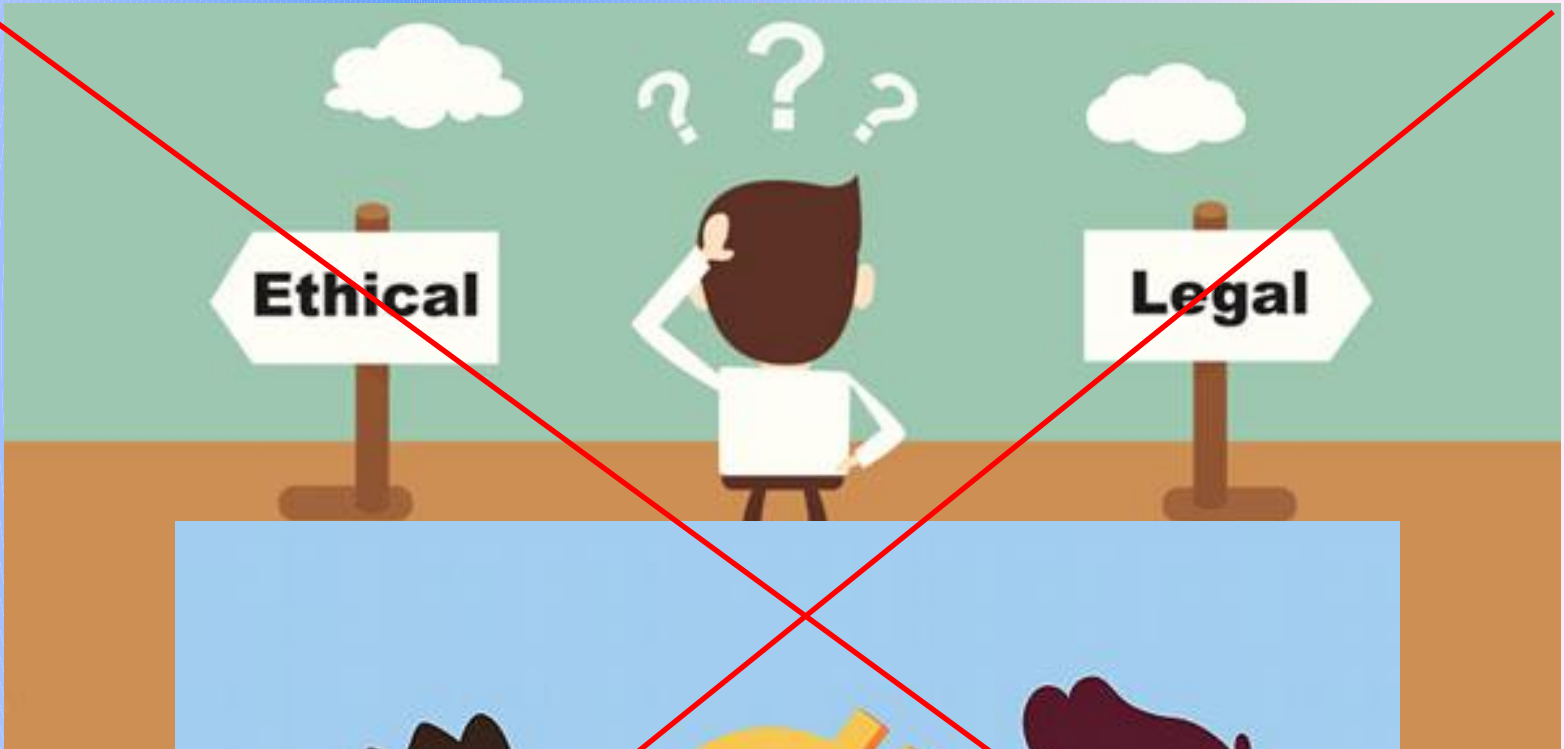


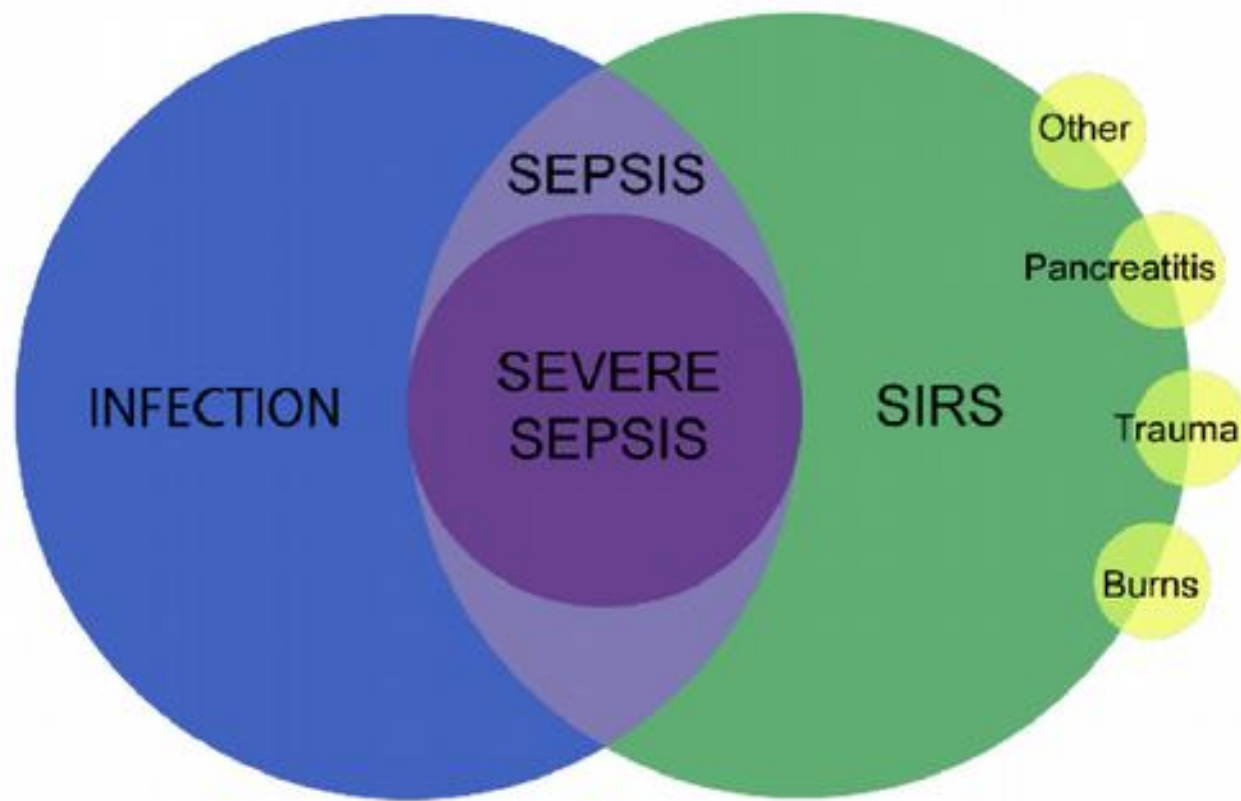
# Chyby při péči o septického pacienta

anestezie a intenzivní medicína

Jan Máca



# Co je to sepse?



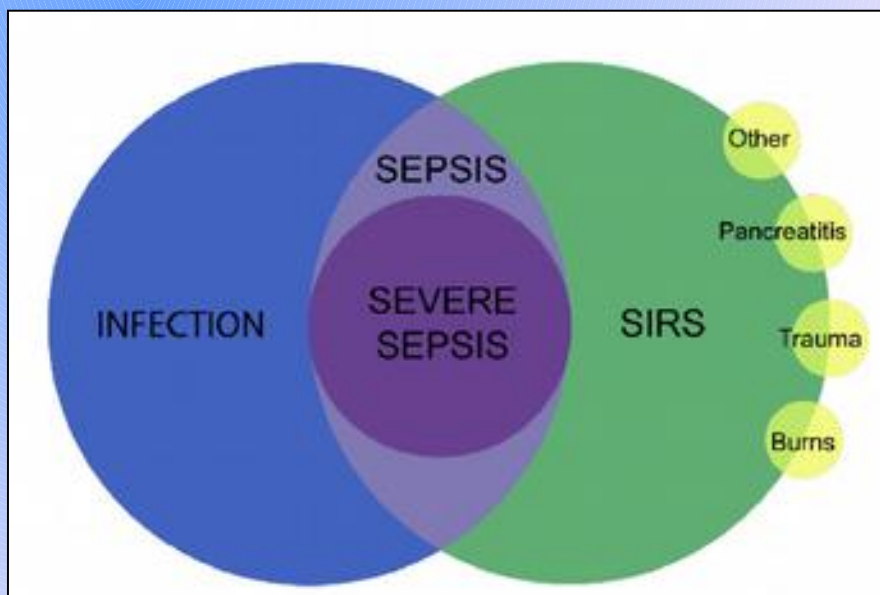
# Co je to sepse?



sepse **není** generalizovaná infekce



sepse je **dysregulovaná**, patologická **reakce** organismu/systému na infekci



**chyby**



**diagnóza**

**terapie**

diagnostika a terapie sepse

=

největší výzva v intenzivní péči

diagnostika a terapie sepse

=

největší výzva **nejen** v intenzivní péči

**diagnóza**



## ACCP/SCCM - 1992

### **Systemic inflammatory response syndrome (SIRS):**

1. tělesná teplota > **38°C** nebo < **36°C**
2. tepová frekvence > **90/min**
3. dechová frekvence > **20/min** nebo PaCO<sub>2</sub> < **32 mmHg**
4. leukocyty > **12.000/mm<sup>3</sup>** nebo < **4.000/mm<sup>3</sup>** nebo > **10 %** nezralých forem (tyčí)

ORIGINAL ARTICLE

# Systemic Inflammatory Response Syndrome Criteria in Defining Severe Sepsis

Kirsi-Maija Kaukonen, M.D., Ph.D., Michael Bailey, Ph.D., David Pilcher, F.C.I.C.M.,  
D. Jamie Cooper, M.D., Ph.D., and Rinaldo Bellomo, M.D., Ph.D.

N Engl J Med 2015

**SIRS** kritéria nemajú optimálnu senzitivitu stran diagnózy sepse  
nerozlišujú medzi adaptivnými a maladaptivnými reakciami na infekciu

1 z 8 pacientů s prokázanou infekcí a orgánovou dysfunkcí nesplní alespoň 2 kritéria SIRS

Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

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

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

JAMA. 2016

sepsis is defined as life-threatening **organ dysfunction** caused by a **dysregulated host response to infection**

**$\Delta$  SOFA**

**$\Delta$  qSOFA**

**organ dysfunction**  $\approx$  acute change in total SOFA score  $\geq 2$  points consequent to the infection

**qSOFA**

**mimo JIP**

### Quick sequential organ failure assessment

- Respiratory rate greater than or equal to 22 breaths per minute
- Altered mentation
- Systolic blood pressure less than 100 mm Hg

screening pacientů s infekcí a vyšším mortalitním rizikem

**mimo JIP**

# SOFA

## Sepsis-related/sequential organ failure assessment

Organ system	1	2	3	4
<b>Respiratory</b> PaO <sub>2</sub> /FIO <sub>2</sub> , (mmHg)	<400	<300	<200	<100
<b>Hematologic</b> Platelets/ nl	<150	<100	<50	<20
<b>Hepatic</b> Bilirubin, mg/dl ( $\mu$ mol/l)	1,2–1,9 (20–32)	2,0–5,9 (33–101)	6,0–11,9 (102–204)	>12,0 (>204)
<b>Cardiovascular</b> Hypotension	MAP <sup>2)</sup> <70 mmHG	Dopamine $\leq 5$ <sup>1)</sup> or dobutamine (any dose)	Dopamine >5 or epinephrine $\leq 0,1$ <sup>1)</sup> or Norepinephrine $\leq 0,1$ <sup>1)</sup>	Dopamine >15 epinephrine > 0 or norepinephrine 0,1
<b>Neurologic</b> Glasgow Coma Score	13–14	10–12	6–9	<6
<b>Renal</b> Creatinine, mg/dl ( $\mu$ mol/l) urine output	1,2–1,9 (110–170)	2,0–3,4 (171–299)	3,5–4,9 (300–440) <500 ml/day	>5,0 (>440) <200 ml/day

na JIP

# Sepsis-3

## septic shock

- persisting **hypotension requiring vasopressors** to maintain MAP  $\geq$  65mmHg
- serum **lactate** level  $>2$  mmol/L (18mg/dL) despite **adequate volume resuscitation**

## **dynamika procesu**

první zhodnocení je obvykle  
na ED/standardním odd.

**acute change in total SOFA score  $\geq$  2 points consequent to the infection**

**přítomnost orgánová dysfunkce  $\rightarrow$  myslet na sepsi  
susp. sepse  $\rightarrow$  pátrat po orgánové dysfunkci**

- **potřeba opakovaného zhodnocení stavu**
- **indikace zvýšení míry monitorace**
- **indikace hospitalizace na JIP**

# původce a markery zánětu

nedostatek **gold standard** diagnostických testů

(např. aspirace sputa, PSB, BAL,...)

pozitivní identifikace patogenu

zkreslení výsledků

chyby v interpretaci výsledků

rychlost diagnostiky

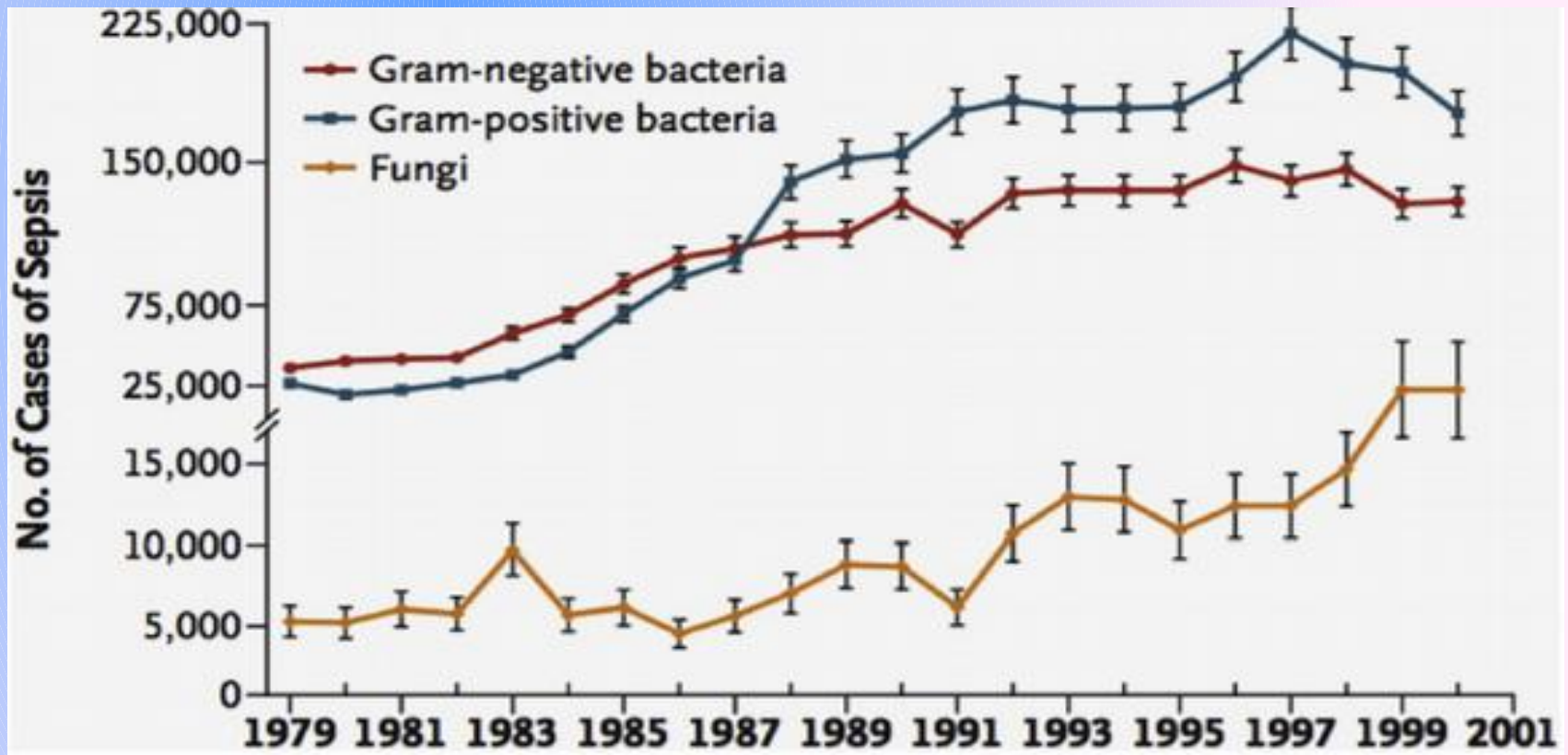
- kultivace            dny
- mikroskopie        hodiny
- PCR                10-tky minut

**biomarkery zánětu - nespecifičnost**

CRP, PCT, presepsin, IL-6, IL-10



## identifikace typu původce



- anamnéza (cestování, předchozí infekce, komorbidity)
- komunitní/nozokomiální vs. health care–associated infection
- lokální mikrobiální podmínky

## Specifické kohorty pacientů

věk (příliš staří/mladí), imunosuprimovaní, podvyživení

### minimální symptomy infekce nebo přítomnost zkreslujících symptomů

- 20-30% geronto-pacientů nevykazuje febrilní stav
- nesouvisející přítomnost alterace vědomí, únavy, nechutenství
- medikace tlumící fyziologickou reaktivitu (b-blokery, kortikoidy)

#### Examples of immunosuppression

##### Pathogenesis

Physiologic

##### Condition

- Extremes of age
- Pregnancy

Acquired

- HIV/AIDS
- Diabetes
- Malnutrition
- Malignancy/chemotherapy
- Radiation treatment
- Medications (steroids)

Congenital

Inherited immunodeficiencies

Other

- Cystic fibrosis
- Systemic inflammation

# problémy a chyby diagnostice - shrnutí

**Chyba: vyloučení diagnózy sepse** v situaci **neinfekční/infekční** příčiny SIRS

**Chyba: stanovení diagnózy sepse** a zahájení terapie (ATB) v situaci **neinfekční** příčiny SIRS

## poddiagnostikování



- opoždění intervencí monitorace (ATB/chirurg)
- IVF



- **zhoršení prognózy a klinického výsledku**

## naddiagnostikování



- neindikovaná ATB terapie a IVF



- **mikrobiální rezistence**
- **tekutinový overload**

terapie

**bundled care?**

# bundles



minimum z historie

The New England Journal of Medicine

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## EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

EMANUEL RIVERS, M.D., M.P.H., BRYANT NGUYEN, M.D., SUZANNE HAVSTAD, M.A., JULIE RESSLER, B.S., ALEXANDRIA MUZZIN, B.S., BERNHARD KNOBLICH, M.D., EDWARD PETERSON, PH.D., AND MICHAEL TOMLANOVICH, M.D., FOR THE EARLY GOAL-DIRECTED THERAPY COLLABORATIVE GROUP\*

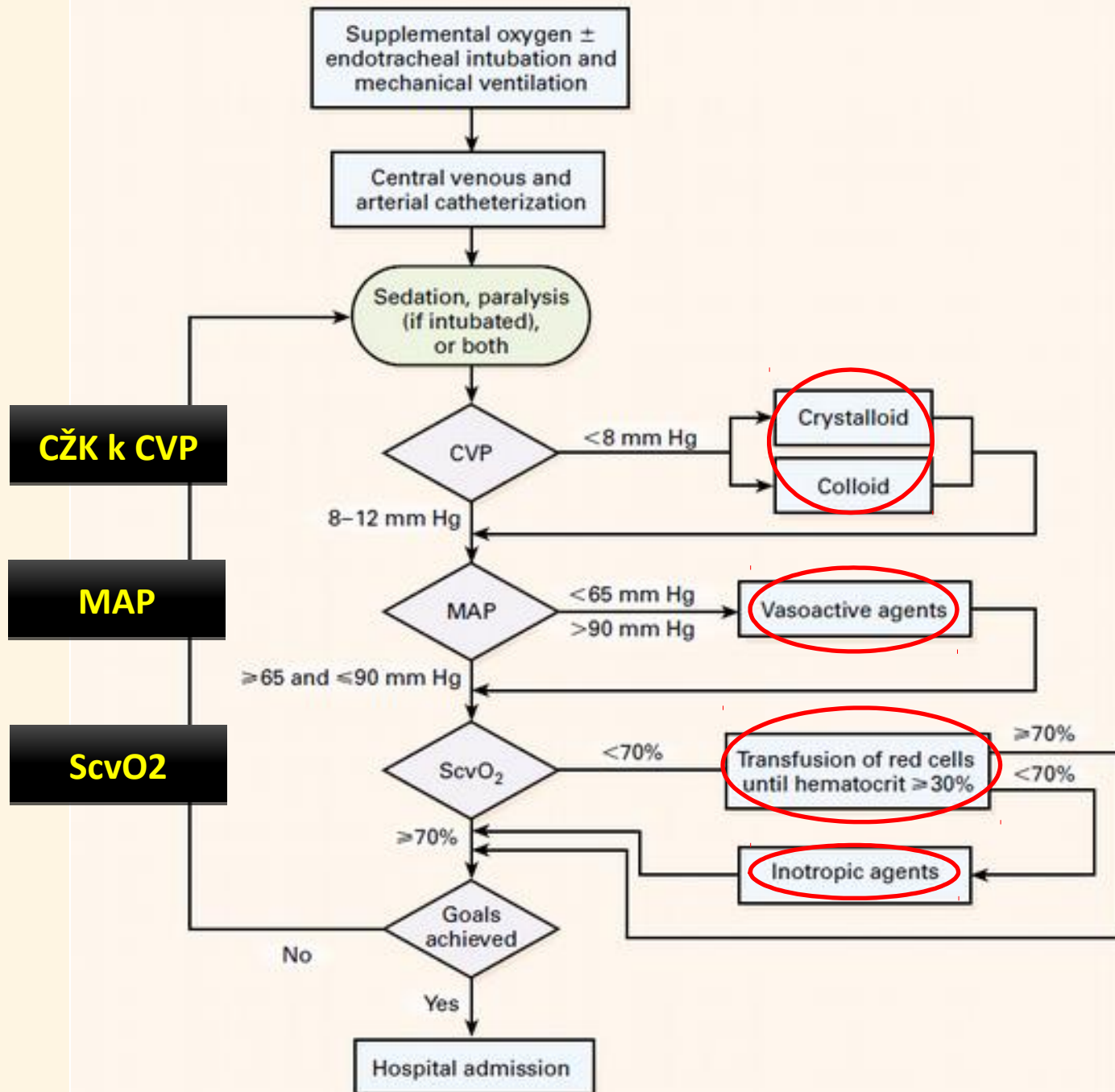
NEJM 2001

monocentrická, ED

**standardní**  
**n=130**

vs.

**EGDT**  
**n=133**



# výsledky

VARIABLE	STANDARD THERAPY (N= 133)	EARLY GOAL-DIRECTED THERAPY (N= 130)	RELATIVE RISK (95% CI)	P VALUE
	no. (%)			
In-hospital mortality†				
All patients	59 (46.5)	38 (30.5)	0.58 (0.38–0.87)	0.009
Patients with severe sepsis	19 (30.0)	9 (14.9)	0.46 (0.21–1.03)	0.06
Patients with septic shock	40 (56.8)	29 (44.6)	0.60 (0.36–0.98)	0.04
Patients with sepsis syndrome	44 (45.4)	37 (41.1)	0.66 (0.42–1.04)	0.07
28-Day mortality†	61 (49.2)	40 (30.8)	0.58 (0.39–0.87)	0.01
60-Day mortality†	70 (56.9)	47 (36.2)	0.67 (0.46–0.96)	0.03
Causes of in-hospital death‡				
Sudden cardiovascular collapse	25/119 (20.9)	10/103 (9.7)	—	0.02
Multiorgan failure	26/119 (21.8)	17/103 (16.2)	—	0.27

„riversománie“

SSC 2004

SSC Bundles 2005

CONFERENCE REPORTS AND EXPERT PANEL



# Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

Andrew Rhodes<sup>1\*</sup>, Laura E. Evans<sup>2</sup>, Waleed Alhazzani<sup>3</sup>, Mitchell M. Levy<sup>4</sup>, Massimo Antonelli<sup>5</sup>, Ricard Ferrer<sup>6</sup>, Anand Kumar<sup>7</sup>, Jonathan E. Sevransky<sup>8</sup>, Charles L. Sprung<sup>9</sup>, Mark E. Nunnally<sup>2</sup>, Bram Rochwerg<sup>3</sup>, Gordon D. Rubinfeld<sup>10</sup>, Derek C. Angus<sup>11</sup>, Djillali Annane<sup>12</sup>, Richard J. Beale<sup>13</sup>, Geoffrey J. Bellinghan<sup>14</sup>, Gordon R. Bernard<sup>15</sup>, Jean-Daniel Chiche<sup>16</sup>, Craig Coopersmith<sup>8</sup>, Daniel P. De Backer<sup>17</sup>, Craig J. French<sup>18</sup>, Seitaro Fujishima<sup>19</sup>, Herwig Gerlach<sup>20</sup>, Jorge Luis Hidalgo<sup>21</sup>, Steven M. Hollenberg<sup>22</sup>, Alan E. Jones<sup>23</sup>, Dilip R. Karnad<sup>24</sup>, Ruth M. Kleinpell<sup>25</sup>, Younsuk Koh<sup>26</sup>, Thiago Costa Lisboa<sup>27</sup>, Flavia R. Machado<sup>28</sup>, John J. Marini<sup>29</sup>, John C. Marshall<sup>30</sup>, John E. Mazuski<sup>31</sup>, Lauralyn A. McIntyre<sup>32</sup>, Anthony S. McLean<sup>33</sup>, Sangeeta Mehta<sup>34</sup>, Rui P. Moreno<sup>35</sup>, John Myburgh<sup>36</sup>, Paolo Navalesi<sup>37</sup>, Osamu Nishida<sup>38</sup>, Tiffany M. Osborn<sup>31</sup>, Anders Perner<sup>39</sup>, Colleen M. Plunkett<sup>25</sup>, Marco Ranieri<sup>40</sup>, Christa A. Schorr<sup>22</sup>, Maureen A. Seckel<sup>41</sup>, Christopher W. Seymour<sup>42</sup>, Lisa Shieh<sup>43</sup>, Khalid A. Shukri<sup>44</sup>, Steven Q. Simpson<sup>45</sup>, Mervyn Singer<sup>46</sup>, B. Taylor Thompson<sup>47</sup>, Sean R. Townsend<sup>48</sup>, Thomas Van der Poll<sup>49</sup>, Jean-Louis Vincent<sup>50</sup>, W. Joost Wiersinga<sup>49</sup>, Janice L. Zimmerman<sup>51</sup> and R. Phillip Dellinger<sup>22</sup>



EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS

EMANUEL RIVERS, M.D., M.P.H., BRYAN W. FRANKLIN, M.D., JANE HAVSTAD, M.A., JULIE RESSLER, B.S.,  
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FOR THE EARLY GOAL-DIRECTED THERAPY COLLABORATIVE GROUP\*

2008-2011

Wall Street Journal, 2008

Alan Jones, 2011



pochybnosti

- mortalita CG
- vyřazení pacientů
- CVK COI
- laktát vs. ScvO<sub>2</sub>
- nejasnosti stran efektu intervencí



# Konfirmační studie

1 *Protocolized Care for Early Septic Shock (ProCESS), 2014*

n=1341

EGDT

protokol

IVF do euvolémie , PRBC (hgb < 75g)

standard care

USA

**no difference 60-day, 90-day a 1-year mortality - 19-21%**

„riversoskepse“

ORIGINAL ARTICLE

## Early, Goal-Directed Therapy for Septic Shock — A Patient-Level Meta-Analysis

The PRISM Investigators\*

2017

metaanalýza ProCESS, ARISE, ProMISe

n=3723

**EGDT**

vs.

**usual care**

90day mortality

**24.9%**

**25.4%**

**EGDT higher cost, more ICU days, more use of vasopressors**

**sickest** - vysoký laktát, PDR (45%), kombinace hypotenze a hyperlaktatemie



### Surviving sepsis campaign bundles

To be completed within **3 hours:**

- Measure lactate level
- Obtain blood cultures before administration of antibiotics
- Administer broad spectrum antibiotics
- Administer 30 mL/kg crystalloid for hypotension or lactate greater than or equal to 4 mmol/L

To be completed within **6 hours:**

- Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation to maintain a mean arterial pressure) greater than or equal to 65 mm Hg
- In the event of persistent arterial hypotension despite volume resuscitation (septic shock) or initial lactate greater than 4 mmol/L:
  - Measure CVP<sup>a</sup>
  - Measure ScvO<sub>2</sub><sup>a</sup>
- Remeasure lactate if initial lactate was elevated<sup>a</sup>

<sup>a</sup> Targets for quantitative resuscitation included in the guidelines area CVP of greater than or equal to 8 mm Hg, ScvO<sub>2</sub> of greater than or equal to 70%, and normalization of lactate.

# The Surviving Sepsis Campaign Bundle: 2018 Update

Mitchell M. Levy, MD, MCCM<sup>1</sup>; Laura E. Evans, MD, MSc, FCCM<sup>2</sup>;  
Andrew Rhodes, MBBS, FRCA, FRCP, FFICM, MD (res)<sup>3</sup>

- **sepsis is a medical emergency**

- **appropriate immediate management in the initial hours after development of sepsis improves outcomes**

- Measure lactate level. Remeasure if initial lactate is >2 mmol/L.
- Obtain blood cultures prior to administration of antibiotics.
- Administer broad-spectrum antibiotics.
- Begin rapid administration of 30ml/kg crystalloid for hypotension or lactate  $\geq 4$  mmol/L.
- Apply vasopressors if patient is hypotensive during or after fluid resuscitation to maintain MAP  $\geq 65$  mm Hg.

3-h and 6-h bundles have been combined into a single “hour-1 bundle”

## SSC bundles - shrnutí

**ATB**

i.v., combination (if multiresistant),  
PCT guided, reevaluation

**IVF**

dynamic variables (PLR, fluid  
challenge, EE occlusion test)  
albumin v.s. krystaloid

**vazopresory**

noradrenalin, vasopressin, cíl >65  
mmHg

**laktát**

lactate clearance

**kotrikoidy**

unclear



30ml/kg za 3 hodiny

nové cíle? timing?  
SEPSISPAM > 85 mmHg

marker hypoperfuze?

HC 200mg/den i.v.  
septický šok

**UPV, TRF, kontrola glykemie, nutrice, analgosedace, imunoglobuliny**

# obecné chyby

protocols?

late recognition

late ATB/no source control/no cultures

late and inadequate IVF

late vasopressors agents

no close monitoring and reevaluation

liberal PRBC

liberal use - dobutamin/dopamin

liberal use – ScvO<sub>2</sub>

best clinical judgement with use of some bundle elements

# golden hour



děkuji za pozornost