Șocul septic

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CATEDRA CHIRURGIE 4

NOUA CLASIFICARE FIZIOPATOLOGICĂ A ŞOCULUI (Antri et all. 2007)

ŞOC HIPOVOLEMIC: ↓ masei sanguine -hemoragie:digestivă (sup sau inf) traumatisme (exteriorizată sau internă -deshidratare:diaree, sdrpoliuropolidip -pierd. de plasmă:arsuri,sechestr spIII	SOC OBSTUCTIV:obstacol în reumplerea cordului -embolie masivă -tamponadă cardiacă (pericardită)
SOC CARDIOGENIC:↓ activ. de pompă a cordului -decompensarea unor MCC -tulb. de ritm (in sp TPSV) -miocardite etc	SOC DISTRIBUTIV (vasoplegie=vasodilat.permanentă) -şoc septic -şoc anafilactic

SEPSIS

- Sindrom clinic definit prin raspunsul sistemic la agresiunea microbiana
- Interactiunea complexa, evolutiva a linilor de mediatori imunomodulatori si populatii celulare diverse, activate ca raspuns la agresiunea initiala, cu instalarea secventiala a disfunctiilor organice multiple.
- Raspuns adaptativ la agresiune? Previne lezarea tisulara ireversibila?

DEFINIŢII

- ± ***Infecţia*** – reacţie inflamatorie generată de pătrunderea microorganismelor într-un ţesut care în mod normal este steril;
- ± ***SIRS*** (sindromul de răspuns inflamator sistemic) –
  - Temperatura > 38º C sau < 36º C
  - Frecvenţa cardiacă > 90 bătăi/minut
  - Frecvenţa respiratorie > 20 respiraţii/minut sau $PaCO_2$< 32mmHg
  - Leucograma >12.000/mm^3 sau < 4000/mm^3 sau >10% forme imature
- ± ***Sepsis*** – SIRS determinat de o infecţie
- ± **Sepsis sever** – sepsis asociat cu disfuncţie de organ sau acidoză metabolică
- ± **Şocul septic** – sepsis asociat cu hipotensiune arterială persistentă în ciuda repleţiei volemice
- ± **Sindromul de disfuncţie/ insuficienţă multiplă de organe** – alterarea acută a funcţiei mai multor organe

ŞOCUL SEPTIC

Şocul septic reprezintă forma cea mai gravă a unei infecţii.

CONTINUUM DE GRAVITATE

SRIS → sepsis → sepsis sever →şoc septic→SDMO →SIMO

Şocul septic este un sepsis grav asociat unei disfuncţii cardio-vasculare:
hipotensiune arterială (TA sistolică < 2 deviaţii standard pentru vârstă, cu toate că reumplerea vasculară depăşeşte 40 ml/kg într-o oră sau necesită administrarea a cel puţin unui produs vaso-activ sau prezenţa a cel puţin 2 semne de hipoperfuzie) lactatemie > 2 ori, acidoza cu deficit de baze > 5 mmol/l, diureza < 0,5 ml/kg/oră, timpul de recolorare cutanat > 5 secunde, diferenţa între temperatura centrală şi temperatura periferică > 30C.
Şocul septic astfel definit nu este o entitate diferită de sepsisul grav, ci o formă mai particulară.

Tranzitia catre sepsis

- Eliberarea de mediatori proinflamatori ca raspuns la infectie depaseste bariere locale si determina un raspuns generalizat- SIRS
- Cauze multifactoriale:
  - Efectele directe ale invaziei microbiene in organism
  - Efectele toxinelor microbiene
  - Eliberare masiva de mediatori proinflamatori
  - Activarea complementului
  - Susceptibilitate genetica pentru aparitia sepsisului
- **SIRS- inflamatie intravasculara maligna**
  - **Inflamatie**- raspunsul in sepsis – exacerbarea raspunsului inflamator normal
  - **Intravasculara**
    - Mediatori in sp interstitial in cadrul interactiunilor intercelulare
    - Sepsis- preluati de fluxul sanguin in circulatia sistemica
  - **Maligna-** necontrolata, disreglata, autointretinuta!

DEFINITII (CONFORM CONFERINTEI DE CONSENS SURVIVING SEPSIS CAMPAIGN, 2008)

SEPSIS infectie dovedita sau suspicionata (pe criterii clinice, bacteriologice si imagistice), care declanseaza un raspuns inflamator sistemic particular

Sindromul răspunsului inflamator sistemic (SRIS) există atunci când un bolnav prezintă cel puţin două, din următoarele patru criterii:

- **temperatura: < 36^0C , > 38^0C**
- **frecventa cardiaca: > 90 batai/minut**
- **hiperventilatie: frecventa respiratorie > 20 respiratii/minut sau PCO_2 < 32 mmHg**
- **nr. leucocite: < 4000, > 12000 sau >10 % forme imature**

SEPSISUL SEVER

Definitie: Sepsis asociat cu disfunctii organice, hipoperfuzie sau hipotensiune

Criterii de diagnostic:

Disfunctiile de organ:

a) Hipoxemia arteriala PaO_2 / Fi O_2 < 300
b) Oligurie acuta: debit urinar < 0,5ml /kg/h pentru cel putin 2 ore
c) Creatinina > 2 mg / dl
d) Anomalii ale coagularii: INR > 1.5, aPTT > 60 s
e) Trombocitopenie: TR < 100000 / mmc
f) Hiperbilirubinemia > 2 mg / dl

SOCUL SEPTIC

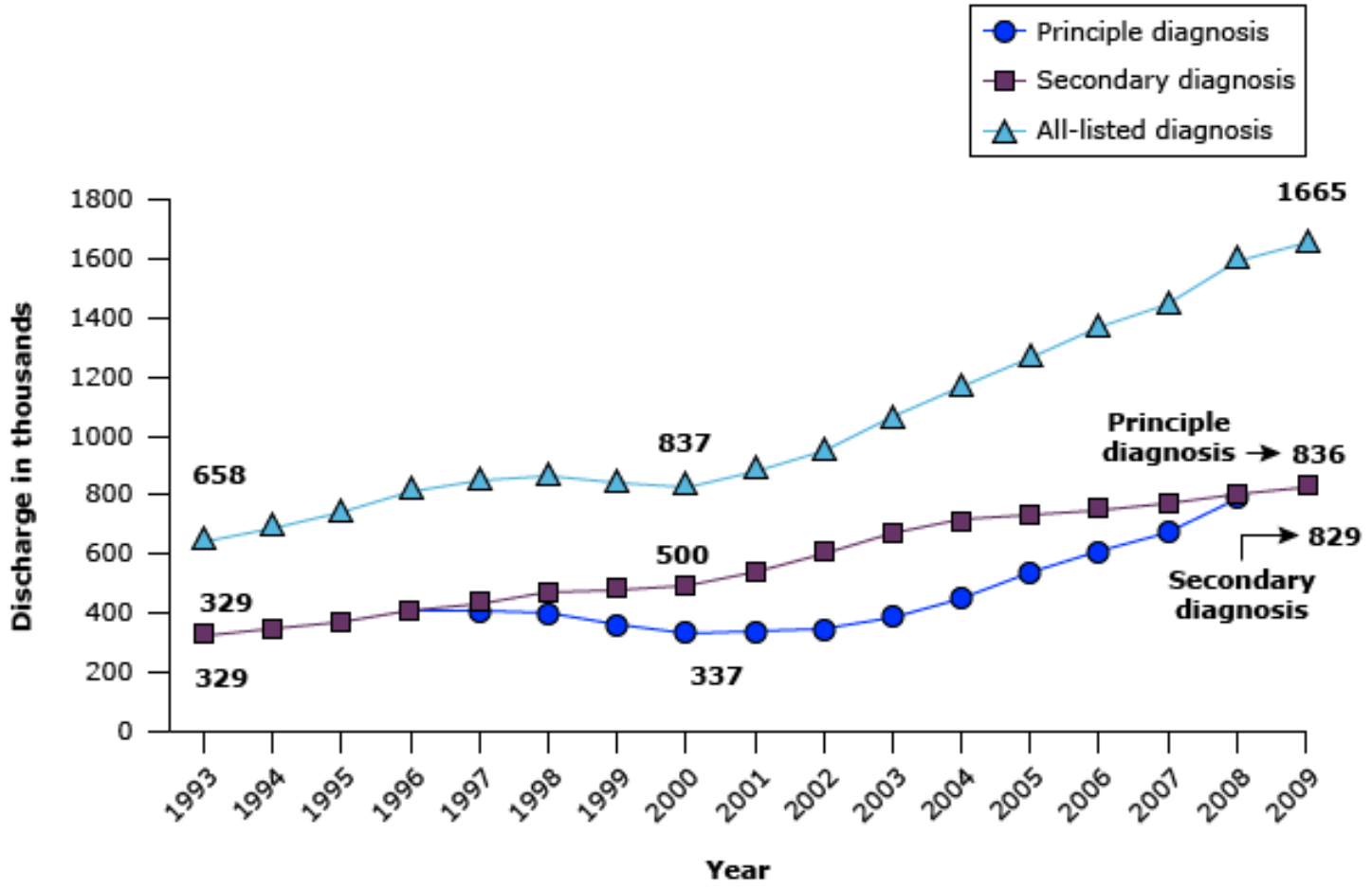
Definitie: Insuficienta circulatorie acuta neexplicata de o alta cauza

Criterii de diagnostic:

a) hipotensiune arteriala persistenta in conditiile unei resuscitari volemice adecvate

b) necesitatea utilizarii de vasopresor pentru mentinerea presiunii arteriale in conditii de normovolemie

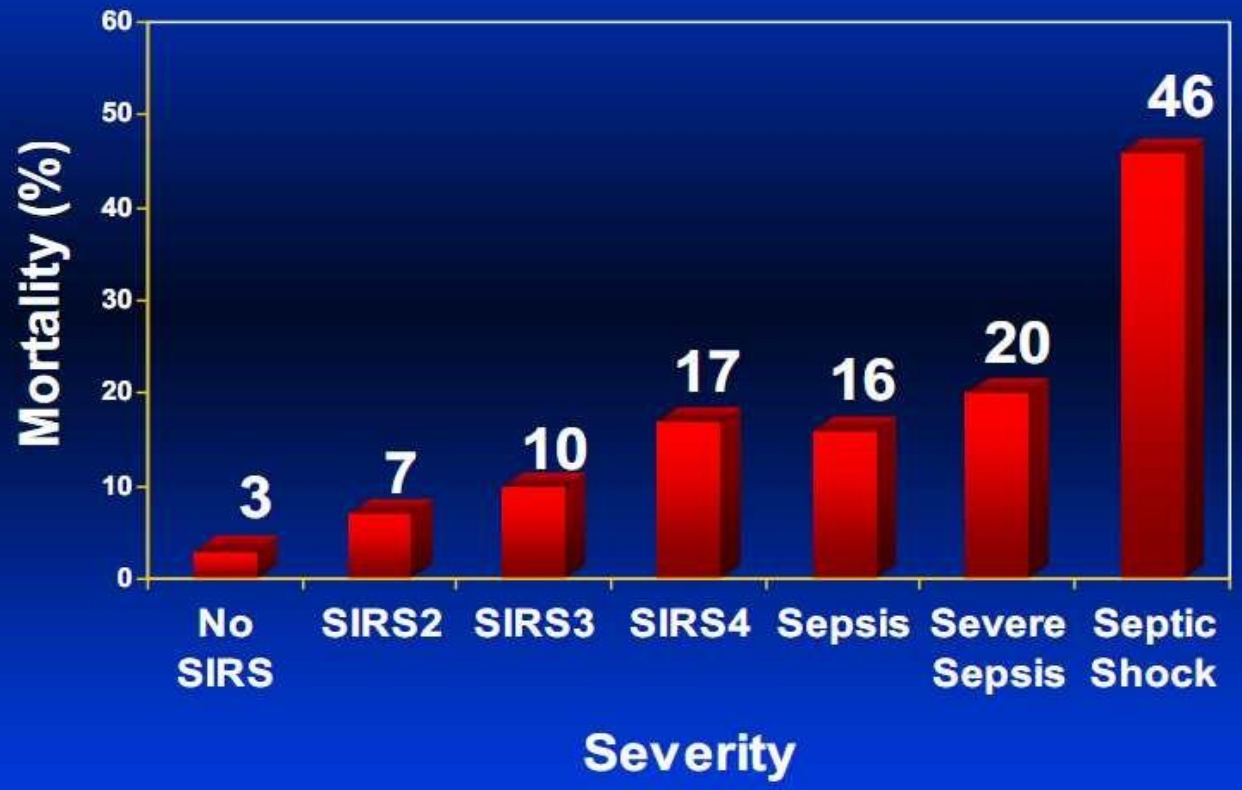
Trends in hospital stays with septicemia 1993-2009



In the United States between 2000 and 2009, hospital stays with a principal diagnosis of septicemia increased 148 percent (10.6 percent annually), while those with secondary diagnoses of septicemia increased by only 66 percent (5.8 percent annually).

Reproduced from: Agency for Healthcare Research and Quality Center for Delivery, Organization, and Markets. Healthcare Cost and Utilization Project, Nationwide Inpatient Sample, 1993-2009.

Outcome of Sepsis is Related to Severity of the Host Response



Rangel-Frausto et al. *JAMA* 1995.

Răspunsul gazdei la infectie

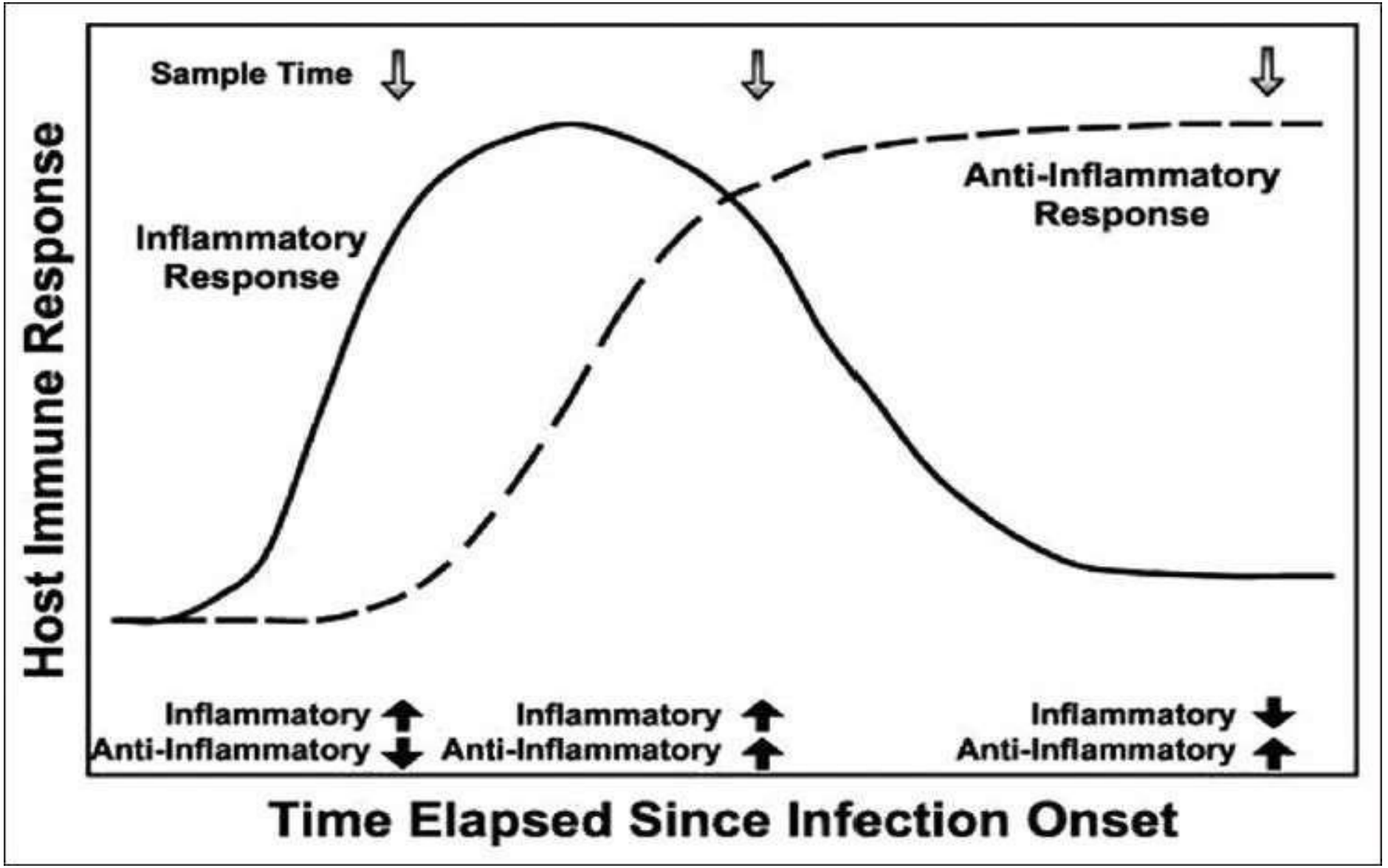
- Inițiat de macrofage când recunosc și cuplează componente microbiene
  - PRP- pattern recognition receptors-
    - Toll like receptors
    - NOD- nucleotide oligomerisation domain leucin rich repeat proteins
    - RIG(retinoic acid inducible gene) –I like helicase
  - TREM-1- triggering receptors expressed on myeloid cells și MDL-1- receptorii mieloizi DAP 12- asociind lectina de pe celulele imune ale gazdei pot recunoaste si cupla componenete microbiene
- Efectele cuplării macrofage- componente microbiene

Biologic effects of proinflammatory cytokines such as TNF and IL-1

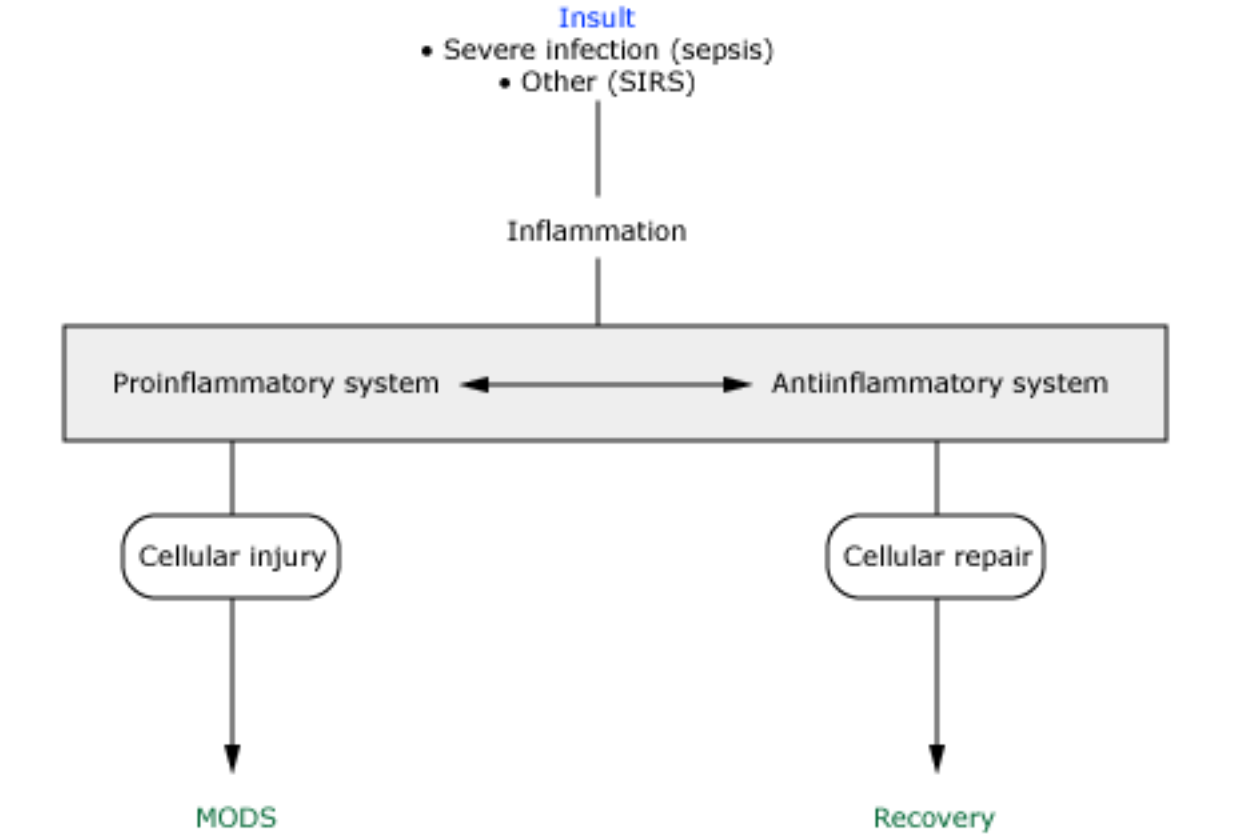
Fever
Hypotension
Acute phase protein response
Induction of IL-6 and IL-8
Coagulation activation
Fibrinolytic activation
Leukocytosis
Neutrophil degranulation and augmented antigen expression (TNF)
Increased endothelial permeability (TNF)
Stress hormone response
Enhanced gluconeogenesis (TNF)
Enhanced lipolysis (TNF)

Pro and anti-inflammatory responses in sepsis

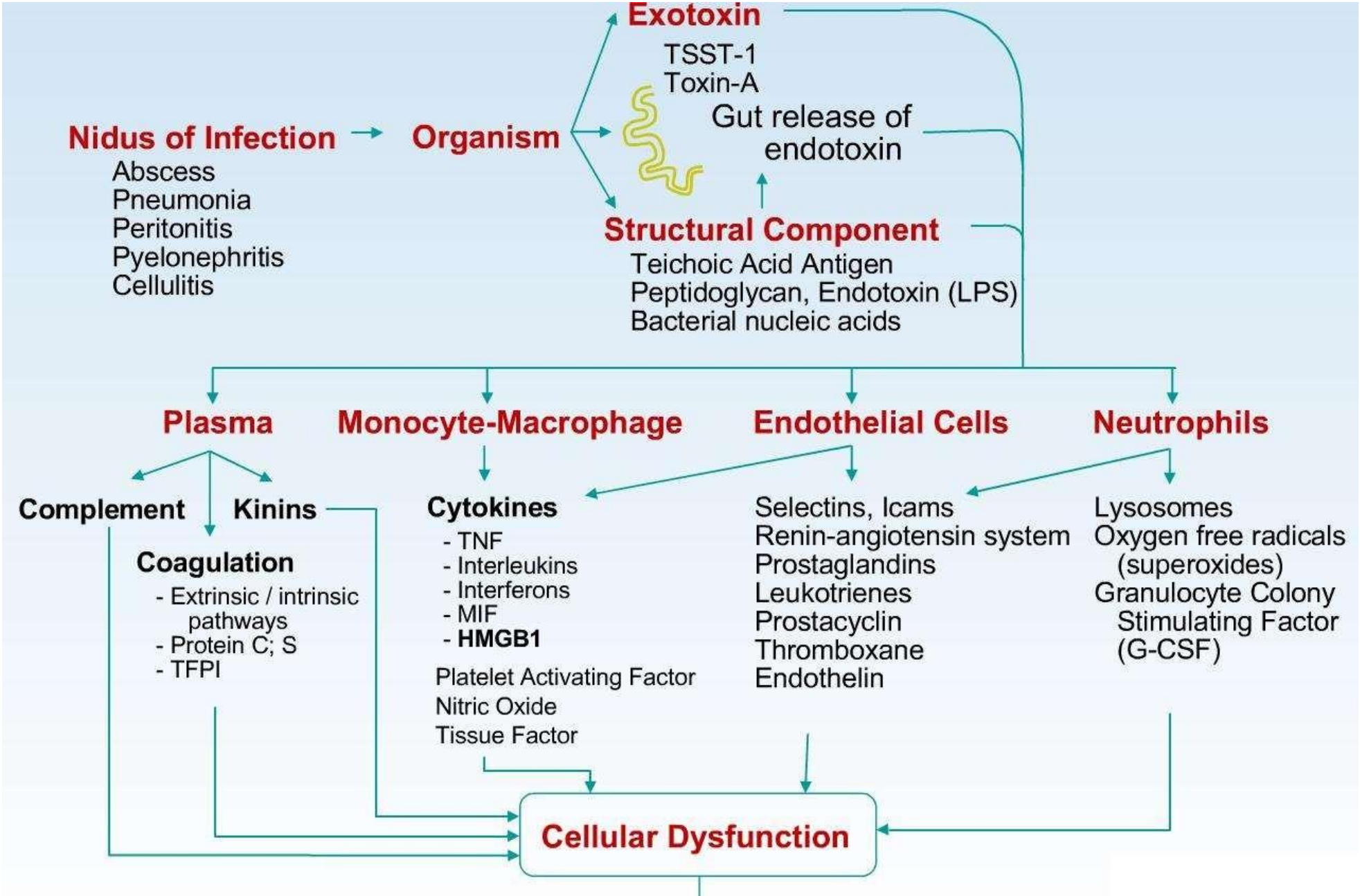
Carrigan SD, Scott D, Tabrizian M. Towards resolving the challenges of sepsis diagnosis. Clin Chem 2004;50:1301-14)



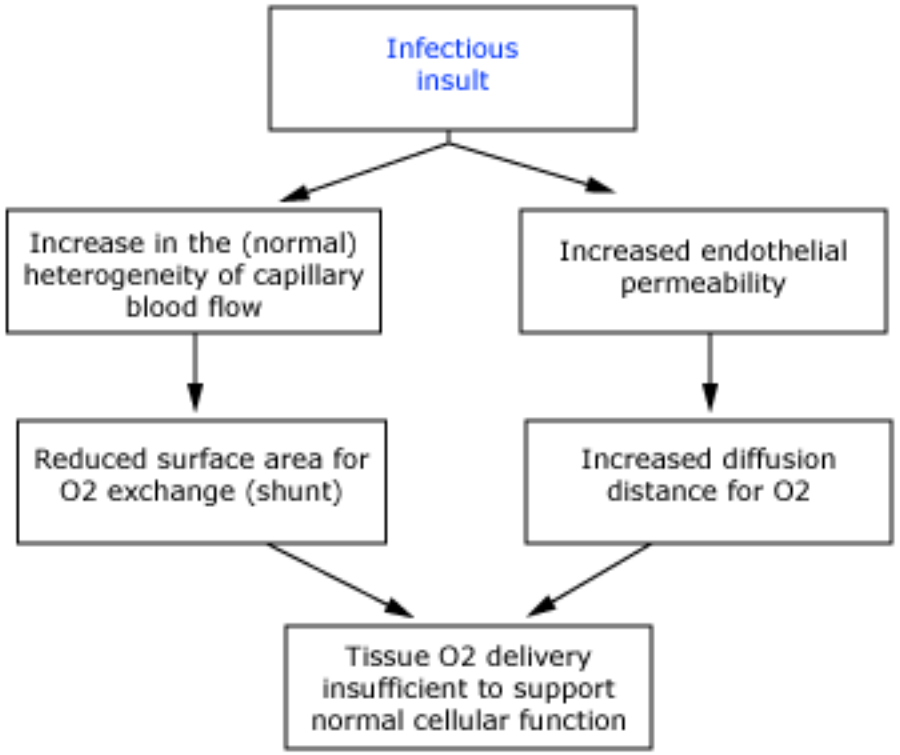
Potential outcomes of mediator release in sepsis



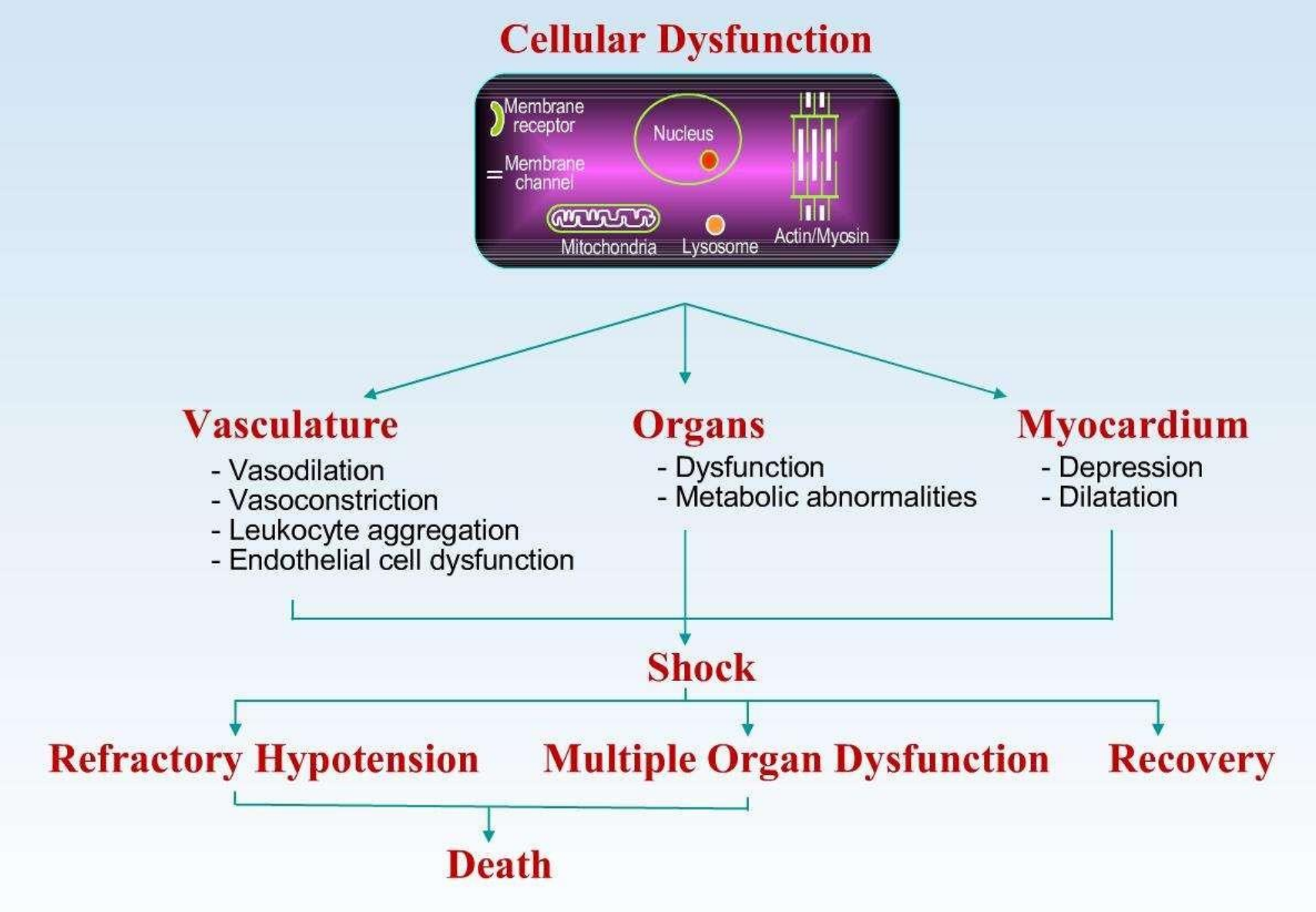
PATOGENEZA SOCULUI SEPTIC



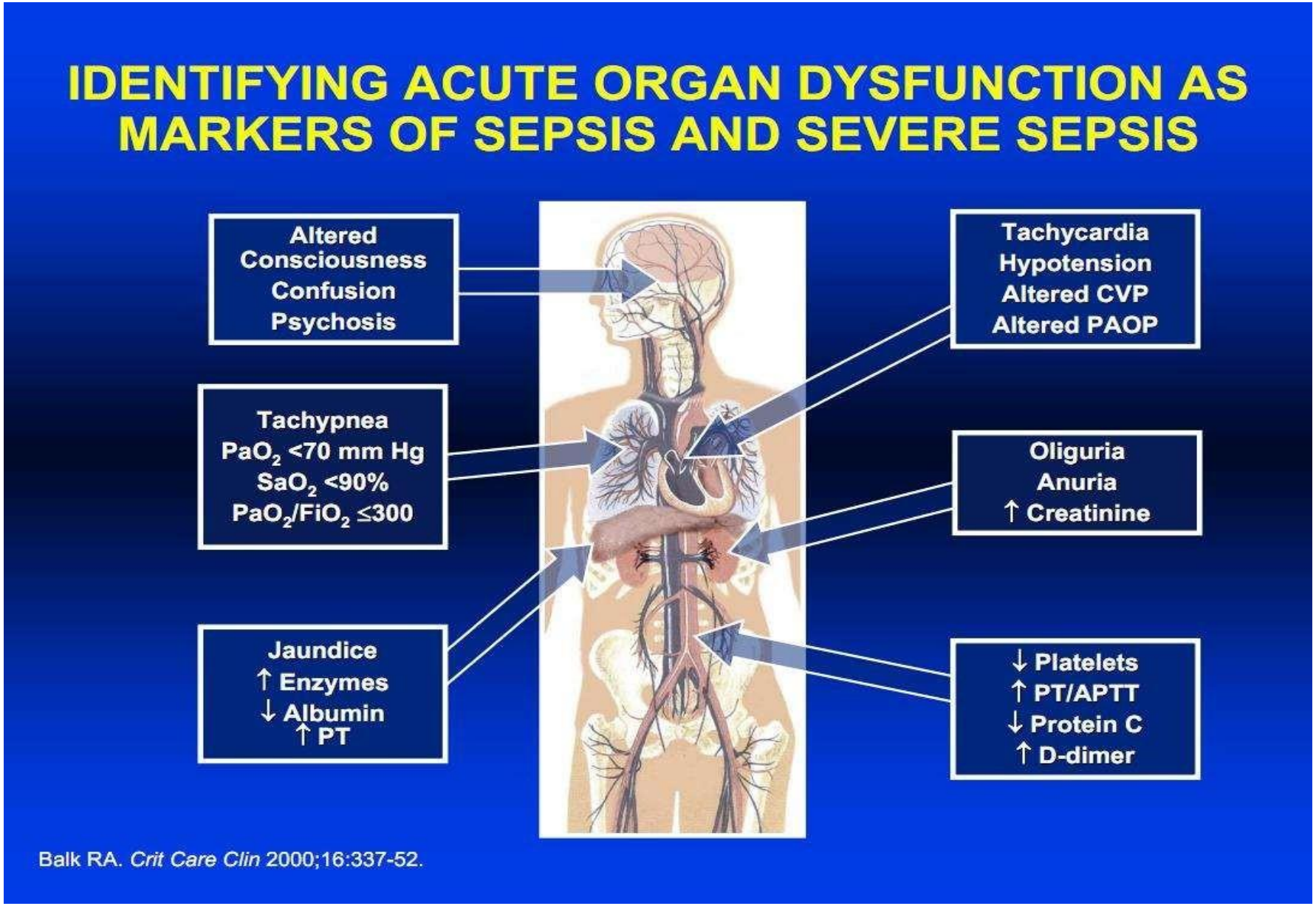
Decreased oxygen extraction in sepsis



PATOGENEZA SOCULUI SEPTIC

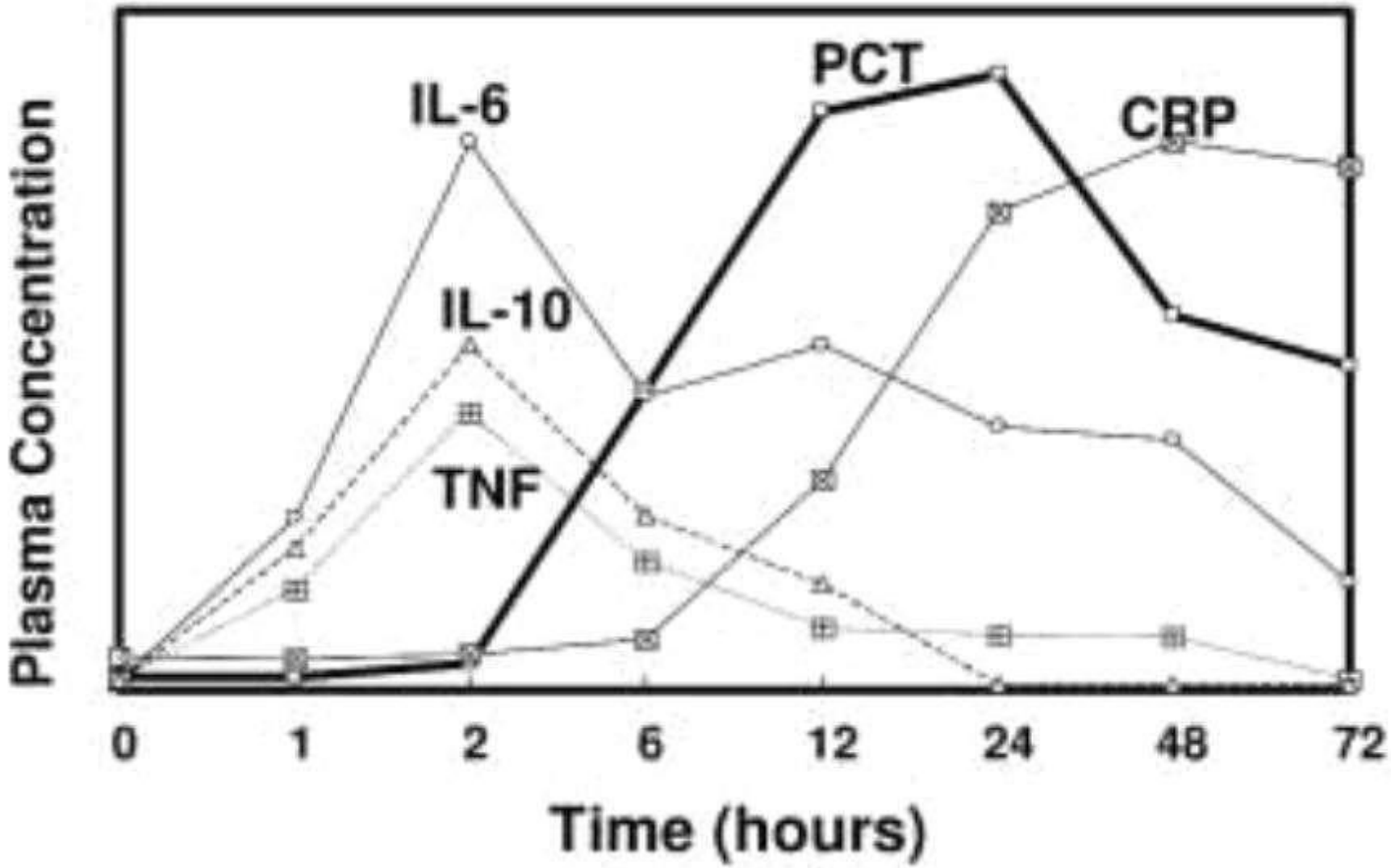


IDENTIFYING ACUTE ORGAN DYSFUNCTION AS MARKERS OF SEPSIS AND SEVERE SEPSIS



Balk RA. *Crit Care Clin* 2000;16:337-52.

Time course of the plasma levels of various parameters of the systemic inflammatory response



Procalcitonina ca biomarker in sepsis

- Ca rapsuns la infectia bacteriana, prin stimularea indusa de cytokine, tesuturile elibereaza PCT
- Rol major- monocitele migrate transendotelial- productie tranzitorie
- Stimul infectios- concentratia plasmatica va creste in 6- 24 ore, T1/2- 20-24 ore
- Indusa si de politrauma, chirurgie majora, arsuri, soc cardiogen- dinamica diferita

PCT in sepsis

- Dinamica paralela cu evolutia infectiei bacteriene- scade aprox 50%/zi
- Nivel de cut off?
  - > 1 mcg/ml- probabilitate inalta
  - < 0.25 mcg/ml- probabilitate redusa

(Schuetz, JAMA, 2013)

- Nu e afectata de corticoterapie
- Nu creste in infectii virale, fungice

Clinical outcomes associated with procalcitonin algorithms to guide antibiotherapy in respiratory tract infections

Schuetz et al, JAMA, 2013; 309(7): 717-718

- 14 RCT, 4000 pacienti, infectii de tract respirator inferior, cu antibioterapie ghidata sau nu de dinamica de procalcitonina
- Obiectiv principal- mortalitatea si esecul terapiei la 30 de zile
- Folosirea PCT nu creste mortalitate in orice tip de infectie de tract respirator inferior
- Mai putine esecuri terapeutice la admisie(OR 7.06 95% CI: 0.61-0.95) si la bolnavi cu CAP(OR 0.77, 95%CI: 0.62- 0.95)
- Scade expunerea la antibiotic- 4 vs 8 zile!- in special in BPOC si exacerbari de bronsite
- PCT safe, scade durata antibioterapiei si reduce riscul de selectare de tulpini multirezistente
- Cost 25- 30 USD
- Dar la pacientul critic?

Alti biomarkeri?

- Proteina C reactiva
- Citokine pro si antinflamatorii– prezinta interes in evaluarea raspunsului inflamator, dar nu permit distinctia intre inflamatie de origine infectioasa sau neinfectioasa (Rheinhart, 2012)
- Receptori solubili
  - TREM1- dozare locala(alveolara) > plasmatica
  - Soluble urokinase- type plasminogen activator receptor(metaanaliza Backes, 2012)- valoare diagnostic redusa, indicator bun de prognostic(concentratii mari- evolutie defavorabila)
- Combinatii de biomarkeri
  - Panel- suPAR, sTREM-1, MIF, CRP, PCT, leucocite(Kofoed, 2007)
  - Proapolipoproteina A+ SAA- serum amyloid A- scor ApoSAA

Pattern hemodinamic

- ✓index cardiac crescut
- ✓rezistente vasculare sistemice scazute
- ✓ presiuni de umplere (PVC, PCP) normale sau usor scazute
- ✓ Δ (a-v) O2 normala sau la limita de jos
- ✓ flux sanguin circulator periferic crescut dar maldistribuit

MONITORIZARE

1. Monitorizare cardio-respiratorie de baza (AV, TA, pulsoximetrie);
2. Monitorizare invaziva tensiune arteriala la pacientii instabili hemodinamic;
3. Cateter venos central (PVC si $ScvO_2$);
4. Monitorizare debit cardiac cateter Swann Ganz sau metode mai putin invazive (ecografie transesofagiana, Doppler esofagian);
5. Ecocardiografia;
6. Systolic/pulse pressure variation SPV, deltaPP si stroke volume variation (SVV)–ventriculul stang ramane dependent de presarcina pana cand SPV < 10 mmHg, deltaPP < 13 % sau SVV < 10 % (acest tip de evaluare se poate face la pacientl sedat, intubat si ventilat);
7. Indicator de perfuzie tisulara – tulburarile in microcirculatie au fost cel mai mult investigate la nivel splanhnic prin diferite tehnici (capnometrie regionala, laser – Doppler flowmetry, indocyanine green dilution); in afara de lactat tonometria gastrica ramane singura solutie care poate evalua eficienta repletiei volemice si vasopresorului asupra perfuziei tisulare; diferenta venoasa-arteriala CO_2 poate fi deasemeni folosita pentru aprecierea perfuziei tisulare.

LACTATUL SERIC

1 ± 0,5mmol/l, > 2mmol/l pts critic

Determinare unică – triaj în ER

>4mmol/l risc de moarte iminent în susp de

Infecţie din ER, chiar dacă TA este N

Treciak S et al, Int Cate Med 2007, 33:970-977

Howell MD at al, Crit Care Med 2007, 33: 1892-1899

Determinări seriate – în TI

CLEARANCE LACTAT

Cl lactat = (lactat prezentare ED-lactat la 6h)/lactat prezentare EDx100

- Monitorizare 72h
- Tratament EGDT
- Mortalitatea ↓cu 10% pt fiecare ↑de 10% a Cl lactatului

Nguyen

PARAMETRII ADITIONALI CARE SUPLIMENTEAZA CRITERIILE DE SIRS

b) PCR

- folosita pentru evaluarea prezentei/severitate raspuns inflamator, apreciere severitate sepsis, diferentiere infectie bacteriana–virala, diferentiere pneumonie–infectie endotraheala, pentru dg de apendicita
- nu creste suplimentar pe cand cresterea procalcitominei reflecta severitatea SIRS
- poate creste: boli autoimune/reumatologice, tumori maligne, postoperator
- creste 24 de ore mai tarziu decat citokinele si PCT

c) IL 6

- citokina proinflamatorie
- produsa de monocite, macrofage, celule endoteriale
- numerosi stimuli inclusiv mediatori proinflamatori si endotoxina determina cresterea IL6
- o valoare mai >1000 pg/ml indica risc crescut de deces datorita sepsisului
- la pacientii critici creste nespecific datorita inflamatiei asociate
- timpul de injumatatire este scurt si nu este indusa preferential de infectiile bacteriene

I. Managementul sepsisului sever

A. Resuscitare initiala
B. Diagnostic
C. Tratament antibiotic
D. Controlul sursei
E. Repletia volemica
F. Vasopresoare
G. Terapia inotropa
H. Corticosteroizi
I. Administrarea de produsi de sange

II. Tratament suportiv sepsis sever

A. Ventilatie mecanica in ALI/ARDS induse de sepsis
B. Sedare analgezie si curarizare in sepsis
C. Controlul glicemiei
D. Terapia de substitutie renala
E. Administrarea de bicarbonate
F. Profilaxia trombozei venoase profunde
G. Profilaxia ulcerului de stress
H. Decontaminare selectiva tract digestiv
I. Consideratii asupra reducerii masurilor suportive

I A. Resuscitarea initiala

1. recomandata la pacientii cu soc indus de sepsis, adica hipoperfzietisulara (hTA persistenta dupa repletie volemica sau lactat > 4 mmol/l) (1C)

   - in primele 6 ore se urmareste obtinerea (1C):

      a) PVC 8-12 mmHg

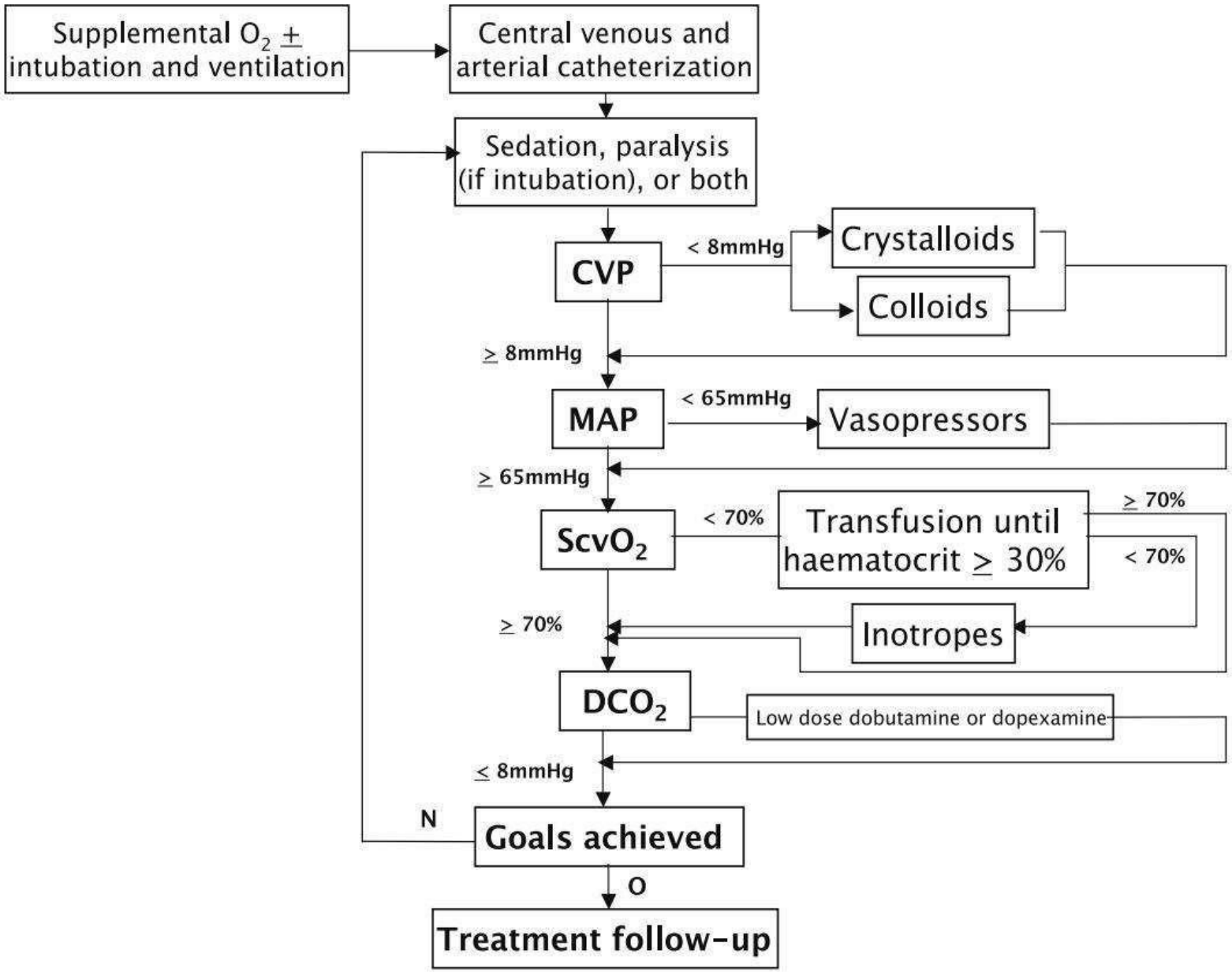
      b) MAP > 65 mmHg

      c) debit urinar > 0.5 ml/kg/h

      d) Scv O_2 > 70%

2. administrarea MER in primele 6 ore, pentru obtinerea unui Ht> 30% daca ScvO2 sau SvO2 < 70 sau 65 % (2C)

Protocol for Early Goal-Directed Therapy, modified from Rivers et al.



I E. Terapia volemica

1. Repletie volemica cu cristaloid (1B);
2. Repletia volemica are drept tinta PVC de 8 mmHg (12 mmHg la cei ventilati mecanic) (1C);
3. Se recomanda continuarea terapiei volemice cat timp exista ameliorarea statusului hemodinamic (1D);
4. Se recomanda repletie volemica in caz de hipovolemie cu 1000 de ml cristaloid /300–500 ml coloid in 30 de minute (1D);
5. Rata de corectie volemica trebuie redusa daca presiunile de umplere cresc fara amelioararea statusului hemodinamic (1D).

I F. Vasopresoare

1. MAP > 65 mmHg (1C)
2. de prima intentie se folosesc noradrenalina/dopamina pentru corectia hipotensiunii in socul septic (1C)
3. adrenalina/fenilefrina/vasopresina nu sunt de prima intentie in tratamentul socului septic (2C)
4. adrenalina este prima alternativa in socul septic ce nu raspunde la noradrenalina si dopamina (2B)
5. nu se recomanda doze mici de dopamina pentru protectie renala (1A)
6. se recomanda monitorizarea invaziva a tensiunii arteriale la toti pacientii ce necesita vasopresor (1D)

Adrenalina are ca dezavantaje:

-tahicardia
-efect nociv pe circulatia splanhnica
-hiperlactemie

Fenilefrina:

-nu produce tahicardie
-vasopresor pur-determina scaderea stroke volume

Dopamina:

-determina crestere TAM, debit cardiac (datorita cresterii stroke volume si tahicardiei)
-influenteaza raspunsul endocrin pe calea axului hipotalamo-hipofizar-CSR
-are efecte imunosupresoare
-este mai eficienta in caz de disfunctie sistolica

Noradrenalina

-este mai puternica decat dopamina
-determina cresterea TAM datorita efectului vasoconstrictor
-modificari minime pe AV
-efecte mai mici pe stroke volume decat dopamina

Vasopresina

-in soc nivelul este crescut precoce
-intre 24 si 48 de ore valorile ajung la normal (deficit relativ de vasopresina)
-doze mici pot fi eficiente in cresterea tensiunii la pacientii refactari la alte vasopresoare.

Critical Care Medicine:
October 2014 - Volume 42 - Issue 10 - p 2158–2168
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Feature Articles

Interaction Between Fluids and Vasoactive Agents on Mortality in Septic Shock: A Multicenter, Observational Study*

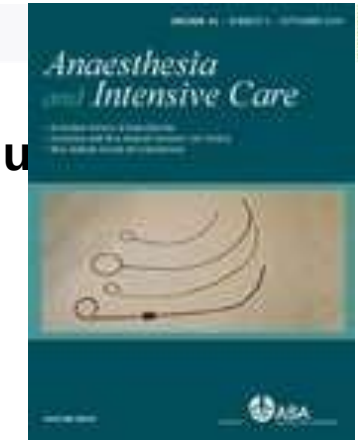
Waechter, Jason MD[1]; Kumar, Anand MD[2]; Lapinsky, Stephen E. MB, MSc[3]; Marshall, John MD[3]; Dodek, Peter MD, MHSc[4]; Arabi, Yaseen MD[5]; Parrillo, Joseph E. MD[6]; Dellinger, R. Phillip MD[7]; Garland, Allan MD, MA[2]; for the Cooperative Antimicrobial Therapy of Septic Shock Database Research Group

- Objective: Fluids and vasoactive agents are both used to treat septic shock, but little is known about how they interact or the optimal way to administer them. We sought to determine how hospital mortality was influenced by combined use of these two treatments.
- Design: Retrospective evaluation using multivariable logistic regression to evaluate the association between hospital mortality and categorical variables representing initiation of vasoactive agents and volumes of IV fluids given 0–1, 1–6, and 6–24 hours after onset, including interactions and adjusting for potential confounders.
- Setting: ICUs of 24 hospitals in 3 countries.
- Patients: Two thousand eight hundred forty-nine patients who survived more than 24 hours after after onset of septic shock, admitted between 1989 and 2007.
- Interventions: None.
- **Measurements and Main Results: Fluids and vasoactive agents had strong, interacting associations with mortality ($p < 0.0001$). Mortality was lowest when vasoactive agents**
  - **were begun 1–6 hours after onset,**
  - **with more than 1 L of fluids in the initial hour after shock onset,**
  - **more than 2.4 L from hours 1–6,**
  - **and 1.6–3.5 L from 6 to 24 hours.**
  - **The lowest mortality rates were associated with starting vasoactive agents 1–6 hours after onset.**
- **Conclusions: The focus during the first hour of resuscitation for septic shock should be aggressive fluid administration, only thereafter starting vasoactive agents, while continuing aggressive fluid administration. Starting vasoactive agents in the initial hour may be detrimental, and not all of that association is due to less fluids being given with such early initiation of vasoactive agents.**

ŞOCUL SEPTIC

FIZIOPATOLOGIE

- Infecţia duce la proliferarea germenilor şi eliberarea lor sau a componentelor (endotoxină, acid tecoic,etc.) în circulaţie
- Răspunsul organismului consta din:
  - Răspuns celular (activarea macrofagelor, monocitelor, neutrofilelor, celulelor endoteliale)
  - Răspuns umoral (citokine: TNF, IL, FAP, PG, LTR, NO,RO,etc.)
  - Activarea complementului şi coagulării
- Hemodinamic:
  - Macrocirculator: alterarea funcţiei sistolice şi diastolice a cordului
    vasodilataţie periferică
  - Microcirculator: inflamaţie endotelială difuză
    şunturi arterio-venoase
    ocluzii în microcirculaţie
  - Metabolic: hipercatabolism



- **Low-dose vasopressin in addition to noradrenaline may lead to faster resolution of organ failu in patients with severe sepsis/septic shock**
- S Bihari, S Prakash, AD Bersten
- Flinders Medical Centre and Flinders University
- **Summary**
- Introduction: Resolution of multi-organ failure may be hastened by adjunctive use of vasopressin in patients with septic shock. We hypothesised that patients who received vasopressin as an addition to noradrenaline in the first 24 hours of presentation would have earlier resolution of organ failure as assed by the sequential organ failure assessment (SOFA score).
Method: The cohort of patients with severe sepsis in the recently published PRICE study (n=50) was retrospectively analysed as patients receiving noradrenaline only (n=30) and compared to patients who received noradrenaline plus vasopressin in the first 24 hours (n=20). We compared the delta SOFA score at 48 and 72 hours between the 2 groups.
Result: There were no baseline difference between the groups including the SOFA score, except for white cell count, which was higher in patients who received both noradrenaline and vasopressin. Vasopressin led to faster resolution of organ failure as evidenced by a greater fall in delta SOFA score at 48 and 72 hours. The median (Inter-quartile range) delta SOFA score at 48 hours was 1 (-1,3) in the noradrenaline group, which was significantly higher than -2 (-3,1) observed in the noradrenaline plus vasopressin group (<0.001). Similarly delta SOFA score at 72 hours was also significantly higher in the former group.
Conclusion: These data support the suggestion that addition of vasopressin to noradrenaline result in faster resolution of organ failure in patients with severe sepsis/ septic shock.

I B. Diagnostic

1. Obtinerea de culturi inainte de inceperea tratamentului antibiotic (1C)
   - doua hemoculturi:
     - una percutan
     - una din fiecare abord vascular existent
   - culturi din:
     - urina
     - lcr
     - leziuni cutanate
     - sectretii traheale

2. Imagistica: Rxcp, ecografie, CT (1C)

I C. Tratamentul antibiotic

1. Inceperea tratamentului antibiotic IV cat mai precoce–prima ora dupa recunoasterea sepsisului sever (1D) si socului septic (1B);
2. Folosirea de antibiotice cu spectru larg, cu buna penetrabilitate la nivelul presupusei surse de sepsis (1B);
3. Evaluare zilnica a tratamentului antibiotic pentru (1C):

   -optimizare efect,

   -prevenirea dezvoltarii rezistentei,

   -scaderea toxicitatii,

   -scaderea costurilor,

   ●in momentul in care agentul patogen este identificat se ajusteaza tratamentul antibiotic scazandu-se astfel riscul de suprainfectie cu microorganisme: Candida, Clostridium dificile, tulpini de enterococ rezistente la vancomicina.
4. Se recomanda asocierea de antibiotice la pacienti cu infectie cunoscuta/suspectata cu Pseudomonas cu sepsis sever. (2D)

I C. Tratamentul antibiotic

5. Se recomanda asocierea de antibiotice la pacientii neutropenici cu sepsis sever. (2D)

   -risc crescut de infectie cu Pseudomonas, Enterobacteriacee, S.aureus, daca neutropenia se mentine in timp Aspergillus

6. Tratamentul empiric nu trebuie administrat mai mult de 3–5 zile (de-zescaladarea trebuie facuta cat mai rapid) (2D)

7. Durata tratamentului antibiotic este de 7 - 10 zile (1D)

   ● durata tratamentului poate creste in caz de (1D) :

   -raspuns clinic lent,

   -focare de infectie ce nu pot fi drenate,

   -status imunologic deficitar.

8. Se recomanda oprirea tratamentului antibiotic, daca nu exista cauza infectioasa pentru evitarea dezvoltarii infectiei cu un agent rezistent si aparitia toxicitatii antibioticului (1D).

Hemoculturile sunt negative in mai mult de 50 % din cazurile de sepsis sever /soc septic

I D. Controlul sursei

1.Diagnosticarea cat mai rapida a unei infectii ce necesita controlul urgent al sursei (fasciita necrozanta, peritonita, colangita, infarct intestinal) (1C); de preferinta in primele 6 ore de la prezentare (1D)

2.Toti pacientii cu sepsis sever trebuie sa fie evaluati pentru rezenta unei surse de infectie ce poate fi indepartata (drenaj abces, debridare, indepartare cateter) (1C);

3.In caz de necroza peripancreatica interventia trebuie intarziata pana cand se produce demarcarea adecvata tesut viabil , tesut necrozat (2B);

4. Daca este necesar controlul sursei se recomanda interventia cat mai putin invaziva (drenaj percutan, endoscopic) (1D);

5.Daca exista suspiciunea ca un abord vascular este sursa de infectie se recomanda indepartarea cat mai rapida dupa stabilirea unui alt abord (1C).

Surse de infectie ce se preteaza controlului sursei

- abces intraabdominal
- perforatie gastro-intestinala
- colangita
- pielonefrita
- ischemie intestinala
- alte infectii : empiem, altrita septica

Controlul sursei poate cauza complicatii

- sangerare
- fistula
- leziune de organ

Evaluation of common sources of sepsis

Suspected site	Symptoms/signs	Microbiologic evaluation
Upper respiratory tract	Pharyngeal inflammation plus exudate ± swelling and lymphadenopathy	Throat swab for aerobic culture
Lower respiratory tract	Productive cough, pleuritic chest pain, consolidative auscultatory findings	Sputum of good quality, rapid influenza testing, urinary antigen testing (eg, pneumococcus, legionella), quantitative culture of protected brush or bronchoalveolar lavage
Urinary tract	Fever, urgency, dysuria, loin pain	Urine microscopy showing pyuria
Vascular catheters: arterial, central venous	Redness or drainage at insertion site	Culture of blood (from the catheter and a peripheral site), culture catheter tip (if removed)
Indwelling pleural catheter	Redness or drainage at insertion site	Culture of pleural fluid (through catheter), culture of catheter tip (if removed)
Wound or burn	Inflammation, edema, erythema, discharge of pus	Gram stain and culture of draining pus, wound culture not reliable
Skin/soft tissue	Erythema, edema, lymphangitis	Culture blister fluid or draining pus; role of tissue aspirates not proven
Central nervous system	Signs of meningeal irritation	CSF microscopy, protein, glucose, culture, bacterial antigen test
Gastrointestinal	Abdominal pain, distension, diarrhea, and vomiting	Stool culture for Salmonella, Shigella, and Campylobacter
Intraabdominal	Specific abdominal symptoms/signs	Aerobic and anaerobic culture of percutaneously or surgically drained abdominal fluid collections
Peritoneal dialysis (PD) catheter	Cloudy PD fluid, abdominal pain, fever	Cell count and culture of PD fluid
Genital tract	Women: Low abdominal pain, vaginal discharge Men: Dysuria, frequency, urgency, urge incontinence, cloudy urine, prostatic tenderness	Women: Endocervical and high vaginal swabs onto selective media Men: Urine Gram stain and culture
Joint	Pain, warmth, decreased range of motion	Arthrocentesis with cell counts, Gram stain, and culture

CSF: cerebrospinal fluid; PD: peritoneal dialysis.

Adapted from: Cohen J, Microbiologic requirements for studies of sepsis. In: Sibbald WJ, Vincent JL (eds), Clinical Trials for the Treatment of Sepsis, Springer-Verlag, Berlin, 1995, p.73.

Source control methods for common ICU infections

Site	Interventions
Sinusitis	Surgical decompression of the sinuses
Pneumonia	Chest physiotherapy, suctioning
Empyema thoracis	Drainage, decortication
Mediastinitis	Drainage, debridement, diversion
Peritonitis	Resection, repair, or diversion of ongoing sources of contamination, drainage of abscesses, debridement of necrotic tissue
Cholangitis	Bile duct decompression
Pancreatic infection	Drainage or debridement
Urinary tract	Drainage of abscesses, relief of obstruction, removal or changing of infected catheters
Catheter-related bacteremia	Removal of catheter
Endocarditis	Valve replacement
Septic arthritis	Joint drainage and debridement
Soft tissue infection	Debridement of necrotic tissue and drainage of discrete abscesses
Prosthetic device infection	Device removal

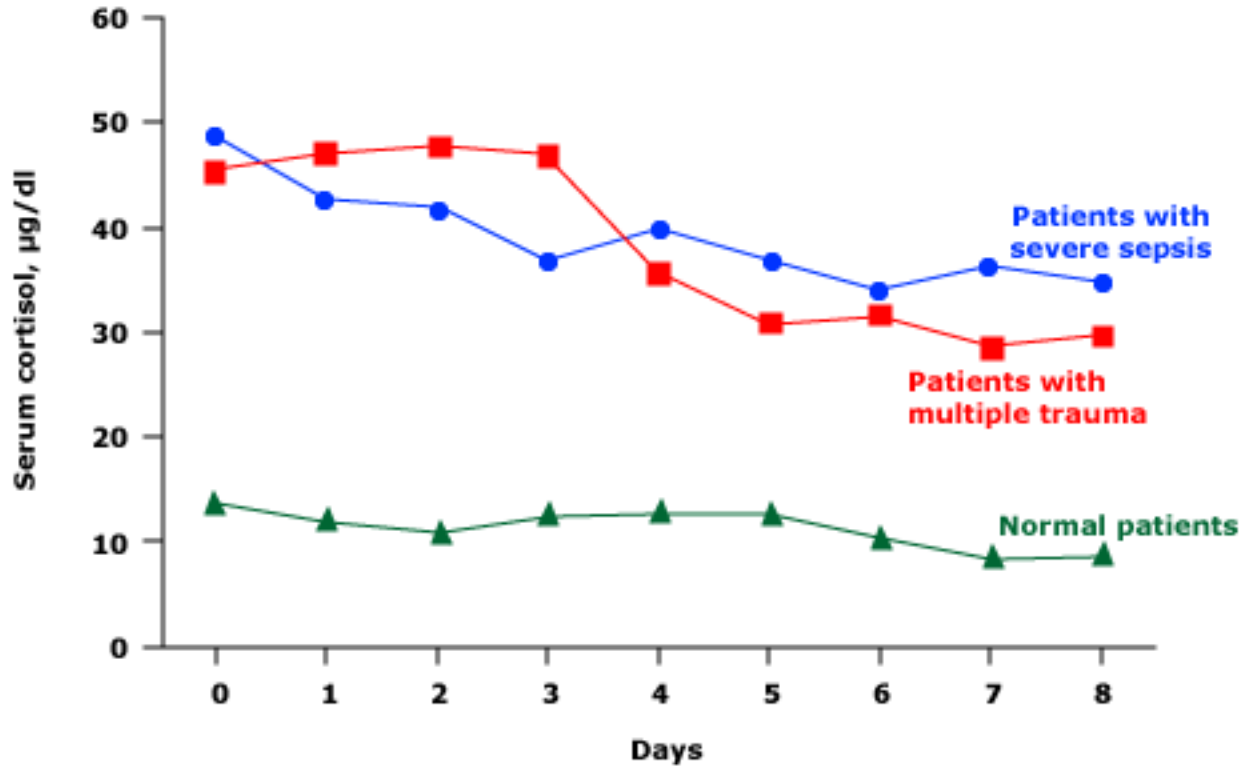
⇦ DIRECT PERITONEAL RESUSCITATION?

Adapted from Marshall, JC, Lowry, SF. Evaluation of the adequacy of source control. In: Sibbald, WJ, Vincent, JL, Clinical Trials for the Treatment of Sepsis. Springer-Verlag, Berlin, 1995 p 329.

I G. Terapia inotropa

1. Se recomanda administrarea de dobutamina in prezenta disfunctiei miocardice sugerata de presiuni crescute de umplere cardiaca si debit cardiac scazut (1C);
2. Nu se recomanda cresterea debitului cardiac la valori supranormale
3. Se recomanda administrarea de HHC iv in socul septic daca tensiunea arteriala nu raspunde la repletia volemica si vasopresor (2C)
4. Nu se recomanda folosirea testului ACTH pentru a identifica pacientii care sa primeasca HHC (2B)
3. Nu se recomanda folosirea dexametazonei daca HHC este disponibil (2B)
4. Se poate folosi fludrocortizon 50 µg/zi po daca HHC nu este disponibil (2C)
5. Se recomanda intreruperea CS cand vasopresorul nu mai este necesar (2D)
6. Se recomanda doze mai mici de 300 mg/zi pentru tratamentul socului septic (1A)
7. Nu se recomanda CS in sepsis in absenta socului (doar daca exista disfunctie endocrina) (1D)

Cortisol levels in normal subjects and the critically ill



Adapted with permission from: Vermes I, Beishuizen A, Hampsink RM, Haanen C. Dissociation of plasma adrenocorticotropin and cortisol levels in critically ill patients: possible role of endothelin and atrial natriuretic hormone. J Clin Endocrinol Metab 1995; 80:1238.

I J. Administrarea de produsi de sange

1. Se recomanda administrarea de MER la Hb < 7 g/dl (valoare tinta Hb = 7-9 g/dl) in absenta ischemiei miocardice, hipoxemiei severe, hemoragiei acute, boala cianogena cardiaca, acidoza lactica (1B)
2. Nu se recomanda utilizarea de eritropoietina (1B)
3. Nu se recomanda administrarea de PPC pentru corectarea tulburarilor de coagulare in absenta sangerarii sau a altor manevre invazive (2D)
4. Nu se recomanda administrarea ATIII in sepsisul sever/soc septic (1B)
5. Nu se recomanda administrarea de CT la TR < 5000/mmc fara sangerare aparenta; se administreaza CT daca TR este intre 5000–30000/mmc cu risc crescut de sangerare;

   -valoarea TR trebuie sa fie mai mare decat 50000 daca se urmareste efectuarea unei interventii chirurgicale sau a unor proceduri invazive (2D).

II C. Controlul glicemiei

1. dupa stabilizarea initiala pacientul cu sepsis sever si hiperglicemie trebuie sa primeasca insulina pentru a scadea nivelul glicemiei (1B);
2. se recomanda folosirea de protocoale adecvate pentru ajustarea dozei de insulina astfel incat glicemia sa fie < 150 mg/dl (2C);
3. pacientii care primesc insulina iv trebuie sa primeasca glucoza si valorile glicemiei sa fie monitorizate la 1–2 ore pana cand se stabilizeaza si ulterior la 4 ore (1C);
4. glicemia masurata pe glucotest trebuie interpretata cu atentie, intrucat valoarea glicemiei poate fi supraestimata (1B).

II F. Profilaxia trombozei venoase profunde

1.la pacientul cu sepsis sever trebuie sa se faca profilaxia TVP cu heparina nefractionata (doze mici tid sau bid) sau HGMM zilnic cu exceptia situatiilor in care exista contraindicatii (1A)

-trombocitopenie
-coagulopatie severa
-sangerare activa
-sangerare recenta intracerebrala

2.la pacientii cu contraindicatie pentru heparina se recomanda folosirea metodelor mecanice GCS jsi ICD (1A)

3.pacientii cu risc crescut de TVP (sepsis sever, istoric TVP, trauma, chirurgie ortopedica) se recomanda combinarea metodei farmacologice cu cea mecanica (2C)

4. se recomanda folosirea HGMM la pacientii cu risc mare de TVP (2C)

Se recomanda monitorizare pentru HIT

II G. Profilaxia ulcerului de stres

- se recomanda folosirea de blocanti de H2 (1A) sau PPI (1B)

II H. Decontaminarea tractului digestiv

-se pot folosi antibiotice nonabsorbabile sau cura scurta de antibiotic iv

II I. Consideratii privind scaderea masurilor suportive

-se constata scaderea anxietatii si depresiei membrilor familiei ca urmare a discutiilor despre diagnostic, prognostic si tratament (1D)

PACHET DE MASURI TERAPEUTICE CARE TREBUIE EFECTUATE IN PRIMELE 6 H DE LA INTERNAREA IN T.I.

1. Oxigenoterapie ± IOT si ventilatie mecanica
2. Cateter venos central si cateter arterial
3. Masurarea lactatului
4. Obtinerea culturilor inaintea administrarii antibioticului (antimicoticului)
5. Administrarea empirica de antibiotic (antimicotic) cu spectru larg in primele 3 h de la prezentarea la UPU sau o ora de la internarea in UTI
6. La prezentare – EGDT (early goal directed therapy) Rivers 2001

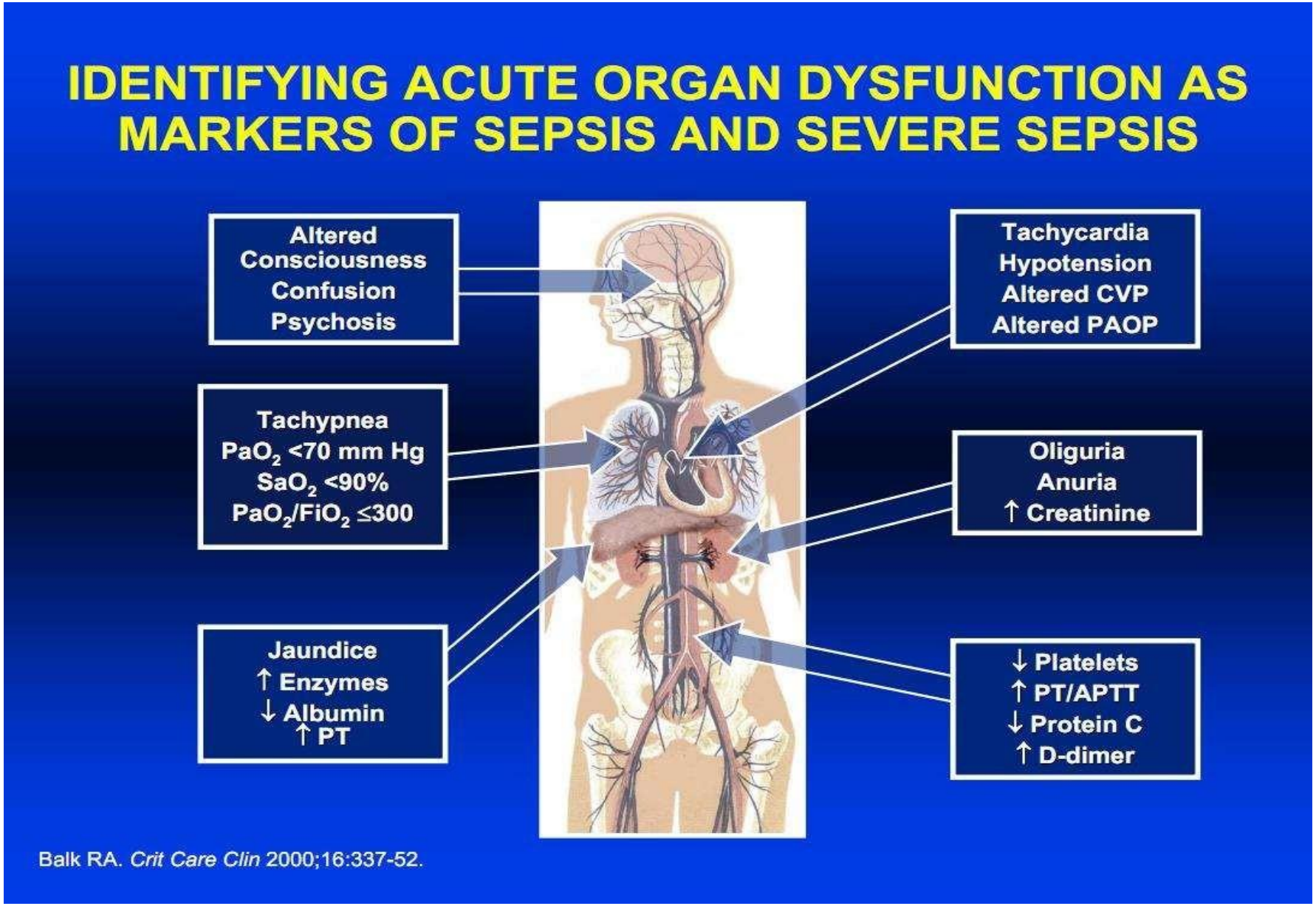
PACHET DE MASURI NECESAR DE APLICAT IN PRIMELE 24 DE ORE DE LA PREZENTARE

1. Administrarea dozelor mici de corticosteroizi in socul septic, conform protocolului unitatii
2. Protocol standardizat al Unitatii de Terapie Intensiva
3. Mentinerea glicemiei mai mare sau egala cu limita inferioara a normalului, dar mai mica de 150 mg /dl (8,3 mmol/l)

PROTOCOL DE TRATAMENT AL UTI

1. Administrarea empirica de antibiotic // antimicotic
2. Mentinerea glicemiei
3. Administrarea de corticosteroizi
4. Ventilatie mecanica
5. Tratamentul acidozei lactice
6. Profilaxia TVP
7. Profilaxia ulcerului de stres
8. Nutritia

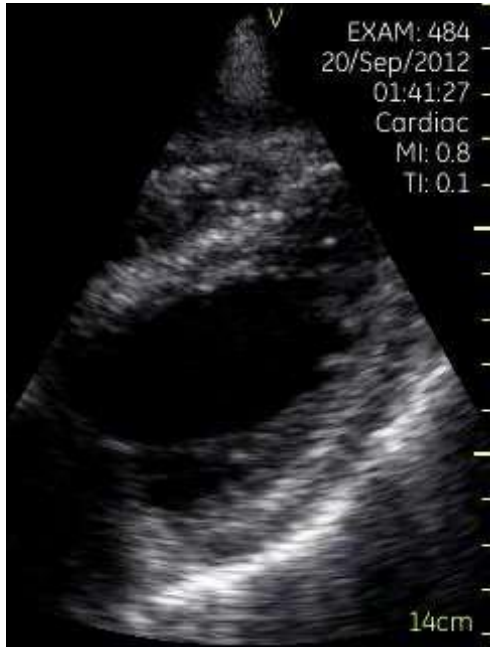
IDENTIFYING ACUTE ORGAN DYSFUNCTION AS MARKERS OF SEPSIS AND SEVERE SEPSIS



Balk RA. *Crit Care Clin* 2000;16:337-52.

Disfuncția miocardică în SS

- HD- hipovolemie absoluta- vasodilatatie periferica- maldistributie fluxuri sanguine regionale- alterarea extractiei de oxygen la nivel tisular
- Dupa expansiune volemica- status hiperdinamic, scadrea rezistentelor vasculare sistemice
- Disfunctie miocardica intrinseca PRECOCE
- **Factor independent de agravare a morbiditatii/mortalitatii(Bouhemad, 2011)**
- Mecanisme:
  - Disfunctie mitocondriala- scad rezervele de ATP
  - SN vegetativ- down regulation pt receptorii adrenergici
  - Perturbarea homeostaziei calcice
  - Alterarea precoce(primele 24 ore) a functiei miofilamentelor(Parillo, 1993)
  - Scade fractia de ejectie- dilatatie biventriculara- creste volumul telediastolic



DISFUNCTIA MIOCARDICA IN SOCUL SEPTIC

- Incidenta aprox: 20- 60% in primele zile de la debut
- Diminuare calcica tranzitorie
- Studii pe modele experimentale animale/autopsie la om- date histopatologice- aspect de cardiopatie de stress/ adrenergica
- Raspuns redus la catecoli in socul septic
- Diagnostic dificil: index cardiac, de regula, crescut
  - Evaluare hemodinamica
  - Markeri biologici:
    - Troponina-
    - BNP-
- Cum alegem inotropul cel mai potrivit?

British Journal of Anaesthesia **112** (1): 102–9 (2014)
Advance Access publication 17 September 2013 · doi:10.1093/bja/aet296

BJA

Early diastolic dysfunction is associated with intensive care unit mortality in cancer patients presenting with septic shock

M. Mourad[1], L. Chow-Chine[1], M. Faucher[1], A. Sannini[1], J. P. Brun[1], J. M. de Guibert[1], L. Fouche[1], J. Lambert[2], J. L. Blache[1] and D. Mokart[1,3*]

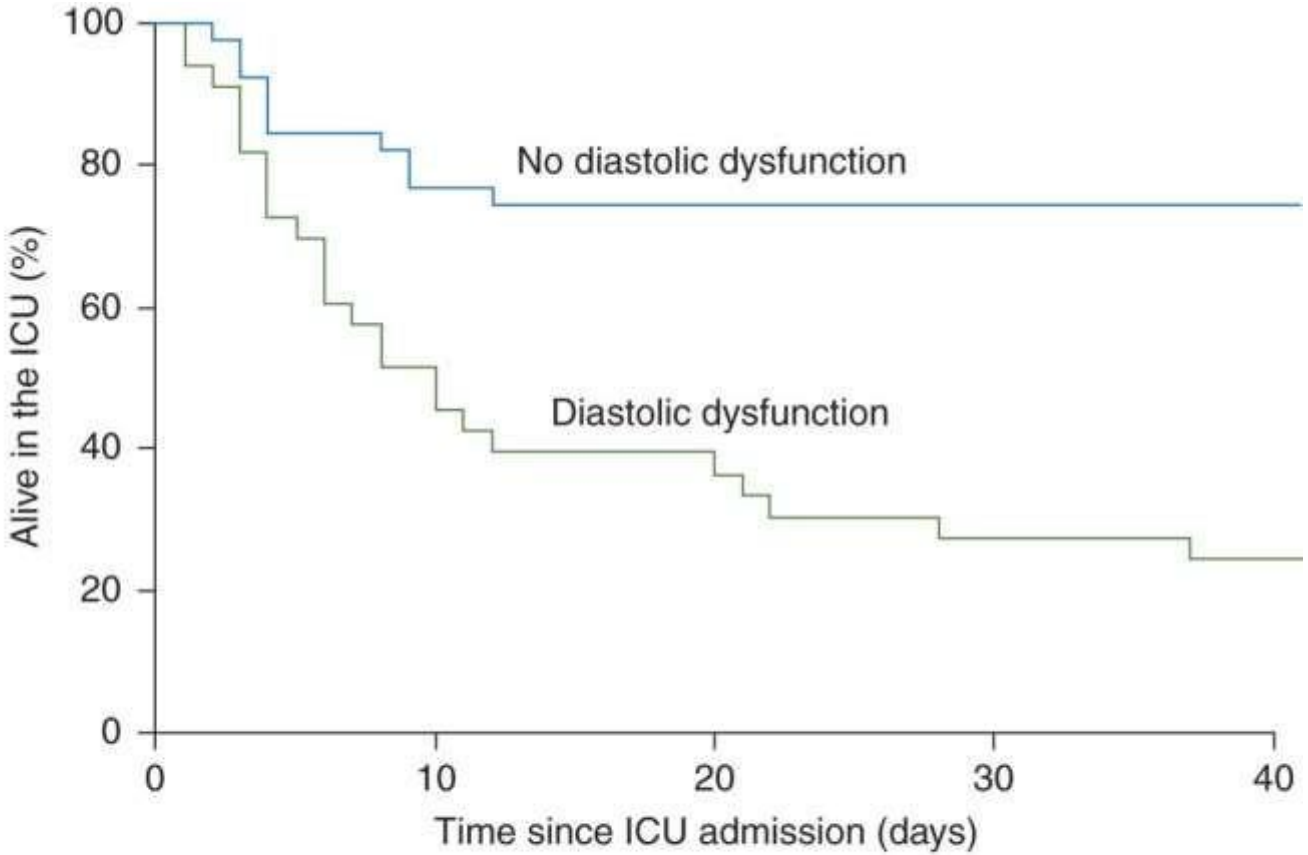
Table 3 Echocardiographic data and ICU mortality, multivariate analysis. The Hosmer–Lemeshow goodness-of-fit ($\chi^2=7.66$; $P=0.47$)

	Multivariate logistic regression analysis		
	ORs	**95% CI**	***P*-value**
$e' \leq 8$ cm s^{-1}	7.7	2.58–23.38	<0.001

Editor's key points

- The body's response to inflammation and sepsis is at least in part dependent on adequate myocardial function.
- Diastolic dysfunction can be detected and quantified by echocardiographic indices such as pulse wave and tissue Doppler.
- The presence or extent of diastolic dysfunction may be an additional factor used to stratify the need for high-level care and response to treatment.
- This study's findings of a strong association between diastolic dysfunction and intensive care unit mortality in patients with sepsis offer inroads into improved treatment options.

ICU survival according to diastolic dysfunction; Gray test: P<0.0001.

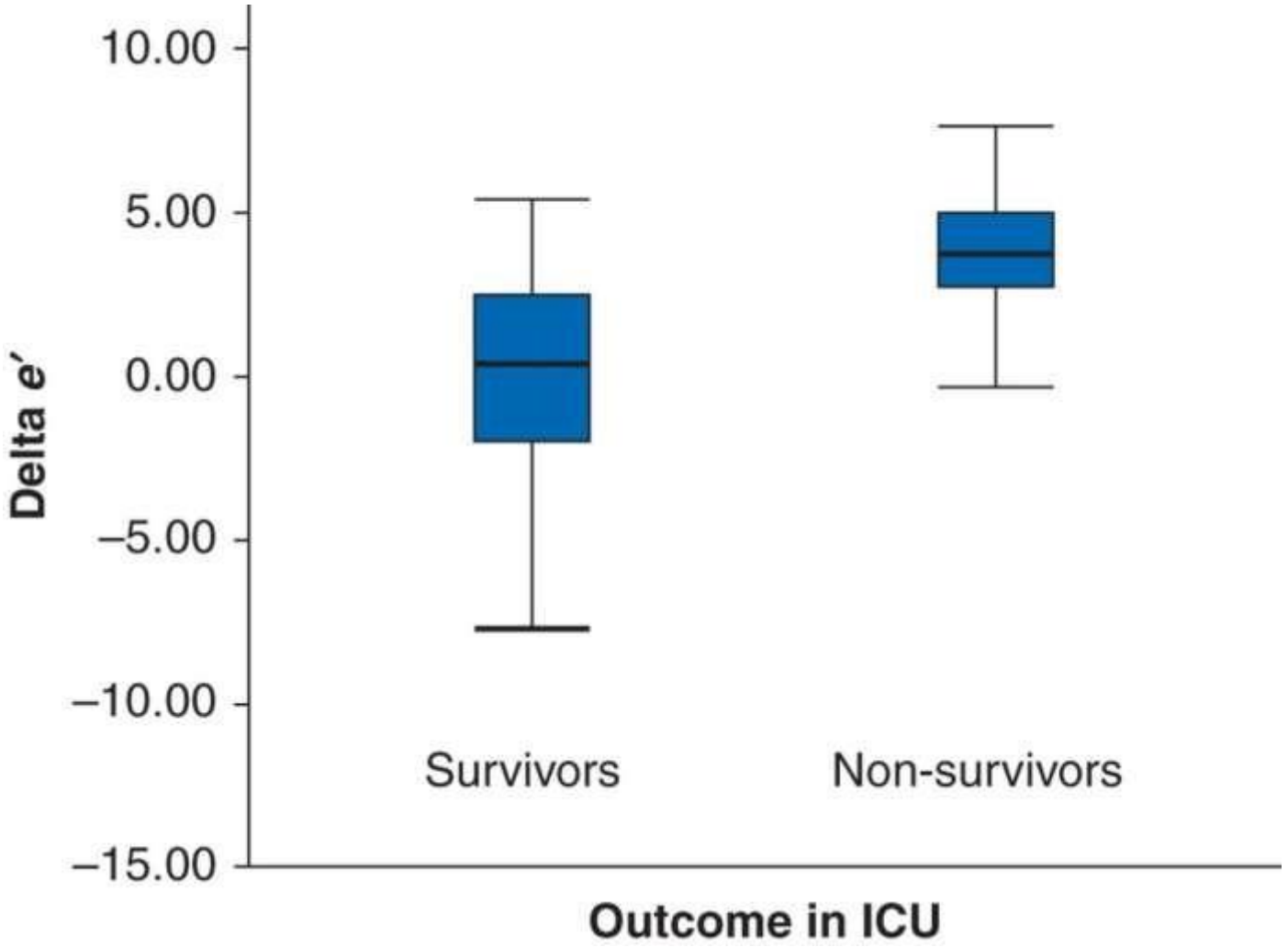


No. still in ICU				
Dysfunction 33	12	6	2	0
No dysfunction 39	13	4	1	1

Mourad M et al. Br. J. Anaesth. 2014;112:102-109

BJA British Journal of Anaesthesia

Delta e′ (theoretical e′−measured e′) represents part of diastolic dysfunction not related to age.



Mourad M et al. Br. J. Anaesth. 2014;112:102-109

BJA British Journal of Anaesthesia

Crit Care Med 2014 Apr;42(4):790-800. doi: 10.1097/CCM.0000000000000107.

Troponin elevation in severe sepsis and septic shock: the role of left ventricular diastolic dysfunction and right ventricular dilatation*.

Landesberg G[1], Jaffe AS, Gilon D, Levin PD, Goodman S, Abu-Baih A, Beeri R, Weissman C, Sprung CL, Landesberg A.

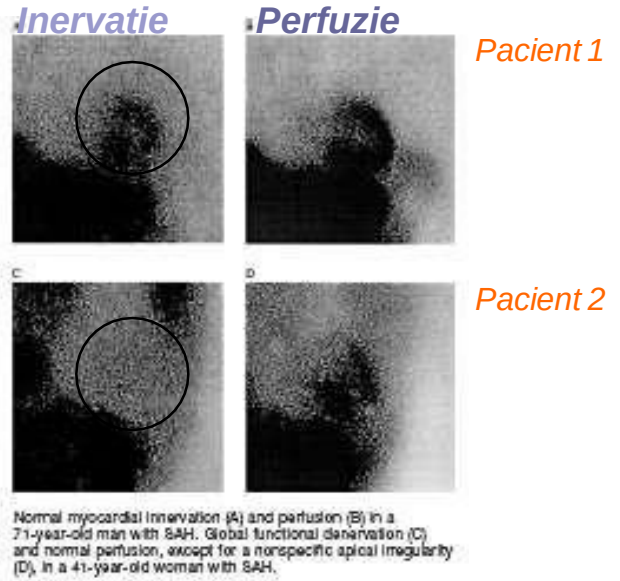
- **OBJECTIVE:**
- Serum troponin concentrations predict mortality in almost every clinical setting they have been examined, including sepsis. However, the causes for troponin elevations in sepsis are poorly understood. We hypothesized that detailed investigation of myocardial dysfunction by echocardiography can provide insight into the possible causes of troponin elevation and its association with mortality in sepsis.
- **DESIGN:**
- Prospective, analytic cohort study.
- **SETTING:**
- Tertiary academic institute.
- **PATIENTS:**
- A cohort of ICU patients with severe sepsis or septic shock.
- **INTERVENTIONS:**
- Advanced echocardiography using global strain, strain-rate imaging and 3D left and right ventricular volume analyses in addition to the standard echocardiography, and concomitant high-sensitivity troponin-T measurement in patients with severe sepsis or septic shock.
- **MEASUREMENTS AND MAIN RESULTS:**
- Two hundred twenty-five echocardiograms and concomitant high-sensitivity troponin-T measurements were performed in a cohort of 106 patients within the first days of severe sepsis or septic shock (2.1 ± 1.4 measurements/patient). Combining echocardiographic and clinical variables, left ventricular diastolic dysfunction defined as increased mitral E-to-strain-rate e'-wave ratio, right ventricular dilatation (increased right ventricular end-systolic volume index), high Acute Physiology and Chronic Health Evaluation-II score, and low glomerular filtration rate best correlated with elevated log-transformed concomitant high-sensitivity troponin-T concentrations (mixed linear model: t = 3.8, 3.3, 2.8, and -2.1 and p = 0.001, 0.0002, 0.006, and 0.007, respectively). Left ventricular systolic dysfunction determined by reduced strain-rate s'-wave or low ejection fraction did not significantly correlate with log(concomitant high-sensitivity troponin-T). Forty-one patients (39%) died in-hospital. Right ventricular end-systolic volume index and left ventricular strain-rate e'-wave predicted in-hospital mortality, independent of Acute Physiology and Chronic Health Evaluation-II score (logistic regression: Wald = 8.4, 6.6, and 9.8 and p = 0.004, 0.010, and 0.001, respectively). Concomitant high-sensitivity troponin-T predicted mortality in univariate analysis (Wald = 8.4; p = 0.004), but not when combined with right ventricular end-systolic volume index and strain-rate e'-wave in the multivariate analysis (Wald = 2.3, 4.6, and 6.2 and p = 0.13, 0.032, and 0.012, respectively).
- **CONCLUSIONS:**
- **Left ventricular diastolic dysfunction and right ventricular dilatation are the echocardiographic variables correlating best with concomitant high-sensitivity troponin-T concentrations. Left ventricular diastolic and right ventricular systolic dysfunction seem to explain the association of troponin with mortality in severe sepsis and septic shock.**

Disfuncția ventriculară miocardita adrenergică- « stunned » myocardium)

Leziuni miocite cardiace și neuronale cu eliberare masivă de catecolamine, cu punct de plecare terminațiile nervoase din miocard

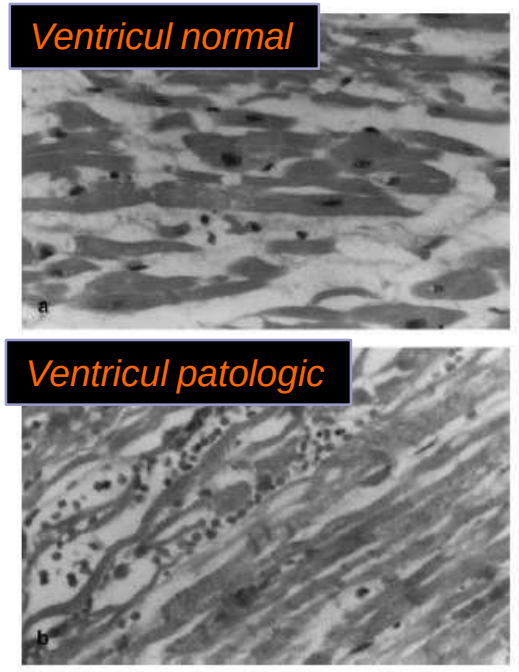
(scintigrafie de perfuzie normală

*Scintigrafie de inervare simpatică sugerează denervare funcțională)***Banki, Circulation 2005**

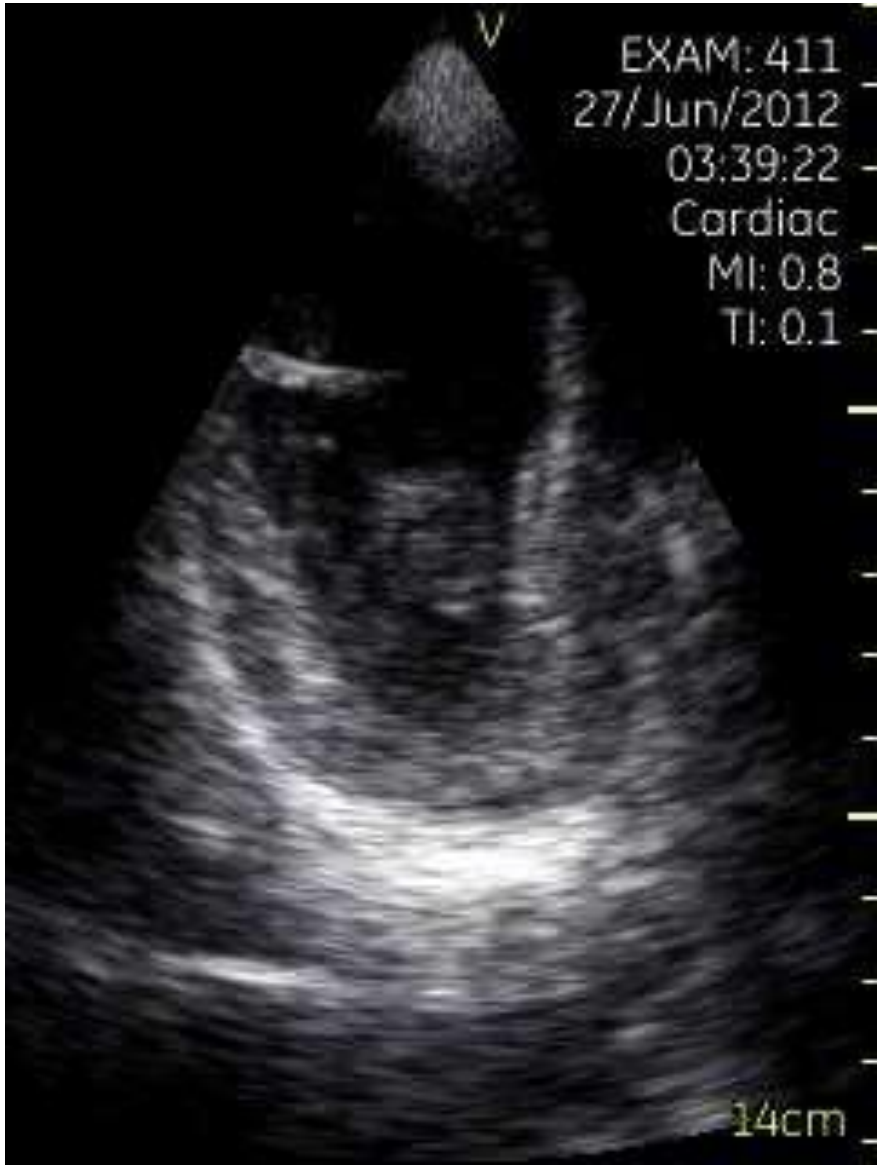


Degenerescență miofibrilară și miocitară cu Infiltrate celulare inflamatorii

Microscopie electronică la pacienți decedați cu HSA, comparativ cu bolnavi decedați cu patologie extracerebrală



Cardiomiopatie catecolică



Réanimation (2014) 23:167-175
DOI 10.1007/s13546-014-0860-6

Place des inotropes en réanimation

Inotropic support in the intensive care unit

L. Satre Buisson · J. Poissy ·

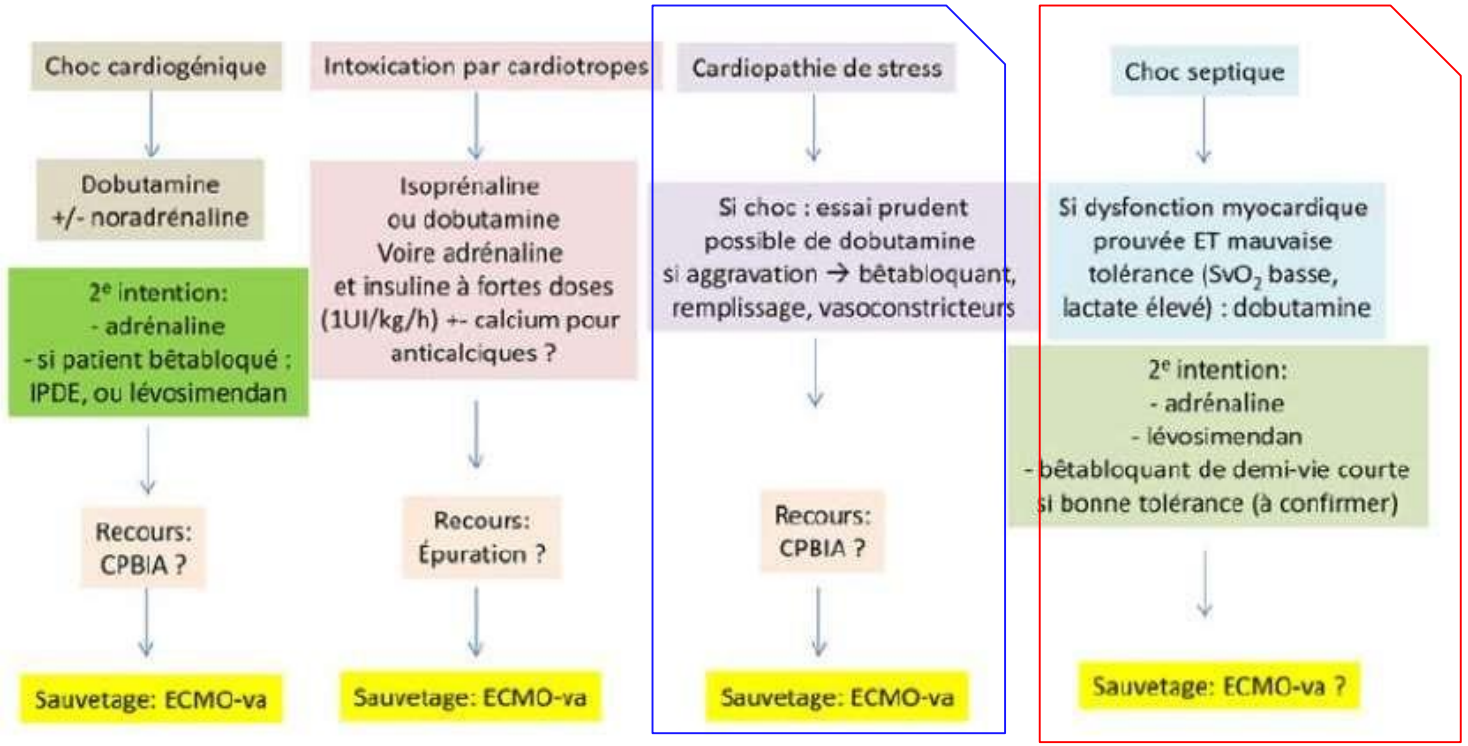
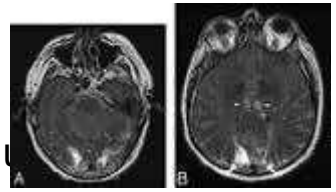


Fig. 2 Orientation thérapeutique dans les situations où les inotropes pourraient être utilisés. CBPIA, ballonnet de contrepulsion intra-aortique ; ECMO-va : *veno-arterial extracorporeal membrane oxygenation* ; IPDE : inhibiteur des phosphodiestérases

Encefalopatia septica/delirium

- Alterare a starii de constienta
- Nu presupune agresiune microbiana directa asupra SNC(dar aceasta trebuie exclusa)- Ebersolt et al, 2007
- Impune eliminarea cauzelor de neurotoxicitate(metabolice, farmacologice)
- **Semnifica evolutia unui sepsis necontrolat**(Bolton, 1993)
- **Factor independent de prognostic agravat pentru morbiditate/ mortalitate/ deficit cognitiv permanent(Cecinski et al, 2011)**
- Esential- diagnostic precoce, tratament preventiv
- Mecanisme:
  - **Complexul neurovascular**: activare endoteliala, alterarea barierei hematoencefalice, alterarea microcirc cerebrale- alterarea aportului de oxygen, hemoragii prin tulburari de coagulare, eliberare glutamate/ leucoencefalopatie/PRES
  - **Disfunctie intercelulara-** disfunctie mitocondriala, stress oxidative(glia si neuroni) in hipocamp si cortexul cerebral cu apoptoza
  - **Microglia**- hiperactivata prin diminuarea inhibitiei colinergice(van Gool, 2010)/ apoptoza/ elibereaza glutamate- effect neuroprotector sau neurotoxic
  - **Alterarea neurotransmisiei**
    - colinergice, betaadrenergice, gabaergice si serotoninergice consecinta finala, cu alterarea starii de constienta- predominant in cortex sih ipocamp- emotie, memorie, comportament
    - Sinteza NT alterata de trecerea aac neurotoxici- amoniu, tirozina, triptofan- prin cresterea conc plasmatice- disfunctie hepatica si liza musculara
    - Tulburari hemodinamice, de hemostaza, hipoxice- produc leziuni cerebrale, agraveaza procese neuroinflamatorii

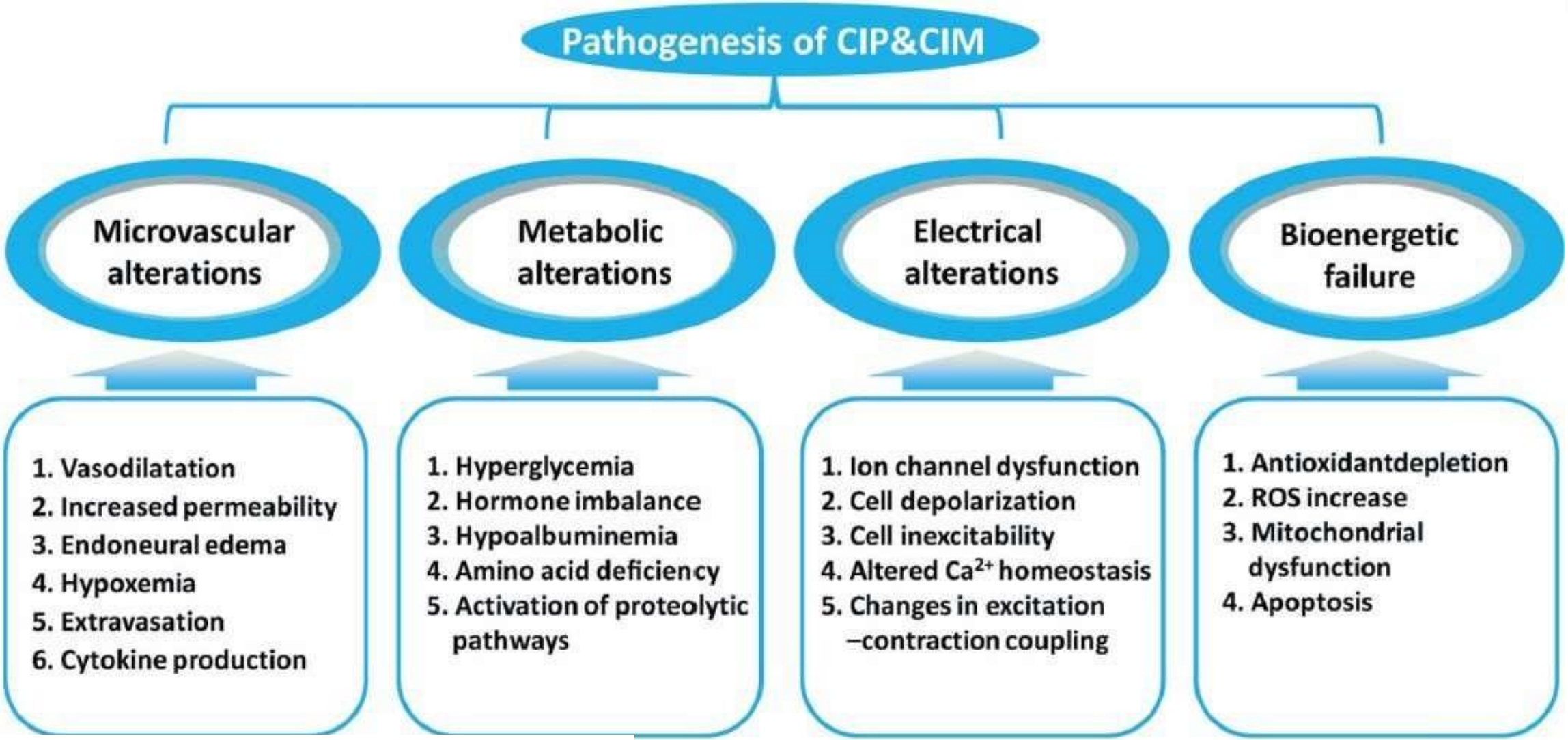


Encefalopatia septica/delirium

- **DIAGNOSTIC**
  - Alterarea starii de constienta- tulburari de somn-delir- coma cu modificarea starii motorii- agitatie/hipoactivitate- mioclonii multifocale, asterixis, rigiditate paratonica
  - Gandire dezorganizata, dezorientare TS, inversarea ritmului nictemeral, halucinatii
  - EEG- trasee cu unde predominant theta/delta, trasee trifazice, burst suppression, status nonconvulsivant
  - Modificari PESS, creste nivel plasmatic NSE, proteina S100 ß
  - Dg diferential- sevraj alcoholic/medicamentos- 5% boln alcoolodependenti spitalizati, la 48-72 de ore de la ultima ingestie- agitatie psihomotorie, zoopsie, manifestari vegetative
- **TRATAMENT**
  - Masuri nefarmacologice- confort fizic si psihologic, kineziterapie
  - Masuri farmacologice
    - Limitarea expunerii la medicamente neurotoxice
    - Controlul durerii si al tulburarilor de somn
- **PROGNOSTIC**
  - GCS≤ 8- Mortalitate 63%, 67%- EEG tip burst suppression (Eidelman, 1996)
  - **Persistenta sau recidiva encefalopatiei- symptom al unui sepsis necontrolat sau abces profund!!!**

Polineuromiopatia bolnavului septic

- Polineuropatia bolnavului critic- polineuropatie axonala sensoriomotorie (Latronico, 2008)
  - 58% la bolnavii cu stationare prelungita in reanimare
  - 70- 80% la bolnavii cu sepsis, soc septic, MSOF
  - 100%- bolnavi cu sepsis + stare de coma!(Latronico, 2005)
- Miopatia bolnavului critic- afectare musculara primara descrisa recent/ incidenta nu este cunoscuta
- Studii EMG/ viteze de conducere nervoasa/ biopsie musculara
- Suspiciune clinica: bolnavi cu stationare prelungita STI si dificultate de sevrare de ventilatia mecanica fara cauza cardiac sau respirator
- Afectare neomogena a grupelor musculare/denervare diafragmatica
- Poate fi diagnosticat de la 72 de ore
- Factori de risc: MSOF + sepsis + hiperglicemie+ ventilatie mecanica prelungita
- Prognostic: factor independent de agravare, risc crescut semnificativ de mortalitate



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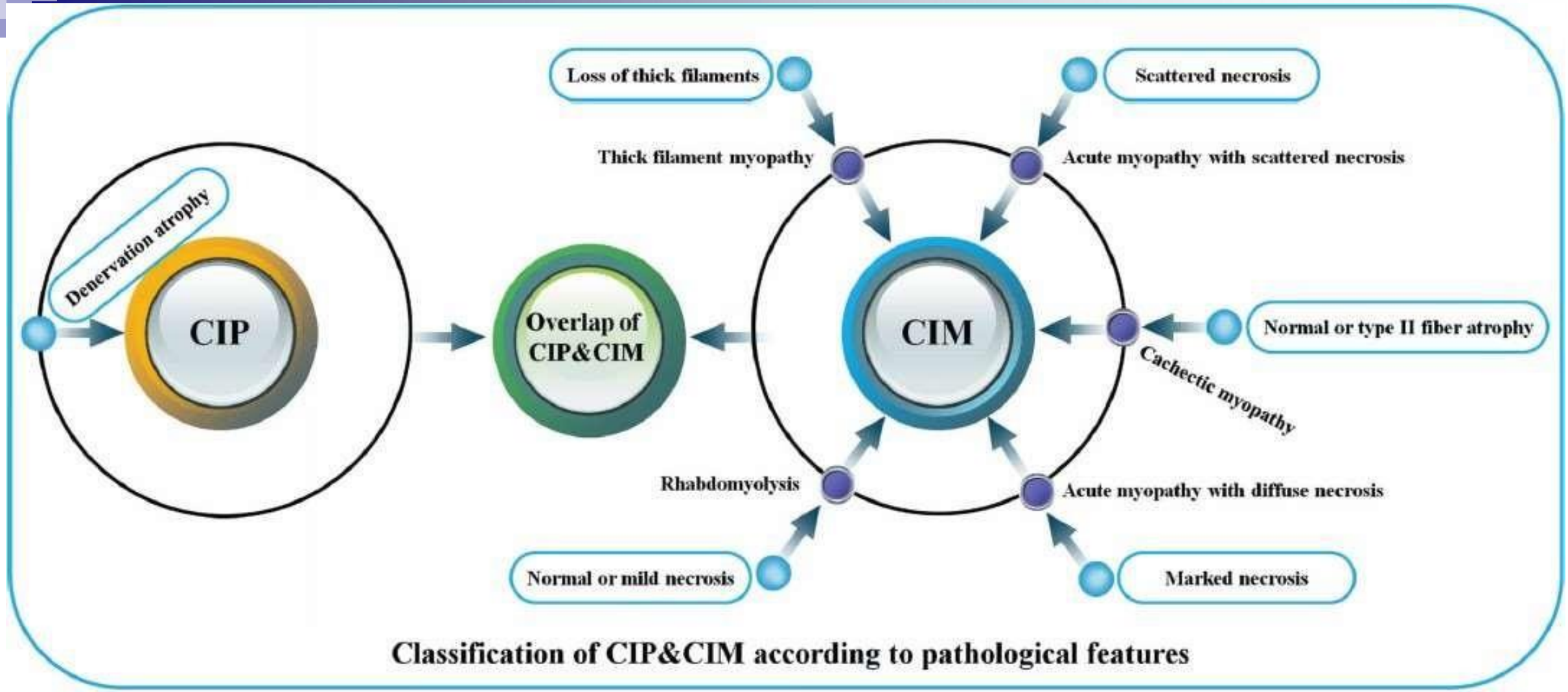
Critical illness polyneuropathy and myopathy: a systematic review

Chunkui Zhou[1, 2], Limin Wu[1, 3], Fengming Ni[4], Wei Ji[5], Jiang Wu[1], Hongliang Zhang[1]



Classification of CIP&CIM according to pathological features

From: **Myopathic Changes Associated With Severe Acute Respiratory Syndrome: A Postmortem Case Series**

Arch Neurol. 2005;62(7):1113-1117. doi:10.1001/archneur.62.7.1113

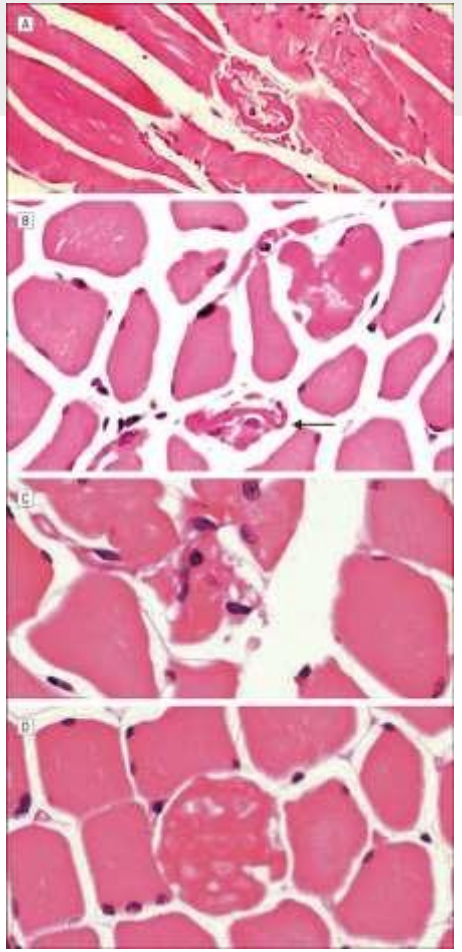


Figure Legend:

Isolated myofiber necrosis seen in 4 cases of severe acute respiratory syndrome. A, Coagulation and fragmentation of cytoplasmic contents (patient 7 in the psoas). B, Karyorrhectic nuclear debris, in the form of fine nuclear dusts, was observed in some fibers (arrow; patient 8 in the psoas). C, Necrotic fibers may have some macrophage infiltration (patient 5 in the quadriceps). D, Necrotic fibers may be completely devoid of macrophages (patient 1 in the quadriceps). (All hematoxylin-eosin, original magnification ×270.)

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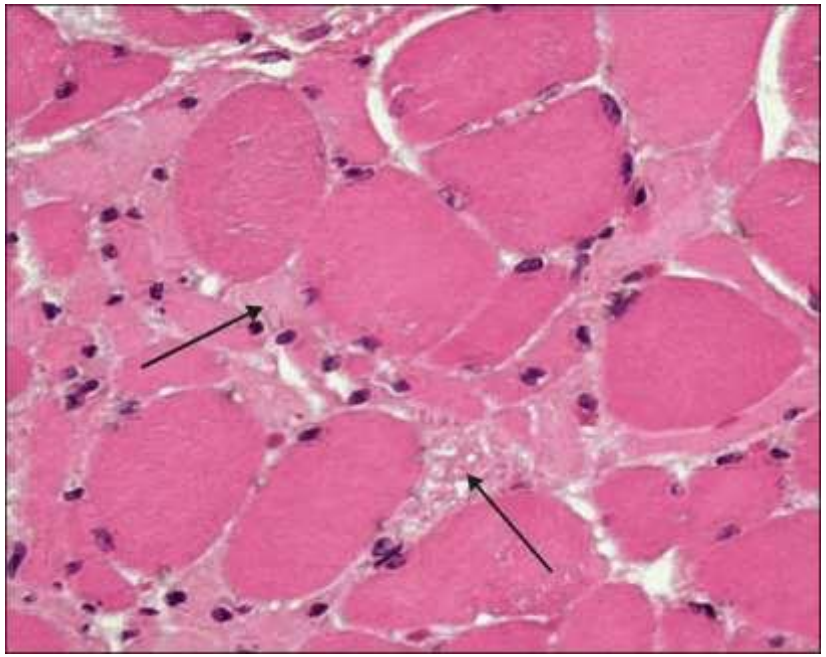
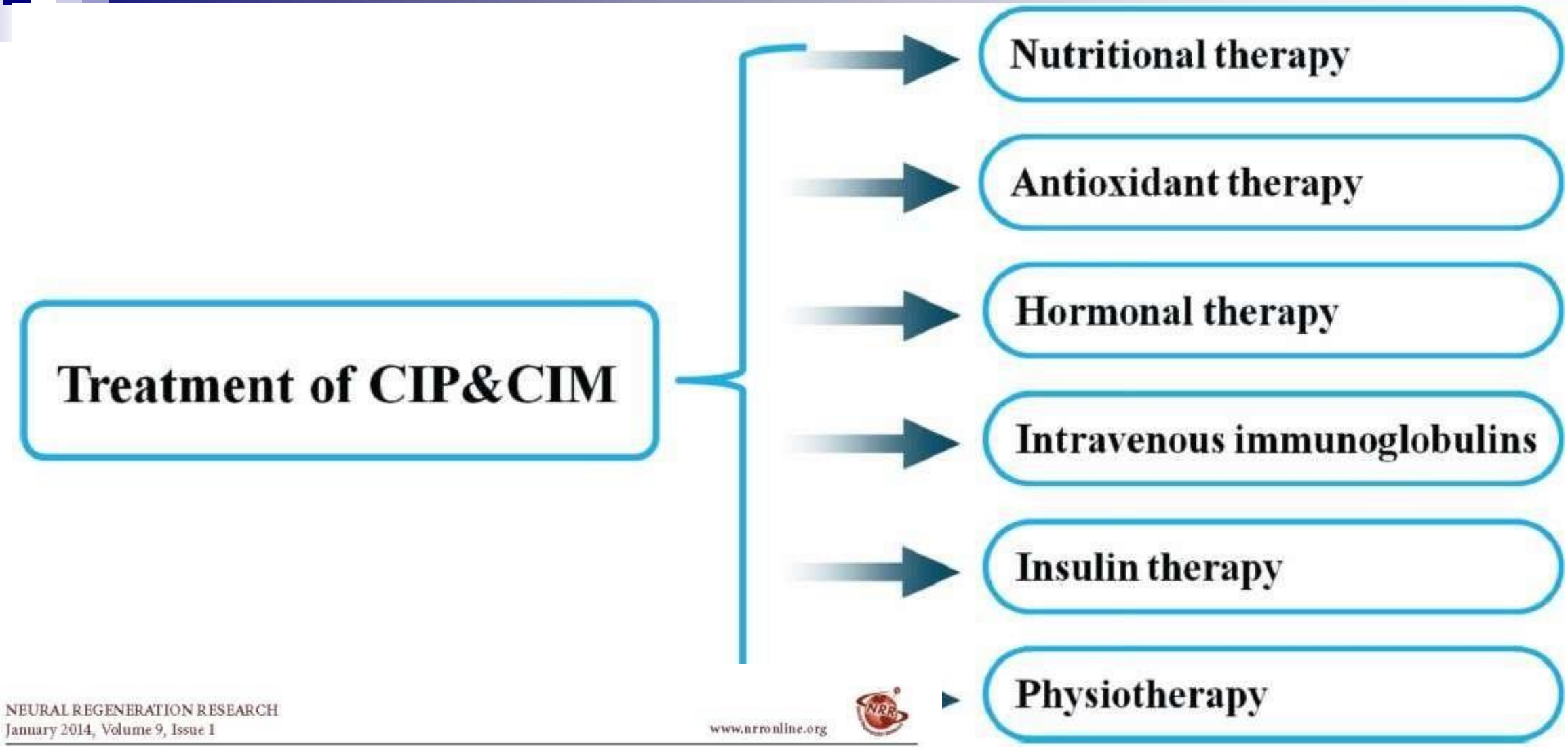


Figure Legend:

Critical illness myopathy from patient 3 in the psoas (hematoxylin-eosin, original magnification ×300). Atrophic fibers stained poorly, and in some fibers, a feathery degeneration of the cytoplasmic content was seen (arrows).



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Polineuromiopatia bolnavului septic

- Tratament- preventiv(Dos Santos 2012)
  - Corectarea diselectrolitemiilor
  - Control glicemie
  - Evitarea factorilor declansatori: aminoglicozide, corticoizi, relaxante musculare
  - Control rapid al sepsis-ului
  - Recuperare neuromotorie/ fiziokinetoterapie initiate rapid
  - Diagnostic- ventilator induced diaphragmatic dysfunction
- Curativ
- Studii electrofiziologice- traheostoma rapid efectuata, estimare prognostic/ aranjamente pentru internare intr-un spital de recuperare cronici neurologie

Disfunctia respiratorie in socul septic

- ALI/ARDS extrapulmonar
- Miopatia diafragmatica indusa de ventilatia mecanica

Disfunctia renala din socul septic

- 20% boln cu sepsis sever, 50%- soc septic(Legrand, 2011) mortalitate- 50- 80- %!!- factor de risc independent!
- Mecanisme:
  - Hipoperfuzie renala- activare endoteliala
  - Activarea celulelor inflamatorii si imunitare
  - Consecinte:
    - Perturbarea microcirculatiei renale- cresterea permeabilitatii- edem interstitial
    - Necroza si apoptoza celulara
    - Modificari functionale tubulare

Tulburari de hemostaza in socul septic

- Activarea coagularii-
  - Inductia expresiei factorului tisular la suprafata celulelor endoteliale si monocite- macrophage de endotoxine/ citokinele inflamatorii
  - Coagulopatie- fenomen difuz
- si inhibitia fibrinolizei- sistemul fibrinolitic nu poate contracara activarea coagularii
- CID- difuzia monomerilor de fibrina si captarea trombocitelor circulante in microtrombi- trombopenie, consum de factori de coagulare

Soc septic- disfunctia sistemului imun

- 2/3 decese apar in faza tardiva a sepsisului prin infectii secundare oportuniste, bacteriene sau fungice(Krishna, 2013)
- “Sepsis – related immunoparalysis”
- Pacientii surviving sepsis- risc de 4x mai mare de reinternare in primul an pentru infectii recurente, cu scaderea persistenta a calitatii vietii(Winters, 2010, Nesseler, 2013, Wang, 2014)
- Mecanisme:
  - In faza antiinflamatorie- anergie- scade secretia de cytokine de celulele T la stimul bacterian
  - Raspunsuri aberante la stimulare bacteriana de celulele splenice si din ggl limfatici
  - Disfunctie macrophage/monocyte
  - Scade secretia de IL2
  - Apoptoza celulelor immune efectoare- limfocite B, celulele T CD4, natural killer- nu declanseaza raspuns inflamator- imunoparalizie/ necroza celulara –da!
  - A nu se confunda cu apoptoza monocitelor din faza initiala- evita o faza hiperinflamatorie

  - Clinic- infectii nosocomiale bacteriene MDR, infectii virale- reactivare virusuri herpetice- CMV, HSV/ fungi

ŞOCUL SEPTIC

CLINIC

- Febră sau hipotermie
- Tahicardie
- Tahipnee
- Alterarea statusului mental (encefalopatia septică)
- Hipotensiune arterială
- Extremităţi calde
- Amplitudine mare a undei de puls
- Timp de umplere capilară normal
- Vene periferice pline
- Oligurie

ŞOCUL SEPTIC

PRINCIPII DE TRATAMENT

SURVIVING SEPSIS CAMPAIGN ± 2004

1. Resuscitarea inițială (primele 6 ore):
   - PVC 8-12mmHg
   - TA medie >65mmHg
   - SvO_2> 70%
   - Debit urinar >0,5ml/kg oră
2. Identificarea germenelui cauzal
   - Hemoculturi
   - Culturi din produsul patologic suspectat
3. Antibioterapia
   - Precoce (în prima oră de la recunoaşterea şocului septic)
   - Empirică (de primă intenție) ± spectru larg, activă pe germenii suspectați
   - Asociere de antibiotice; doze mari; administrare intravenoasă, adaptată farmacocineticii
   - La 48 ore ± terapie de dezescaladare
4. Controlul sursei
   - Intervenție chirurgicală pentru îndepărtarea focarului

ŞOCUL SEPTIC

PRINCIPII DE TRATAMENT

5. Terapia volemică (cristaloide sau coloide)
   - Normalizarea volumului intravascular şi PVC
6. Terapia cu vasopresoare
   - Normalizarea TA şi a perfuziei organelor
7. Terapia cu inotrope
   - Normalizarea debitului cardiac
   - Se preferă dobutamina (la nevoie, cu noradrenalină)
8. Terapia cu corticoizi
   - HHC 50 mg/6 ore
9. Terapia cu proteina C activată (Xygris)
   - Acţiune anticoagulantă şi antiinflamatorie
10. Administrarea de sânge
    - Refacerea transportului de oxigen
    - Hb 7-9g/l

ŞOCUL SEPTIC

PRINCIPII DE TRATAMENT

11. Suportul ventilator
    - Ventilaţia protectivă a plămânului
12. Sedarea, analgezia şi relaxarea musculară
    - Analgezie de calitate întotdeauna, sedare la pacientul ventilat mecanic, relaxare musculară numai dacă e necesar
13. Controlul glicemiei
    - Menţinerea glicemiei < 150mg%
14. Epurarea extrarenală
    - Hemofiltrare veno-venoasă continuă / hemodializă intermitentă
15. Terapia cu bicarbonat
    - Combaterea acidozei metabolice la pH <7,15
16. Profilaxia trombozei venoase profunde
    - Heparine cu greutate moleculară mică
17. Profilaxia ulcerului de stress
    - omeprazol
18. Luarea în consideraţie a limitării suportului vital
    - În cazurile fără şanse de vindecare – sedare, analgezie şi hidratare

Protocol for Resuscitation of Adult Hypotensive Patients With Suspected Sepsis

Culture relevant body fluids, including blood.
Infuse a balanced electrolyte solution of 500 mL/15 min. Monitor the systolic blood pressure response.
Insert a central venous or pulmonary artery catheter.
- **If after a 500-mL bolus of saline the patient remains hypotensive and CVP is <8-12 mm Hg or PAWP is <8-12 mm Hg, infuse another 500-mL bolus of fluid; repeat as needed.**
- **If CVP is >15 or PAWP is 15-20 and the patient remains hypotensive (<65 mm Hg), start an infusion of the inotropedobutamine or dopamine. The goal is a mean systemic pressure >65 mm Hg and a pulse rate <120 beats/min.**

Determine the cardiac index and systemic vascular resistance.
- **If after infusion of fluid and inotropes SVR is <600, infuse avasopressor—either norepinephrine or vasopressin—to increase SVR.**

Monitor mixed venous oxygen saturation and urine output as an indication that therapeutic interventions have improved perfusion.
CVP, central venous pressure; PAWP, pulmonary artery wedge pressure; SVR, systemic vascular resistance.

Tratamentul şocului septic

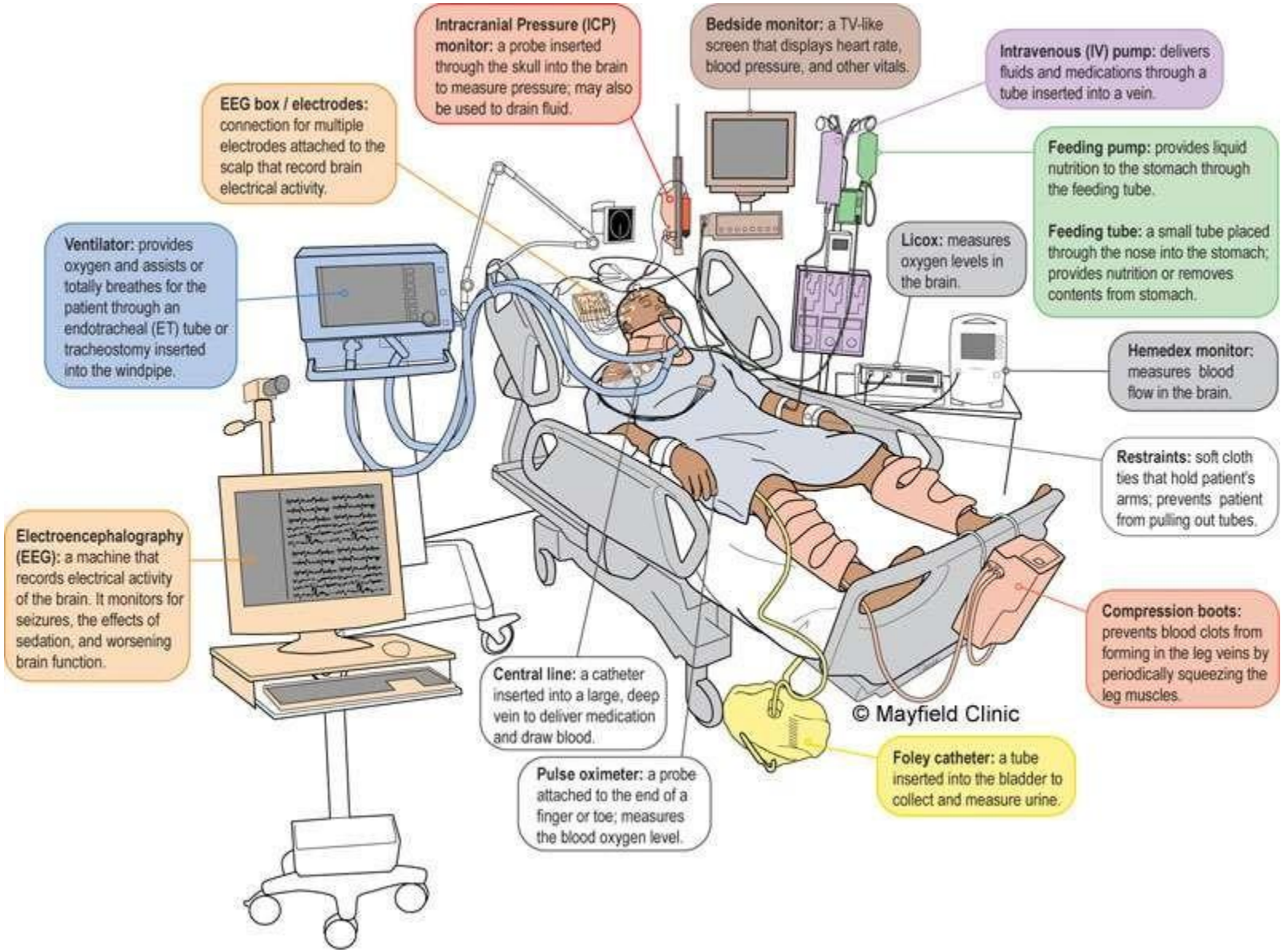
Controlul infecţiei: drenajul şi antibioterapia – tratamentul definitiv
Corecţia deficielor lichidiene
Suportul farmacologic:
    dobutamina, dopamina, noradrenalina,
Manipulările răspunsurilor umorale:
    Tratamentul polimedicamentos titrat sau antimediator seriat
    Imunoterapia, steroizi, octreotida
    Anticoagulantele (antitrombina III)

Sepsis – factori de prognostic negativ

- Raspunsul gazdei
  - - absenta febrei/hipotermia, leucopenia
  - Comorbiditati, virsta ≤ 40 ani, fibrilatie atriala recent instalata, dependent de alcool, imunosupresie
- Locul infectiei
  - Mortalitate 50- 55% cand locul infectiei este necunoscut, gastrointestinal, pulmonar; 30%- urinar, 75%- intestin ischemic(Knaus, 1992, Krieger, 1983, Leligdowicz, 2014)
- Tipul infectiei: nosocomiala, fungi noncandida, infectii polimicrobiene
- Terapia antimicrobiana- adecvata, instituita precoce- scade mortalitatea cu 50%(!), antibioterapia anterior cu 90 zile creste risc de mortalitate in sepsis cu Gram negative(Johnson, 2011)
- Restabilirea perfuziei- esecul restabilirii precoce a perfuziei- corelat cu rata mortalitatii

Sepsis sever/soc sepsis- reducerea ratei mortalitatii

- Precoce
  - Repletie hidrica adecvata in primele ore
  - Antibioterapie adecvata din prima ora
  - Culturi pt diagnostic
- Ulterior
  - Monitorizare si tratament disfunctii de organ
  - Atentie: disf miocardica, encefalopatia septica, disf renala, imunoparalizie si infectii secundare, polineuromiopatie (inclusiv diafragmatica, VAP- preventiv), sepsis nosocomial!


Intracranial Pressure (ICP) monitor: a probe inserted through the skull into the brain to measure pressure; may also be used to drain fluid.
Bedside monitor: a TV-like screen that displays heart rate, blood pressure, and other vitals.
Intravenous (IV) pump: delivers fluids and medications through a tube inserted into a vein.
EEG box / electrodes: connection for multiple electrodes attached to the scalp that record brain electrical activity.
Feeding pump: provides liquid nutrition to the stomach through the feeding tube.
Feeding tube: a small tube placed through the nose into the stomach; provides nutrition or removes contents from stomach.
Licox: measures oxygen levels in the brain.
Ventilator: provides oxygen and assists or totally breathes for the patient through an endotracheal (ET) tube or tracheostomy inserted into the windpipe.
Hemedex monitor: measures blood flow in the brain.
Restraints: soft cloth ties that hold patient's arms; prevents patient from pulling out tubes.
Electroencephalography (EEG): a machine that records electrical activity of the brain. It monitors for seizures, the effects of sedation, and worsening brain function.
Compression boots: prevents blood clots from forming in the leg veins by periodically squeezing the leg muscles.
Central line: a catheter inserted into a large, deep vein to deliver medication and draw blood.
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Pulse oximeter: a probe attached to the end of a finger or toe; measures the blood oxygen level.
Foley catheter: a tube inserted into the bladder to collect and measure urine.