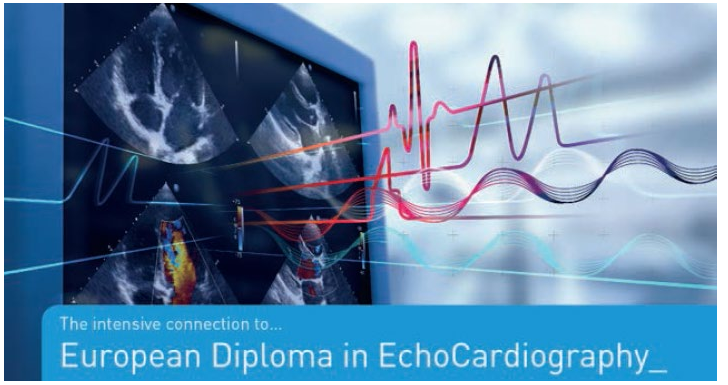
Šokové stavy a indikace k antibiotické léčbě

Martin Balik
Complex Cardiac Center, Dept. of Anaesthesia and Intensive Care
1st Medical Faculty, Charles University
Prague, Czechia, EU



Conflict of interest

- Research grants: AZV 18-06-00417 (Prospective randomized double-blind study of efficacy and safety of 1c class antiarrhythmic agent (propafenone) for supraventricular arrhythmias in septic shock), Gilead Sciences (Immune boosting in severe Covid19)
- Research support: ESICM Stoutenbeek Award (Dutch Society of Critical Care)
- Inventor and patent holder: Lactocitrate®, EU patent (EP2609915B1), Canadian patent (No.2799624)
- Speaker Fees: FMC, GML-Biomedica, Gilead Sciences, Bbraun, AOP Orphan
- Grant to organize educational meetings: None
- Advisory board: None

Rozhodovací algoritmus (propedeutika, 12svEKG a základní TTE)…:Hypotenze, tachy/bradykardie, oligurie, MAC, laktatémie…

1.) Obstrukční šok – ANO

NE

2.) Kardiogenní šok – ANO

NE

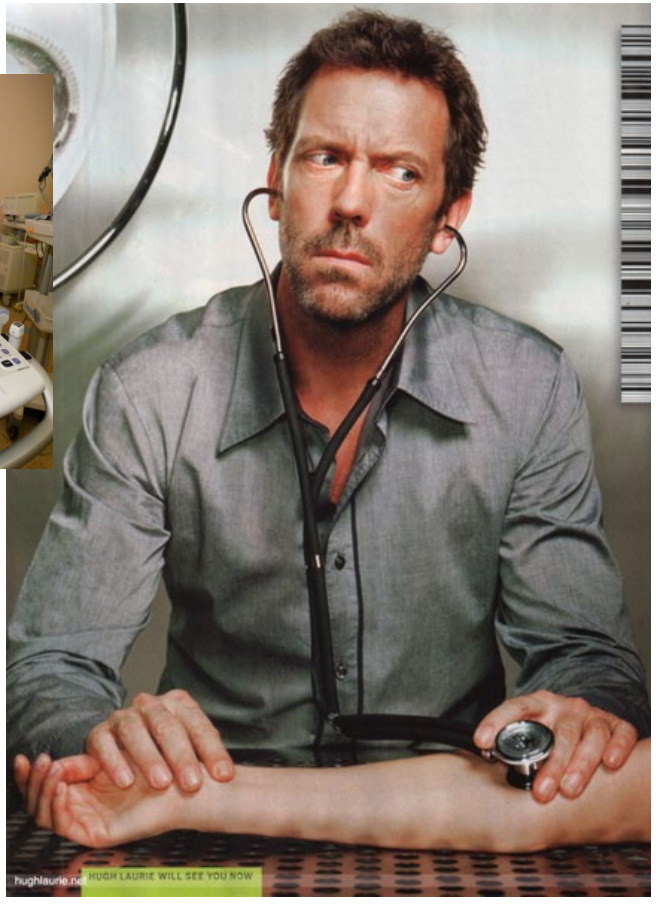
3.) Hypovolemický šok – ANO

NE

4.) Distribuční šok: sepse ?, - ANO
anafylaxe ?, neurogenní ?

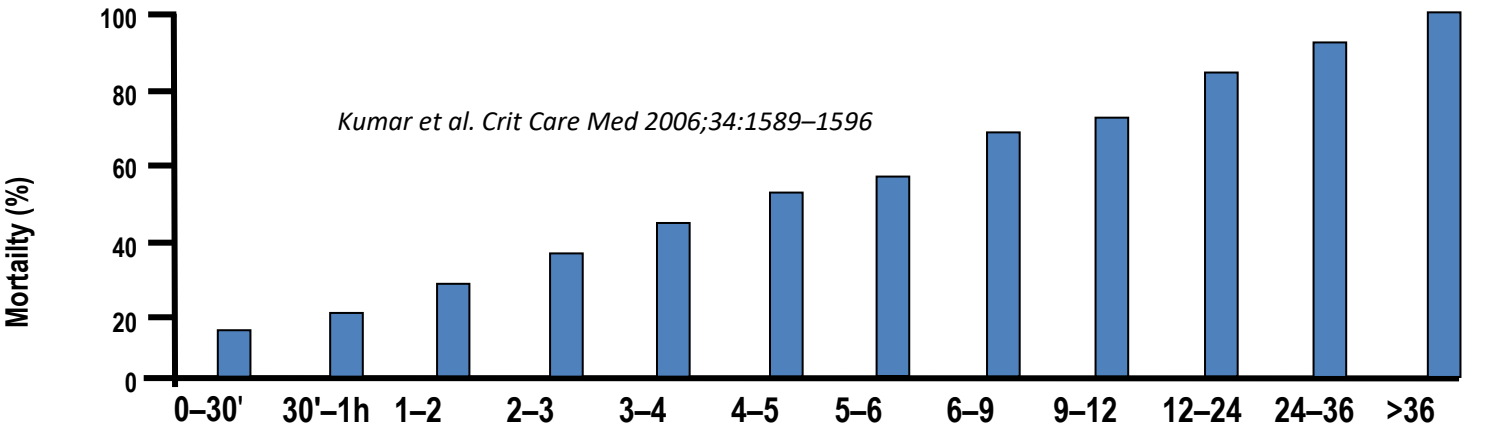
NE

5.) Endokrinní (hypoadrenal., hypothyr., DKA), intoxikace



Hit hard, hit first – but what…?

- Unstable patient after shock…..
- Risk of late antibiotic administration (SSC:1h, mortality +7.8%/1h of delay !)



Duration of hypotension prior to effective antimicrobial therapy: impact on survival

General side effects of antibiotics

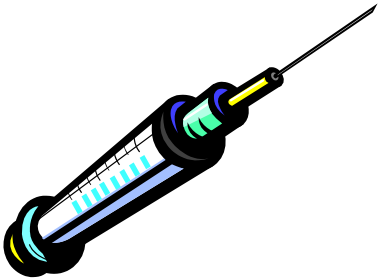
- Elimination of the community flora during the first 48h
- Opening patients to colonisations with MDRB
- High MIC in current nosocomial bugs supports selection of MDRB
- End-organ toxicity of the reserve antibiotics
- Lack of monitoring (colimycin and its 9 active metabolites….)
- Poor attention to PK/PD – misinterpretation, changes of Vd and Cl in shock
- Lack of qualification in Intensive Medicine and uncertainty in every patient´s instability leads to overuse of antibiotics (…CRP ?)

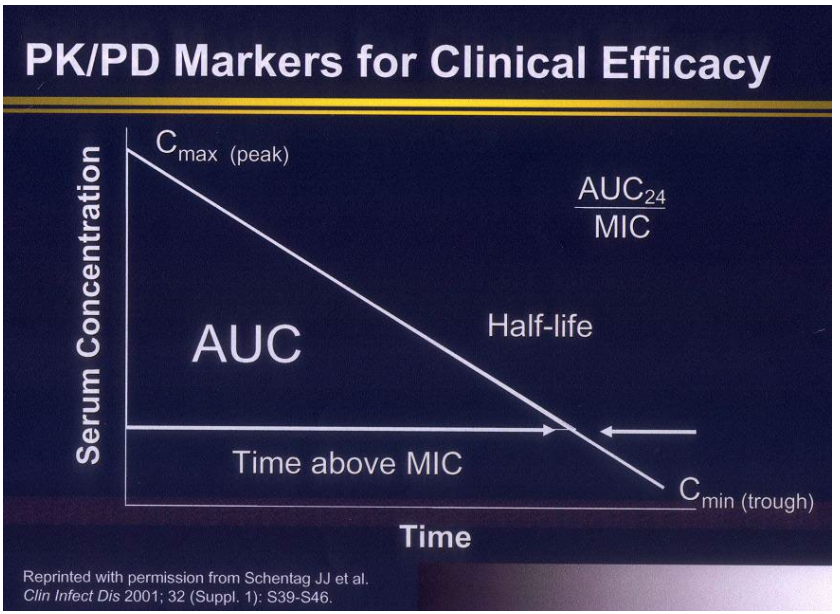
PK/PD versus MIC konkrétního mikroba

- Time-over-MIC dependent antibiotika:
  - betalaktamy
  - glykopeptidy

(cíl >50% dávk intervalu nad MIC: ±4-8 mg/l)

- AUC dependent antibiotika
  - fluochinolony
- Peak a post-atb effect
  - aminoglykosidy



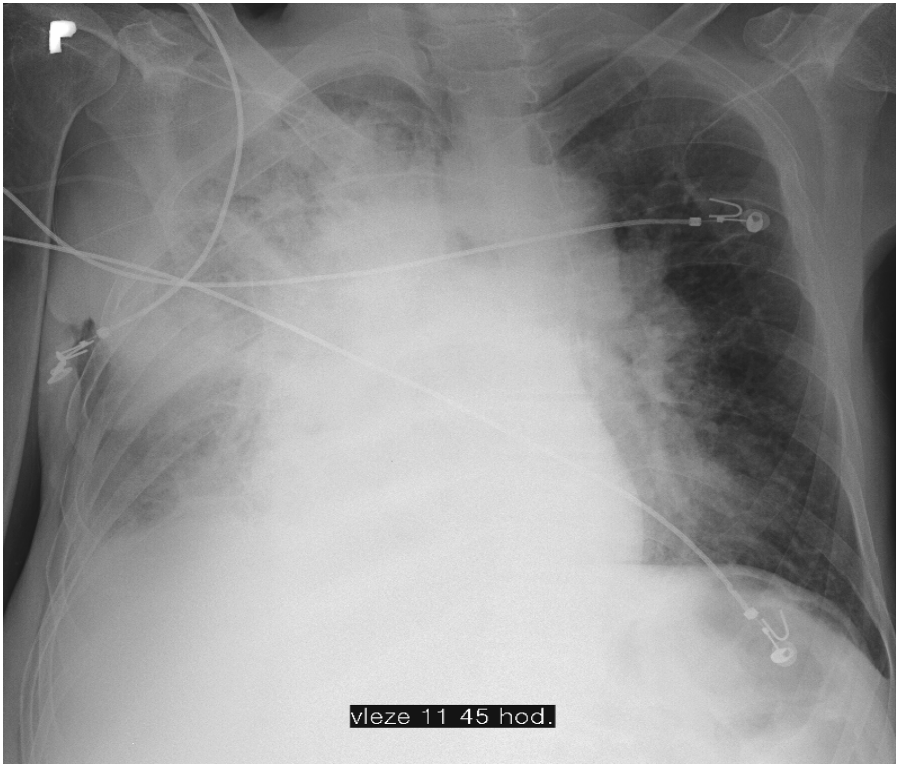


Šok a změny distribuce tělesných tekutin

- Proporcionální závažnosti a trvání šoku – vzestup ECW……
  C = dose / Vd…….Cl = Vd * Ke……. $T_{1/2}$ = ln2 * Vd / Cl
- Alterace kapilární permeability - ⬆ ECW/TBW a ⬆ ECW/ICW
- Katabolizmus a ztráta tělesného proteinu, nekrosa a apoptosa buněk – ⬆ ECW/ICW
- TBW se může měnit jen málo, stejně jako tělesná hmotnost
- **Steady state nastává za 4-5 eliminačních T1/2 antibiotika, obvykle za 48h: Dříve nemá smysl nabírat hladiny !**
- **Vankomycin – random u kont podání (ráno)**
- **Aminoglykosidy – trough před podáním (ordinujte proto 06-12….)**

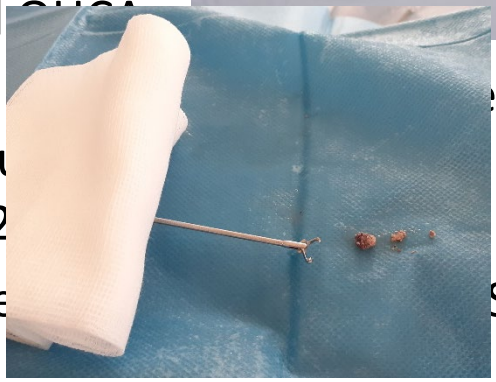
Risk factors of infection in shock

- Aspiration
- Prolonged gut hypoperfusion
- Lung contusion – is this CAP ?
- TTM – hypothermia
- Periresuscitation „semi-sterile“ line insertions



Aspiration = bronchoscopy

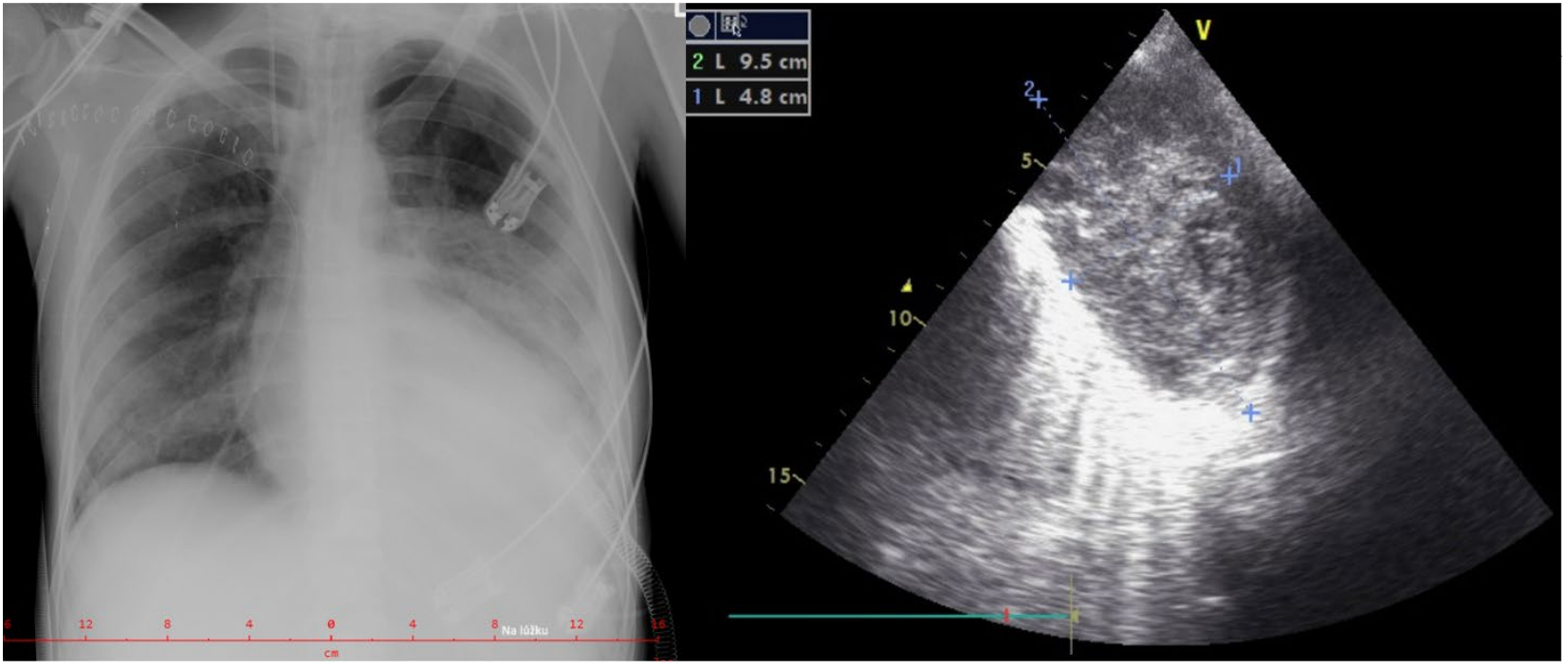
- Reported in 28% of OHCA
- Likely more in purely paramedic-managed
- Antibiotics with impact on morbidity only
  aspiration (Noc M, et al: Prophylactic versu
  antibiotics in CPR patients, Resuscitation 2
- FOB 24/7 managed by intensivists as prere



+36h

Immediately after FOB

Pleural pathologies – is this pneumonia ?



Gut reperfusion as indication to antibiotics


Observational Study

Medicine

The association of ea
resuscitation followin
arrest with neurologi
A retrospective observation

Christoph Schriefl, MD[a,*], Philipp Steininger,
Michael Poppe, MD[a], Florian Ettl, MD[a], Alexan
Heidrun Losert, MD[a], Michael Schwameis, MD
Christian Schoergenhofer, MD[c]

Intensive Care Med
https://doi.org/10.1007/s00134-022-06637-w

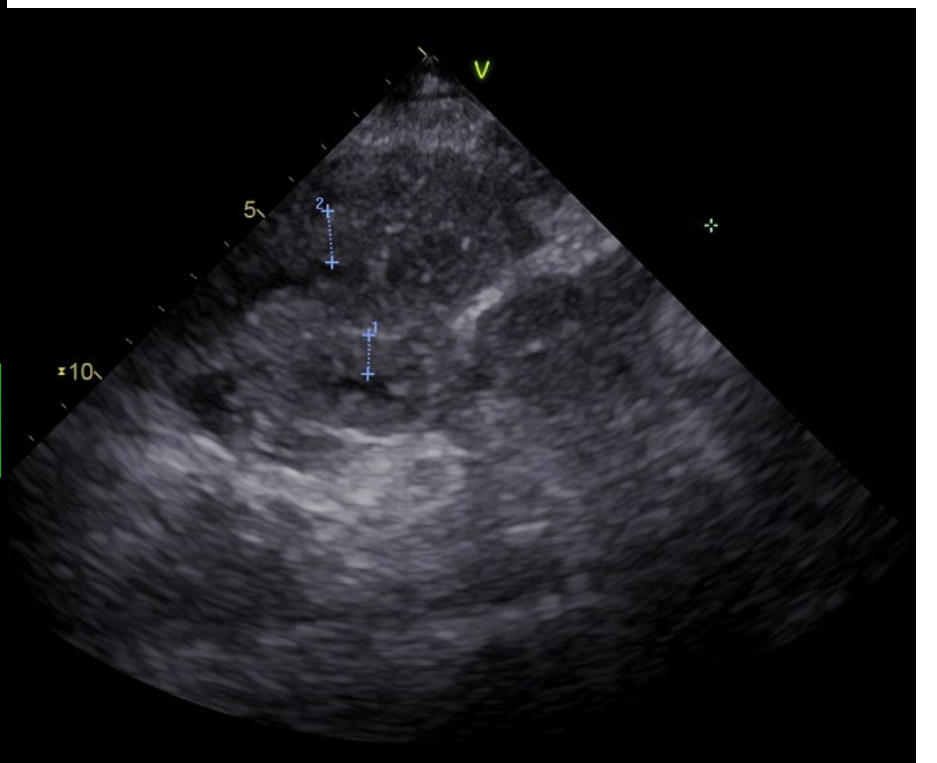
ORIGINAL

Factors associated with acute mesenteric ischemia among critically ill ventilated patients with shock: a post hoc analysis of the NUTRIREA2 trial

Gaël Piton[1,56*], Amélie Le Gouge[2,3], Julie Boisramé-Helms[4,5], Nadia Anguel[6], Laurent Argaud[7],

- Post-CPR diarrhoea (min 2x >12h post ROSC)
- Pathophysiology of NOMI – link to catecholamines and haemodynamic instability
- Multivariate odds ratio for a poor neurologic outcome 5.90, 95%CI 1.28-27, p=0.02

Reperfusion gut after OHCA



- A reperfusion swelling of the small bowel in the patient on Ecpella. Note the thickened gut wall of 9-11 mm.

Mild hypothermia as predisposing factor to VAP ?

RESEARCH ARTICLE

acta Anaesthesiologica Scandinavica

Increased risk of ventilator-associated pneumonia in patients after cardiac arrest treated with mild therapeutic hypothermia

Julia Hasslacher[1] | Fabian Steinkohl[2] | Hanno Ulmer[3] | Georg Lehner[1] | Sebastian Klein[1] | Timo Mayerhoefer[1] | Michael Joannidis[1]

- 23% VAP, 6% microbiol confirmed

	All patients ($n = 171$)	VAP ($n = 39$)	No VAP ($n = 132$)	p-value
CRP max [mg/dl], median (IQR)	14.8 (8.6–21.7)	20.4 (14.5–27.2)	12.3 (7.6–18.9)	.0001
PCT max [µg/L], median (IQR)	2.8 (0.6–14.1)	3.3 (1.1–12.3)	2.2 (0.5–14.4)	.188
Leucocyte count max [G/L], median (IQR)	17.2 (13.1–22.9)	18.2 (14.2–23.9)	16.5 (12.8–22.8)	.171
Mild therapeutic hypothermia, *n* (%)	81 (47)	24 (62)	57 (43)	.044

Should we use antibiotics preventively ?

The NEW ENGLAND JOURNAL of MEDICINE

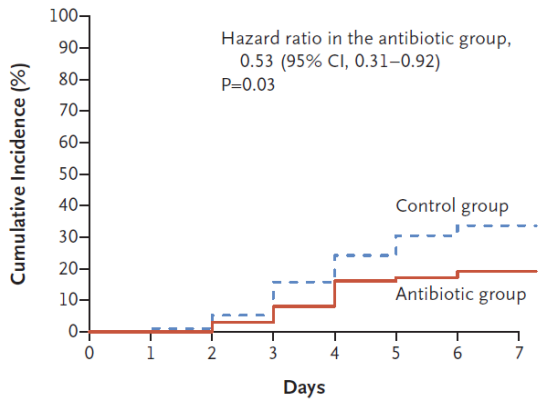
ORIGINAL ARTICLE

Prevention of Early Ventilator-Associated Pneumonia after Cardiac Arrest

B. François, A. Cariou, R. Clere-Jehl, P.-F. Dequin, F. Renon-Carron, T. Daix, C. Guitton, N. Deye, S. Legriel, G. Plantefève, J.-P. Quenot, A. Desachy, T. Kamel, S. Bedon-Carte, J.-L. Diehl, N. Chudeau, E. Karam, I. Durand-Zaleski, B. Giraudeau, P. Vignon, and A. Le Gouge, for the CRICS-TRIGGERSEP Network and the ANTHARTIC Study Group*

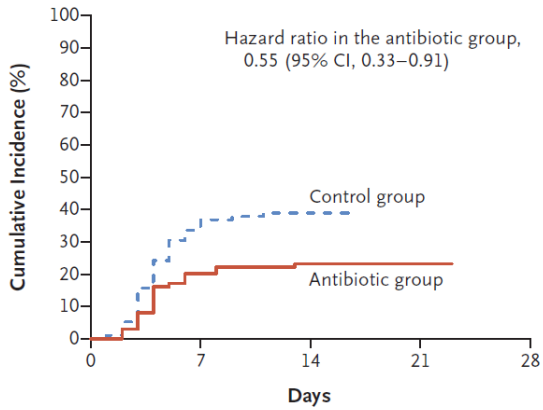
- Excluded aspirated patients
- Excluded primary infections , known MDRB colonisations
- Only shockable rhythms
- **48h of potentiated ampicilin**

A Early Ventilator-Associated Pneumonia



No. at Risk								
Control group	95	93	82	65	48	38	29	18
Antibiotic group	99	96	86	63	48	33	28	22

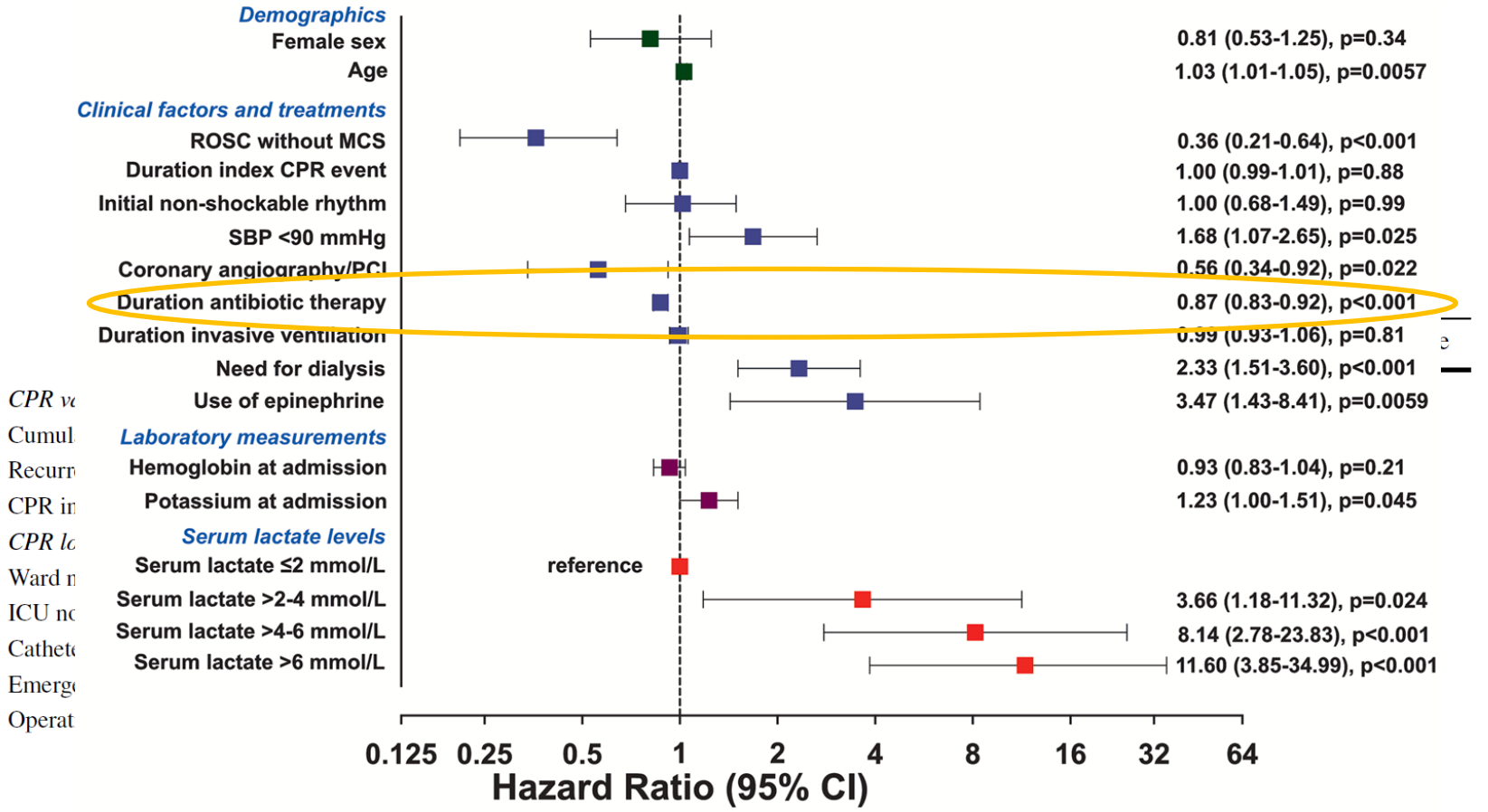
B Any Ventilator-Associated Pneumonia



No. at Risk					
Control group	95	18	2	0	0
Antibiotic group	99	22	6	1	0

Complication	Antibiotic Group (N=99)	Control Group (N=95)	Hazard Ratio (95% CI)	P Value
	number (percent)			
Ventilator-associated pneumonia†‡	23 (23)	37 (39)	0.55 (0.33–0.91)	
Early‡	19 (19)	32 (34)	0.53 (0.31–0.92)	0.03
Late	4 (4)	5 (5)		

Antibiotics – for how long ?



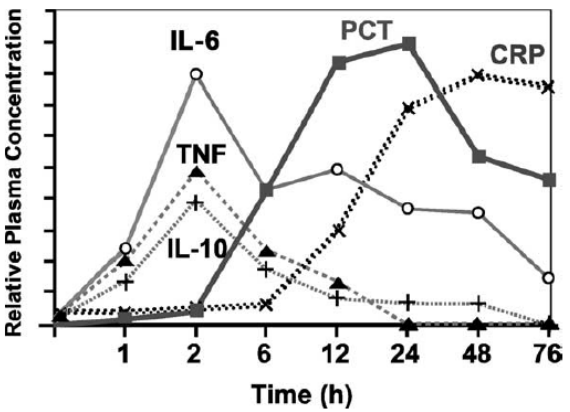
Some ot the available markers may help…..or add to confusion…..

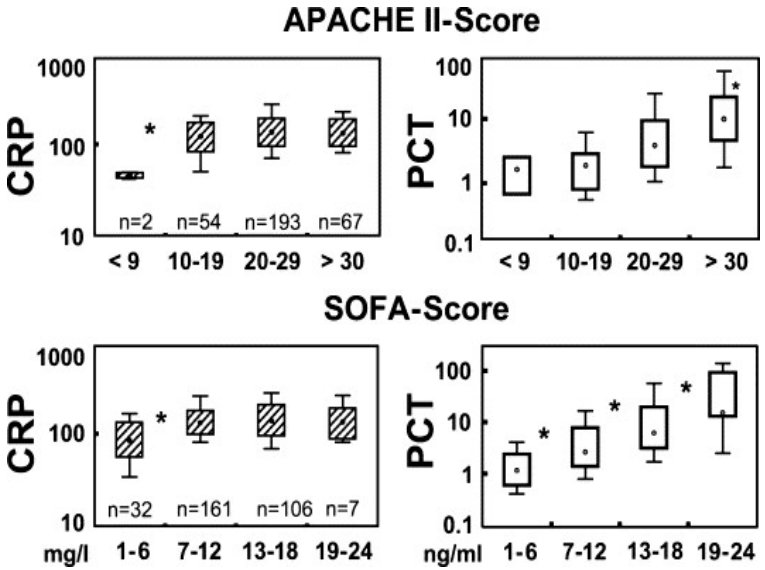
push start : results in 17 minutes

- CRP
- PCT
- Immature granulocytes
- Presepsin
- D-dimer
- TnI or hsTnI
- Myoglobin
- BNP or NTproBNP
- NGAL
- ……

Procalcitonin and CRP

- CRP - normal with high NPV
- PCT: Relationship to illness severity scores – morbidity
- PCT: Relationship to mortality
- PCT correlation with bacteraemia (*Jones A. Infectious diseases 2007, ROC 0.84)*



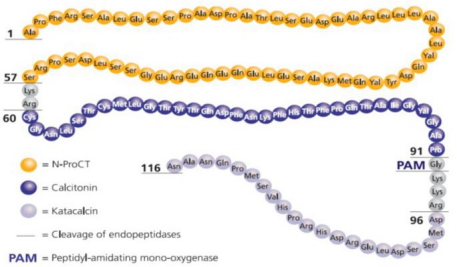


Meisner M: Clin Chim Acta 2002

PCT variable cut offs for infection

- Cardiogenic shock, CPR
- Endovascular interventions
- Impact of dialysis, AKI
- Cardiac surgery
- Trauma
- Burns

Diagnosis	Cut-off (ng/ml)	Sensitivity/specificity (%)
Meningitis (bacterial/viral)	1.8	100
		100
	0.5	69
		100
Pneumonia (bacterial/viral)	2	63
		96
Pneumonia (bacterial/atypical germs)		–
		–
Pancreatitis (infected/sterile necrosis)	1.8	94
		90
Septic shock	1.5	100
		72



Meisner M: Clin Chim Acta 2002, Ann Lab Med 2014
Morgenthaler N: Clin Lab 2002

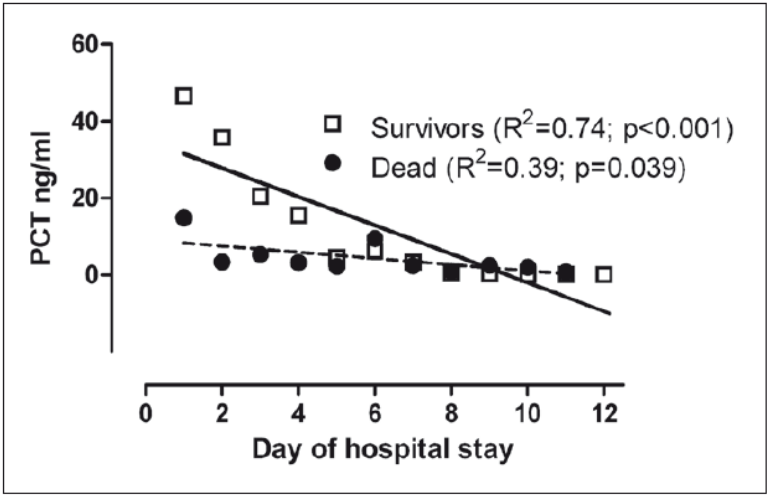
PCT and cardiogenic shock

Cardiogenic shock	Initially low, but increasing within 1-3 days, if vasopressor support is required	May be intermediate to high (e.g. >0.5 ng/mL to >10 ng/mL)
After prolonged resuscitation, myocardial infarction	Peak Day 1	Only In case of prolonged CPR, levels are related with prognosis after CPR. Very faint increase after myocardial infarction.

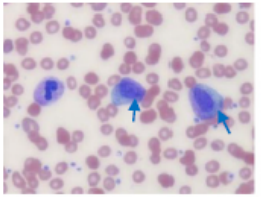
- Cardiogenic shock in STEMI and PCI with no infection
- High basal PCT with steady decrease in survivors

Picariello C. HSR proceedings in intensive care and cardiovascular anesthesia 2014

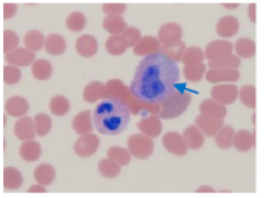
Meisner M: Clin Chim Acta 2002, Ann Lab Med 2014



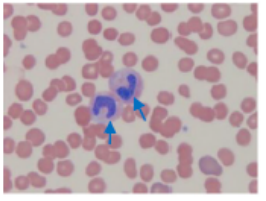
Immature neutrofils



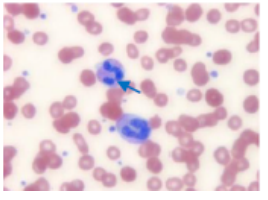
Myelocyte (indicated by arrow)
Size: 12 - 18µm
Nucleus: Round or oval with no nucleoli
Cytoplasm: Bluish-pink containing primary and secondary granules
Nucleus : Cytoplasm ratio 2 : 1



Metamyelocyte (indicated by arrow)
Size: 10 – 18µm
Nucleus: Indented or kidney-shaped
Cytoplasm: Pinkish-blue containing secondary granules
Nucleus : Cytoplasm ratio 1.5 : 1



Band Cell (indicated by arrow)
Size: 10 – 16µm
Nucleus: Horseshoe shaped
Cytoplasm: Light pink containing many small secondary granules
Nucleus : Cytoplasm ratio 1 : 2

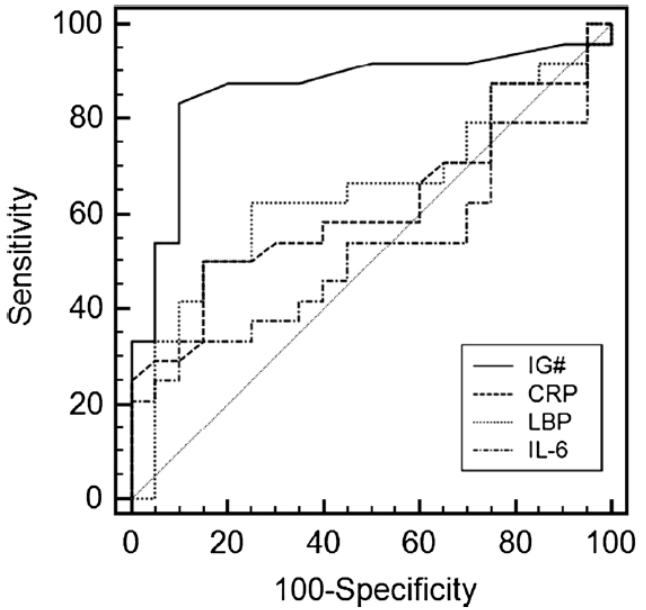


Mature Neutrophil (indicated by arrow)
Size: 10 – 16µm
Nucleus: Definite lobes separated by a narrow filament
Cytoplasm: Light pink with many small secondary granules
Nucleus : Cytoplasm ratio 1 : 3

Mare TA, 2015

Immature granulocytes

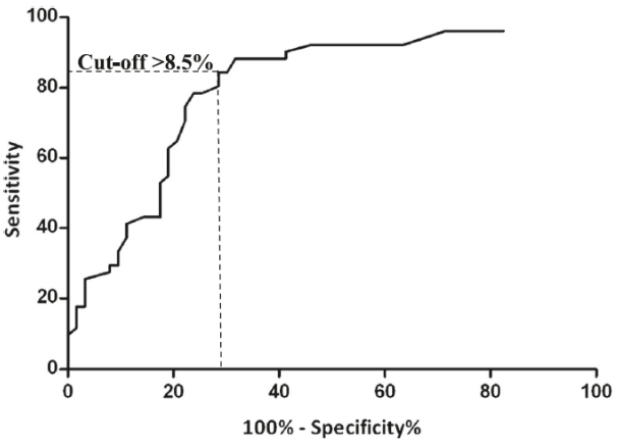
- correlating with mortality, *Mare TA. Critical care 2015*
- IG+WBC similar ROC AUC as CRP+WBC, *Van der Geest PJ. Journal of Critical Care 2014.*



Nierhaus A. BMC Imunology 2013

	WBC	CRP	IG percentage
Cutoff value	>12.6 10^9/L	>99 mg/L	>0.4%
Sensitivity	45	77	58
Specificity	93	71	80
PPV	93	85	86
NPV	45	59	48

PPV indicates positive predictive value; NPV, negative predictive value.



Mare TA. Critical Care 2015

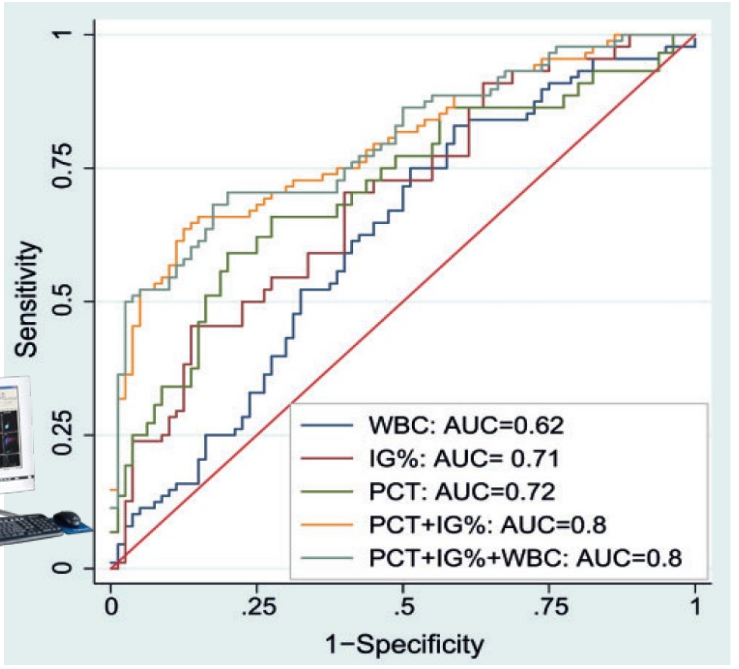
Interactive CardioVascular and Thoracic Surgery (2019) 1–7
doi:10.1093/icvts/ivy360

ORIGINAL ARTICLE

Cite this article as: Porizka M, Volny L, Kopecky P, Kunstyr J, Waldauf P, Balik M. Immature granulocytes as a sepsis predictor in patients undergoing cardiac surgery. Interact CardioVasc Thorac Surg 2019; doi:10.1093/icvts/ivy360.

Immature granulocytes as a sepsis predictor in patients undergoing cardiac surgery†

Michal Porizka[a,*], Lukas Volny[a], Petr Kopecky[a], Jan Kunstyr[a], Petr Waldauf[b] and Martin Balik[a]



tody		01/06/16		
	0	2CH-RES2	2CH-RES2	2CH-RES2
eumoniae				negativ.
Texty hematologie				
Laboratorní poznámka			Komentář	
Krevní obraz				
Leukocyty		16,55	30,88	24,16
Erytrocyty		3,41	4,09	4,39
Hemoglobin		97	114	124
Hematokrit		0,305	0,368	0,396
Stř.obj.erytr.		89,4	90,0	90,2
Barvivo erytr.		28,4	27,9	28,2
Stř.barev.kon.		318	310	313
Distr.křiv.ery		17,3	17,2	16,6
Trombocyty		187	222	185
Stř.obj.trombo		9,6	9,4	9,4
Destičkový hematokrit		0,180	0,210	0,170
Distr.křiv.tr.		9,9	9,3	8,9
Dif.stroj. relativní				
Neutrofily		89,9	93,9	92,5
Lymfocyty		5,0	2,4	4,1
Monocyty		3,3	2,8	3,1
Eozinofily		1,6	0,6	0,1
Bazofily		0,2	0,3	0,2
Dif.stroj. absolutní				
Neutrofily abs.		14,87	28,99	22,36
Lymfocyty abs.		0,82	0,73	0,98
Monocyty abs.		0,55	0,88	0,74
Eozinofily abs.		0,27	0,19	0,02
Bazofily abs.		0,04	0,09	0,06
Ostatní hematologie-				
Nezralé granulocyty %		0,8	1,2	1,0
Nezralé granulocyty abs.		0,14	0,36	0,25
Normoblasty strojově		0,10	0,10	0,00
Normoblasty absolutní		0,02	0,04	0,01

- automatic analyser Sysmex
  - promyelocytes, metamyelocytes
  - no bands
  - normal< 0.6%

Composite endpoint IG%+PCT

Dark side of antibiotics – if administered in every shock patient….

Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis

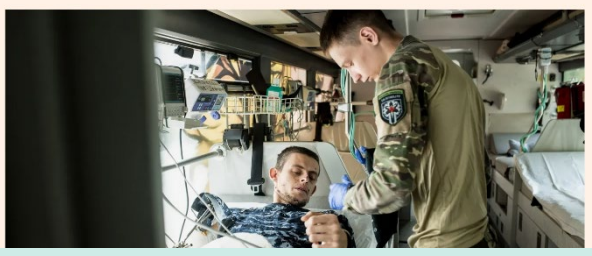
*Antimicrobial Resistance Collaborators**

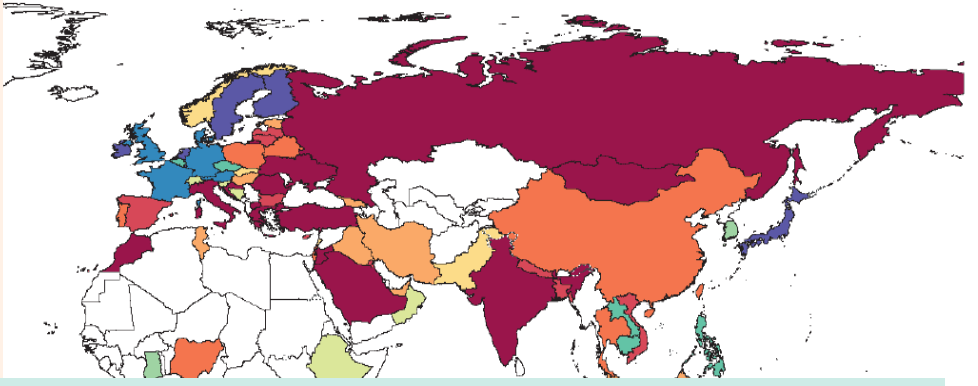
Lancet 2022; 399: 629–55

Antibiotic resistance + Add to myFT

Ukraine infections show rising threat from antibiotic resistance

Economic and political fallout from war distracts governments from health threats





Abstract

Blood and surveillance cultures from an injured service member from Ukraine grew *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Enterococcus faecium*, and 3 distinct *Pseudomonas aeruginosa* strains. Isolates were nonsusceptible to most antibiotics and carried an array of antibiotic resistant genes, including carbapenemases (bla_{IMP-1}, bla_{NDM-1}, bla_{OXA-23}, bla_{OXA-48}, bla_{OXA-72}) and 16S methyltransferases (*armA* and *rmtB4*).

Pandemic 2020-2022 and MDRB

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.journals.elsevier.com/journal-of-critical-care

The threat of multidrug-resistar
Gram-negative respiratory infec

Daniel Reynolds[1], Jason P. Burnham[2], Cristina Vazc
Kevin Betthauser[3], Scott T. Micek[3] and Marin H. Kc

The impact of obesity on the outcome of severe SARS-CoV-2 ARDS in a high volume ECMO centre: ECMO and corticosteroids support the obesity paradox

M. Balik [a,*], E. Svobodova [a], M. Porizka [a], M. Maly [a], P. Brestovansky [a], L. Volny [a], T. Brozek [a], T. Bartosova [a], I. Jurisinova [a], Z. Mevaldova [a], O. Misovic [a], A. Novotny [a], J. Horejsek [a], M. Otahal [a], M. Flaksa [a], Z. Stach [a], J. Rulisek [a], P. Trachta [a], J. Kolman [a], R. Sachl [a], J. Kunstyr [a], P. Kopecky [a], S. Romaniv [a], M. Huptych [b], M. Svarc [c], G. Hodkova [c], J. Fichtl [c], F. Mlejnsky [c], T. Grus [d], J. Belohlavek [e], M. Lips [a], J. Blaha [a]

microorganisms

MDPI

Review

Multi-Drug Resistance Bacterial Infections in Critically Ill Patients Admitted with COVID-19

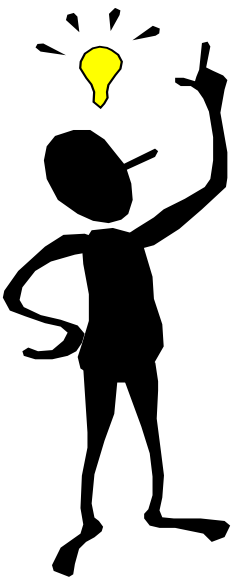
Daniela Pasero [1,2,*], Andrea Pasquale Cossu [2] and Pierpaolo Terragni [1,2]

timicrobial resistance by pathogen–
nce; AGR: aminoglycoside resistance;
CR: carbapenem resistance; FQR: fluoroquinolone resistance.

- 29% bacterial superinfections, of these 32-50% MDRB
- Mortality linked to MDRB - not to SARS-CoV-2 mutations !...spring 2021...

Conclusion and take home mesage

- Antibiotics related questions in shock
  - Sepsis ?
  - Prolonged LCO/gut hypoperfusion ?
  - Post-resuscitation diarrhoea ? – implies bacteremia
  - Confirmed aspiration ? – bronchoscopy warranted
  - CA vs HA flora…..off hospital >3 months ?
  - Shock in patient on immunosuppresants ?
- Indication based on markers like PCT (> 2-2.5 ng/ml), immature granulocytes (IG%)
- Differentiate non-infection associated findings
  - lung contusion, pleural effusion
- Terminate therapy within 5-7 days
- Individualize therapy !



Děkuji za pozornost !

Complex Cardiovascular Center
1St. Medical Faculty of Charles University,
General University Hospital

U nemocnice 2; 128 08, Prague, EU
T: +420 224 962 243
F: +420 224 962 118
E: martin.balik@vfn.cz
www.karim-vfn.cz