Παθοφυσιολογία του τραυματία

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Πρόεδρος Ελληνικής Εταιρείας Καρδιοαναπνευστικής Αναζωογόνησης


return
shift
Conflict of Interest
YES
NO

Βαρύτητα του τραύματος

Parameter	Injury Description	Grade
Injury severity score (ISS)	A2 + B2 + C2 (A, B, C are the AIS scores of the three most injured ISS body regions)	34
Head and neck AIS	Subarachnoid hemorrhage	3
Face AIS	Aches around glob	1
Chest AIS	Chest wall stiffness	1
Abdomen AIS	Mild liver contusion	3
Extremities AIS	Bilateral femoral fracture	4
External AIS	Multiple abrasions	1

Abbreviation: AIS, abbreviated injury scale.

Cut-off 16, ευαισθησία 20%

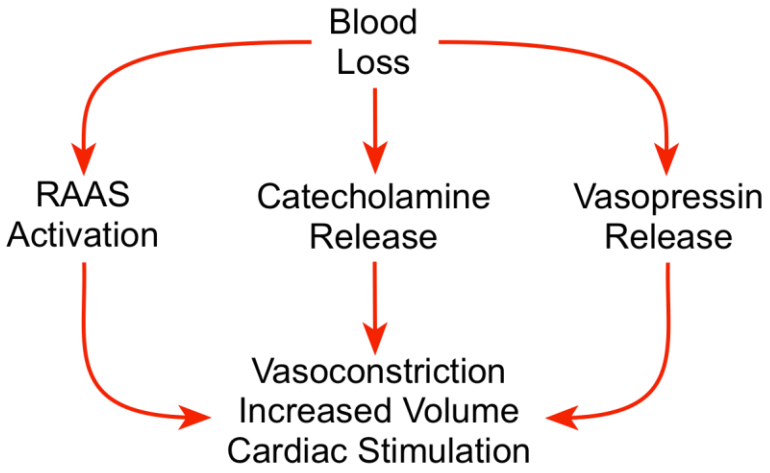
AIS > 2 points and at least one of the following covariables

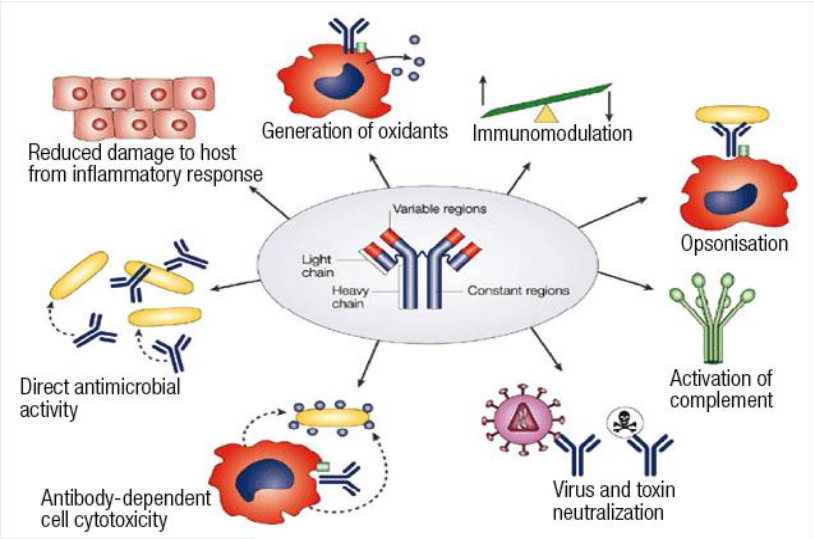
- hypotension (systolic blood pressure < 90 mm Hg)
- level of consciousness (Glasgow Coma Scale [GCS] score < 8)
- acidosis (base excess >= 6.0)
- coagulopathy (international normalized ratio 1.4/partial thromboplastin time > 40 s)
- age (>70 years).

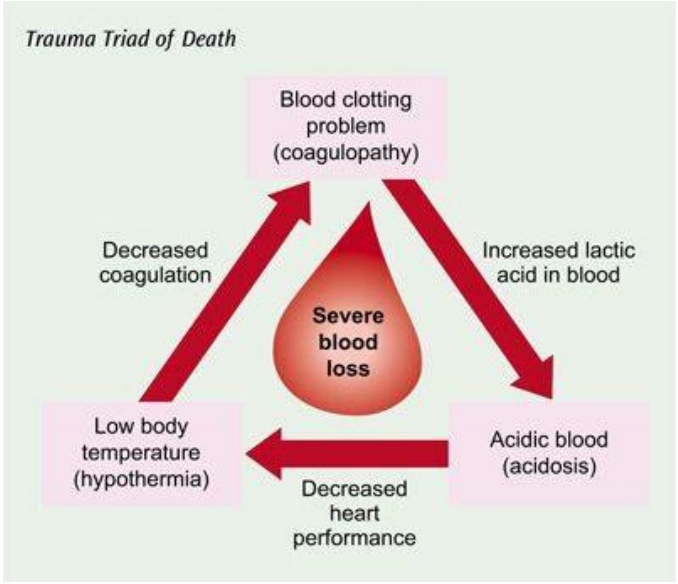
Frenzel et al. Does the applied polytrauma definition notably influence outcome and patient population? - a retrospective analysis. Scand J Trauma Resusc Emerg Med 2017;25(1):87

Pothmann et al. Assessment of polytraumatized patients according to the Berlin Definition: does the addition of physiological data really improve interobserver reliability? PLoS ONE 2018:13–18 .

Θνητότητα σχετίζεται με την παθοφυσιολογία







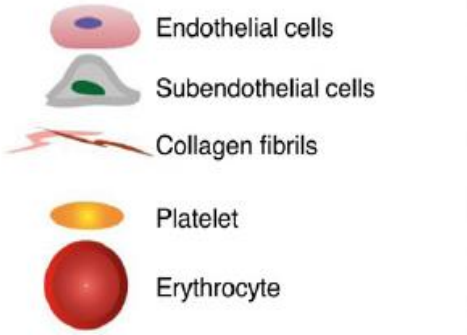
The NIH- funded Glue grant project

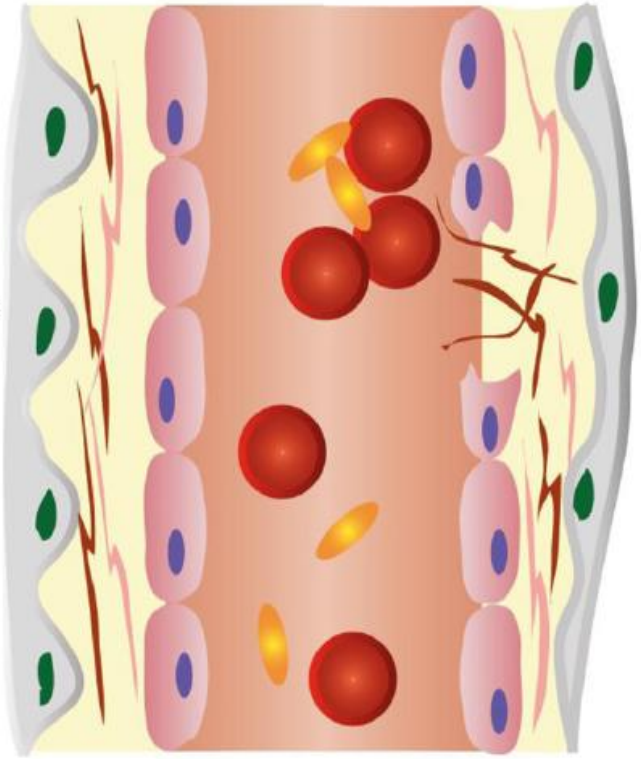
Normal Endothelium

Functional aspects:

Physiologic barrier to maintain

Energy support and fluid balance





Endothelium
after hemorrhage/shock

Signs of dysfunction:

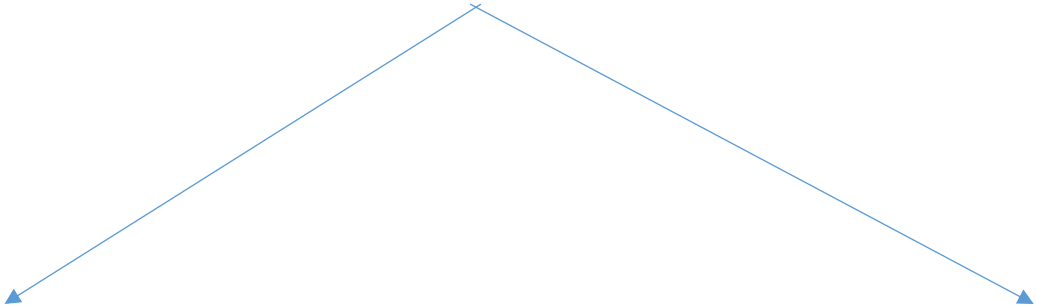
Swollen
Leaky
Less endothelium, circulation
Sticking of blood cells
Blockage /hemostasis

Clinical signs:

- **requirement of volume**
- **requirement of vasopressors**
- **coagulopathy/platelet count down**
- **pos. I/O ratio**

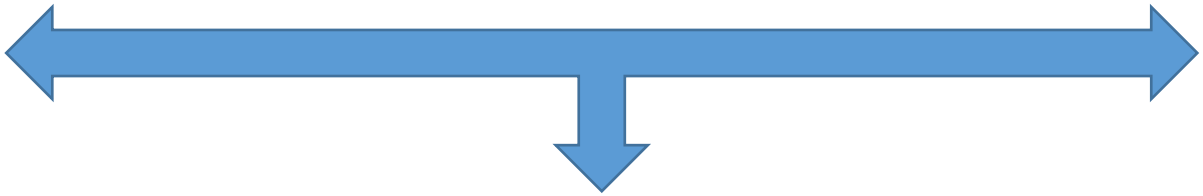
Η παθοφυσιολογία όμως φαίνεται όλο και πιο περίπλοκη

- Ενεργοποίηση κυτταρικών σημάτων κινδύνου ανεξάρτητα από το είδος του τραύματος: Αρκεί η απώλεια επαρκούς ποσότητας αίματος



Damage associated molecular patterns (DAMPs)
Αφορούν το ανθρώπινο σώμα

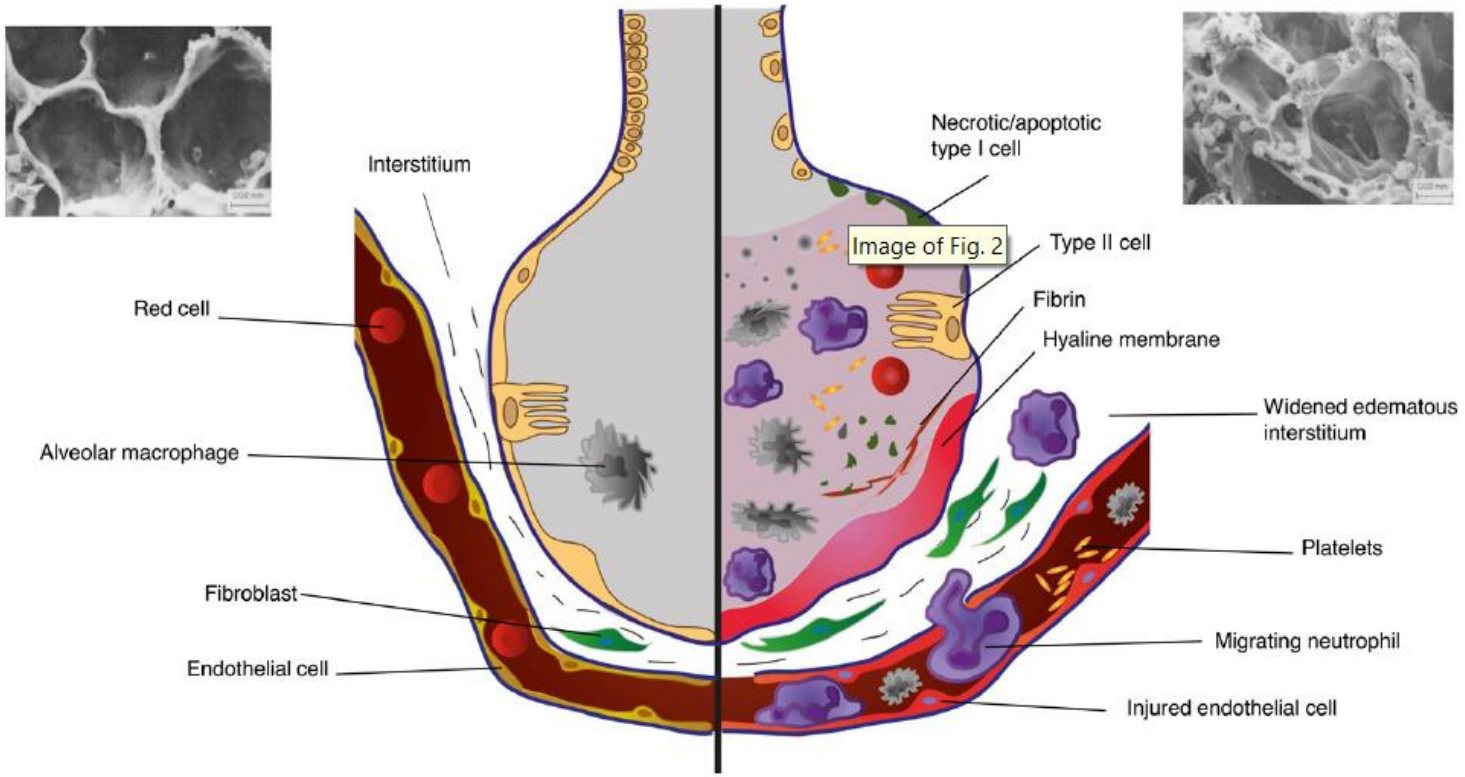
Pathogen associated molecular patterns (PAMPs)
Παθογόνα και ενδοτοξίνες

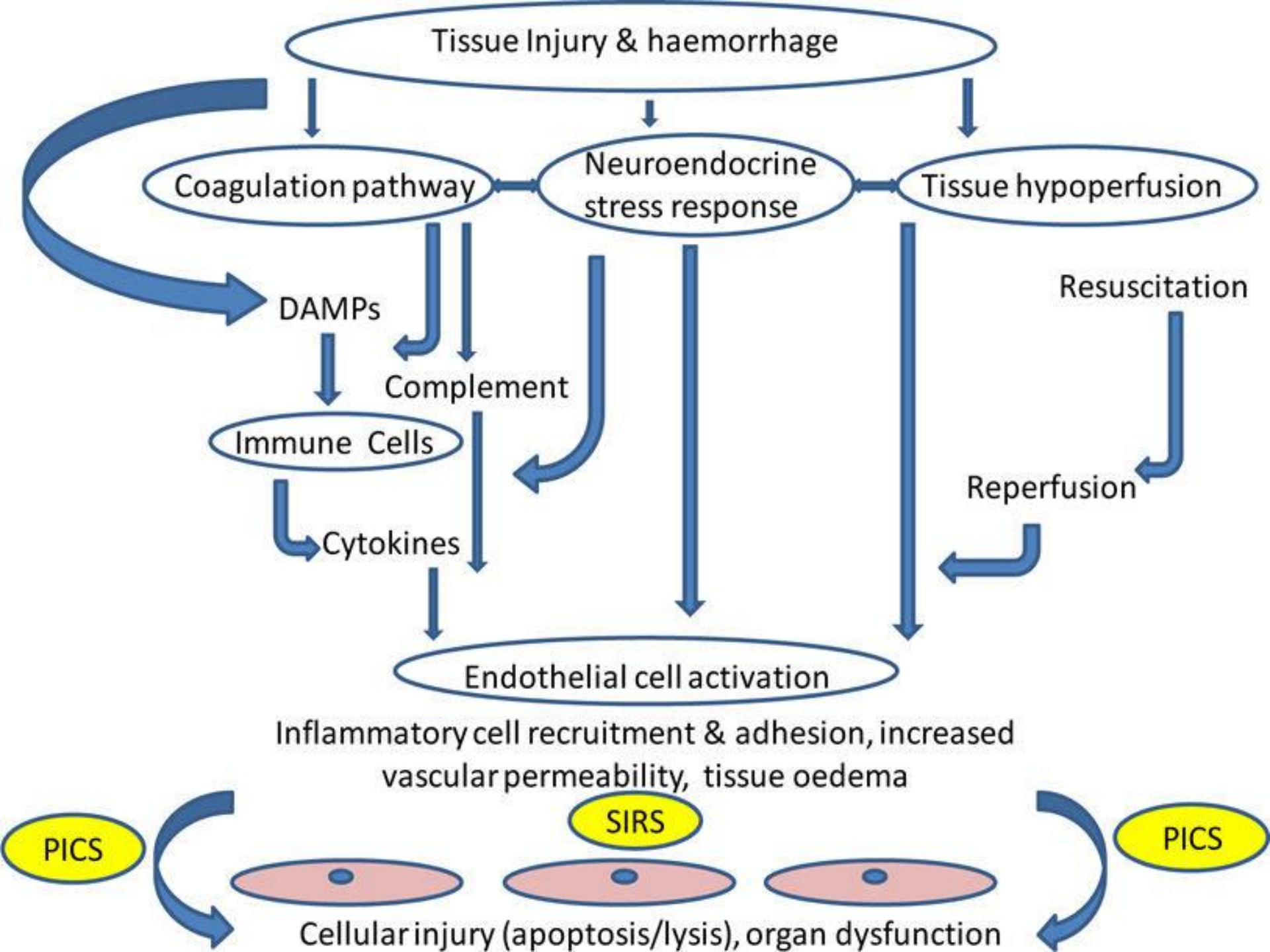


Κοινή φλεγμονώδη αντίδραση

Ένα παράδειγμα

Loss of volume into the «third space» in the lung due to endothelial damage and increased permeability



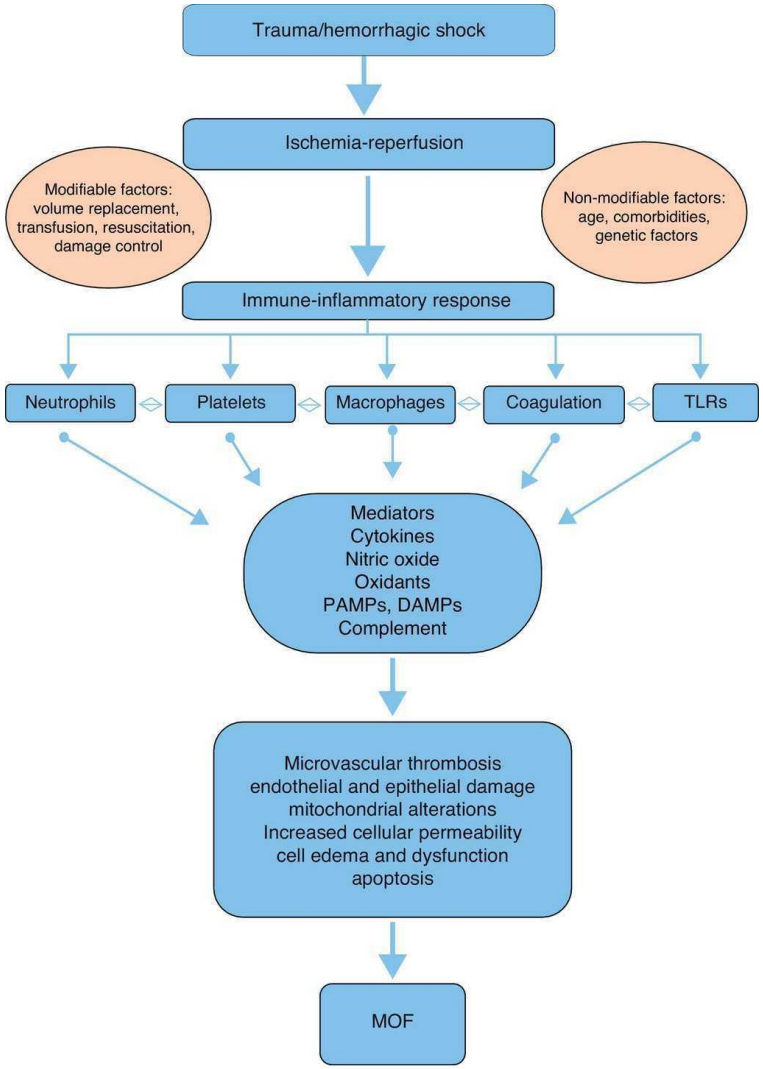

Tissue Injury & haemorrhage
Coagulation pathway
Neuroendocrine stress response
Tissue hypoperfusion
DAMPs
Complement
Resuscitation
Immune Cells
Reperfusion
Cytokines
Endothelial cell activation
Inflammatory cell recruitment & adhesion, increased vascular permeability, tissue oedema
PICS
SIRS
PICS
Cellular injury (apoptosis/lysis), organ dysfunction

SHOCK, Vol. 47, No. 4, pp. 429–435, 2017

CONTEMPORARY PATTERNS OF MULTIPLE ORGAN DYSFUNCTION IN TRAUMA

Joanna M. Shepherd, Elaine Cole, and Karim Brohi

Centre for Trauma Sciences, Blizard Institute, Queen Mary University of London, London, UK



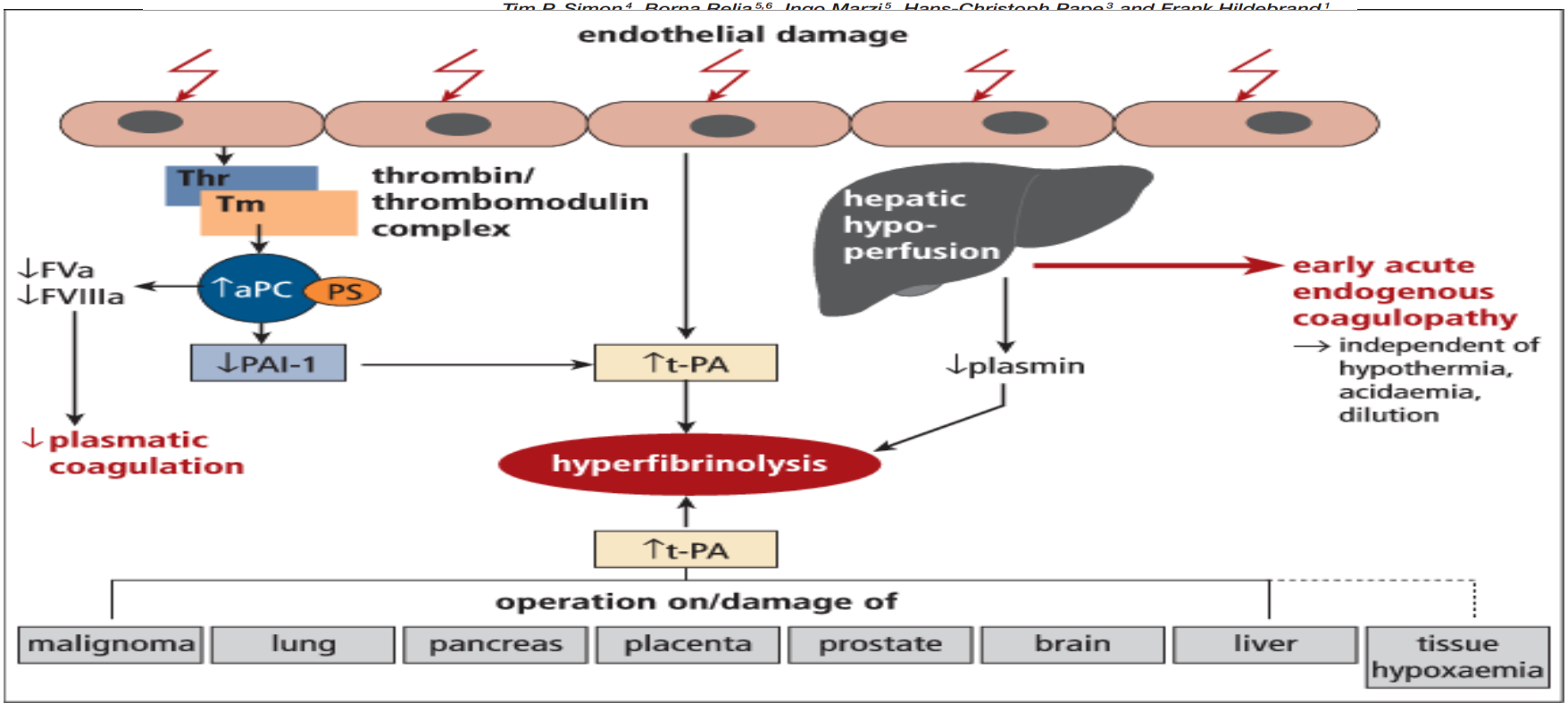
Υποάδρευση: Δυσλειτουργία του ενδοθηλίου

frontiers in Immunology

ORIGINAL RESEARCH
published: 09 January 2020
doi: 10.3389/fimmu.2019.03028

Trauma Severity and Its Impact on Local Inflammation in Extremity Injury—Insights From a Combined Trauma Model in Pigs

Klemens Horst[1,2*], *Johannes Greven*[1,2], *Hannah Lüken*[1], *Qiao Zhi*[2], *Roman Pfeifer*[3], *Tim P. Simon*[4], *Borna Relja*[5,6], *Ingo Marzi*[5], *Hans-Christoph Pape*[3] *and Frank Hildebrand*[1]



Genomic Storm theory

Physiol Genomics 32: 299–310, 2008.
First published November 6, 2007; doi:10.1152/physiolgenomics.00086.2007.

Comparison of longitudinal leukocyte gene expression after burn injury or trauma-hemorrhage in mice

James A. Lederer,[1] Bernard H. Brownstein,[2] M. Cecilia Lopez,[3] Sandra MacMillan,[2] Adam J. Delisle,[1] Malcolm P. MacConmara,[1] Mashkoor A. Choudhry,[4] Wenzhong Xiao,[5] Steven Lekousi,[6] J. Perren Cobb,[2] Henry V. Baker,[3] John A. Mannick,[1] Irshad H. Chaudry,[4] and the Inflammation and the Host Response to Injury Collaborative Research Program Participants

[1]*Department of Surgery, ...ham and Women's Hospital/Harvard Me...cal Scho... Boston, Ma...chusetts; [2]Department ... Washington ...iversity School of Medicine, St. Louis, Missouri; [3]De...tment of Mole...lar Genetics and ...icrob... Ga...vil... ...a, ...irmi...m, ... [5]Stanford ...nivers... ...fo... ...ifor...a; [6]De...tme... Mo...cul... B...ogy ... ...as...etts*

Ουδετερόφιλα

Submitted 13 April 2007; accepted in final form 31 October 20...

Lederer JA, Brownstein BH, Lopez MC, MacMillan S, Delisle AJ, MacConmara MP, Choudhry MA, Xiao W, Lekousi S, Cobb JP, Baker HV, Mannick JA, Chaudry IH, and the Inflammation and the Host Response to Injury Collaborative Research Program Participants. Comparison of longitudinal leukocyte gene expression after burn injury or trauma-hemorrhage in mice. *Physiol Genomics* 32: 299–310, 2008. First published November 6, 2007; doi:10.1152/physiolgenomics.00086.2007.—A primary objective of the large collaborative project entitled "Inflammation and the Host Response to Injury" was to identify leukocyte genes that are differentially expressed after two different types of injury in mouse models and to test the hypothesis that both forms of injury would induce similar changes in gene expression. We report

monly seen early after traumatic, thermal, or major surgical procedure (2, 17, 21, 23, 27, 30, 32). However, surgeons and critical care specialists have also recognized that patients who have suffered major burns often have a clinical course quite different from that of patients who have sustained significant traumatic injury (12, 29, 30, 33). Unfortunately, up to the present day, similarities and differences in the molecular mechanisms involved in the response to these two forms of injury have been difficult to quantify.

The availability of gene microarray technology has made it possible to study the effects of both thermal and traumatic injury on the transcriptome in cell populations of interest.

JEM

Brief Definitive Report

Journal of Experimental Medicine

A genomic storm in critically injured humans

Wenzhong Xiao,[1,4] Michael N. Mindrinos,[4] Junhee Seok,[4] Joseph Cuschieri,[9] Alex G. Cuenca,[8] Hong Gao,[4] Douglas L. Hayden,[6] Laura Hennessy,[9] Ernest E. Moore,[10] Joseph P. Minei,[11] Paul E. Bankey,[12] Jeffrey L. Johnson,[10] Jason Sperry,[13] Avery B. Nathens,[14] Timothy R. Billiar,[13] Michael A. West,[15] Bernard H. Brownstein,[16] Philip H. Mason,[5] Henry V. Baker,[8] Celeste C. Finnerty,[17] Marc G. Jeschke,[18] M. Cecilia López,[8] Matthew B. Klein,[9] Richard L. Gamelli,[19] Nicole S. Gibran,[9] Brett Arnoldo,[11] Weihong Xu,[4] Yuping Zhang,[4] Steven E. Calvano,[20] Grace P. McDonald-Smith,[5] David A. Schoenfeld,[2] John D... ...orey,[21] J. Perren Cobb,[3] H. Shaw Warren,[2] Lyle L. Moldawer,[8] David ... Herndon, ... St... F. L... ...d V. ... ...ald... To... ...s, a... th... Inflam...mat...n ...d Ho... ...es...ons... ...t... Inj...y ...arg...-S... C...lab...rative ...es...rc... Progr...

[1]Departm... of Surgery, [2]Department ... Medicine, and [3]Department of Anesthesiology, Critic... ...are Medicine, and Pain Medicine ...assachusetts General Ho...al, Harvard Medical School, Boston, MA 02114
[4]Stanford Genome Technology Center, Stanford University, Palo Alto, CA 94304
[5]Department of Surgery and [6]Department of Medicine, [7]Massachusetts General Hospital, Boston, MA 02114
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[9]Department of Surgery, Harborview Medical Center, University of Washington School of Medicine, Seattle, WA 98104
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[12]Department of Surgery, University of Rochester Medical Center, Rochester, NY 14642
[13]Department of Surgery, University of Pittsburgh Medical Center Presbyterian University Hospital, Pittsburgh, PA 15213
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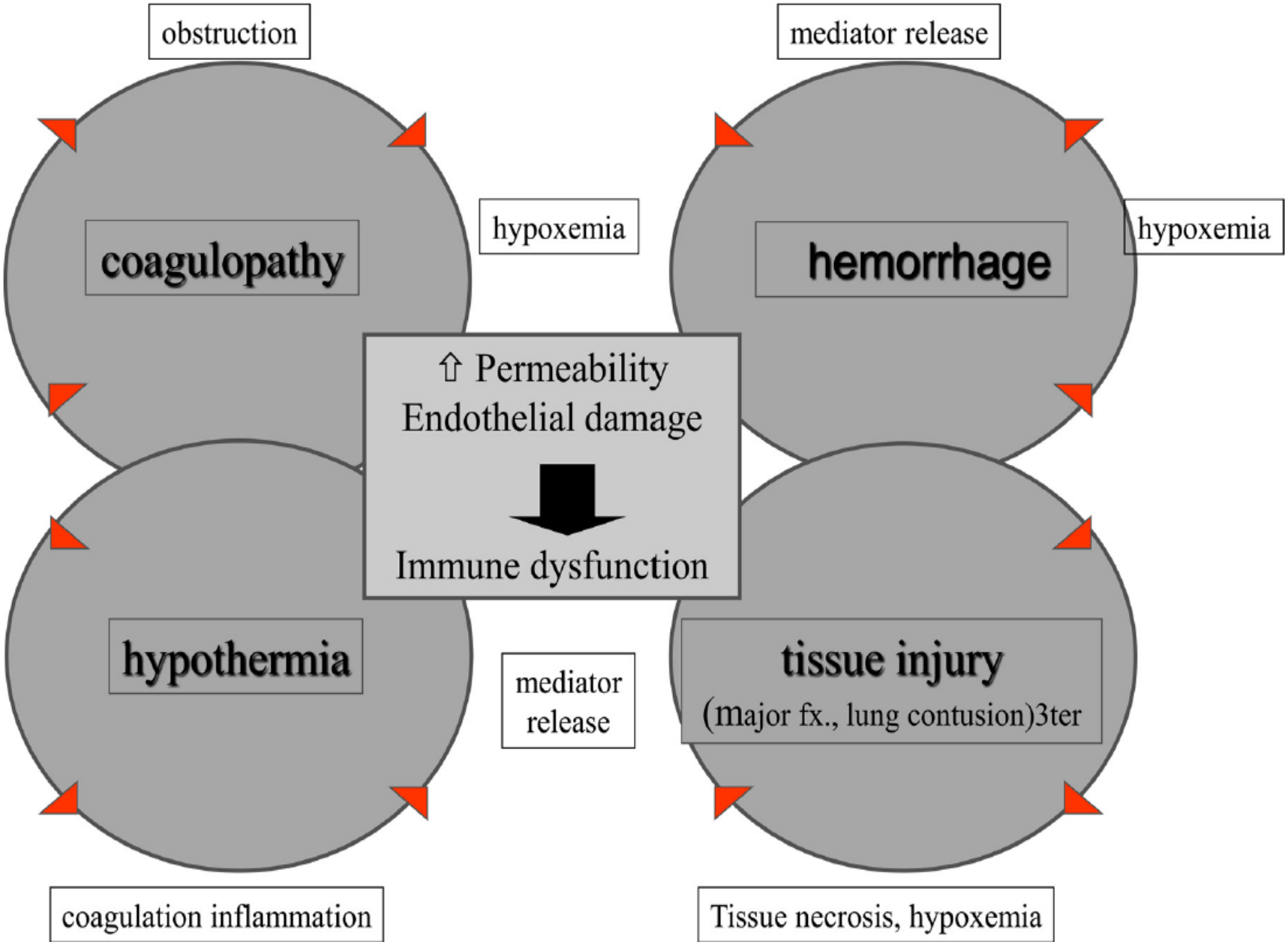
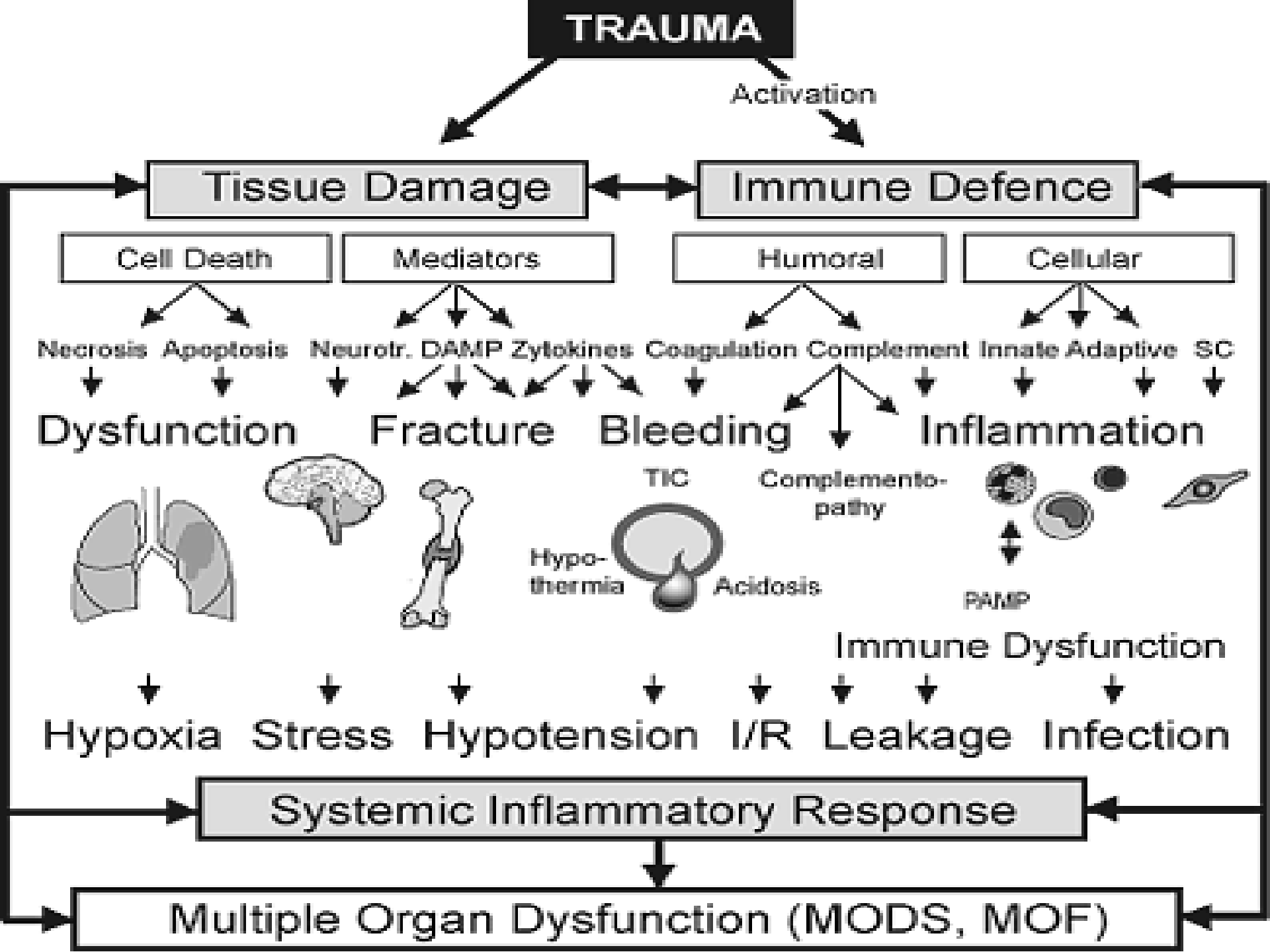
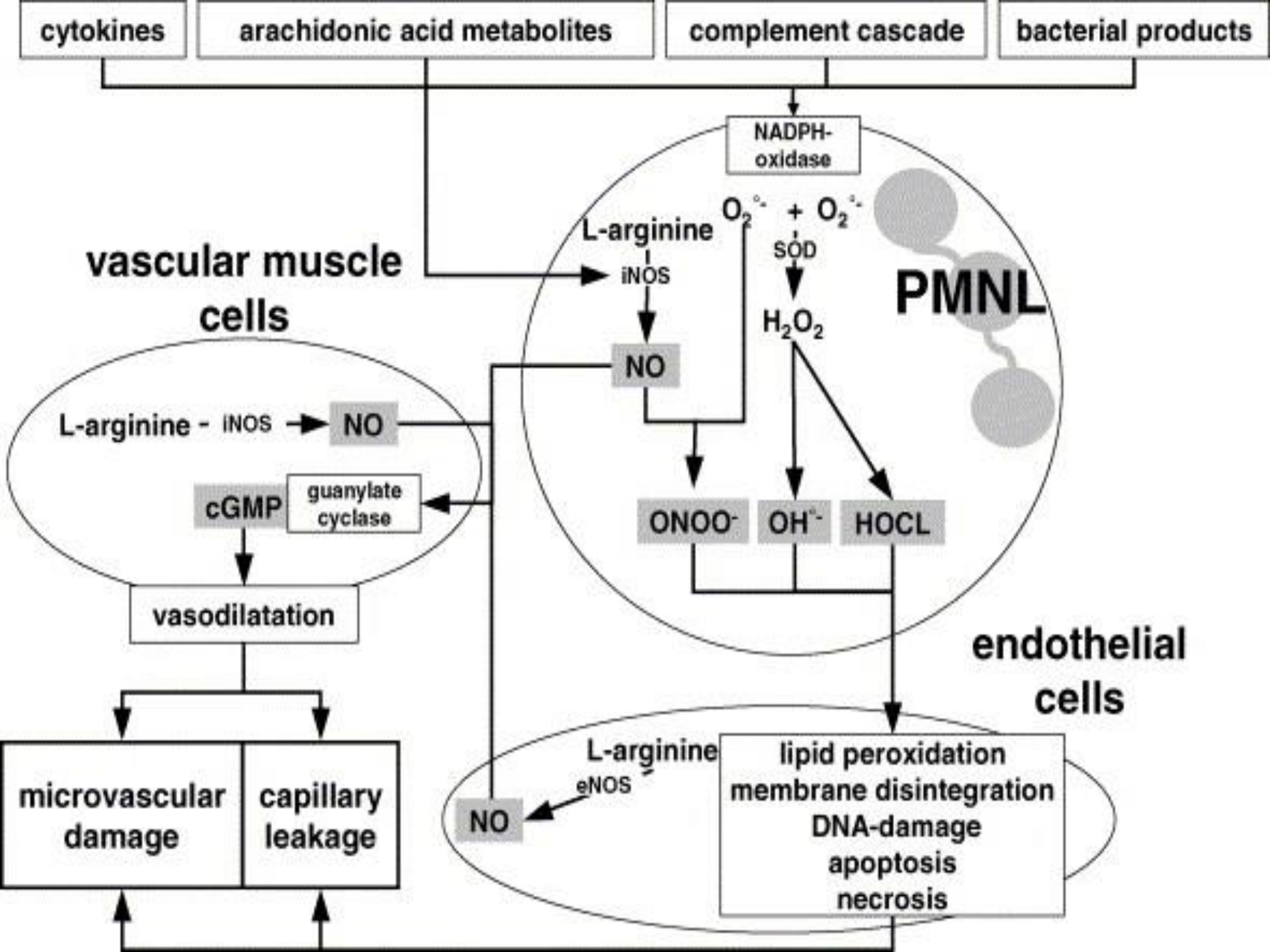
[21]Department of Molecular Biology, Lewis-Sigler Institute for Integrative Genomics, Princeton University, Princeton, NJ 08544

Σε όλη τη νοσηλεία

Polytrauma: four interactive cycles




TRAUMA
Activation
Tissue Damage
Immune Defence
Cell Death
Mediators
Humoral
Cellular
Necrosis
Apoptosis
Neurotr.
DAMP
Zytokines
Coagulation
Complement
Innate
Adaptive
SC
Dysfunction
Fracture
Bleeding
Inflammation
TIC
Hypo-
thermia
Acidosis
Complemento-
pathy
PAMP
Immune Dysfunction
Hypoxia
Stress
Hypotension
I/R
Leakage
Infection
Systemic Inflammatory Response
Multiple Organ Dysfunction (MODS, MOF)


cytokines
arachidonic acid metabolites
complement cascade
bacterial products
NADPH-oxidase
L-arginine
iNOS
$O_2^{\cdot-}$ + $O_2^{\cdot-}$
SOD
H_2O_2
PMNL
NO
vascular muscle cells
L-arginine - iNOS → NO
cGMP
guanylate cyclase
vasodilatation
$ONOO^-$
$OH^{\cdot-}$
HOCL
endothelial cells
L-arginine
eNOS
NO
lipid peroxidation
membrane disintegration
DNA-damage
apoptosis
necrosis
microvascular damage
capillary leakage

European Journal of Trauma and Emergency Surgery
https://doi.org/10.1007/s00068-018-0980-1

ORIGINAL ARTICLE

Resuscitation with centhaquin and 6% hydroxyethyl starch 130/0.4 improves survival in a swine model of hemorrhagic shock: a randomized experimental study

Zinais Kontouli[1] · Chryssoula Staikou[2] · Nicoletta Iacovidou[1,3,4] · Ioannis Mamais[5,6,7] · Evaggelia Kous Apostolos Papalois[9] · Panagiotis Papapanagiotou[4] · Anil Gulati[10] · Athanasios Chalkias[4,11,13] · Theodoros Xanthos[12]

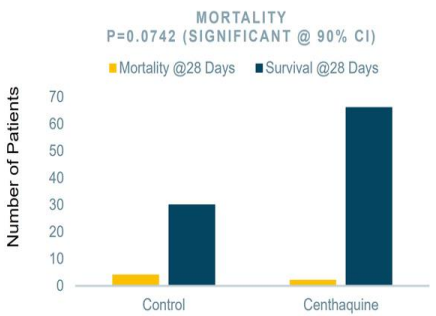
Received: 4 January 2018 / Accepted: 10 July 2018

Centhaquine

A Resuscitative Agent Free of Arterial Constriction

Phase III Trial Mortality Outcome

Significant improvement over standard of care in reducing mortality



Control (mortality)	11.76%
Centhaquine (mortality)	2.94%

Which Multicenter Randomized Controlled Trials in Critical Care Medicine Have Shown Reduced Mortality? A Systematic Review. Santacruz, Carlos A.; Pereira, Adriano J.; Celis, Edgar; Vincent, Jean-Louis. Critical Care Medicine: 2019: 47, 1680-1691.

No pharmacological intervention consistently reduced mortality

Phase II + III Control (N=56)	**10.71%**
Phase II + III Centhaquine (N=91)	**2.20%**
Odds ratio 5.340 (95% CI 1.27-26.50)	**P=0.0271**

- Gulati et al., (2021) Drugs 2021, June 01; 1-22; doi: 10.1007/s40265-021-01547-5
- Gulati et al., 2021 Adv Ther. 2021 May 10. doi: 10.1007/s12325-021-01760-4.
- Gulati et al., (2020) Drugs Fut 2020, 45(3): 153; doi: 10.1358/dof.2020.45.3.3098155.

JOURNAL OF SURGICAL RESEARCH 200 (2016) 227–235

Available online at www.sciencedirect.com
ScienceDirect
journal homepage: www.JournalofSurgicalResearch.com

Centhaquin improves survival in a swine model of hemorrhagic shock

Panagiotis Papapanagiotou, MSc,[a,b,1] Theodoros Xanthos, PhD,[a,b,1] Anil Gulati, PhD,[c] Athanasios Chalkias, PhD,[a,b,] Apostolos Papalois, PhD,[d] Zinais Kontouli, MSc,[a] Athanasios Alegakis, PhD,[e] and Nicoletta Iacovidou, PhD[b,f]*

Drugs (2021) 81:1079–1100
https://doi.org/10.1007/s40265-021-01547-5

ORIGINAL RESEARCH ARTICLE

A Multicentric, Randomized, Controlled Phase III Study of Centhaquine (Lyfaquin®) as a Resuscitative Agent in Hypovolemic Shock Patients

Anil Gulati[1] · Rajat Choudhuri[2] · Ajay Gupta[3] · Saurabh Singh[4] · S. K. Noushad Ali[5] · Gursaran Kaur Sidhu[6] · Parvez David Haque[7] · Prashant Rahate[8] · Aditya R. Bothra[9] · Gyan P. Singh[10] · Sanjiv Maheshwari[11] · Deepak Jeswani[12] · Sameer Haveri[13] · Apurva Agarwal[14] · Nilesh Radheshyam Agrawal[15]

Accepted: 25 May 2021 / Published online: 1 June 2021

Abstract

Introduction Centhaquine (Lyfaquin®) showed significant safety and efficacy in preclinical and clinical phase I and II studies.

Methods A prospective, multicentric, randomized phase III study was conducted in patients with hypovolemic shock, systolic blood pressure (SBP) ≤ 90 mmHg, and blood lactate levels ≥ 2 mmol/L. Patients were randomized in a 2:1 ratio to the centhaquine group ($n = 71$) or the control (saline) group ($n = 34$). Every patient received standard of care (SOC) and was followed for 28 days. The study drug (normal saline or centhaquine 0.01 mg/kg) was administered in 100 mL of normal saline infusion over 1 h. The primary objectives were to determine changes (mean through 48 h) in SBP, diastolic blood pressure (DBP), blood lactate levels, and base deficit. The secondary objectives included the amount of fluids, blood products, and vasopressors administered in the first 48 h, duration of hospital stay, time in intensive care units, time on ventilator support, change in acute respiratory distress syndrome (ARDS), multiple organ dysfunction syndrome (MODS), and the proportion of patients with 28-day all-cause mortality.

Results The demographics of patients and baseline vitals in both groups were comparable. The cause of hypovolemic shock


The Road Ahead
2014
Wall Street
2014
Main Street
steve@greenberg-art.com
GREENBERG

Ευχαριστώ πολύ