IL PAZIENTE SETTICO PRIMA CHE VADA IN SHOCK

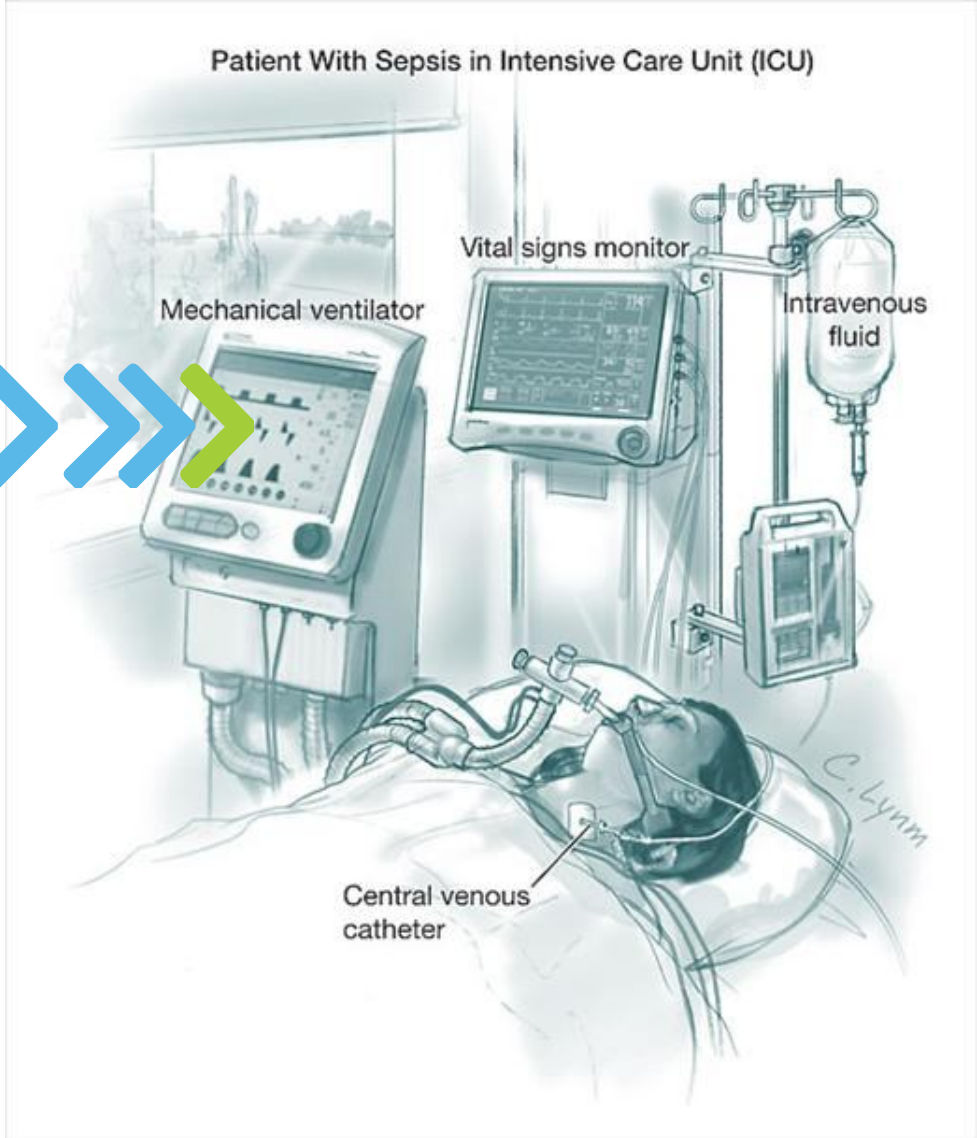
Controversie e novità

Dott. P. POZZESSERE

Medicina e Chirurgia d'Accettazione e d'Urgenza
Azienda Ospedaliera Policlinico BARI

Rimini, 20 ottobre 2012

Paziente con febbre



La sepsi è una malattia sensibile al tempo al pari dell'IMA, del trauma e dell'ictus ischemico

Possiamo parlare di «Golden Hour» anche per il paziente settico?

Antibiotic Therapy

- Begin antibiotics as early as possible, and always within the first hour of recognizing severe sepsis and septic shock.

Key-points

- **Novità e controversie nella fisiopatologia dello shock settico, implicazioni terapeutiche.**

- **Novità e controversie nella diagnosi precoce dello shock settico.**

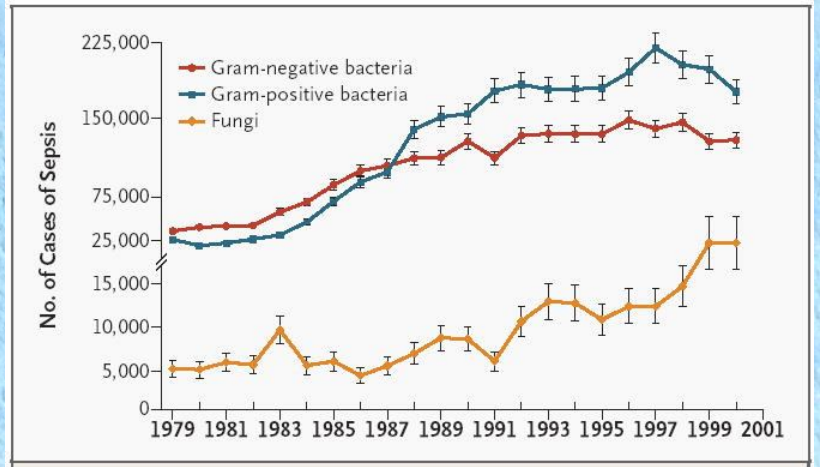


Figure 3. Numbers of Cases of Sepsis in the United States, According to the Causative Organism, 1979–2000.

Points represent the number of cases for the given year, and bars the standard error.

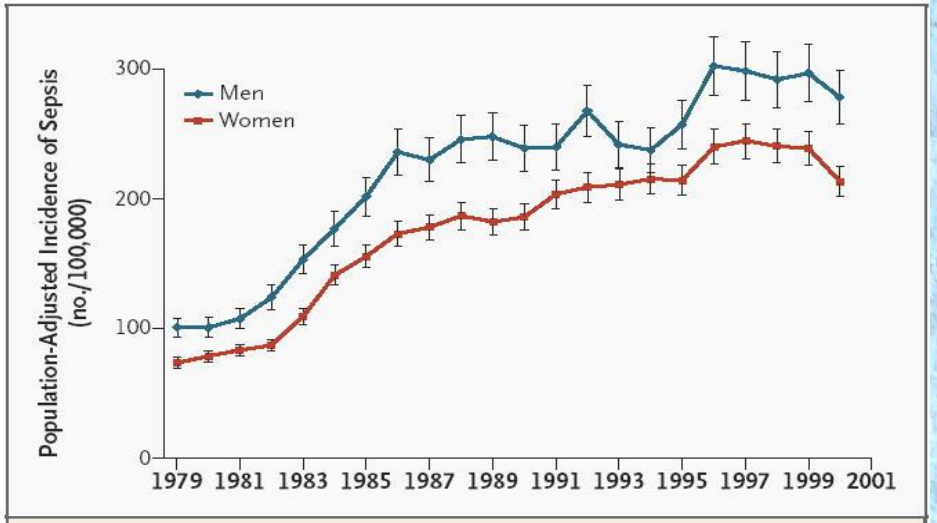
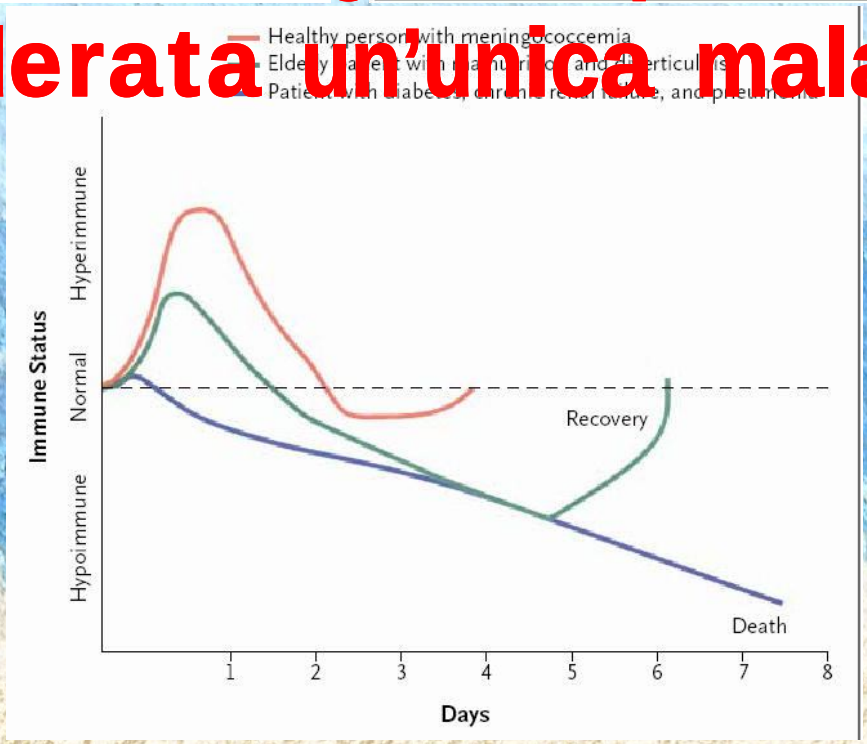


Figure 1. Population-Adjusted Incidence of Sepsis, According to Sex, 1979–2000.

Points represent the annual incidence rate, and bars the standard error.

È troppo eterogenea per essere considerata un unica malattia



Fattori che influenzano la risposta del paziente settico

- **P** redisposition

  (età,gender,comorbidità, int.chirurgici, polimorfismo genetico).
- **I** nfection

  (sede, tipo di germe, resistenza ad antibiotici).
- **R** esponse
- **O** rgan disfunction

Current insights in sepsis: from pathogenesis to new treatment targets

W. Joost Wiersinga

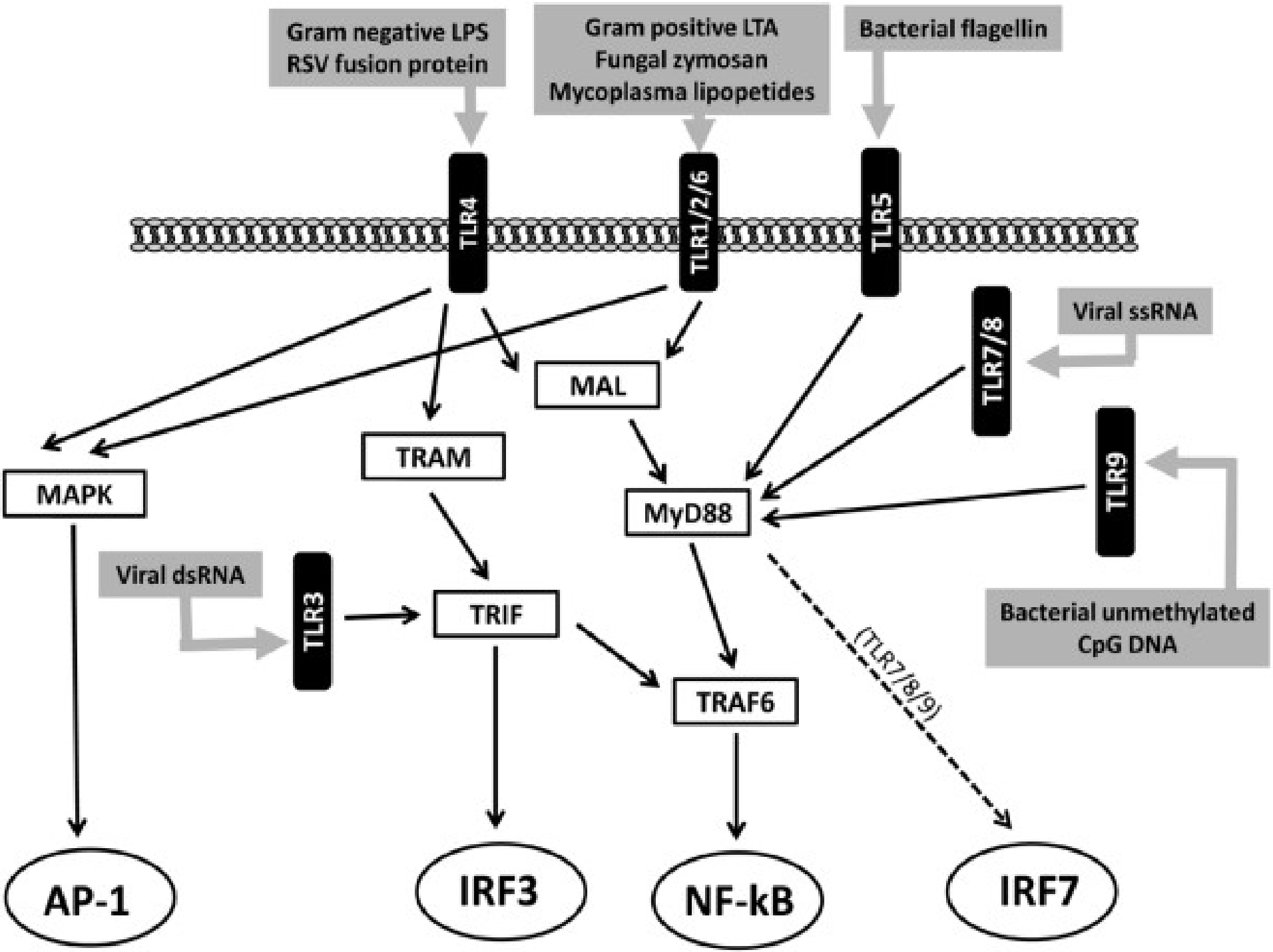
Current Opinion in Critical Care 2011, 17:480–486

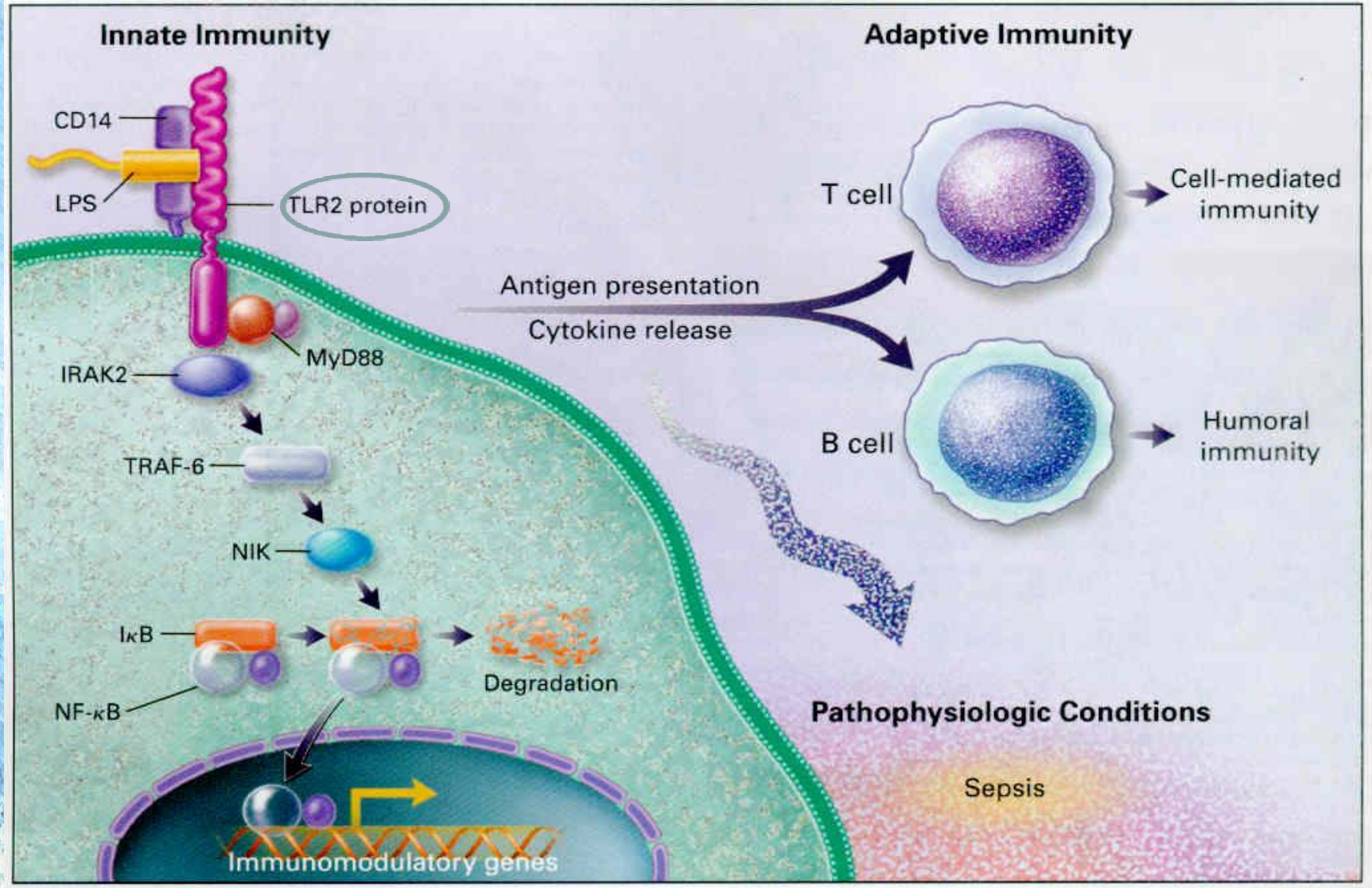
La sepsi può essere vista come una disregolazione del sistema immune mediato dai recettori PRR (pathogen-recognition receptor) conseguente all'invasione di agenti patogeni con conseguente alterazione dell'equilibrio tra risposta infiammatoria e antinfiammatoria.

Pattern-recognition receptors (PRR)

Sono i componenti chiave del sistema immunitario, riconoscono i patogeni e innescano la risposta immune.

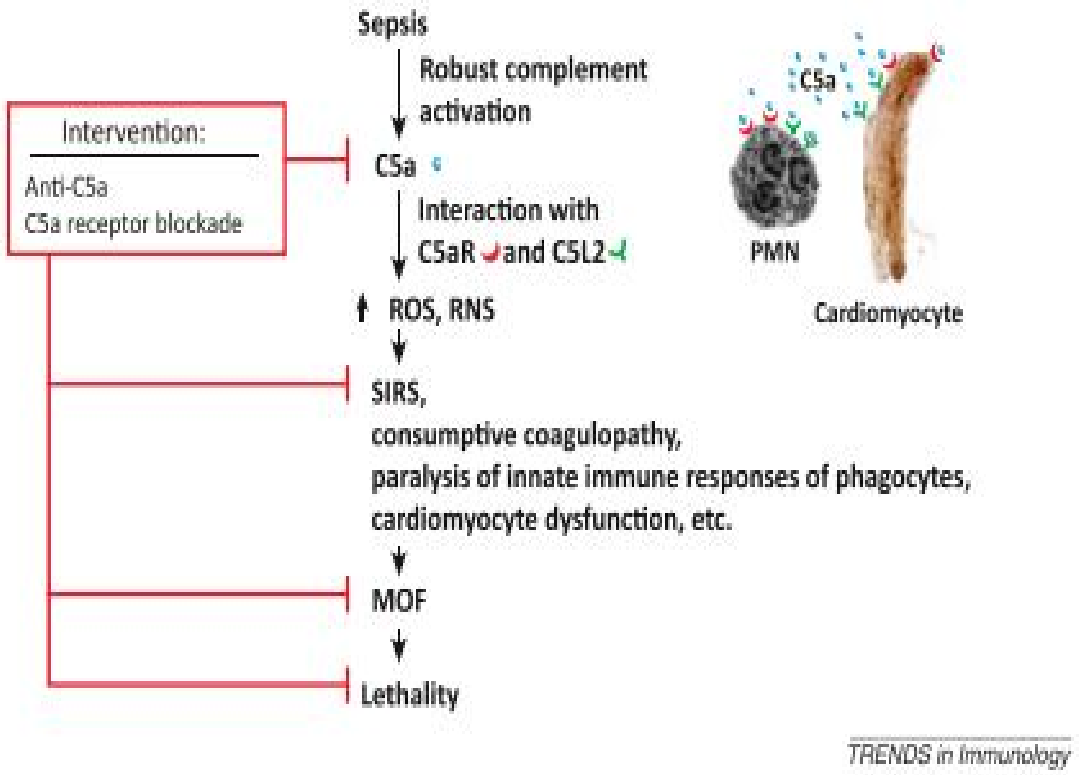
- ✓ **TLR (Transmemrane toll-like receptors)**
  sulla superficie cellulare(TLR1-2-4-5-6-10)
  intracellulare (TLR3-7-8).
- ✓ **NLR (Citoplasmatici): NLRP(14 membri) e RIG-I-like helicase**


Gram negative LPS
RSV fusion protein
Gram positive LTA
Fungal zymosan
Mycoplasma lipopetides
Bacterial flagellin
TLR4
TLR1/2/6
TLR5
TLR7/8
Viral ssRNA
MAL
TRAM
MAPK
MyD88
TLR9
Viral dsRNA
TLR3
TRIF
Bacterial unmethylated
CpG DNA
(TLR7/8/9)
TRAF6
AP-1
IRF3
NF-kB
IRF7


Innate Immunity
Adaptive Immunity
CD14
LPS
TLR2 protein
MyD88
IRAK2
TRAF-6
NIK
IκB
NF-κB
Degradation
Immunomodulatory genes
Antigen presentation
Cytokine release
T cell
Cell-mediated immunity
B cell
Humoral immunity
Pathophysiologic Conditions
Sepsis

NEJM 2003

Sepsi e attivazione del complemento



TRENDS in Immunology

«Cytokine storm» è comune nelle ICU

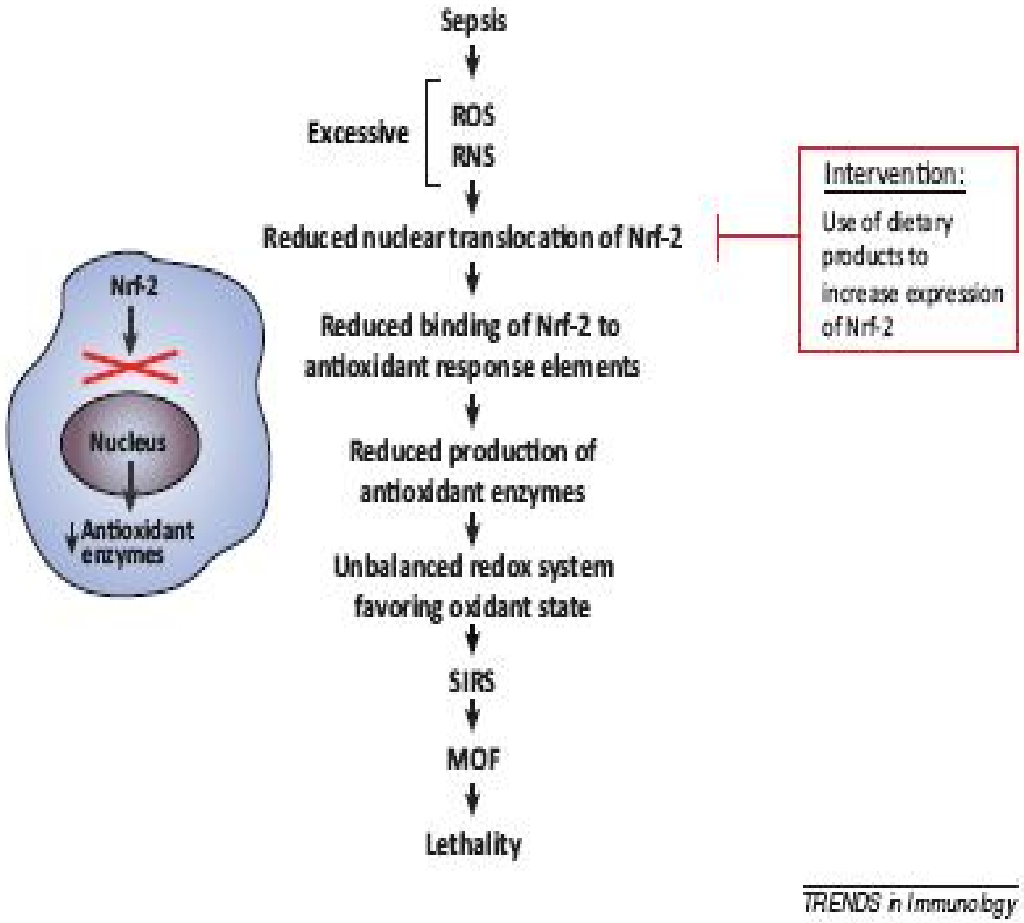
Cytokine Storm

CYTOKINE STORM

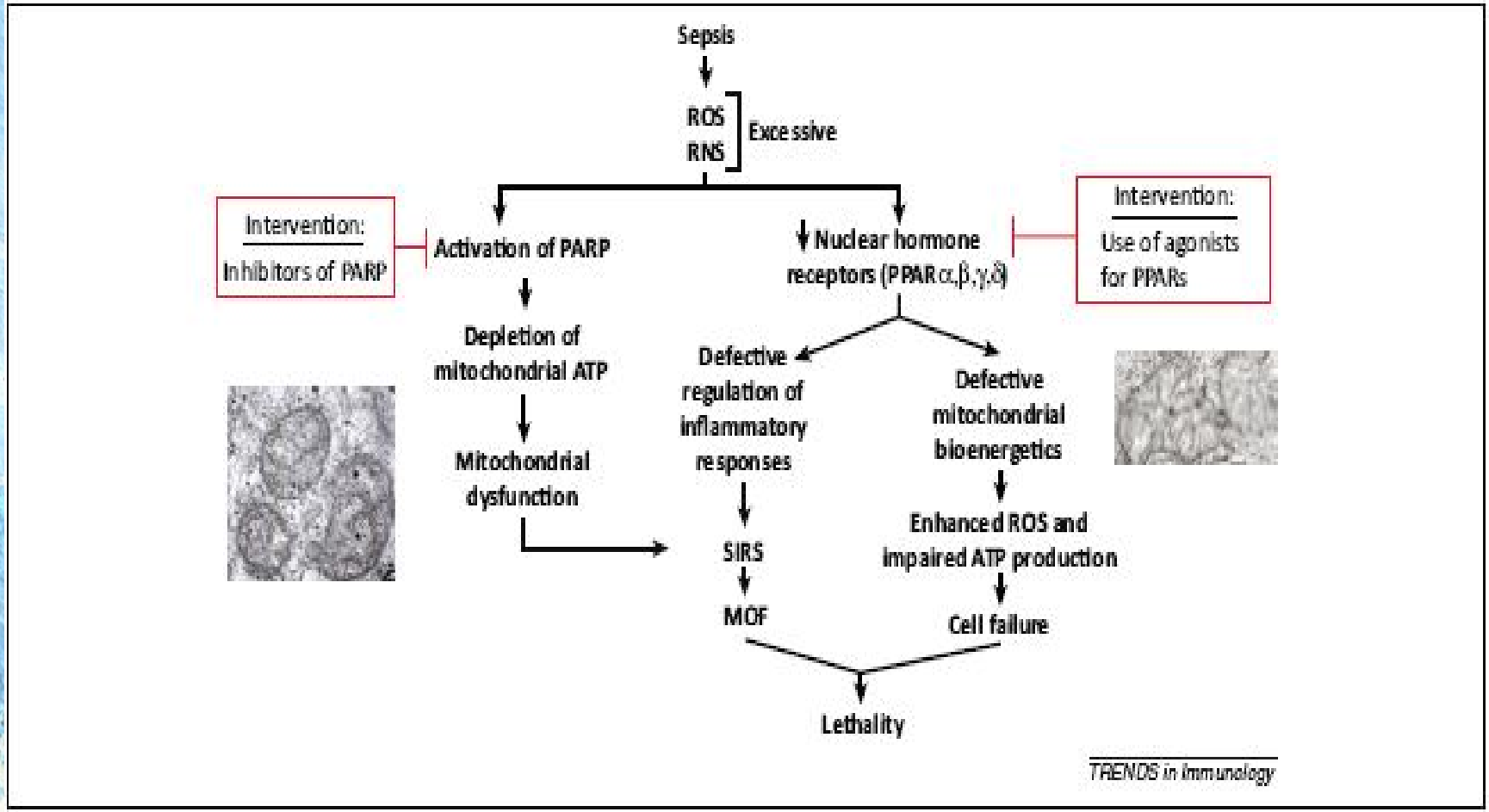
Citochina	Nome	Ruolo
Proinfiammatorie	TNF, IL1, IL6, IL8, MIF, MIP	Attivazione di neutrofili,linfociti, endotelio vascolare, PG, iNOsintetasi
Antinfiammatorie	IL4, IL10, IL13, IL7, IL5	Inbiscono il rilascio di TNF, IL1, IL8
Chemiochine	IL8, MIP1α-β, MCP1-3	Attivano PMN e Macrofagi
Mediatori lipidici	PAF, PG, Tx, FT →	Attivazione dell'endotelio, del tono vascolare, e della via della coagulazione
Radicali dell'ossigeno	Radicali superossido e idrossilico, NO	Regolazione del tono vascolare, proprietà antimicrobiche

Cohen *Nature* 2002 420:885-91

Sepsi e sistema redox



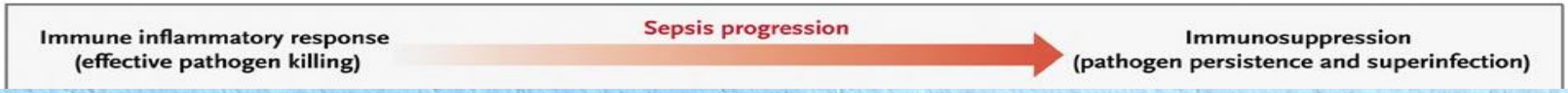
Sepsi e sistema redox



SIRS

Si realizza nelle fasi precoci della sepsi ed è caratterizzata da una risposta precoce proinfiammatoria mediata da componenti molecolari (*cytokine storm* e proteine della fase acuta) e componenti cellulari (leucociti e endotelio).

In pochi casi ha una prognosi infausta in tempi brevi.

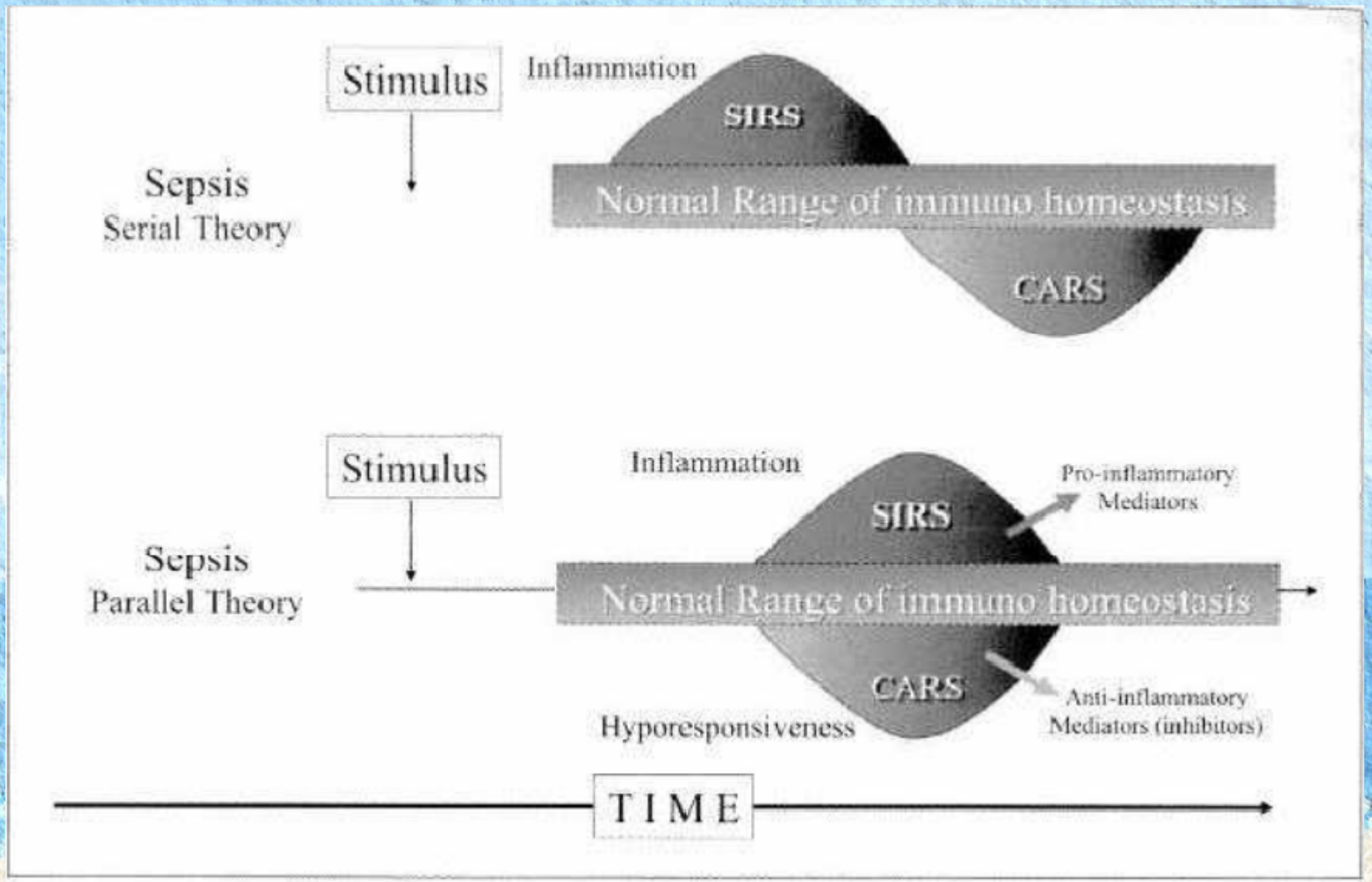


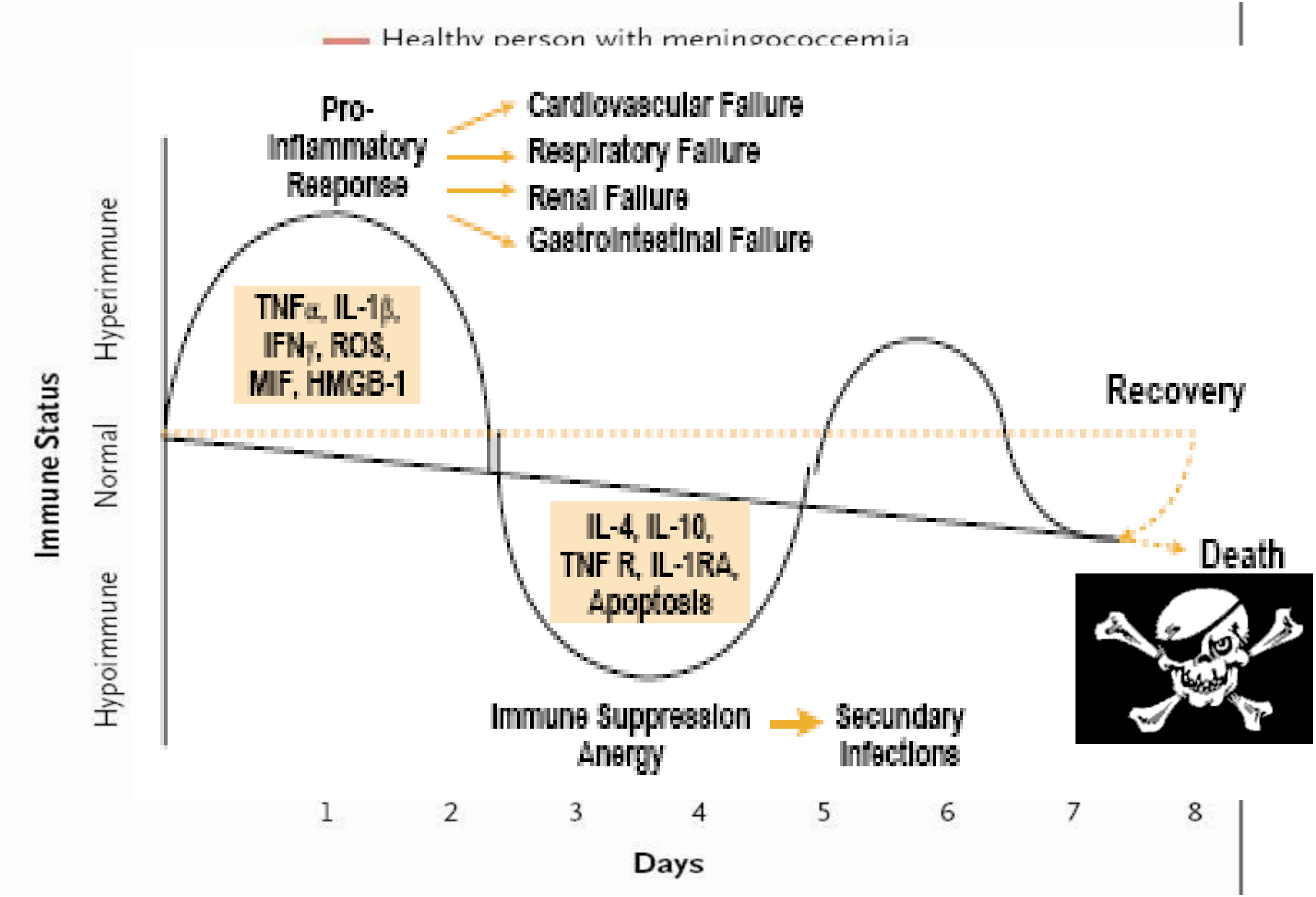
Compensatory Anti-inflammatory Response Syndrome

Kumpf O. et al *J Innate Immun 2010*

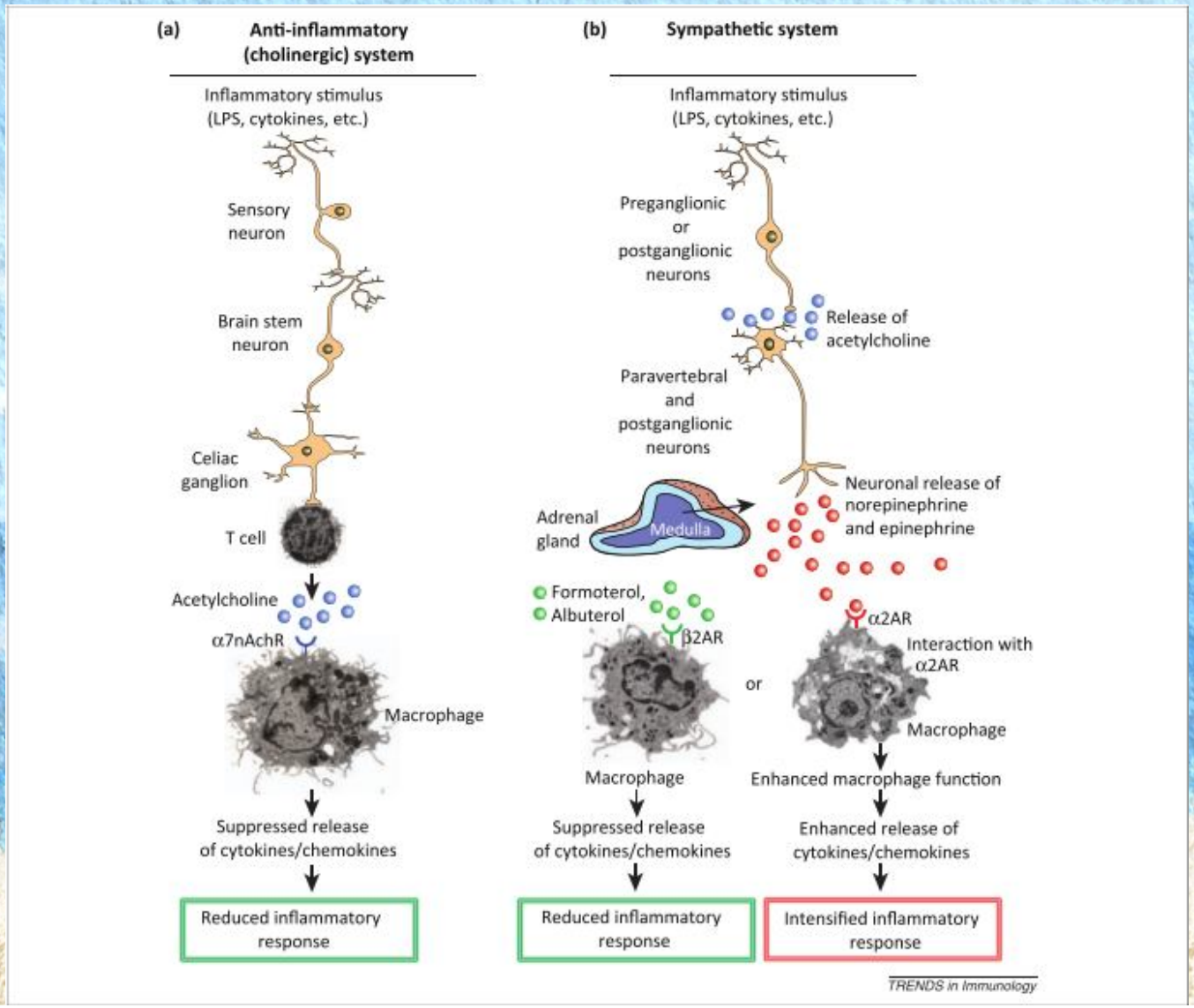
- Predomina nelle fasi tardive
- Si caratterizza per infezioni secondarie
- I pazienti sopravvissuti all'insulto iniziale soccombono per MOFS gg o settimane più tardi.

Hotchkiss et al. *Nat Med 2009.*


Stimulus
Inflammation
SIRS
Sepsis
Serial Theory
Normal Range of immuno homeostasis
CARS
Stimulus
Inflammation
Pro-inflammatory
Mediators
SIRS
Sepsis
Parallel Theory
Normal Range of immuno homeostasis
CARS
Anti-inflammatory
Mediators (inhibitors)
Hyporesponsiveness
TIME


Healthy person with meningococcemia
Pro-Inflammatory Response
Cardiovascular Failure
Respiratory Failure
Renal Failure
Gastrointestinal Failure
TNFα, IL-1β, IFNγ, ROS, MIF, HMGB-1
Recovery
Death
IL-4, IL-10, TNF R, IL-1RA, Apoptosis
Immune Suppression Anergy
Secundary Infections
Immune Status
Hyperimmune
Normal
Hypoimmune
1
2
3
4
5
6
7
8
Days

Ruolo del sistema nervoso simpatico e parasimpatico nella sepsi



Meccanismi d'immunosoppressione

Shift from an inflammatory (Th1) to an antiinflammatory (Th2) response

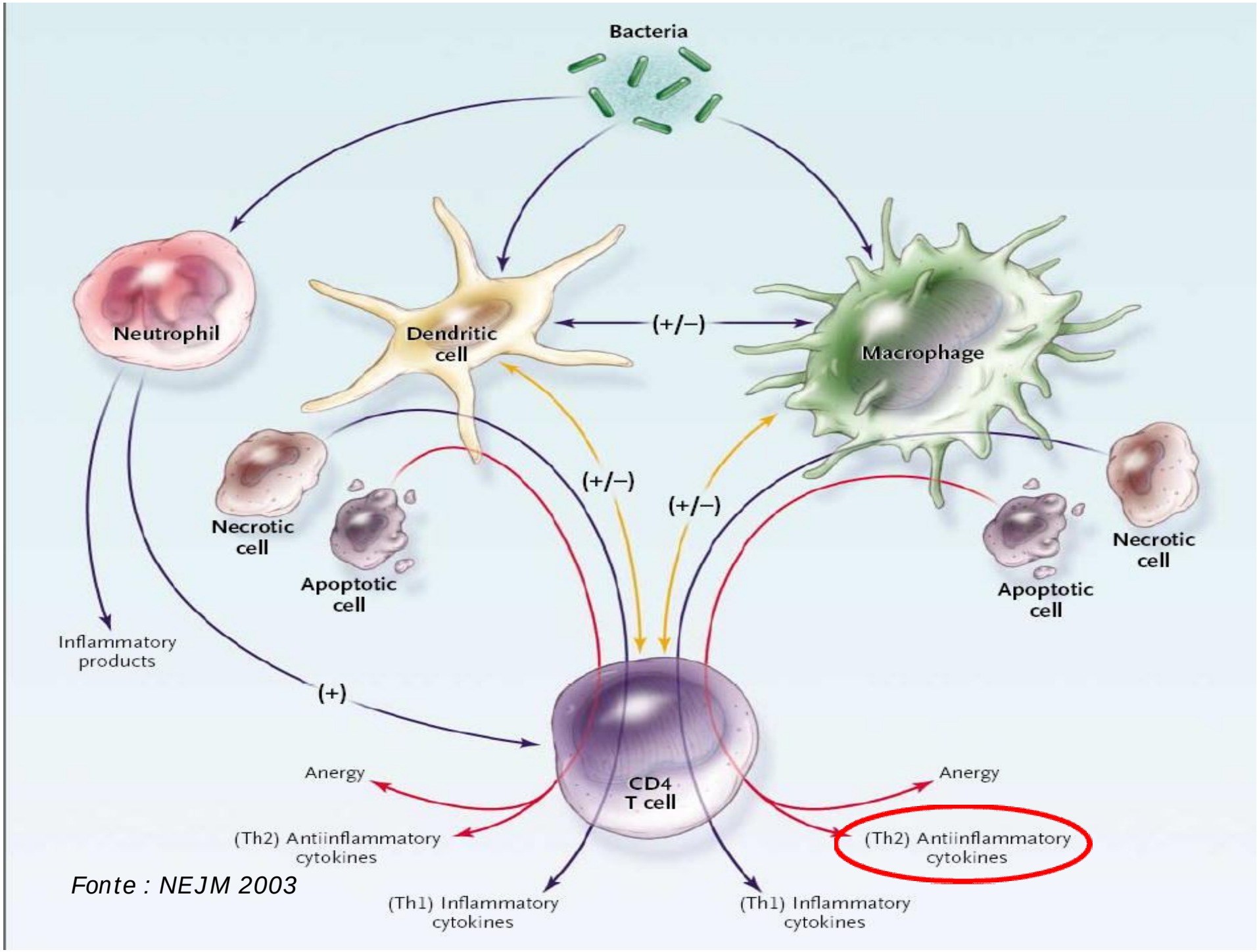
Anergy

Apoptosis-induced loss of CD4 T cells, B cells, and dendritic cells

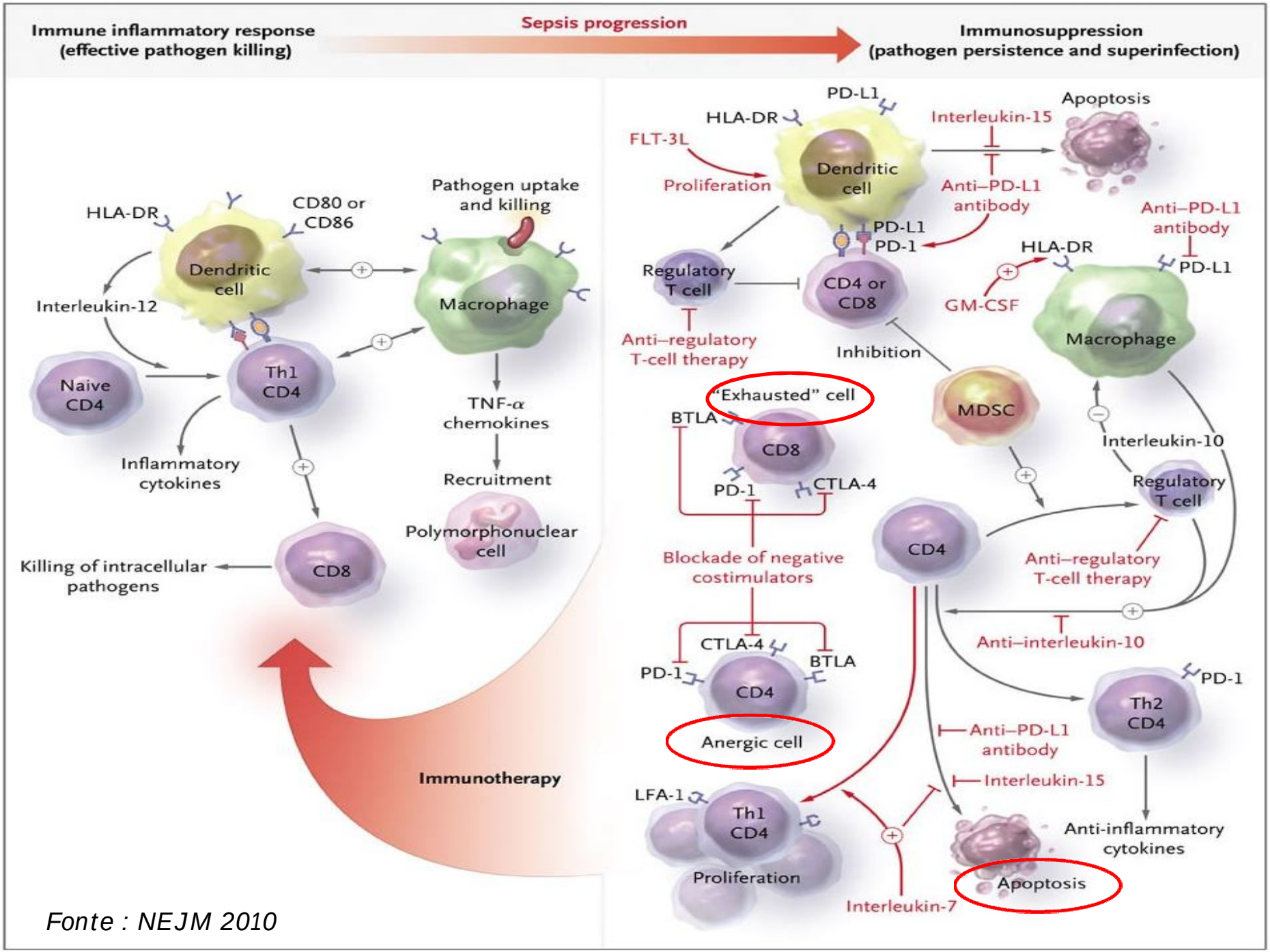
Loss of macrophage expression of major-histocompatibility-complex class II and costimulatory molecules

Immunosuppressive effect of apoptotic cells

* Th1 denotes type 1 helper T cell, and Th2 type 2 helper T cell.



Fonte : NEJM 2003



Fonte : NEJM 2010

Table 1. Pathways and Mediators of Sepsis, Potential Treatments, and Results of Randomized, Controlled Trials (RCTs).*

Pathway	Mediators	Treatment	Results of RCTs
	Superantigens: TSST-1	Anti-TSST-1	Not evaluated
	Streptococcal exotoxins (e.g., streptococcal pyrogenic exotoxin A)	Antistreptococcal exotoxins	Not evaluated
	Lipopolysaccharide (endotoxin)	Antilipopolysaccharide[9]	Negative
Innate immunity	TLR-2, TLR-4	TLR agonists[10] and antagonists	Not evaluated
	Monocytes, macrophages	GM-CSF, interferon gamma[11]	Not evaluated
	Neutrophils	G-CSF†	Not evaluated
Adaptive immunity	B cells (plasma cells and immunoglobulins)	IgG	Not evaluated
	CD4+ T cells (Th1, Th2)		
Proinflammatory pathway	TNF-α	Anti–TNF-α[13,14]	Negative
	Interleukin-1β	Interleukin-1–receptor antagonist[15]	Negative
	Interleukin-6	Interleukin-6 antagonist	Not evaluated
	Prostaglandins, leukotrienes	Ibuprofen,[16] high-dose corticosteroids[17]	Negative
	Bradykinin	Bradykinin antagonist[18]	Negative
	Platelet-activating factor	Platelet-activating factor acetyl hydrolase[19]	Negative
	Proteases (e.g., elastase)	Elastase inhibitor‡	Negative
	Oxidants	Antioxidants (e.g., *N*-acetylcysteine)[20]	Not evaluated
	Nitric oxide	Nitric oxide synthase inhibitor[21]	Negative
Procoagulant pathway	Decreased protein C	Activated protein C[5]	Positive
	Decreased protein S	Protein S[22]	Not evaluated
	Decreased antithrombin III	Antithrombin III[23]	Negative
	Decreased tissue factor–pathway inhibitor	Tissue factor–pathway inhibitor[24]	Negative
	Increased tissue factor	Tissue factor antagonist[25]	Not evaluated
	Increased plasminogen-activator inhibitor 1	Tissue plasminogen activator	Not evaluated
Antiinflammatory	Interleukin-10	Interleukin-10§	Not evaluated
	TNF-α receptors	TNF-α receptors[13]	Negative
Hypoxia	Hypoxia-inducing factor 1α, vascular endothelial growth factor	Early, goal-directed therapy[2] Supernormal oxygen delivery Erythropoietin[26]	Positive Negative Not evaluated
Immunosuppression or apoptosis	Lymphocyte apoptosis	Anticaspases[27]	Not evaluated
	Apoptosis of intestinal epithelial cells	Anticaspases[27]	Not evaluated
Endocrine	Adrenal insufficiency	Corticosteroids[28]	Mixed results¶
	Vasopressin deficiency	Vasopressin[29]	Not evaluated
	Hyperglycemia	Intensive insulin therapy[30,31]	Not evaluated‖

* TSST denotes staphylococcal toxic shock syndrome toxin 1, GM-CSF granulocyte–macrophage colony-stimulating factor, G-CSF granulocyte colony-stimulating factor, Th1 type 1 helper T cells, and Th2 type 2 helper T cells. Organism features means components of bacteria that are toxic to the host and that are potential therapeutic targets in sepsis.

† G-CSF is effective in patients with sepsis who have profound neutropenia.[12]

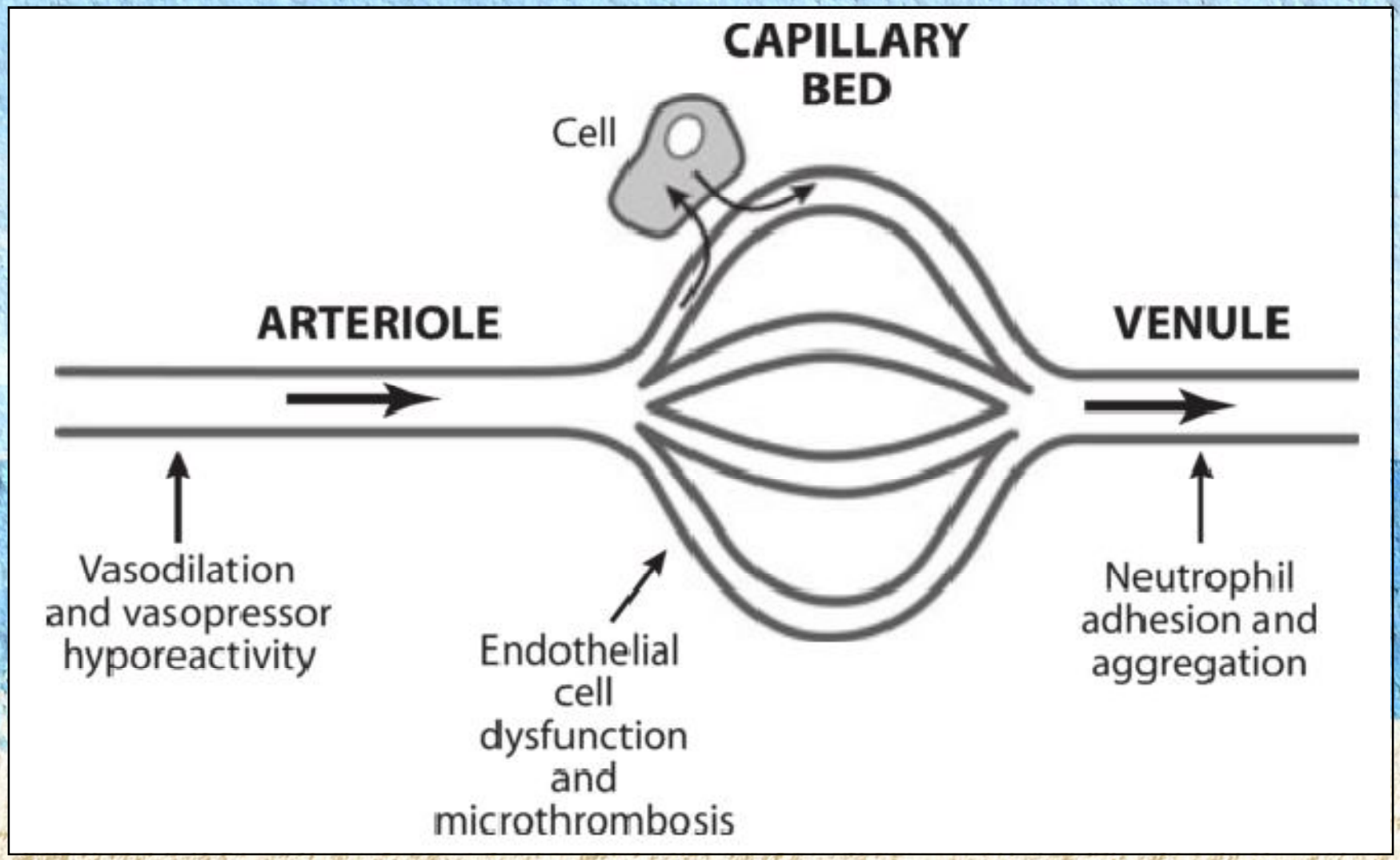
‡ Elastase inhibitor was ineffective in a phase 2 trial involving patients with acute lung injury.

§ Interleukin-10 was ineffective in a phase 2 trial involving patients with acute lung injury.

¶ Corticosteroids had no effect on overall 28-day mortality but decreased mortality in a subgroup of patients with no response to corticotropin (see text for details). Additional trials of corticosteroids in patients with septic shock are in progress.

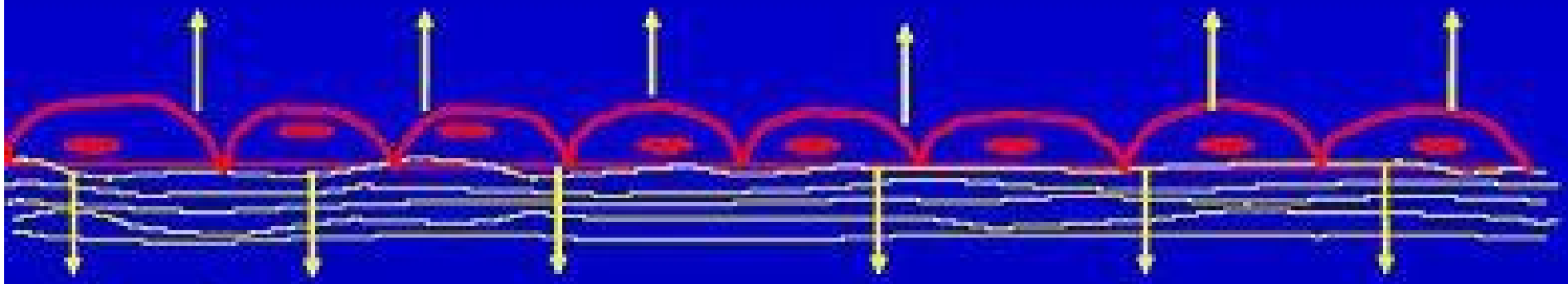
‖ Intensive insulin therapy decreased the mortality rate among critically ill surgical patients but has not yet been evaluated in patients with sepsis.

Unità microcircolatoria



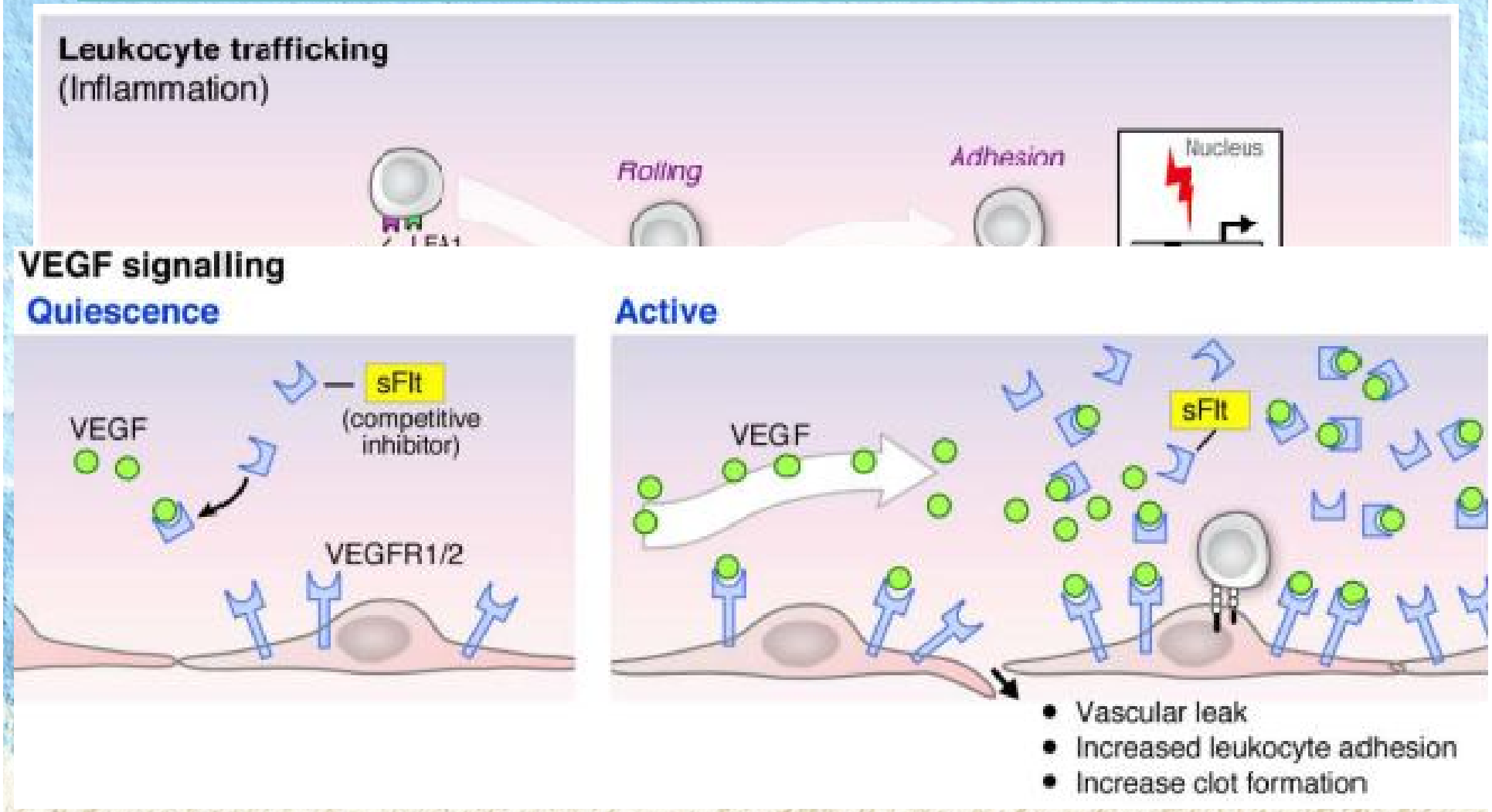
FUNZIONE PARACRINA DELL'ENDOTELIO

- MODULAZIONE DELLA COAGULAZIONE
- MODULAZIONE DELLE INTERAZIONI ENDOTELIO- CELLULE EMATICHE



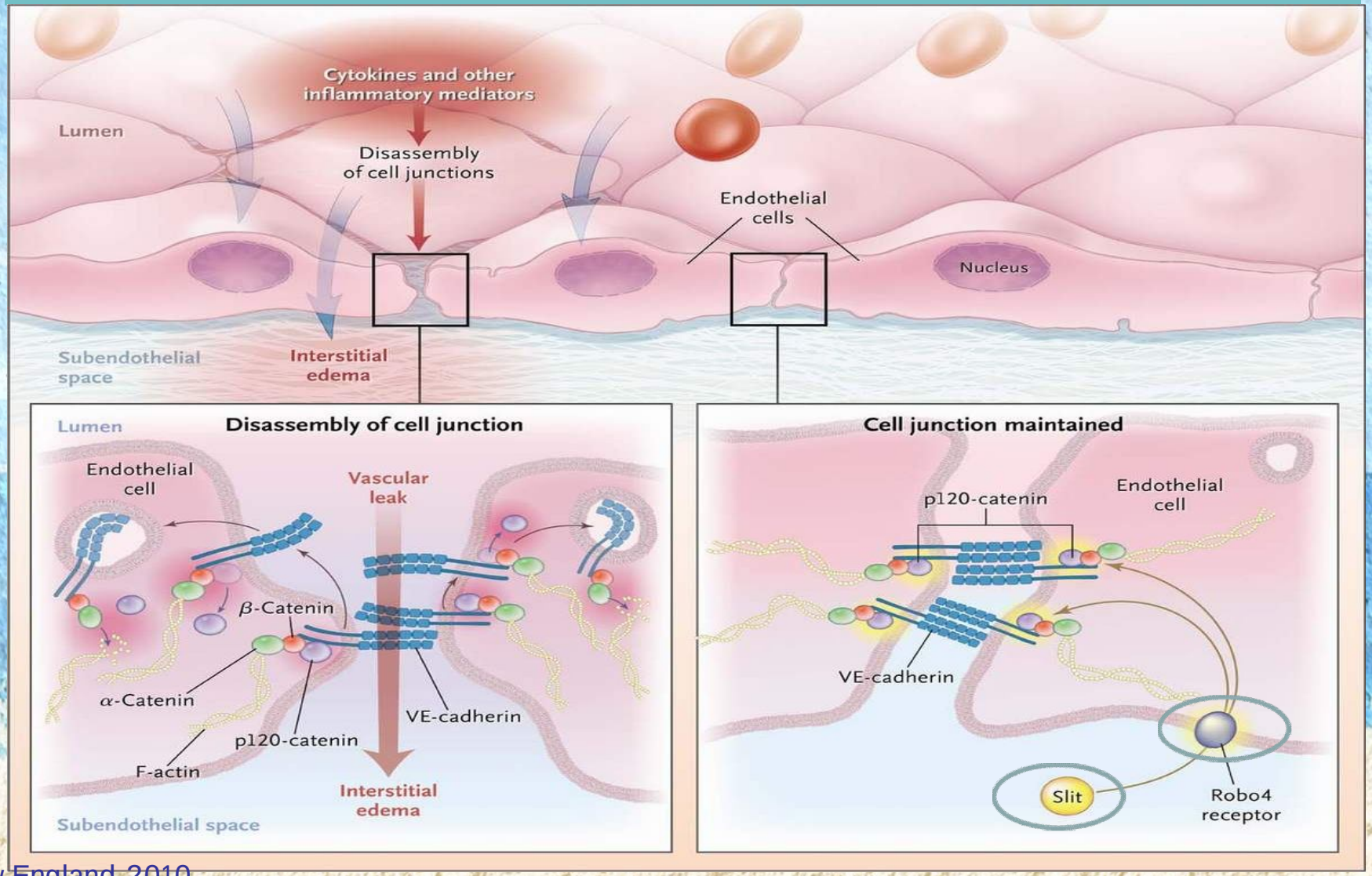
- MODULAZIONE DELLA PERMEABILITA' VASALE
- MODULAZIONE DEL TONO VASALE
- MODULAZIONE DELLA STRUTTURA VASALE

Attivazione dell'endotelio nella sepsi



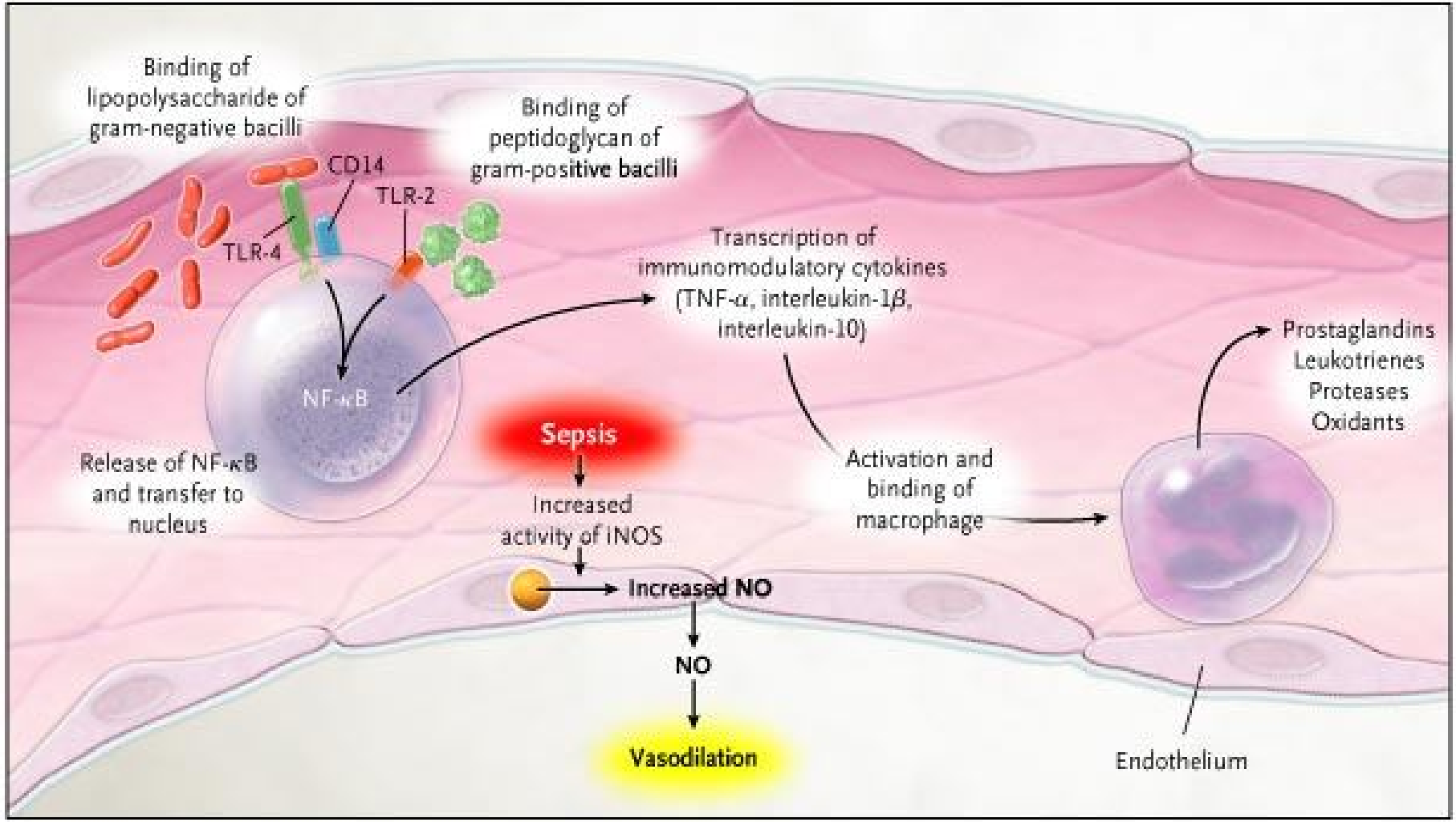
Fonte: Shapiro et al. Critical Care 2010, 14:R182

Citochine ed edema endoteliale

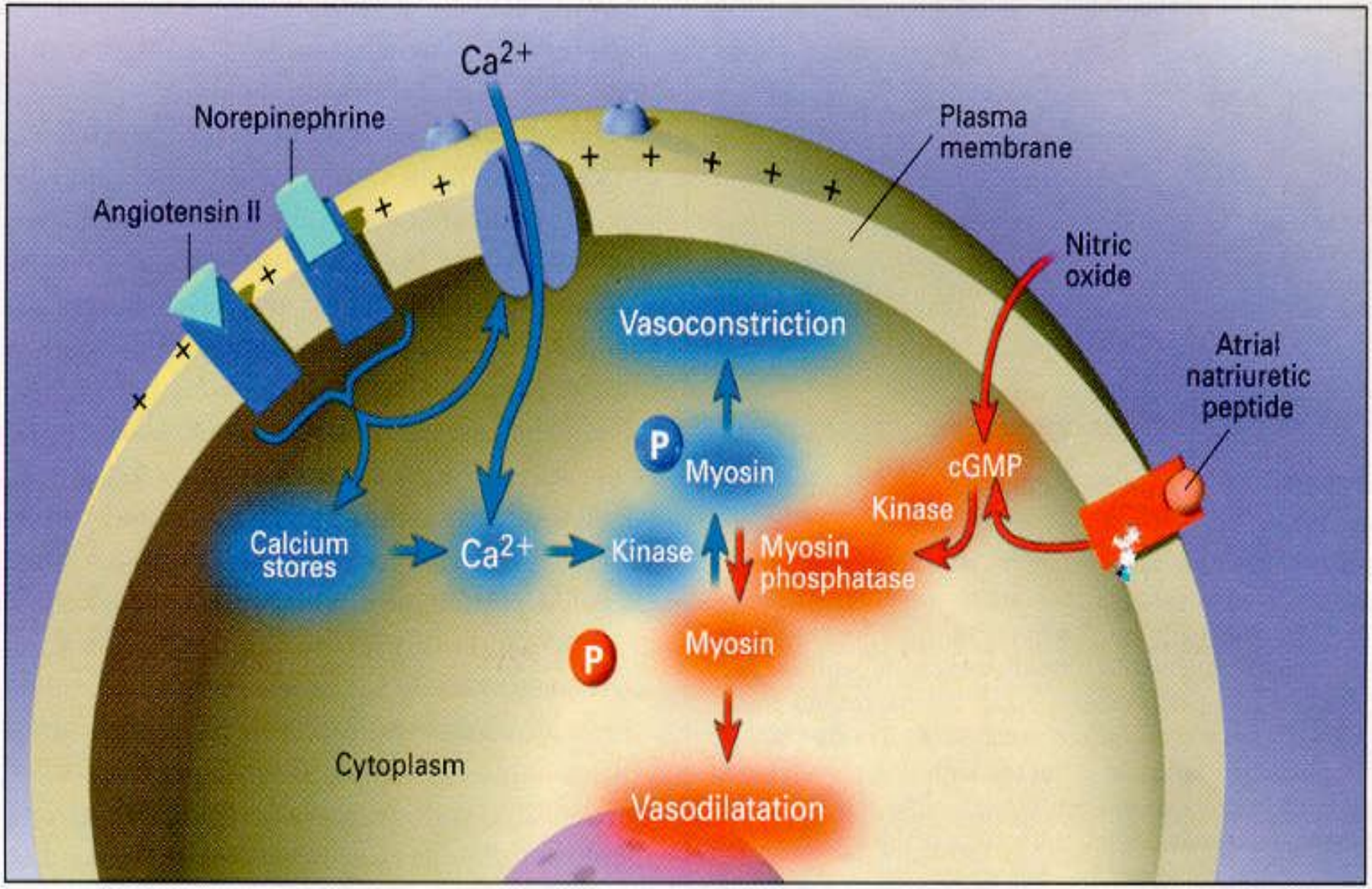


New England 2010

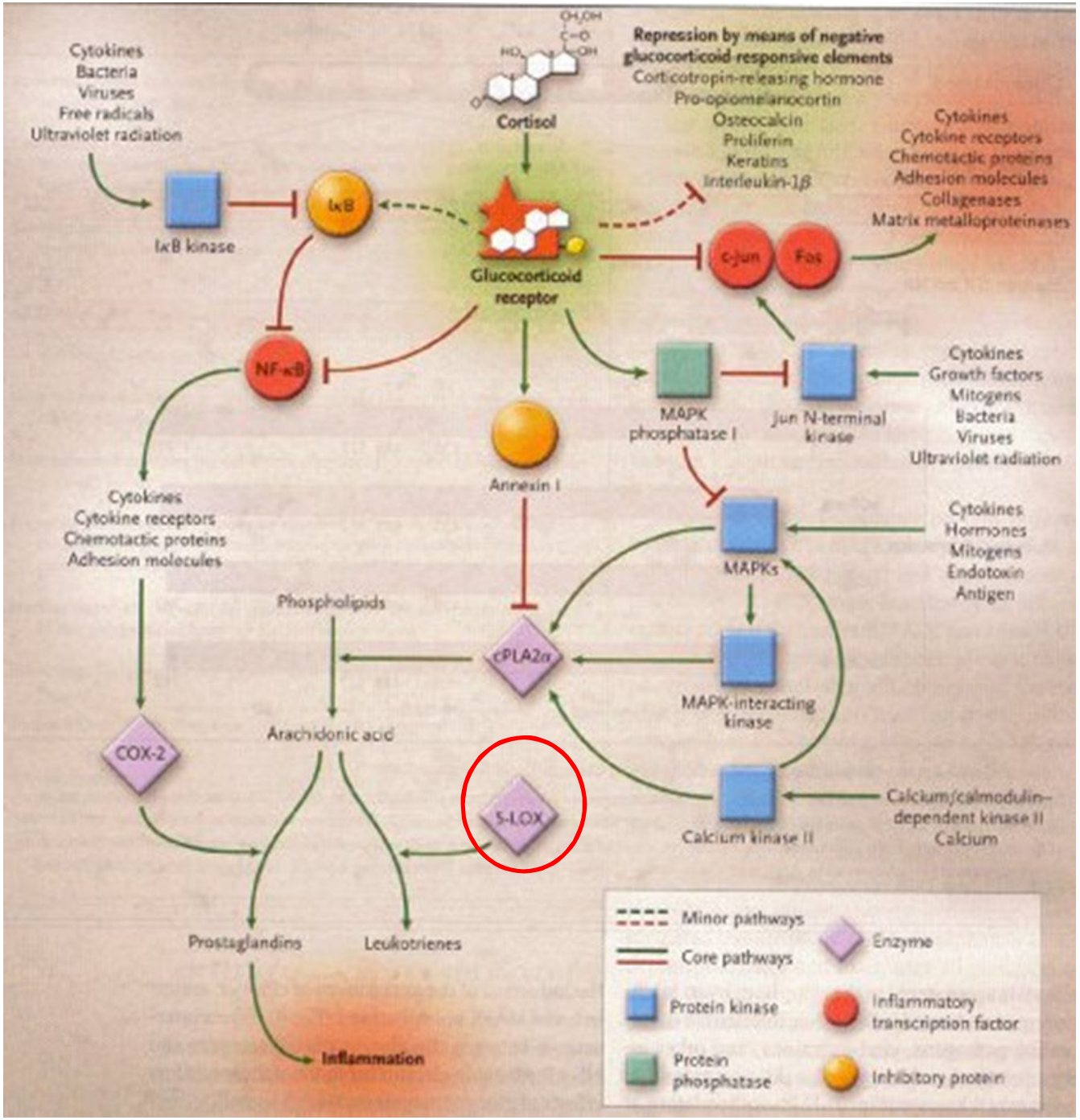
Citochine e vasodilatazione



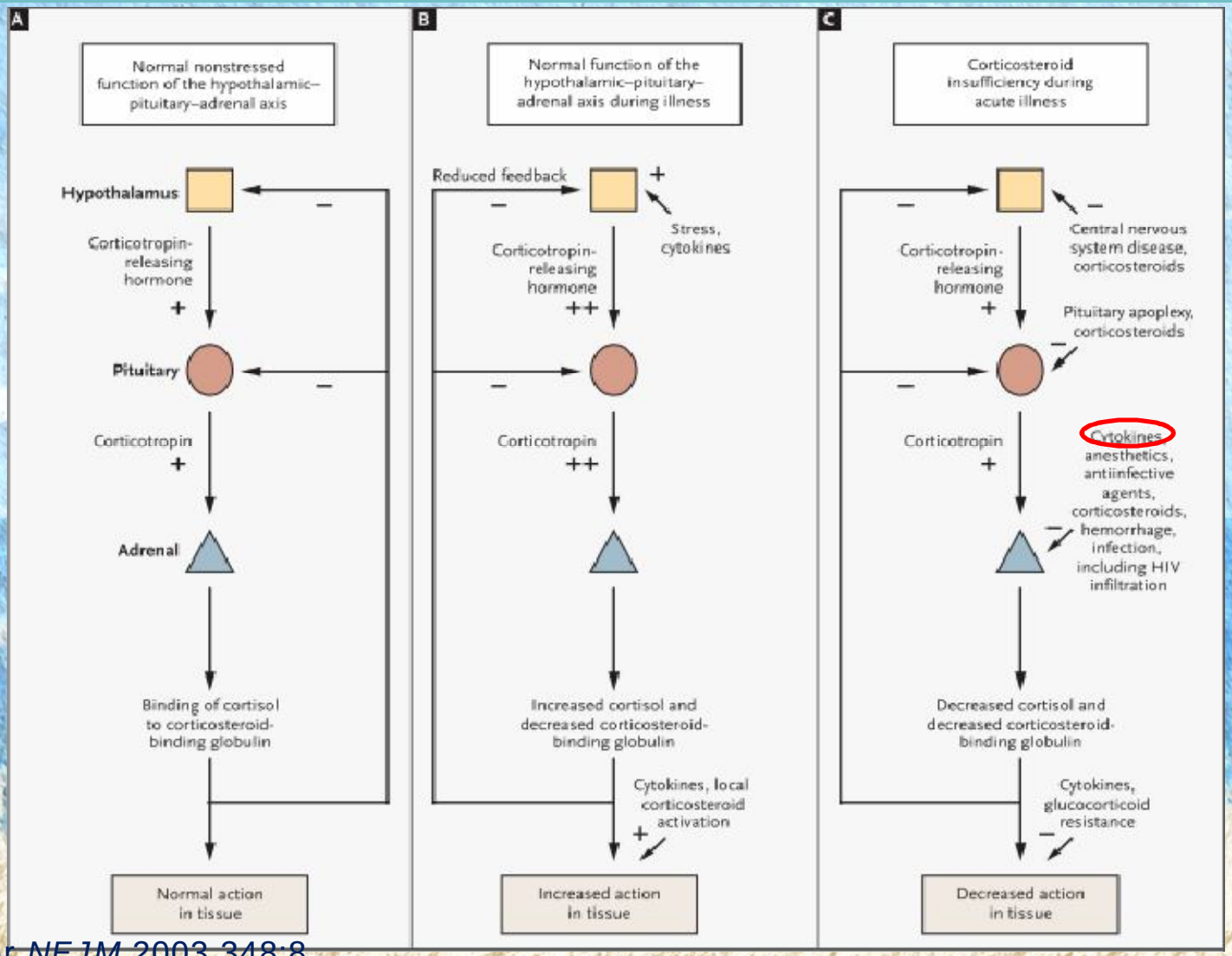
New England 2006



New England 2001


Cytokines
Bacteria
Viruses
Free radicals
Ultraviolet radiation
IκB kinase
IκB
Cortisol
Repression by means of negative glucocorticoid-responsive elements
Corticotropin-releasing hormone
Pro-opiomelanocortin
Osteocalcin
Proliferin
Keratins
Interleukin-1β
Cytokines
Cytokine receptors
Chemotactic proteins
Adhesion molecules
Collagenases
Matrix metalloproteinases
Glucocorticoid receptor
c-Jun
Fos
NF-κB
MAPK phosphatase I
Jun N-terminal kinase
Cytokines
Growth factors
Mitogens
Bacteria
Viruses
Ultraviolet radiation
Annexin I
Cytokines
Cytokine receptors
Chemotactic proteins
Adhesion molecules
MAPKs
Cytokines
Hormones
Mitogens
Endotoxin
Antigen
Phospholipids
cPLA2α
MAPK-interacting kinase
COX-2
Arachidonic acid
5-LOX
Calcium kinase II
Calcium/calmodulin-dependent kinase II
Calcium
Prostaglandins
Leukotrienes
Inflammation
Minor pathways
Core pathways
Enzyme
Protein kinase
Inflammatory transcription factor
Protein phosphatase
Inhibitory protein

Citochine e ins.corticosteroidea



Fonte: Cooper *NEJM* 2003 348:8

Corticosteroids in the Treatment of Severe Sepsis and Septic Shock in Adults

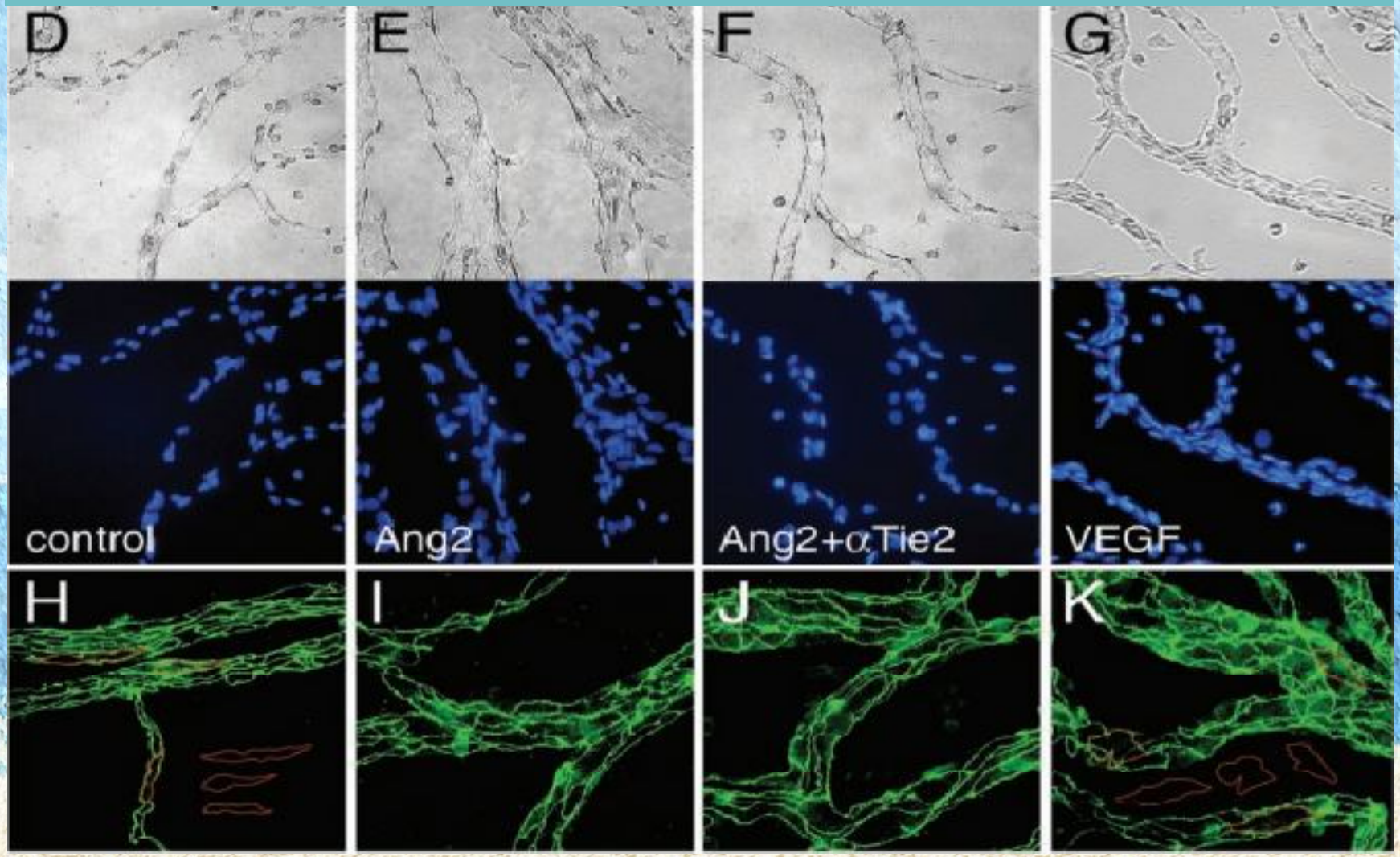
A Systematic Review

Djillali Annane, MD

Meta-analysis of a subgroup of 12 trials investigating prolonged low-dose corticosteroid treatment suggests a favorable effect on all-cause mortality. According to these findings, corticosteroids should be considered at a daily dose of 200 to 300 mg of hydrocortisone (or equivalent) as intravenous bolus or continuous infusion.

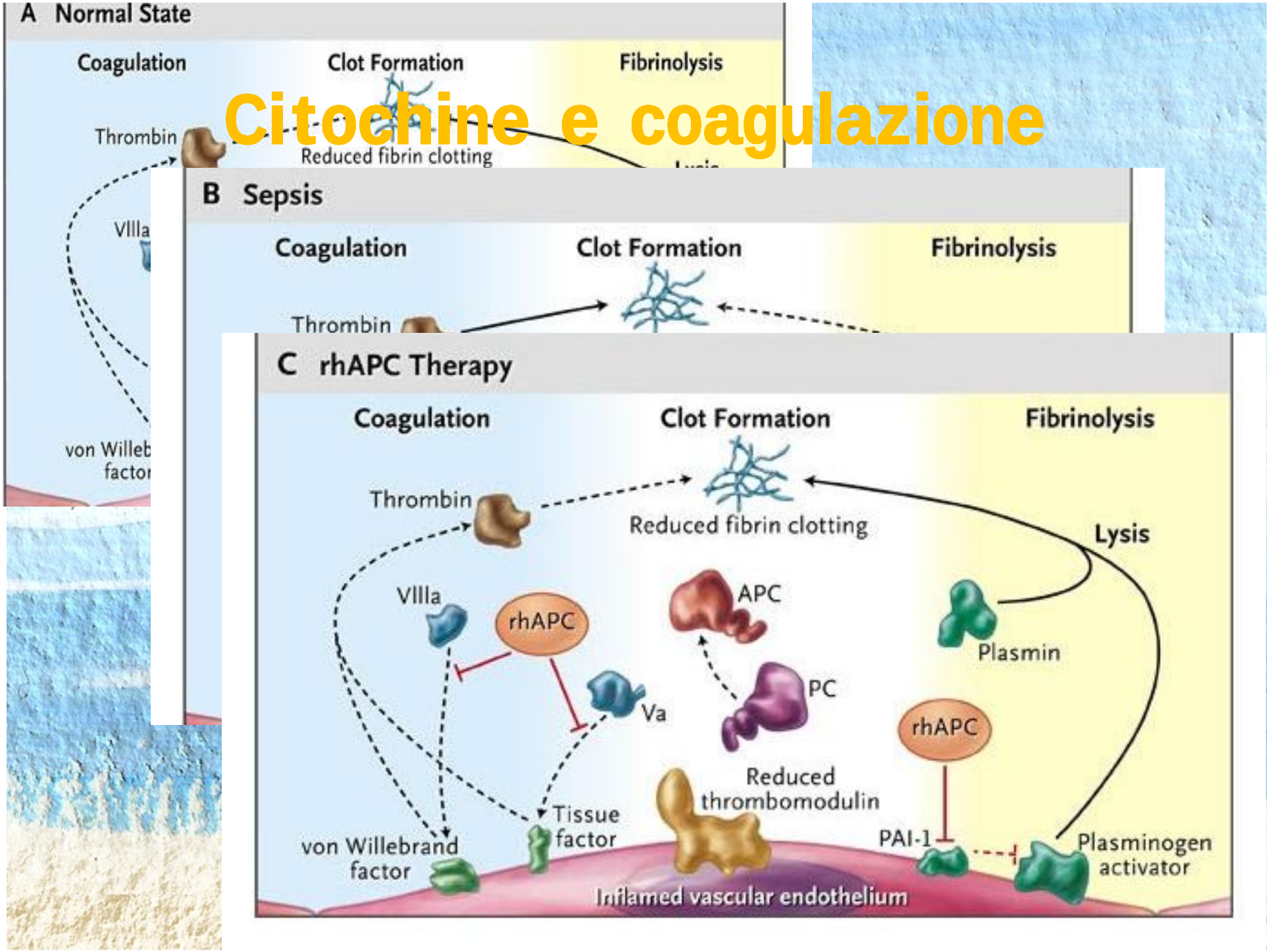
JAMA, June 10, 2009—Vol 301, No. 22

Citochine e angiogenesi

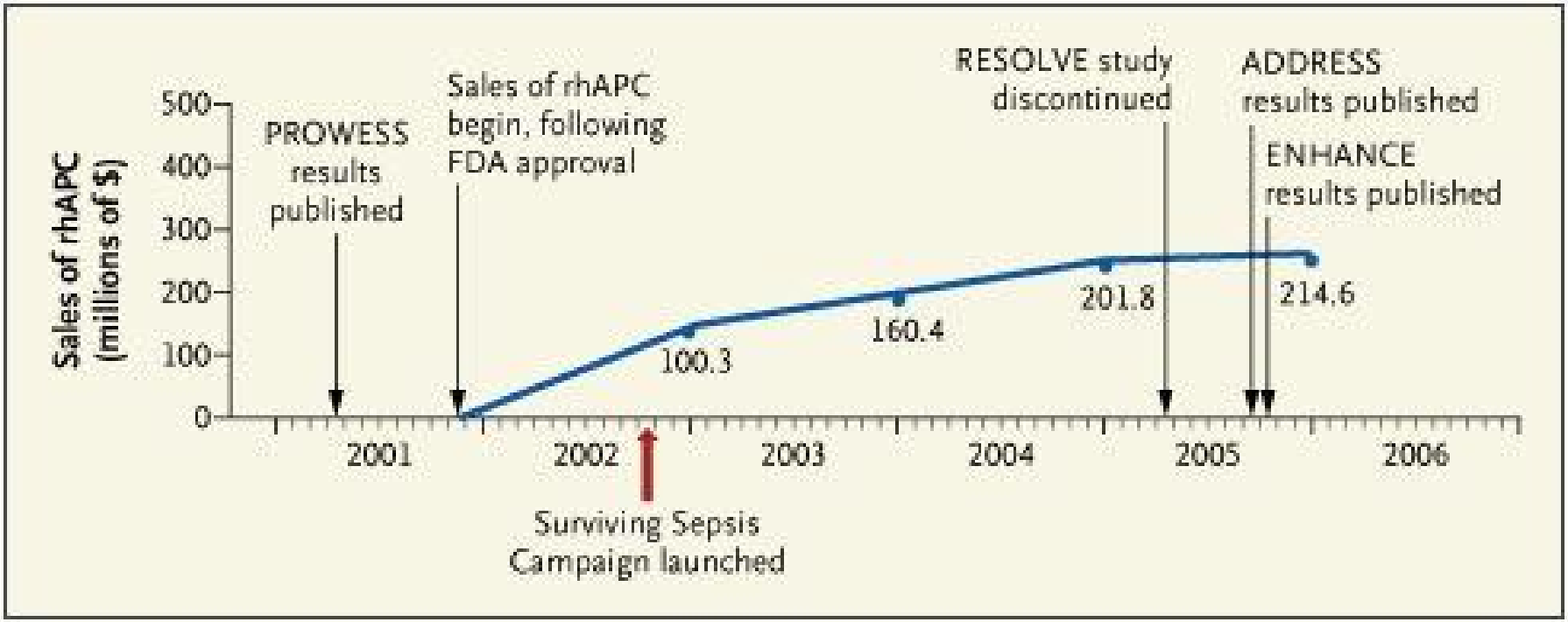


Fonte Lobov *Cell Biol* 2002 99;17: 11205-11210

Citochine e coagulazione



Utilizzo dell'rhAPC



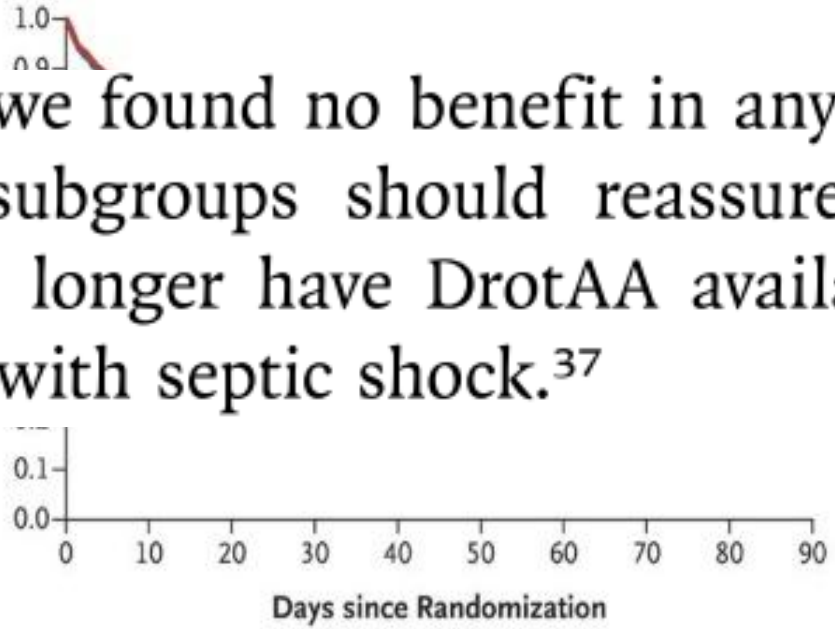
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 31, 2012 VOL. 366 NO. 22

Drotrecogin Alfa (Activated) in Adults with Septic Shock

V. Marco Ranieri, M.D., B. Taylor Thompson, M.D., Philip S. Barie, M.D., M.B.A., Jean-François Dhainaut, M.D., Ivor S. Douglas, M.D., Simon Finfer, F.R.C.P., Bengt Gårdlund, M.D., John C. Marshall, M.D., Andrew Rhodes, M.D., Antonio Artigas, M.D., Ph.D., Didier Payen, M.D., Ph.D., Jyrki Tenhunen, M.D., Ph.D., Hussein R. Al-Khalidi, Ph.D., Vivian Thompson, M.P.H., Jonathan Janes, M.B., B.Ch., William L. Macias, M.D., Ph.D., Burkhard Vangerow, M.D., and Mark D. Williams, M.D., for the PROWESS-SHOCK Study Group*

A Probability of Survival



The fact that we found no benefit in any of the prespecified subgroups should reassure clinicians who no longer have DrotAA available to treat patients with septic shock.[37]

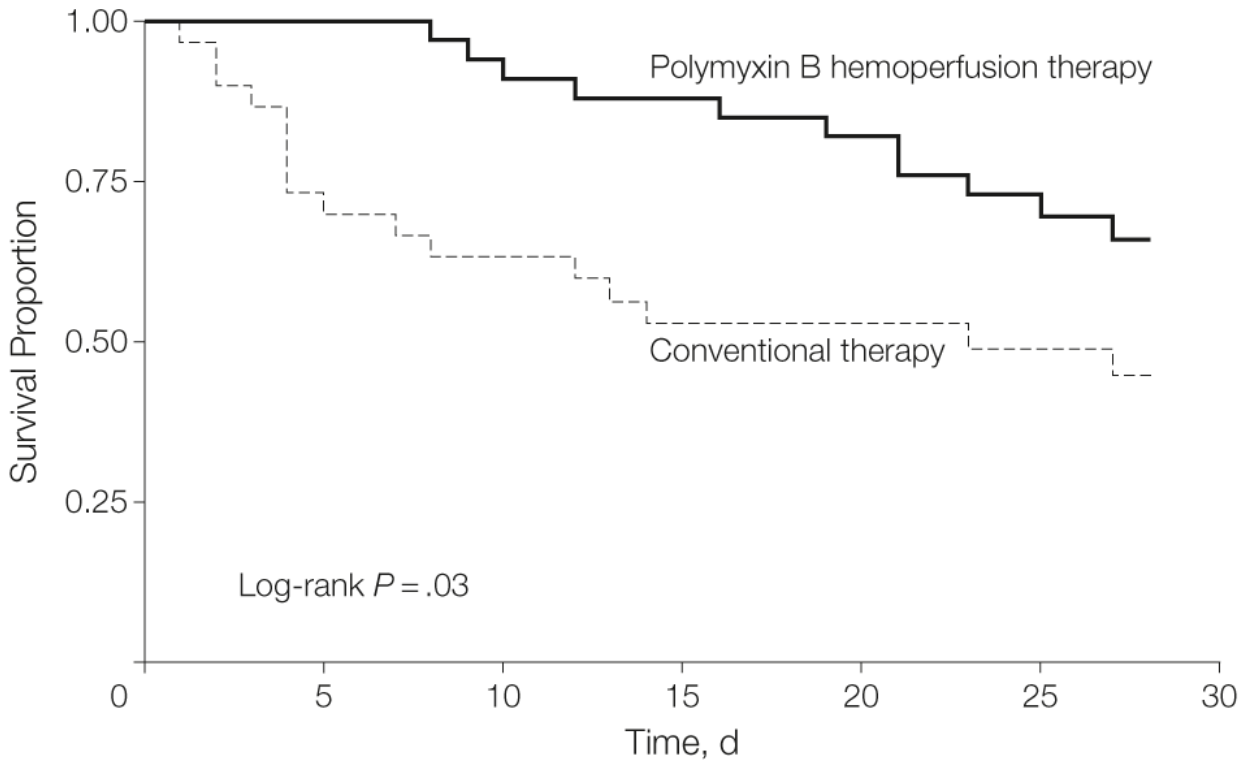
No. at Risk

Placebo	845	703	656	622	593	579	569	563	557	553
DrotAA	851	701	645	616	596	584	576	567	561	555

Early Use of Polymyxin B Hemoperfusion in Abdominal Septic ShockThe EUPHAS Randomized Controlled Trial

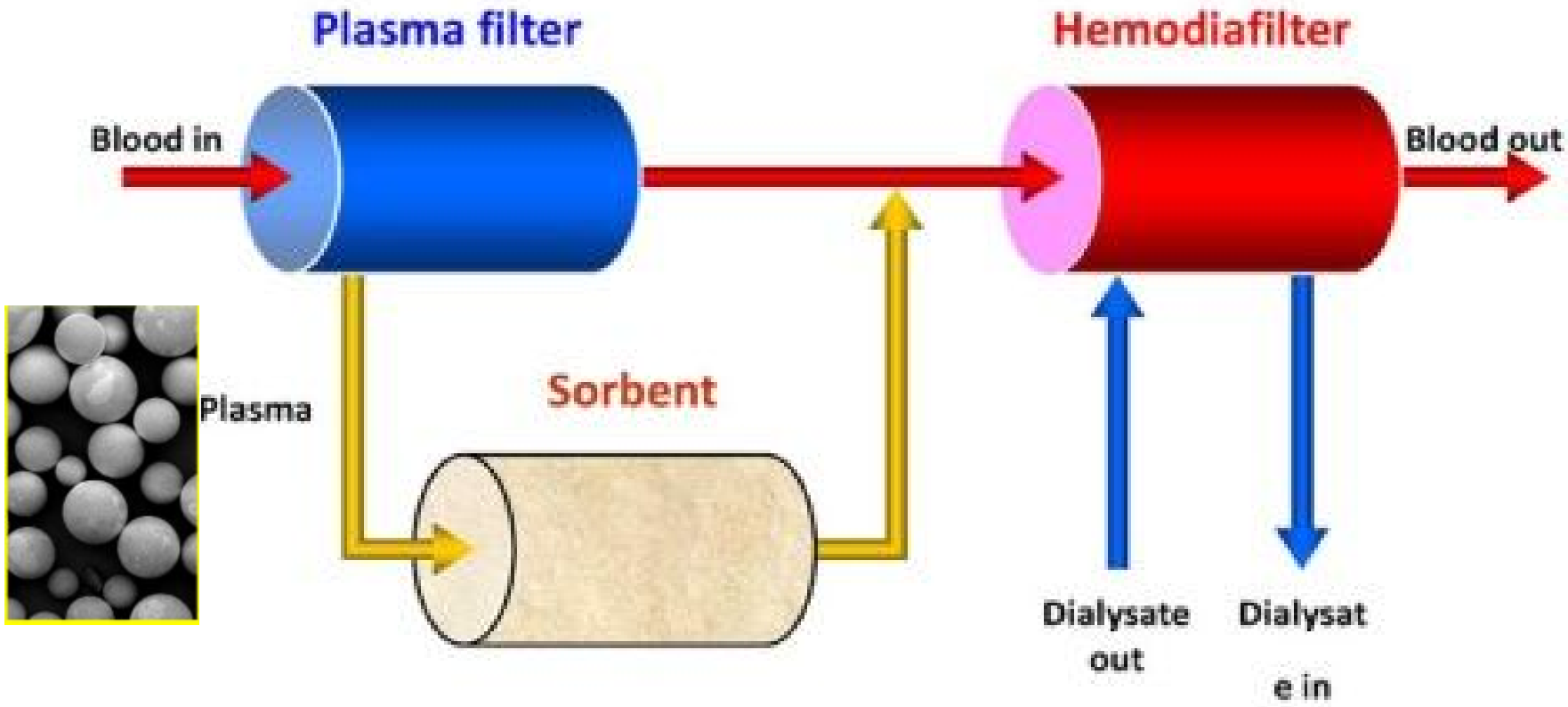
Dinna N. Cruz, MD, MPH; Massimo Antonelli, MD; Roberto Fumagalli, MD; Francesca Foltran, MD; Nicola Brienza, MD, PhD; Abele Donati, MD; Vincenzo Malcangi, MD; et al.

JAMA. 2009;301(23):2445-2452.



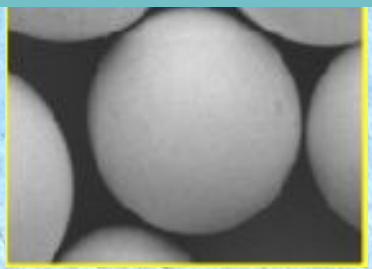
No. at risk							
Polymyxin B hemoperfusion therapy	34	34	32	30	27	22	18
Conventional therapy	30	22	19	15	15	12	11

Couple Plasma Filtration Adsorption (CPFA)



La rimozione delle citochine da parte delle resine idrofobiche è dovuto al legame con l'α2 microglobulina, il carrier palsmatico delle citochine

Cosa assorbono le resine in CPFA



Citochine

- IL5
- IL6
- IL7
- IL8
- IL10
- IL12
- IL16
- IL18
- IL1α
- IL18

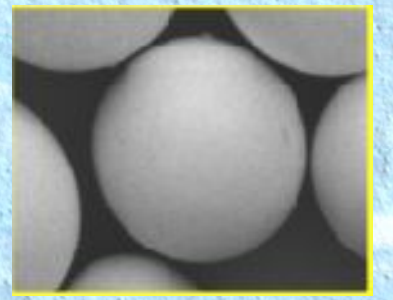
Mediatori della sepsi

- MIPα
- MIPβ
- TNFα
- MCP1
- RANTES
- ENA 78
- Tissue Factor
- TIMP-1
- VEGF

Cosa non assorbono le resine in CPFA

Adsorbimento non significativo

- Albumina
- Eparina
- Citrato
- Anticorpi
- Ferritina
- GMC-sf
- Tiroxina
- Adiponectina
- Fattore vW
- Endotossina



Basso adsorbimento

- Insulina
- EGF
- ICAM
- VCAM
- MCP

CPFA used successfully in non-ARF patients

Official Journal of the European Society of Intensive Care Medicine and the European Society of Pediatric & Neonatal Intensive Care

European Society of Intensive Care Medicine

INTENSIVE CARE MEDICINE

Hemodynamic response to coupled plasmafiltration-adsorption in human septic shock

Marco Formica, Carlo Olivieri, Sergio Livigni, Giulio Cesano, Antonella Vallero, Mariella Maio and Ciro Tetta

Intensive Care Med (2003) 29: 703-708

Objective: The objective was to examine the effect of repeated applications of coupled plasmafiltration-adsorption on the hemodynamic response in septic shock patients hospitalized in intensive care units (ICUs).

Conclusion: Coupled plasmafiltration-adsorption was a feasible and safe extracorporeal treatment and exerted a remarkable improvement in the hemodynamics, the pulmonary function, and the outcome in septic shock patients with or without concomitant ARF.

PROTOCOLLO DI STUDIO

COMPACT

COMbining **P**lasma-Filtration and **A**dsorption **C**linical **T**rial

Efficacia e sicurezza della CPFA (plasmafiltrazione associata ad adsorbimento) nello shock settico in Terapia Intensiva

progetto sperimentale

GiViTI

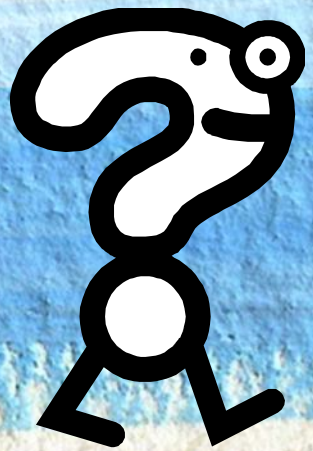
(Gruppo italiano per la Valutazione degli interventi in Terapia Intensiva)

Clintrials.gov-Protocol Registration Receipt 2006-05-31

A systems approach to the early recognition and rapid administration of best practice therapy in sepsis and septic shock

Duane Funk[a,b], Frank Sebat[c] and Anand Kumar[a,d]

Current Opinion in Critical Care 2009, 15:301–307



accp/sccm consensus conference

Definitions for Sepsis and Organ Failure and Guidelines for the Use of Innovative Therapies in Sepsis

THE ACCP/SCCM CONS
Roger C. Bone, M.D., F.C
Robert A. Balk, M.D., F.C
Frank B. Cerra, M.D.
R. Phillip Dellinger, M.D.,

Sepsis = the systemic respons
more of the following con
temperature >38°C or <
minute; (3) respiratory rate
<32 mm Hg; and white blood cell count
<4,000/cu mm, or >10% immature (band) for

Severe sepsis = sepsis associated with organ dysf
fusion, or hypotension. Hypoperfusion and pe
ties may include, but are not limited to lactic
or an acute alteration in mental status

Septic shock = sepsis-induced with hypotension
fluid resuscitation along with the presence o
malities that may include, but are not limited
oliguria, or an acute alteration in mental statu
receiving inotropic or vasopressor agents may
at the time that perfusion abnormalities are m

Sepsis-induced hypotension = a systolic blood pre
or a reduction of ≥40 mm Hg from baseline
other causes for hypotension.

Multiple organ dysfunction syndrome (MODS) =
organ function in an acutely ill patient such
cannot be maintained without intervention.

2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference

Mitchell M. Levy, MD, FCCP; Mitchell P. Fink, MD, FCCP; John C. Marshall, MD; Edward Abraham, MD; Derek Angus, MD, MPH, FCCP; Deborah Cook, MD, FCCP; Jonathan Cohen, MD; Steven M. Opal, MD; Jean-Louis Vincent, MD, FCCP, PhD; Graham Ramsay, MD; For the International Sepsis Definitions Conference

Septic Shock

Septic shock in adults refers to a state of acute circulatory failure characterized by persistent arterial hypotension unexplained by other causes. Hypotension is defined by a systolic arterial pressure below 90 mm Hg (or, in children, <2 SD below normal for their age), a MAP <60, or a reduction in systolic blood pressure of >40 mm Hg from baseline, despite adequate volume resuscitation, in the absence of other causes for hypotension.

Table 1. Diagnostic criteria for sepsis

Infection,[a] documented or suspected, and some of the following:[b]

General variables
- Fever (core temperature >38.3°C)
- Hypothermia (core temperature <36°C)
- Heart rate >90 min^{-1} or >2 SD above the normal value for age
- Tachypnea
- Altered mental status
- Significant edema or positive fluid balance (>20 mL/kg over 24 hrs)
- Hyperglycemia (plasma glucose >120 mg/dL or 7.7 mmol/L) in the absence of diabetes

Inflammatory variables
- Leukocytosis (WBC count >12,000 μL^{-1})
- Leukopenia (WBC count <4000 μL^{-1})
- Normal WBC count with >10% immature forms
- Plasma C-reactive protein >2 SD above the normal value
- Plasma procalcitonin >2 SD above the normal value

Hemodynamic variables
- Arterial hypotension[b] (SBP <90 mm Hg, MAP <70, or an SBP decrease >40 mm Hg in adults or <2 SD below normal for age)
- SvO_2 >70%[d]
- Cardiac index >3.5 $L \cdot min^{-1} \cdot M^{-2}$[3]

Organ dysfunction variables
- Arterial hypoxemia (PaO_2/FIO_2 <300)
- Acute oliguria (urine output <0.5 $mL \cdot kg^{-1} \cdot hr^{-1}$ or 45 mmol/L for at least 2 hrs)
- Creatinine increase >0.5 mg/dL
- Coagulation abnormalities (INR >1.5 or aPTT >60 secs)
- Ileus (absent bowel sounds)
- Thrombocytopenia (platelet count <100,000 μL^{-1})
- Hyperbilirubinemia (plasma total bilirubin >4 mg/dL or 70 mmol/L)

Tissue perfusion variables
- Hyperlactatemia (>1 mmol/L)
- Decreased capillary refill or mottling

2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference

I 10 segni vitali

Table 1 The 10 signs of vitality

Ten signs of vitality	Triggering parameter
Temperature	$\leq 36^{\circ}C$
Pulse	<50 or >100/min
Pain	New or significant increase
Respiratory rate	<6 or >20/min
SaO_2	$<90\%$ and increased *fiO2*
Blood pressure	SBP $<$ 90 mmHg, MAP $<$ 60 mmHg
Level of consciousness	Anxiety/lethargy
Capillary refill	>3 s
Urinary output	<30 ml/h $\times$ 5 h (<100 ml/4 h – excluding renal failure)
$ScvO_2$/base deficit	$<65\%$ or B deficit ≥ 5 or lactic acid > 2.0

The seven signs of vitality in bold are key in deciding if the patient has a perfusion deficit and is at risk. MAP, mean arterial pressure; SBP, systolic blood pressure.

D. Funk et al.

Current Opinion in Critical Care 2009, 15:301–307

Lactate as a hemodynamic marker in the critically ill

Brian M. Fuller[a] *and R. Phillip Dellinger*[b]

Curr Opin Crit Care 2012, 18:267–272

È prodotto da tutti i tessuti, ma soprattutto dal muscolo scheletrico, cervello, intestino e gl.rossi.
(B. Levy *Lancet* 2005).

Cut-off: 2,5 mmol/L (Shapiro N, *Ann Emer Med* 2005).

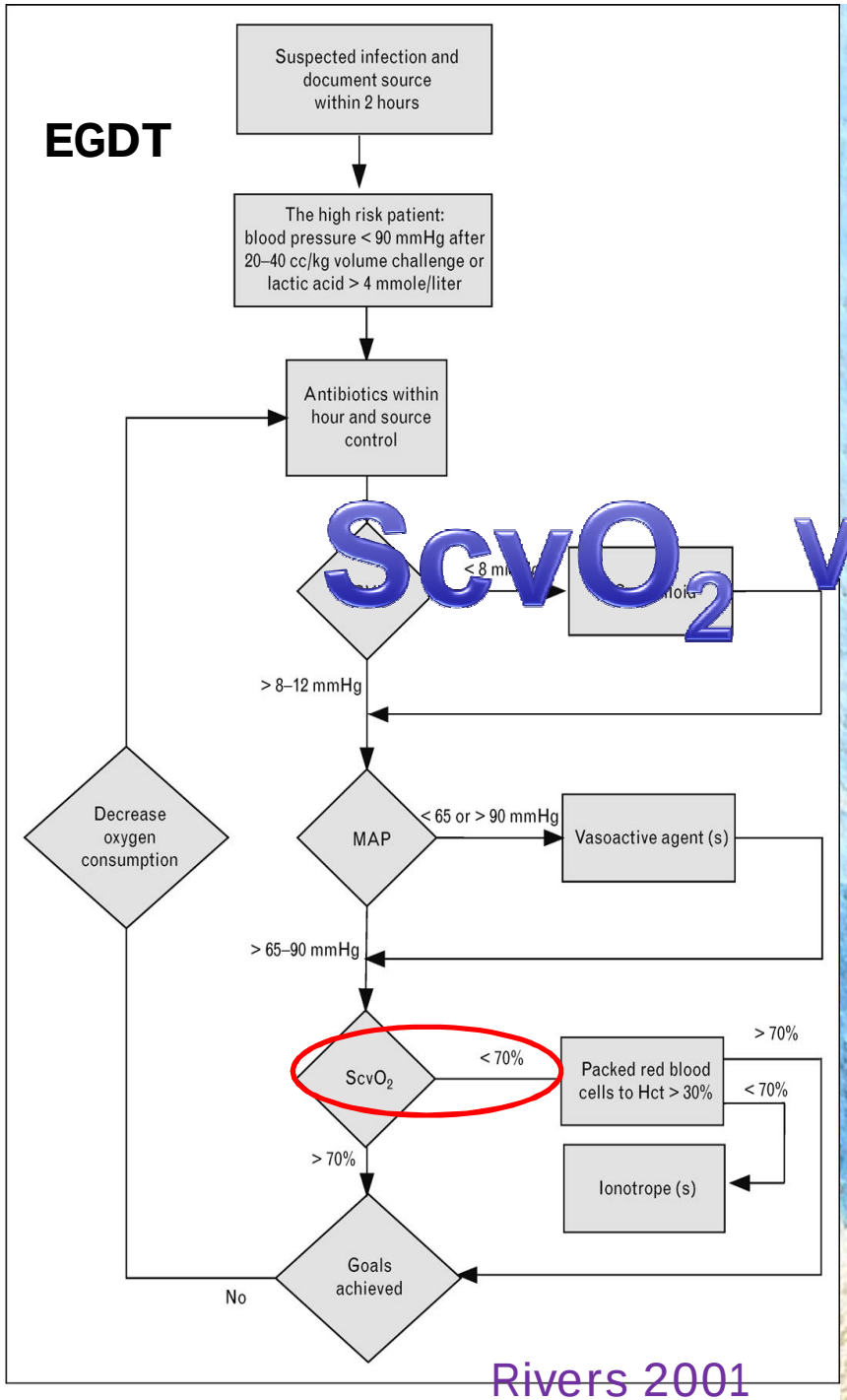
Anche un lieve incremento o un singolo valore elevato si associa ad un aumento della mortalità
(Arnold *Shock* 2009).

Lattato/mortalità

Capacità d'identificare un'esito infausto	>2mmol/l	> 4 mmol/l
Sensibilità	89%	62%
Specificità	42%	88%
Valore predittivo positivo	58%	80%

$$\text{Lactate clearance} = \frac{\text{Lactate start} - \text{Lactate 6h}}{\text{Lactate start}} \text{ X } 100$$

$ScvO_2$ vs Clearance del lattato



Rivers 2001

Reproduced from [61].

Parametri d'ipoperfusione

SvO2

Inadeguatezza del trasporto rispetto alla domanda

Lattati

Inadeguatezza dell'estrazione rispetto alla domanda

ScVO2 vs Clearance lattati

	$ScVO_2$	Clearance lattati
PRO	È stato dimostrato la sua utilità nella EGDT*	Supportato da 2 studi multicentrici**
	Supportato da LG***	Dati supportati da numerosi studi cohorte
	Diagnosi precoce di scompenso cardiaco	
	Miglior indice della performance cardiaca	Miglior indice di stress cellulare
CONTRO	Valori normali o alti nei pazienti settici [1]	Valori normali nei pz settici [2]
	No terapia nei valori elevati	Valori elevati anche per altri motivi

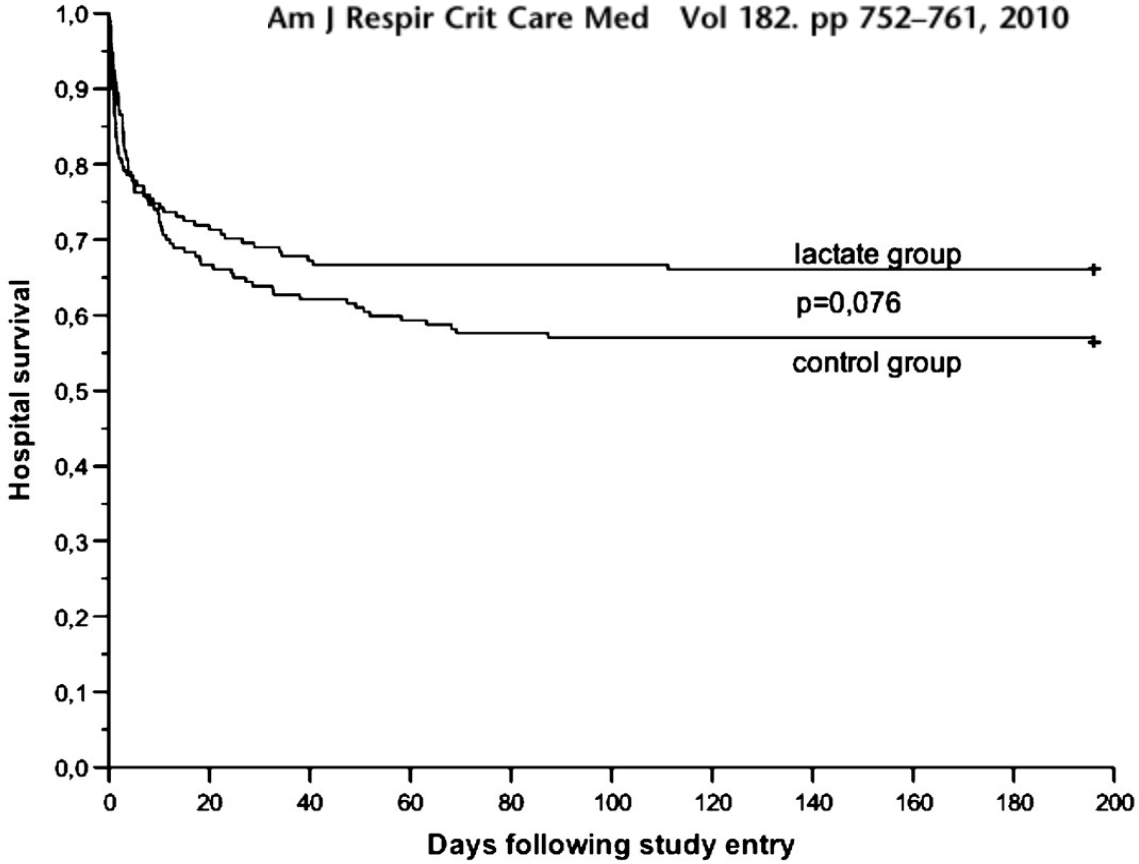
*Otero 2006; ** Jansen 2012, Jones 2010; ***SSC 2008;
[1] Pope 2010; [2] Hernandez 2011;

Early Lactate-Guided Therapy in Intensive Care Unit Patients

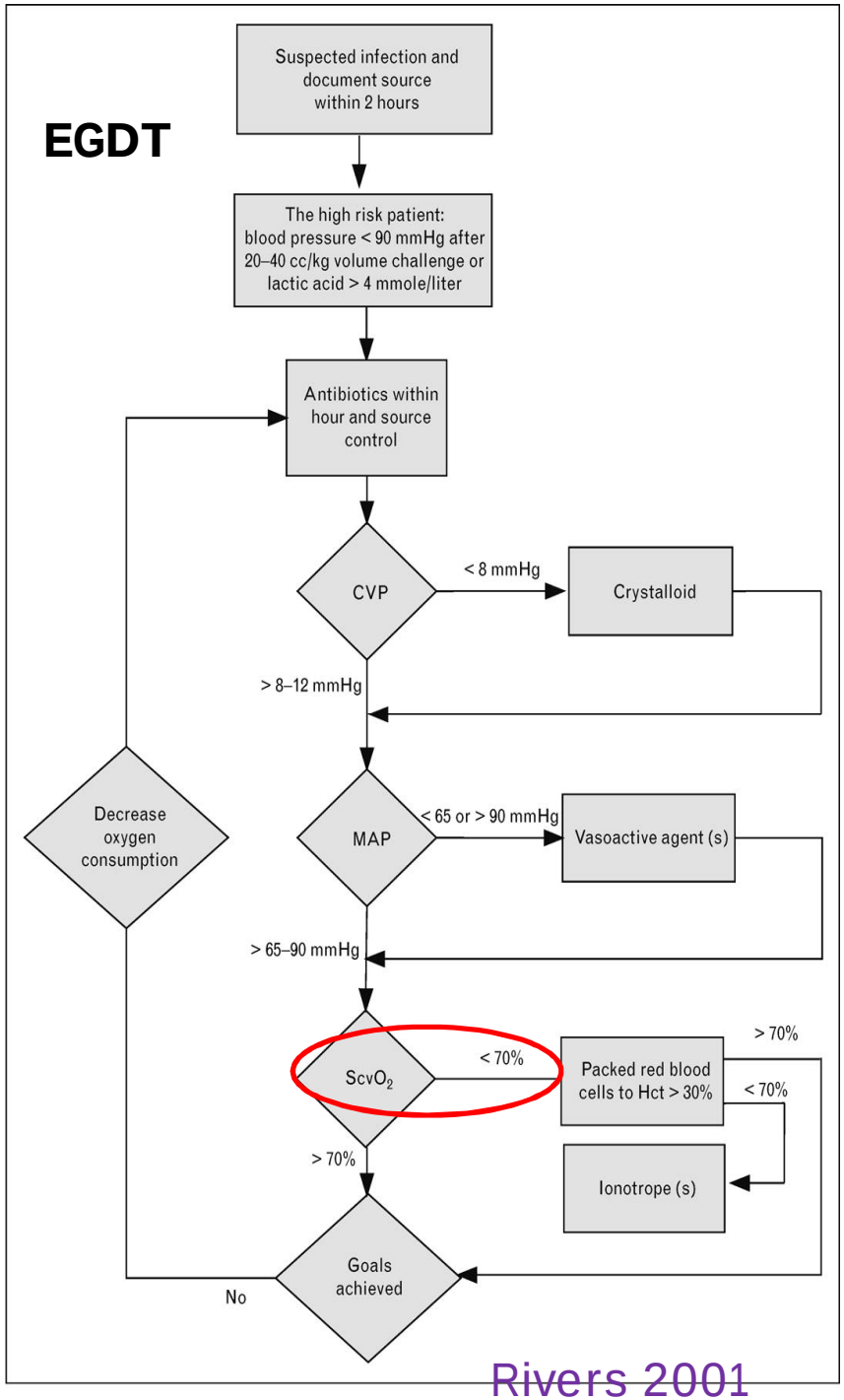
A Multicenter, Open-Label, Randomized Controlled Trial

Tim C. Jansen[1], Jasper van Bommel[1], F. Jeanette Schoonderbeek[3], Steven J. Sleeswijk Visser[4], Johan M. van der Klooster[5], Alex P. Lima[1], Sten P. Willemsen[2], and Jan Bakker[1], for the LACTATE study group*

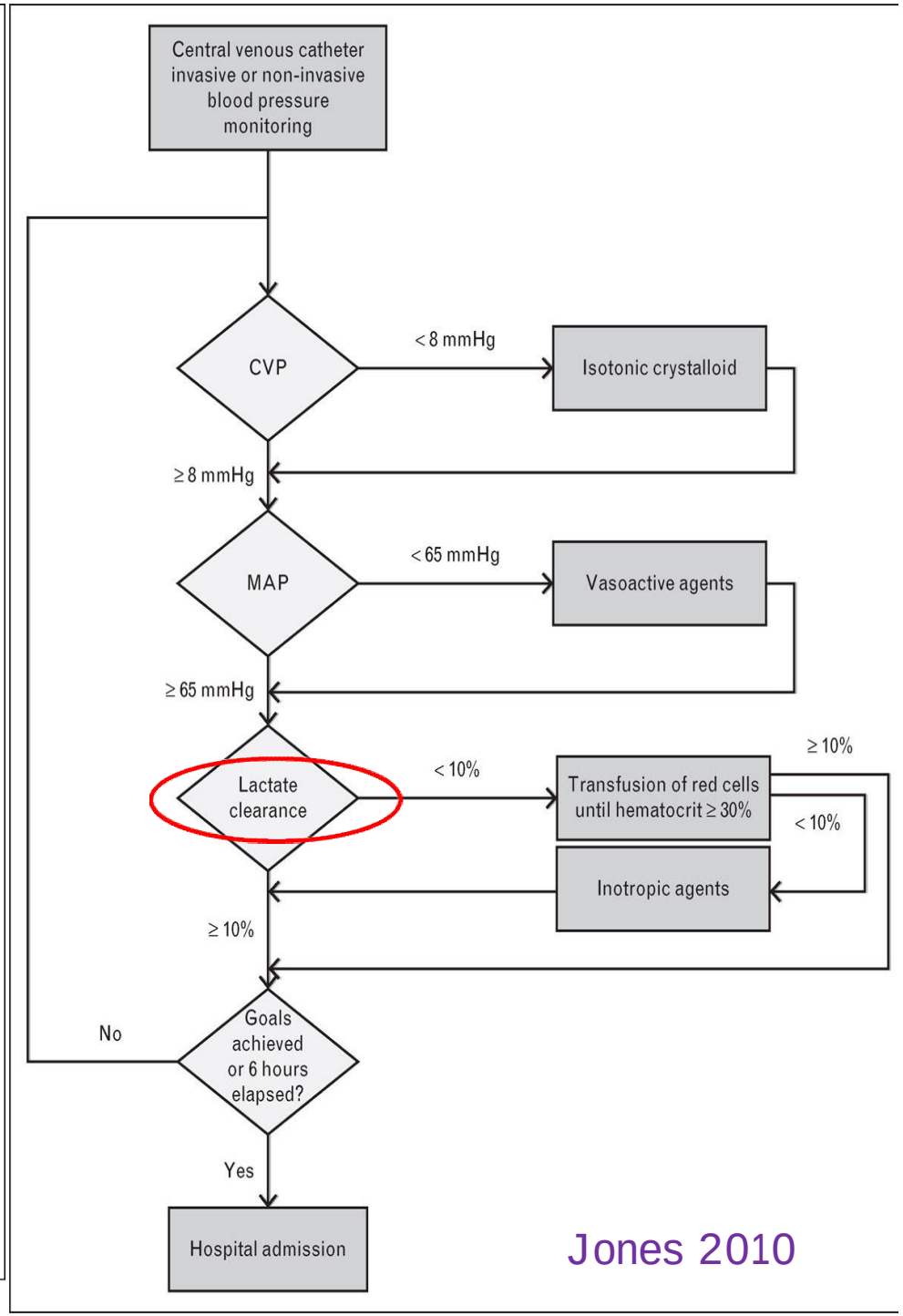
Am J Respir Crit Care Med Vol 182. pp 752–761, 2010



Number at risk:											
Control	177	118	110	105	102	101	101	101	101	101	100
Lactate	171	122	115	114	114	114	113	113	113	113	113

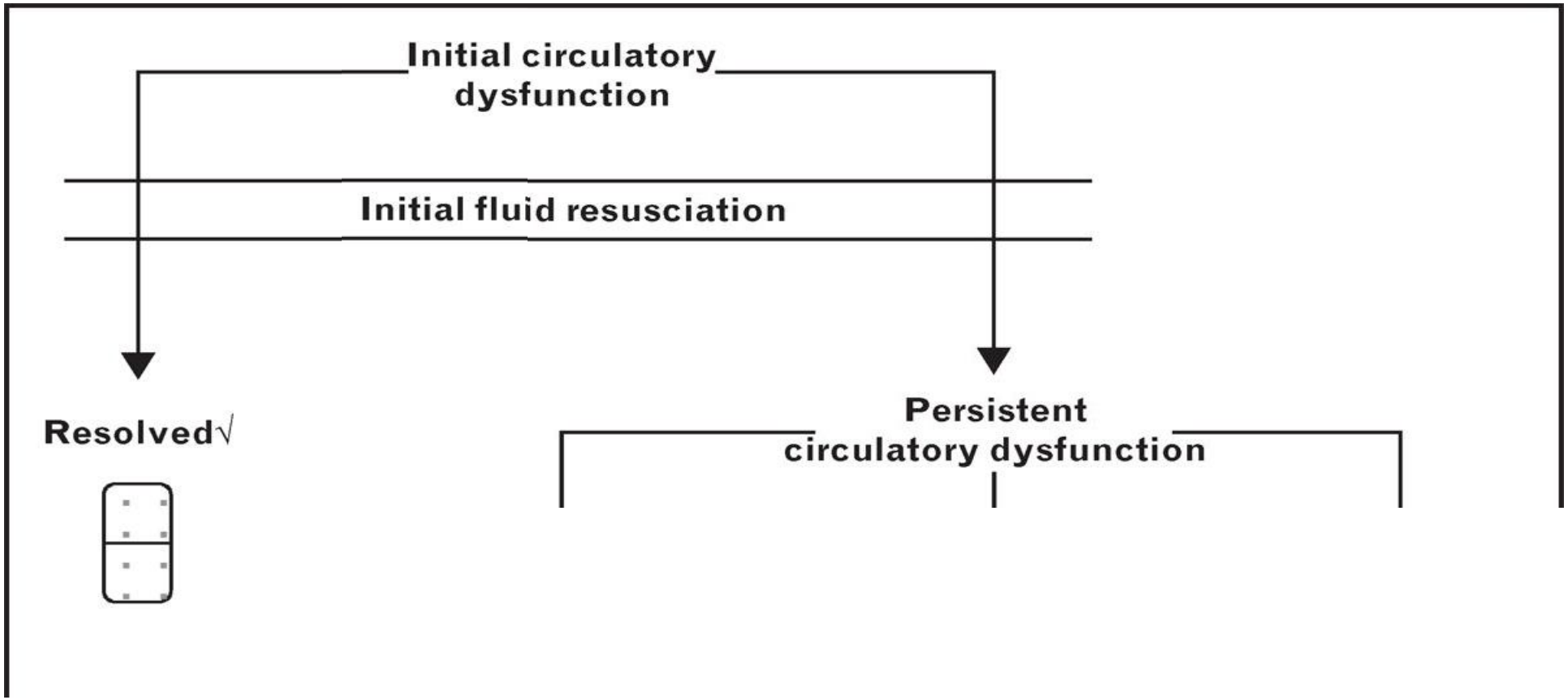


Rivers 2001



Jones 2010

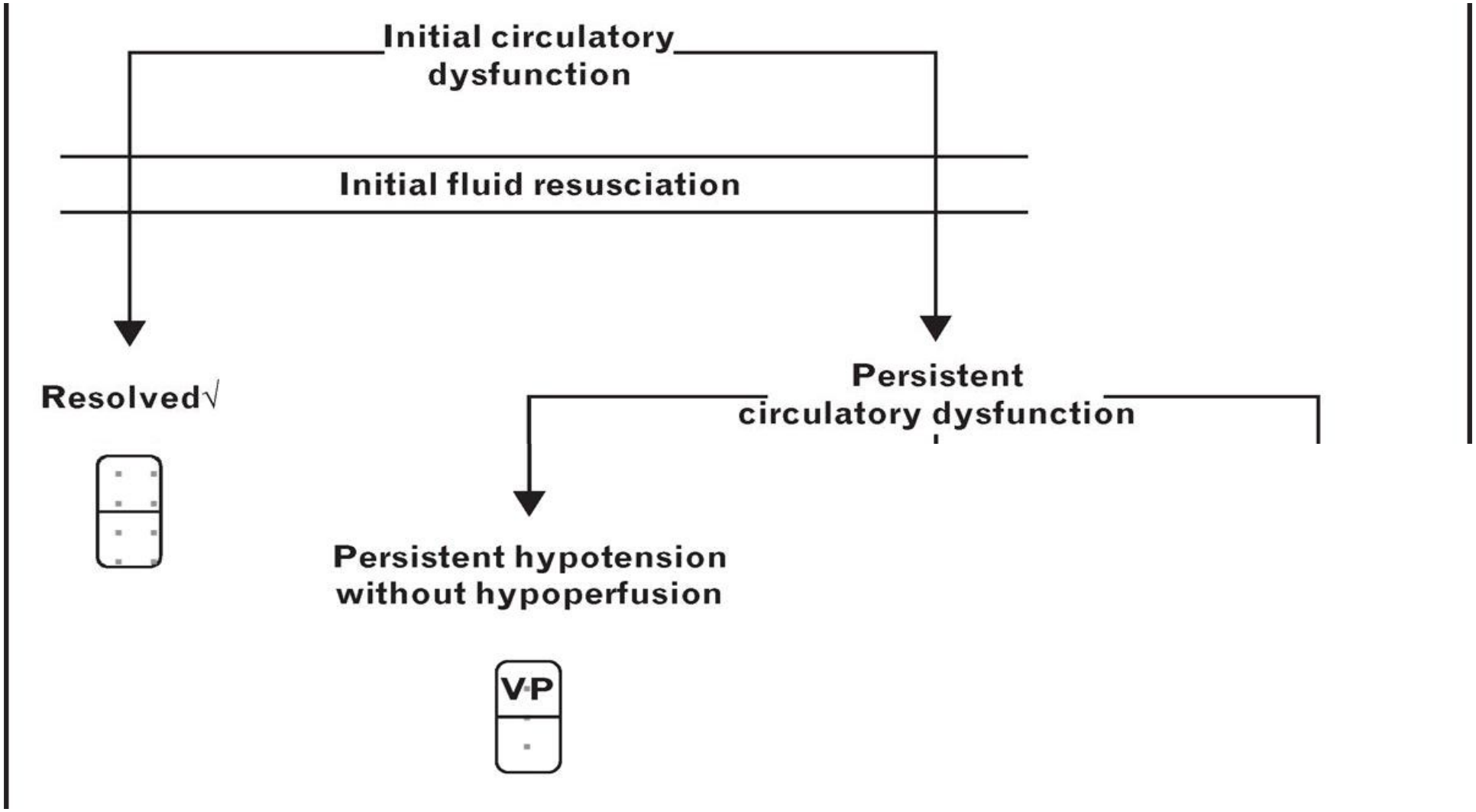
Reproduced from [61].


Initial circulatory dysfunction
Initial fluid resusciation
Resolved√
Persistent circulatory dysfunction

«Disfunzione circolatoria»

- **Alterazioni vascolari**
  - Vasoplegia
  - Edema capillare
  - Disomogenea distribuzione del flusso sanguigno
- **Depressione miocardica**
  - Diminuita frazione d'eiezione
- **Alterazione del microcircolo**

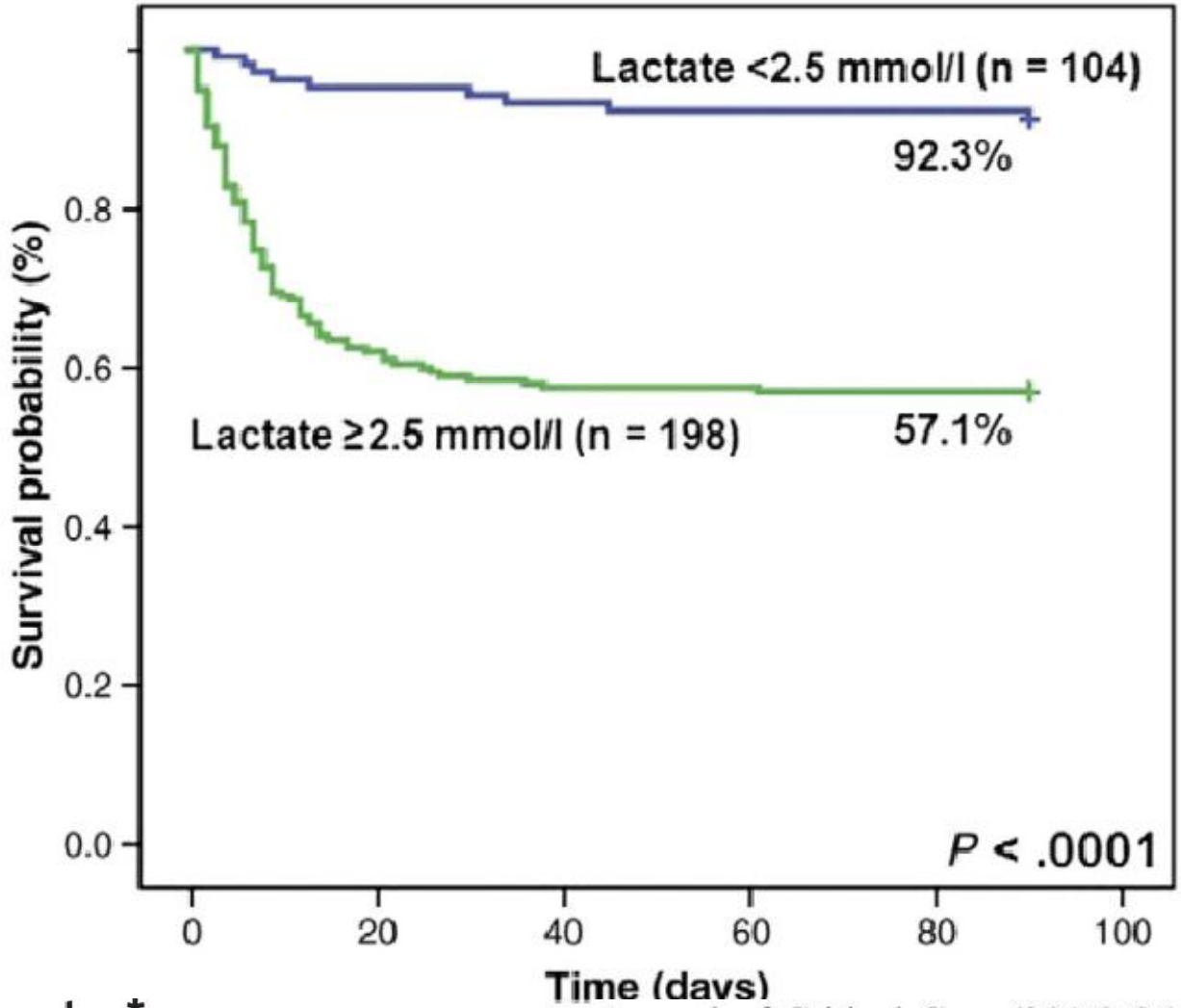
  → ipossia e MOFS



VP= VasoPressor
HP= HyPoperfusion

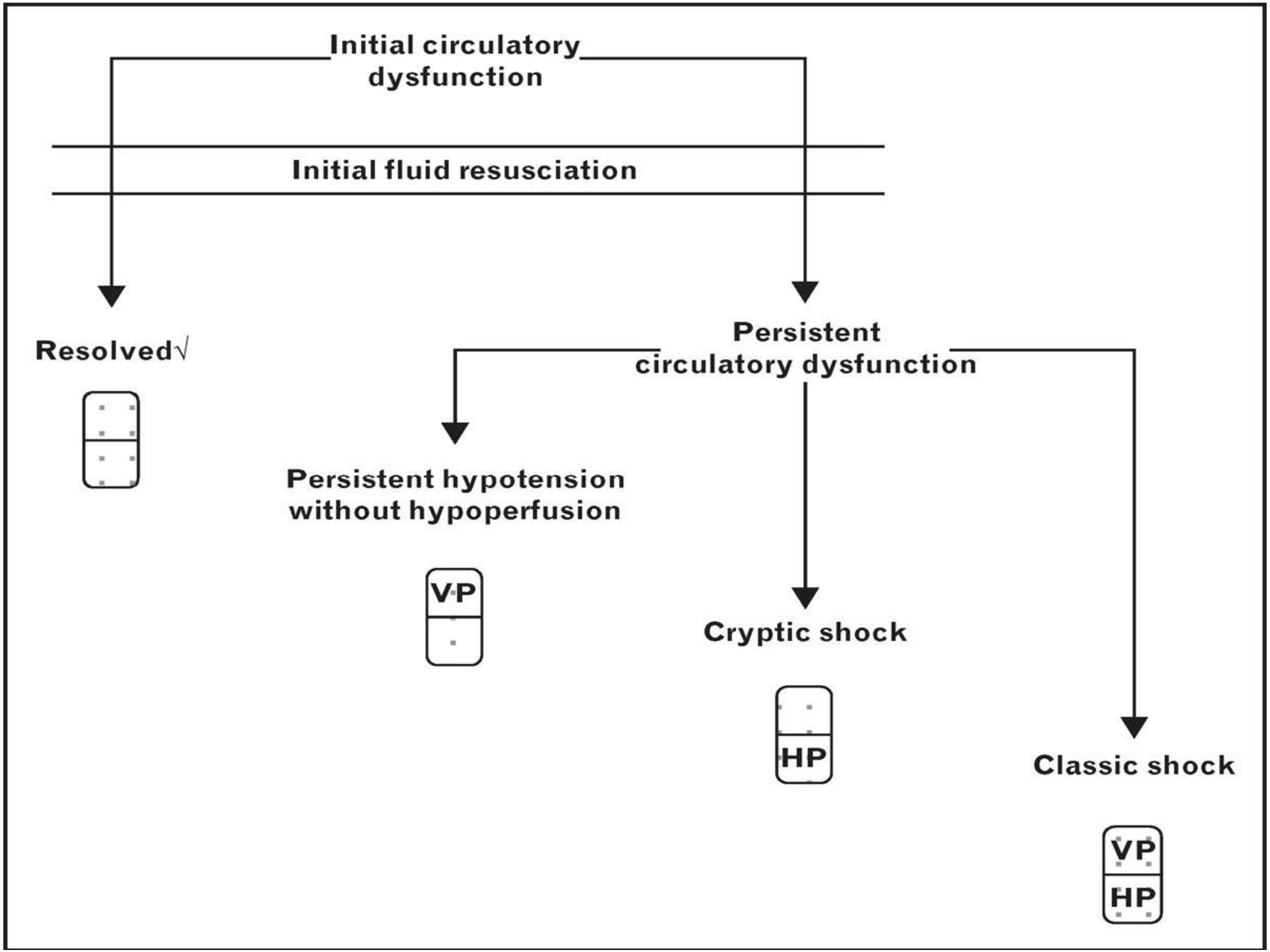
Paz settici con lattati normali

Journal of Critical Care



Glenn Hernandez*,

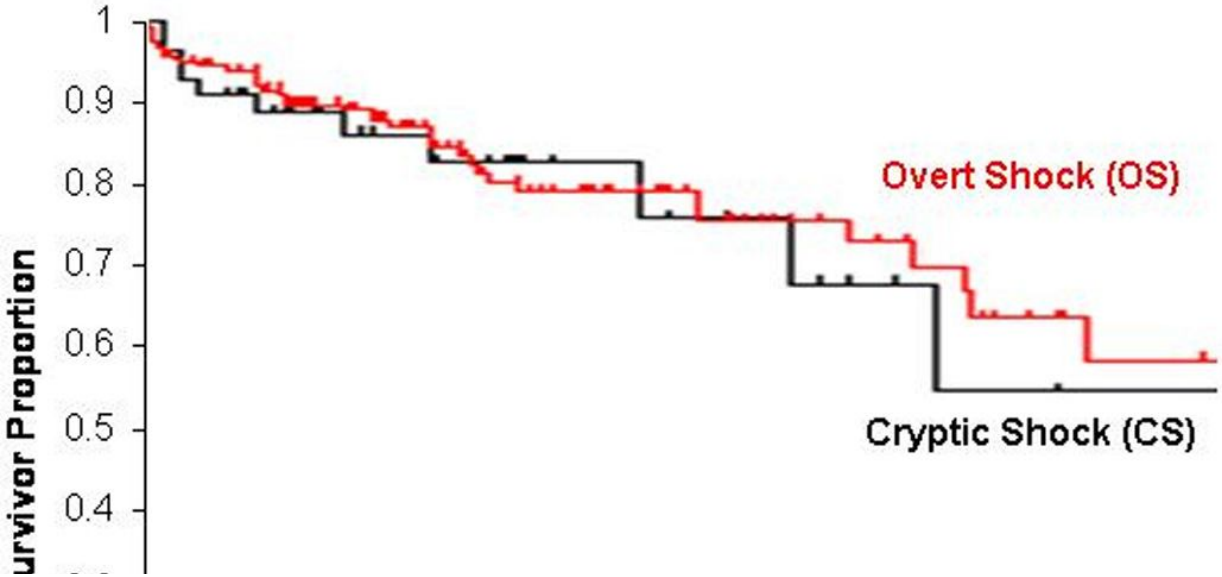
Journal of Critical Care (2011) **26**, 435.e9–435.e14


Initial circulatory dysfunction
Initial fluid resusciation
Resolved√
Persistent circulatory dysfunction
Persistent hypotension without hypoperfusion
VP
Cryptic shock
HP
Classic shock
VP
HP

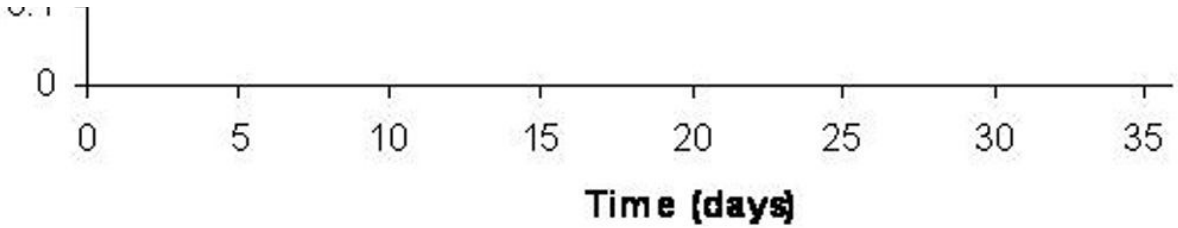
Outcomes of Patients Undergoing Early Sepsis Resuscitation for Cryptic Shock Compared with Overt Shock

Michael A. Puskarich, **Stephen Trzeciak**, **Nathan I. Shapiro**, **Alan C. Heffner**, **Jeffrey A. Kline**, and **Alan E. Jones on behalf of On behalf of the Emergency Medicine Shock Research Network (EMSHOCKNET)**

Resuscitation. 2011 October ; 82(10): 1289–1293.

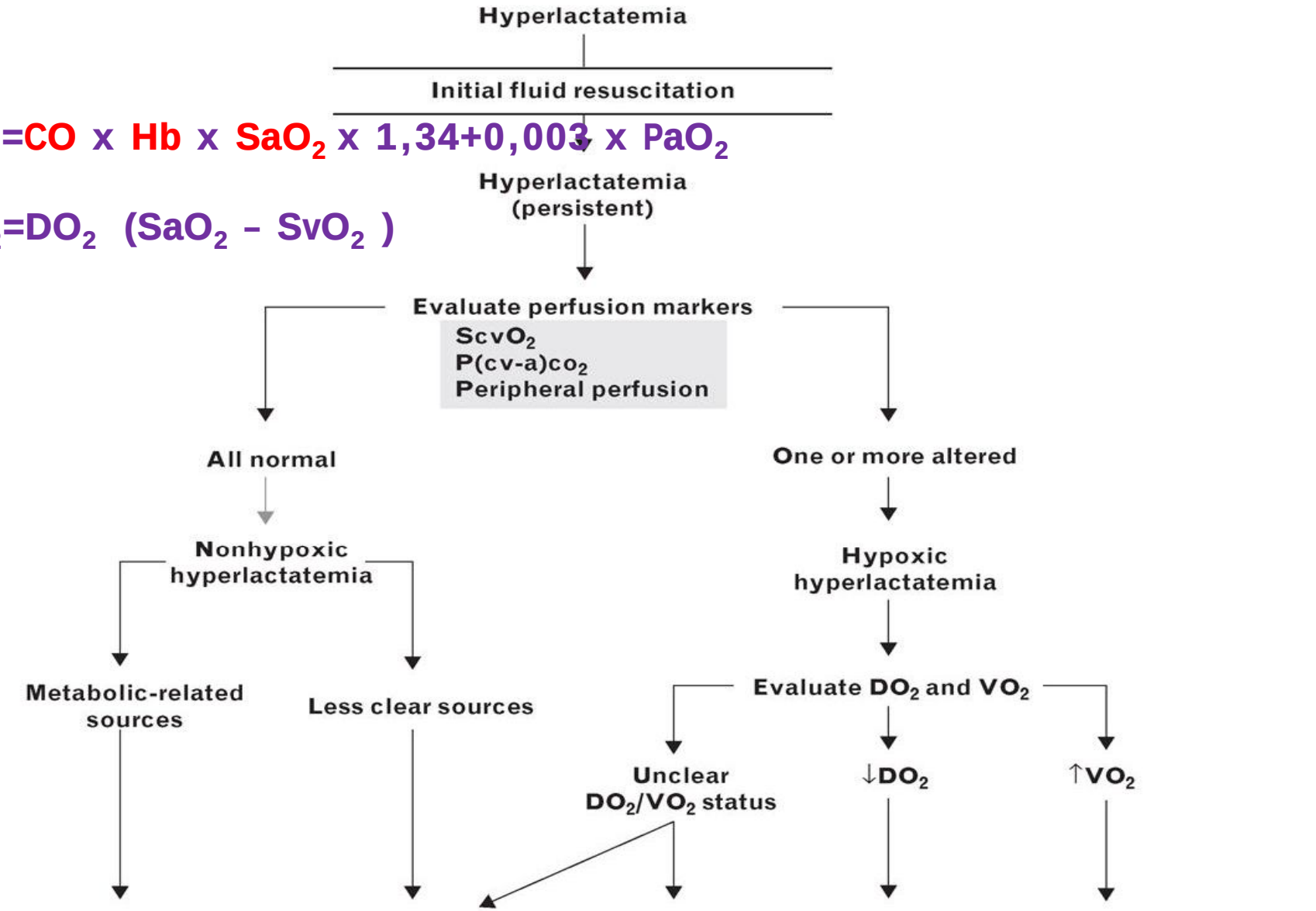


Conclusion—Severe sepsis with cryptic shock carries a mortality rate not significantly different from that of overt septic shock. These data suggest the need for early aggressive screening for and treatment of patients with an elevated serum lactate in the absence of hypotension.



$DO_2 = CO \times Hb \times SaO_2 \times 1{,}34 + 0{,}003 \times PaO_2$

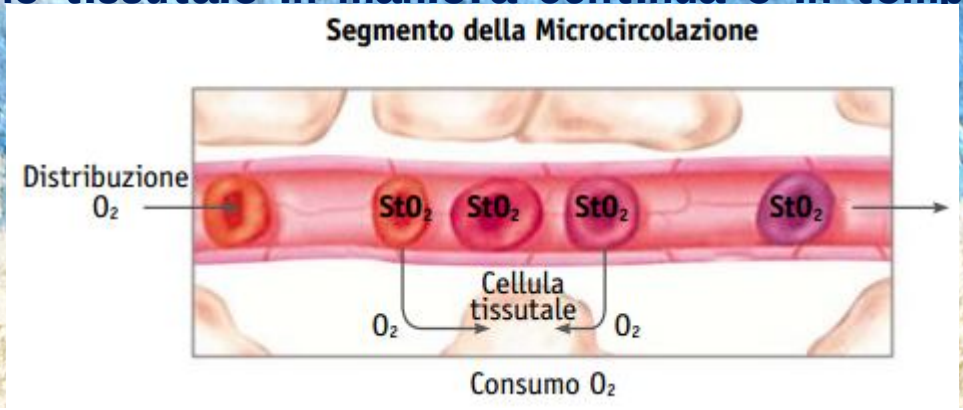
$VO_2 = DO_2 \ (SaO_2 - SvO_2)$



Sustained hyperadrenergia hyperinflammation Hypermetabolism Liver dysfunction Others	Microcirculatory derangements?	Regional hypoxia?	↓Preload ↓Cardiac output Anemia	↑Work or breathing Fever Pain Agitation

Saturazione tissutale di O2

La StO2 è un nuovo parametro che sfrutta la differenza di assorbimento tra l'Hb ossigenata e quella deossigenata, oltre che essere indice dell'Hb tissutale.
I tessuti periferici sono i primi ad essere ipoperfusi e gli ultimi a riperfondersi durante la rianimazione.
Monitora la perfusione tissutale in maniera continua e in tempo reale.



Near Infrared Spectroscopy

	SaO_2	SpO_2	SvO_2	$ScvO_2$	StO_2
Misura di	O_2 Arterioso	Saturazione di O_2 Arterioso (Pulsossimetro)	Saturazione Venosa mista di O_2	Saturazione Venosa centrale di O_2	Saturazione Tissutale di O_2
Misura % della Saturazione di O_2 dell'Emoglobina	Sì	Sì	Sì	Sì	Sì
Sito della misurazione	Arteria	Arteria (con polso)	Arteria polmonare	Vena Cava Superiore o Inferiore, Atrio Destro	Microcircolazione Periferica
Metodo di Misura	Prelievo Arterioso, emogasanalisi	Pulsossimetro/ Saturimetro	Catetere in Arteria Polmonare	Catetere Venoso Centrale	**InSpectra™ StO_2** Tissue Oxygenation Monitor
Significato del Parametro	Legame di O_2 a livello dei Polmoni	Legame di O_2 a livello dei Polmoni	Valutazione Sistemica del Consumo di O_2	Valutazione Regionale del Consumo di O_2	Valutazione Perfusione dei Tessuti
Valore Soglia di Misurazione	95 %	85 %	70 %	75 %	75 %[1]
Intervallo Normale**	95–100 %	96–100 %	60–80 %	> 70 % (5–10 % > SvO_2)	72–95 %[2]
Modifiche durante Shock e Rianimazione	Quando il cuore o le funzioni polmonari sono compromesse		Quando il consumo di O_2 sistemico cambia		Risposta immediata alle variazioni dello stato di perfusione periferica

StO2: evidenze cliniche

- È stato utilizzato nel trauma severo, shock emorragico, cardiogeno, ins.cardiaca severa e shock settico
- StO2<70% si associa ad una malattia più severa e ad una più alta mortalità (Lima 2009).
- Bassi livelli di StO2 si associano a iperlattacidemia (Lima 2009).
- La StO2 non varia dopo un'emorragia di 500 cc.(Jeger 2010).
- I livelli basali di StO2 nei paz settici sono leggermente più bassi che nei volontari sani (Creteur 2007)
- La posizione ma non la profondità della sonda è rilevante nella valutazione della perfusione tissutale durante l'ipovolemia.

«Critical care is
a need and not a place»

Grazie !