a multicentre, open-label, Bayesian, randomised, controlled, phase 3 trial

Al-Khafaji, Claude Galphin, Ronald Rains, Danielle Davison, Ashita Tolwani, Jen-Ting Chen, ffrey DellaVolpe, George W Williams, Kianoush B Kashani, Kyle J Gunnerson, opa Kohli-Seth, Sugeet Jagpal, David Klein, Esha Kamaluddin, Debra M Foster,

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et of septic shock with high endotoxin activity and multiorgan failure, is ought to identify the effect of endotoxin removal from the blood with

omised, controlled, phase 3 trial at 19 US hospitals, enrolling adults (aged

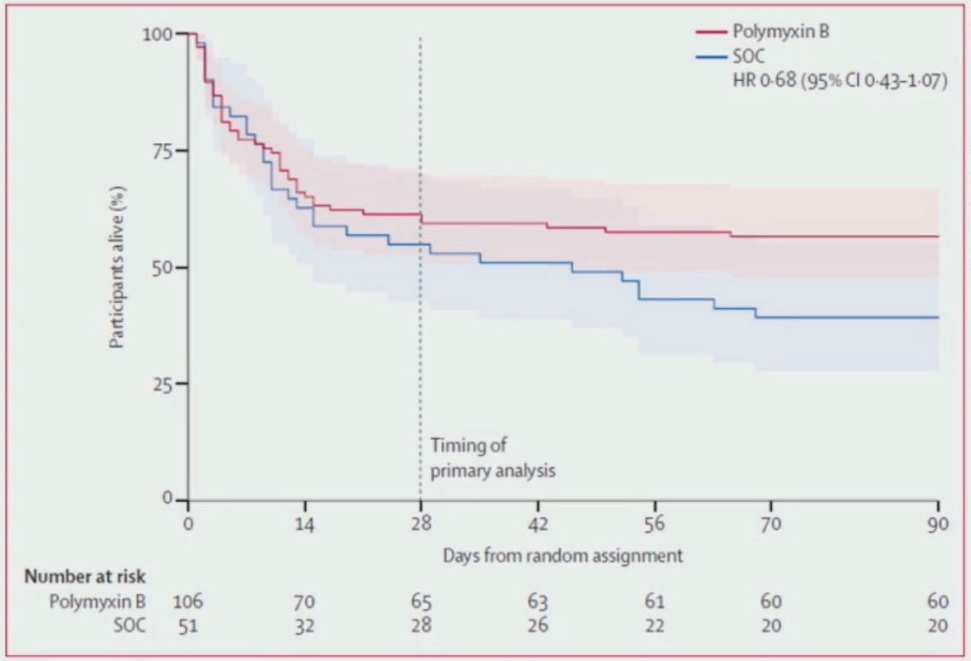
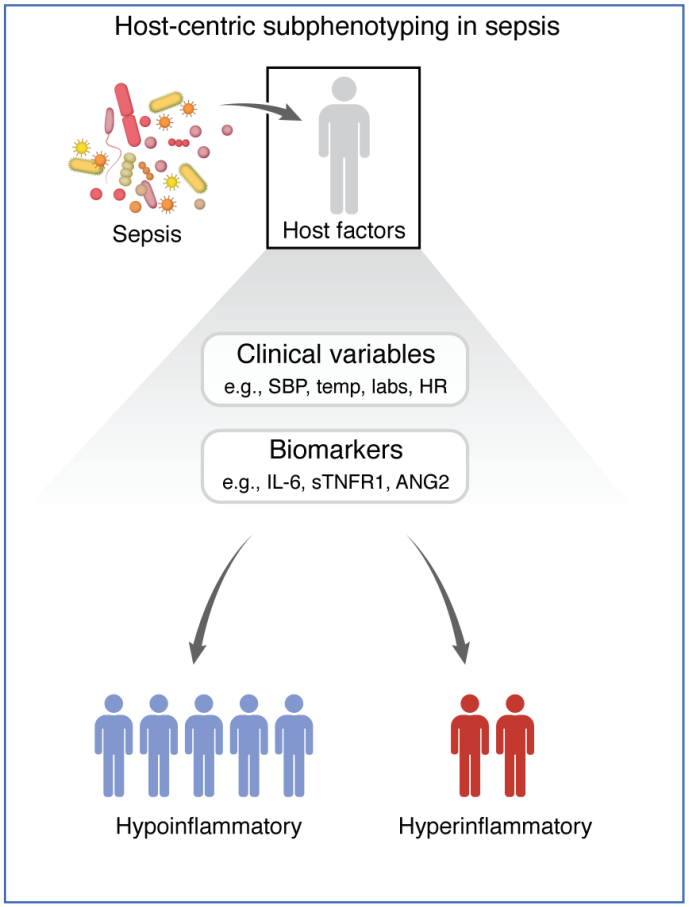
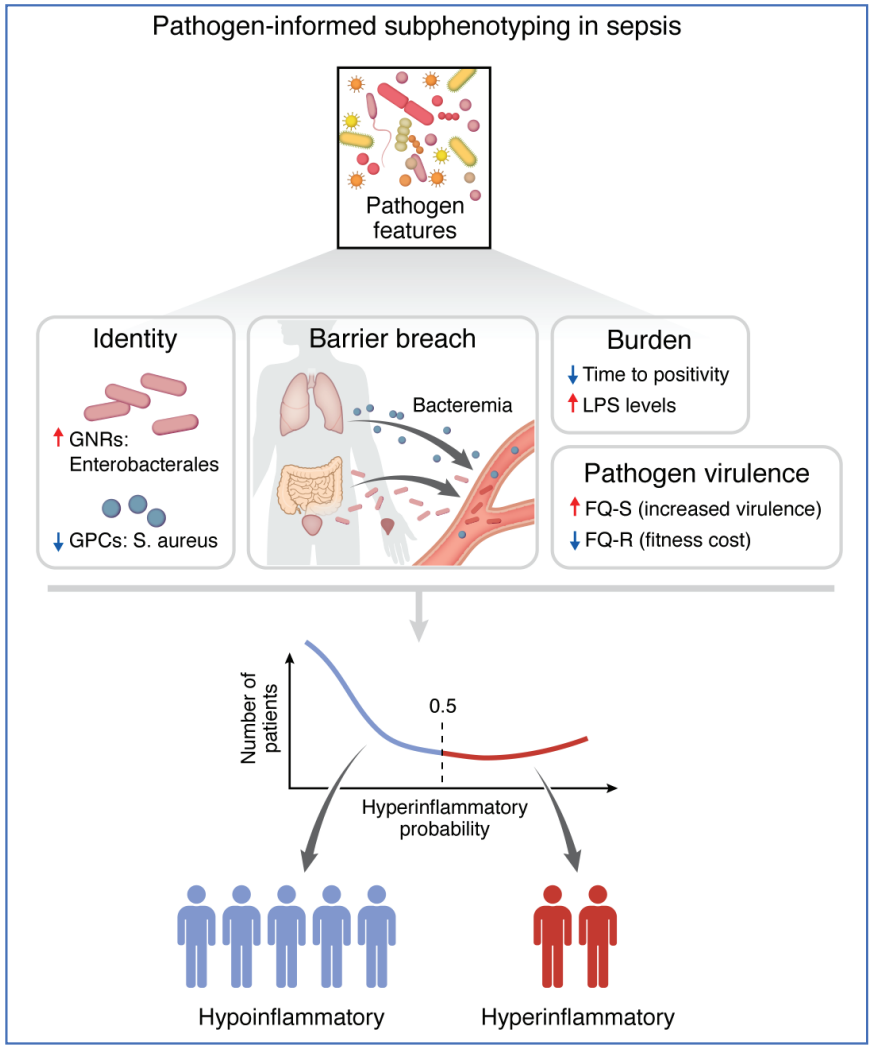


Figure 3: Kaplan–Meier graph of the cumulative survival at 90 days
The solid lines depict the percentage of patients alive in each group and the shaded areas depict the 95% CIs. Results are shown for Tigris only (ie, not including the prior distribution). The HR up to 28 days was 0·84 (95% CI 0·50–1·40). Results for prior distribution are shown in the appendix (p 142). HR=hazard ratio. SOC=standard of care.

Endotoxic septic shock defined by high endotoxin activity and multiorgan failure, polymyxin B haemoadsorption was associated with a high probability of lower mortality at 28 days and 90 days





Redefine critical illness based on biological mechanisms, rather than clinical syndromes

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ImmunoConcEpT

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Director: Déchanet-Merville Julie
Deputy director: Blanco Patrick

université de BORDEAUX

Inserm

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DEWITTE
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PR - Univ. Bordeaux

Groupe SEPSIS

ImmunoConcEpT

The ImmunoConcEpT lab focuses on the immune system and its pathologies; it regroups most investigators involved in this field on the Bordeaux campus.

IMMUNOLOGY from CONCEPT and EXPERIMENTS to TRANSLATION

Team 1 Vulnerability and ageing of the immune system *Julie Déchanet-Merville / Victor Appay*	**Team 2** Origins and pathogenesis of Autoimmune and Inflammatory disorders
Team 3 Immunology of Cancer and Inflammatory Diseases	**Team 4** Conceptual Biology and Medicine