

Antibiotikus terápia COVID-19 betegekben

Molnár Zsolt



TM KETLAK

KORONAVÍRUS
ELLENI TRANSZLÁCIÓS
LAKOSSÁGTÁMOGATÓ
AKCIÓ- ÉS KUTATÓCSOPORT

Patofiziológia

32

NATURE

JULY 4, 1936

A Syndrome produced by Diverse Nocuous Agents

EXPERIMENTS on rats show that if the organism is severely damaged by acute non-specific nocuous agents such as exposure to cold, surgical injury, production of spinal shock (transection of the cord), excessive muscular exercise, or intoxications with sublethal doses of diverse drugs (adrenaline, atropine, morphine, formaldehyde, etc.), a typical syndrome appears, the symptoms of which are independent of the nature of the damaging agent or the pharmacological type of the drug employed, and represent rather a response to damage as such.



János (Hans) Selye
1907-1982

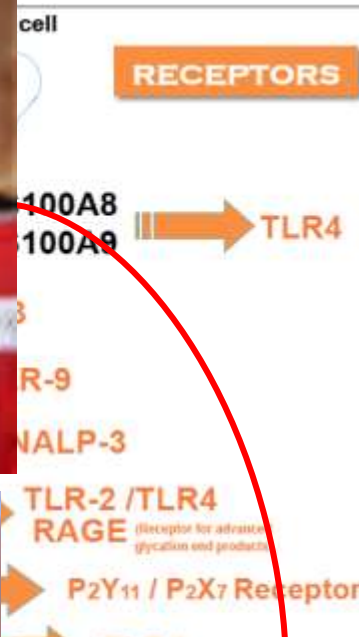
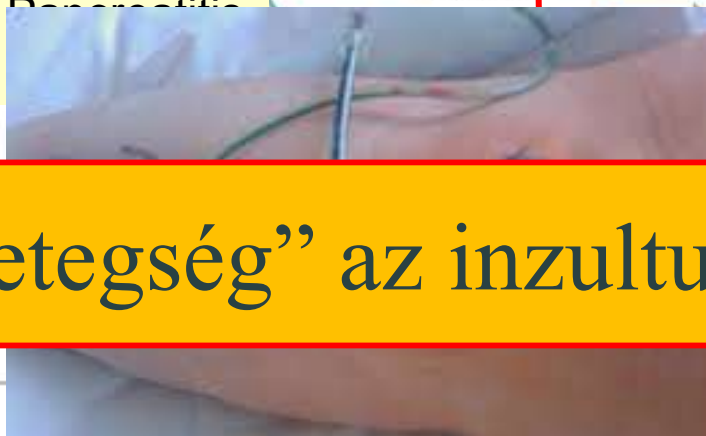
Injury: DAMP or PAMP

DAMP

Damage Associated Molecular Pattern



Dependent on



PAMP

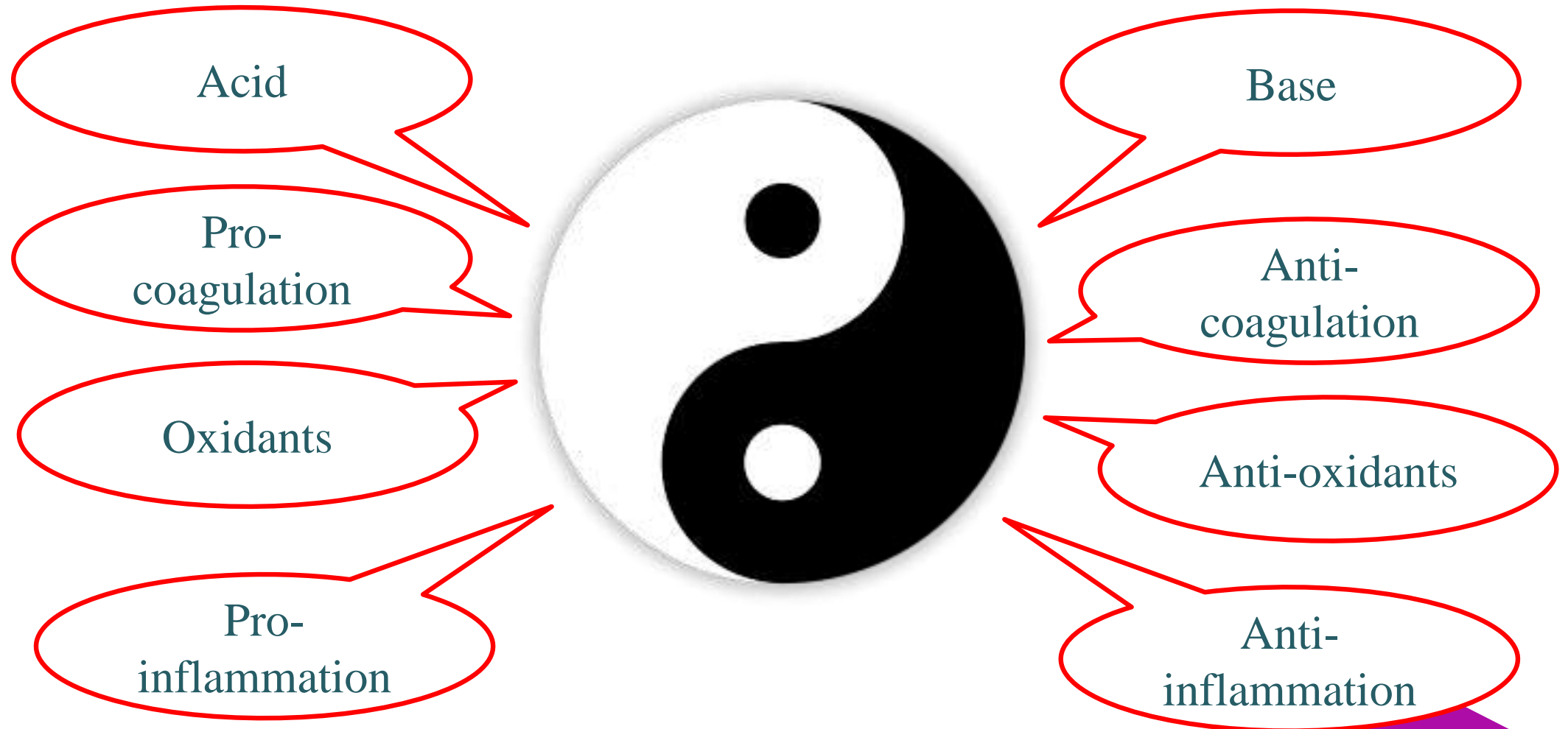
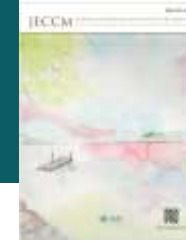
Pathogen Associated Molecular Pattern



A „betegség” az inzultusra adott „normális reakció”

Interpreting biomarkers in infectious diseases in intensive care unit: the potential role of procalcitonin

Fatime Hawchar, Zsolt Molnar



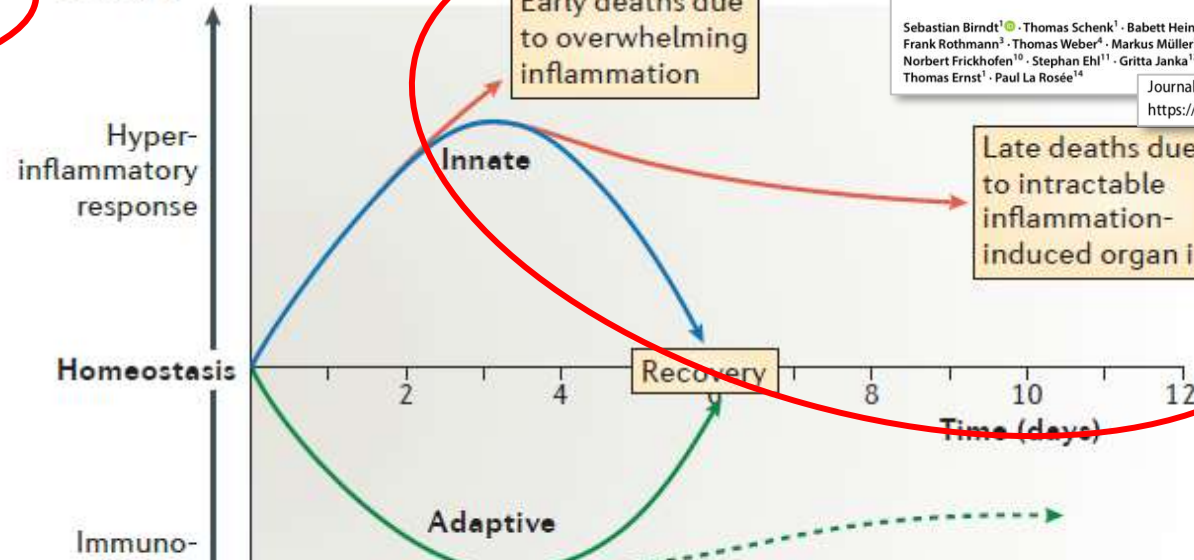
Sepsis-induced immunosuppression: from cellular dysfunctions to immunotherapy

Richard S. Hotchkiss¹, Guillaume Monneret² and Didier Payen³

Nature Reviews | Immunology Volume 13 | December 2013 | 862-874

Pro-
inflammation

Theory 2



Hemophagocytic lymphohistiocytosis in adults: collaborative analysis of 137 cases of a nationwide German registry

Sebastian Birndt¹ · Thomas Schenk¹ · Babett Heinevetter¹ · Frank M. Brunkhorst² · Georg Maschmeyer³ · Frank Rothmann³ · Thomas Weber⁴ · Markus Müller⁵ · Jens Pansse⁶ · Olaf Penack⁷ · Roland Schroers⁸ · Jan Braess⁹ · Norbert Frickhofen¹⁰ · Stephan Ehrl¹¹ · Gritta Janka¹² · Kai Lehmborg¹³ · Mathias W. Pletz¹⁴ · Andreas Hochhaus¹ · Thomas Ernst¹ · Paul La Rosée¹⁴

Journal of Cancer Research and Clinical Oncology (2020) 146:1065–1077
<https://doi.org/10.1007/s00432-020-03139-4>

Ezért volt a „SIRS” hibás koncepció

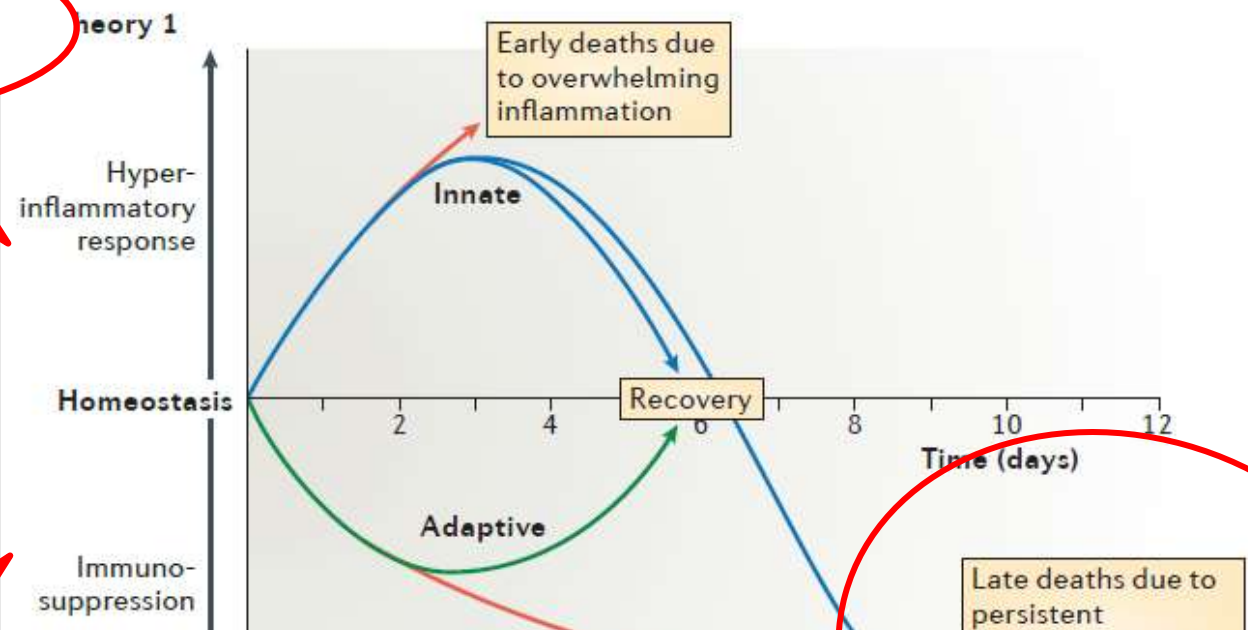
inflammation

Sepsis-induced immunosuppression: from cellular dysfunctions to immunotherapy

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Pro-
inflammation



Bakterialis szuper-infekció COVID-19 betegekben (is)

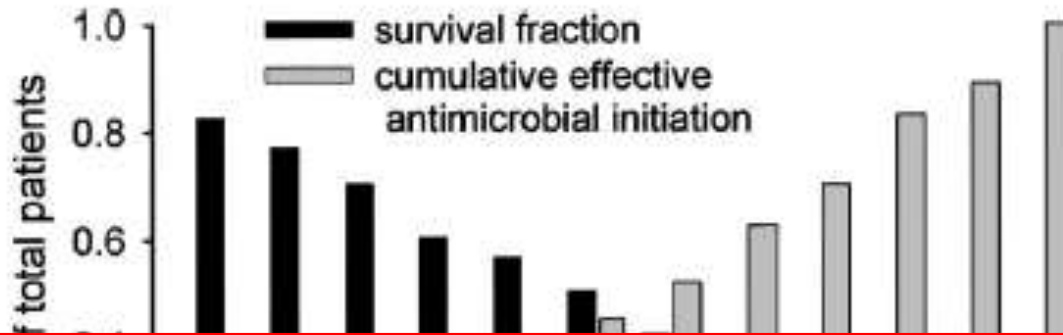
inflammation

A mantra:
„Adj antibiotikumot 1 órán belül!”

Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock*

Anand Kumar, MD; Daniel Roberts, MD; Kenneth E. Wood, DO; Bruce Light, MD; Joseph E. Parrillo, MD; Satendra Sharma, MD; Robert Suppes, BSc; Daniel Feinstein, MD; Sergio Zanotti, MD; Leo Taiberg, MD; David Gurka, MD; Aseem Kumar, PhD; Mary Cheang, MSc

(Crit Care Med 2006; 34:1589–1596)



1. Sedation caused hypotension – neglected
2. „Absence of definitive...evidence of infection” in 21%
3. 558 pts received appropriate AB pre-hypotension– mortality 47.8%!
– excluded!!

Each hour of delay in antimicrobial administration over the ensuing 6 hrs was associated with an average decrease in survival of 7.6%.

Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock

R. Phillip Dellinger, MD; Jean M. Carlet, MD; Henry Masur, MD; Herwig Gerlach, MD, PhD; Thierry Calandra, MD; Jonathan Cohen, MD; Juan Gea-Banacloche, MD, PhD; Didier Keh, MD; John C. Marshall, MD; Margaret M. Parker, MD; Graham Ramsay, MD; Janice L. Zimmerman, MD; Jean-Louis Vincent, MD, PhD; Mitchell M. Levy, MD; for the Surviving Sepsis Campaign Management Guidelines Committee

Intensive Care Med
DOI:10.1007/s00134-017-4683-8

CONFERENCE REPORTS AND EXPERT PANEL

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

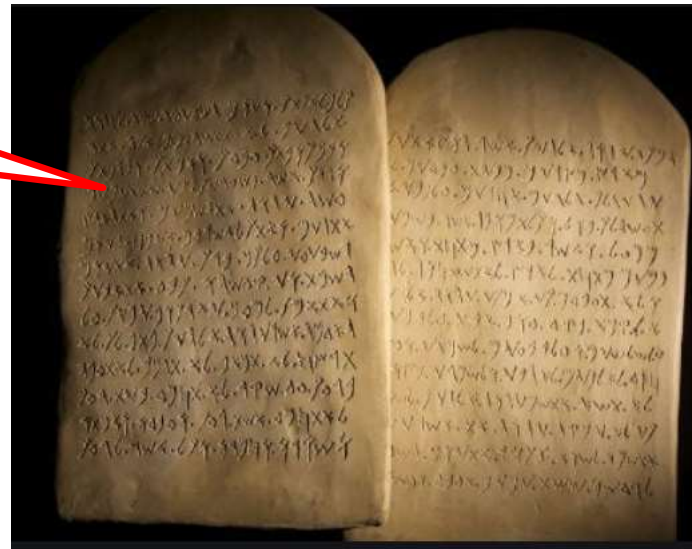


C. Antibiotic Therapy

1. Intravenous antibiotic therapy should be started within the first hour of recognition of severe sepsis, after appropriate cultures have been obtained.

Grade E

Give AB
ASAP!!



D. ANTIMICROBIAL THERAPY

1. We recommend that administration of IV antimicrobials be initiated as soon as possible after recognition and within 1 h for both sepsis and septic shock (strong recommendation, moderate quality of evidence; grade applies to both conditions).

Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with Coronavirus Disease 2019 (COVID-19)

Authors

Waleed Alhazzani^{1,2}, Morten Hylander Moller^{3,4}, Yaseen M. Arabi⁵, Mark Loeb^{1,2}, Michelle Ng Gong⁶, Eddy Fan⁷, Simon Oczkowski^{1,2}, Mitchell M. Levy^{8,9}, Lennie Derde^{10,11}, Amy Dzierba¹², Bin Du¹³, Michael Aboodi⁶, Hannah Wunsch^{14,15}, Maurizio Cecconi^{16,17}, Younsuck Koh¹⁸, Daniel S. Chertow¹⁹, Kathryn Maitland²⁰, Fayez Alshamsi²¹, Emilie Belley-Cote^{1,22}, Massimiliano Greco^{16,17}, Matthew Laundry²³, Jill S. Morgan²⁴, Jozef Kesecioglu¹⁰, Allison McGeer²⁵, Leonard Mermel⁸, Manoj J. Mammen²⁶, Paul E. Alexander^{2,27}, Amy Arrington²⁸, John Centofanti²⁹, Giuseppe Citerio^{30,31}, Bandar Baw^{1,32}, Ziad A. Memish³³, Naomi Hammond^{34,35}, Frederick G. Hayden³⁶, Laura Evans³⁷, Andrew Rhodes³⁸

Recommendation:

43. In mechanically ventilated patients with COVID-19 and respiratory failure, we **suggest** using empiric antimicrobials/antibacterial agents, over no antimicrobials (Weak recommendation, low quality evidence).

Remark: if the treating team initiates empiric antimicrobials, they should assess for de-escalation daily, and re-evaluate the duration of therapy and spectrum of coverage based on the microbiology results and the patient's clinical status.

Felveszel egy COVID-19 beteget, súlyos hipoxiás légzési elégtelenség, gépi lélegeztetés miatt az ITO-ra, az SBO-ról. Elindítanál-e empirikus AB-t a felvételt követő 1 órán belül, ha a PCT: 0.1 ng/mL?

- Mindenképpen
- Nem tudom eldönteni
- Nem

Antibiotics for Sepsis: Does Each Hour Really Count, or Is It Incestuous Amplification?



American Journal of Respiratory and Critical Care Medicine Volume 196 Number 7 | October 1 2017

“A ’minden óra késlekedés az AB adásban emberéletekbe kerül’ doktrina kvázi vallási rangra emelkedett. És, mint a legtöbb ,kvázi vallásnak’ ennek az alapja is sokkal inkább hit és remény, mint szigorú tények.”

“Azonban, a ’minden óra késedelem” mantrát folyamatosan duruzsolják az egészségügyi dolgozók, kórházi vezetés, fenntartók és kormányzati testületek fülébe. Minőségbiztosítási programokat alapoznak rá, és elmaradása finanszírozás elvonással jár.”



Likelihood of infection in patients with presumed sepsis at the time of intensive care unit admission: a cohort study

Peter M. C. Klein Klouwenberg^{1,2,3*}, Olaf L. Cremer¹, Lonneke A. van Vught⁴, David S. Y. Ong^{1,2,3}, Jos F. Frencken^{1,3}, Marcus J. Schultz⁵, Marc J. Bonten^{2,3} and Tom van der Poll⁴

2,579 pts

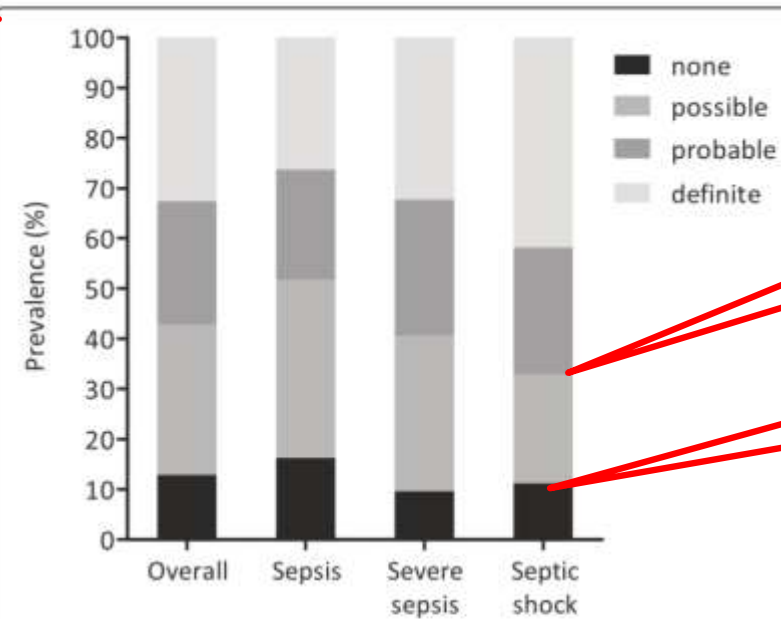


Fig. 1 Plausibility of infection stratified by clinical severity upon presentation in patients with presumed sepsis. Comparison between the clinical diagnosis of infection at the time of ICU admission and the actual presence of infection as determined by post-hoc evaluation

Impact of compliance with infection management guidelines on outcome in patients with severe sepsis: a prospective observational multi-center study

Frank Bloos^{1,2*}, Daniel Thomas-Rüddel^{1,2}, Hendrik Rüddel¹, Christoph Engel³, Daniel Schwarzkopf², John C Marshall⁴, Stephan Harbarth⁵, Philipp Simon⁶, Reimer Riessen⁷, Didier Keh⁸, Karin Drey⁹, Manfred Weiß¹⁰, Susanne Toussaint¹¹, Dirk Schädler¹², Andreas Weyland¹³, Maximilian Ragaller¹⁴, Konrad Schwarzkopf¹⁵, Jürgen Eiche¹⁶, Gerhard Kuhnle¹⁷, Heike Hoyer⁸, Christiane Hartog¹², Udo Kaisers⁹ and Konrad Reinhart^{1,2} for the MEDUSA Study Group

Surgical source control required (n = 234)^f

Time to antimicrobial therapy >1 hour ^b	0.80 (0.38 to 1.72)	0.552
Initial SOFA score ^c	1.19 (1.08 to 1.31)	<0.001
Age ^d	1.06 (1.03 to 1.08)	<0.001
Maximum lactate (day 1) ^e	1.08 (1.00 to 1.13)	0.046
Time to source control >6 hours	2.36 (1.22 to 4.71)	0.012
Intra-abdominal focus	1.08 (0.54 to 2.18)	0.822
Urogenital focus	0.43 (0.12 to 1.34)	0.165

Egy eretnek gondolat:
Az AB nem oki – sokkal inkább adjuváns terápia

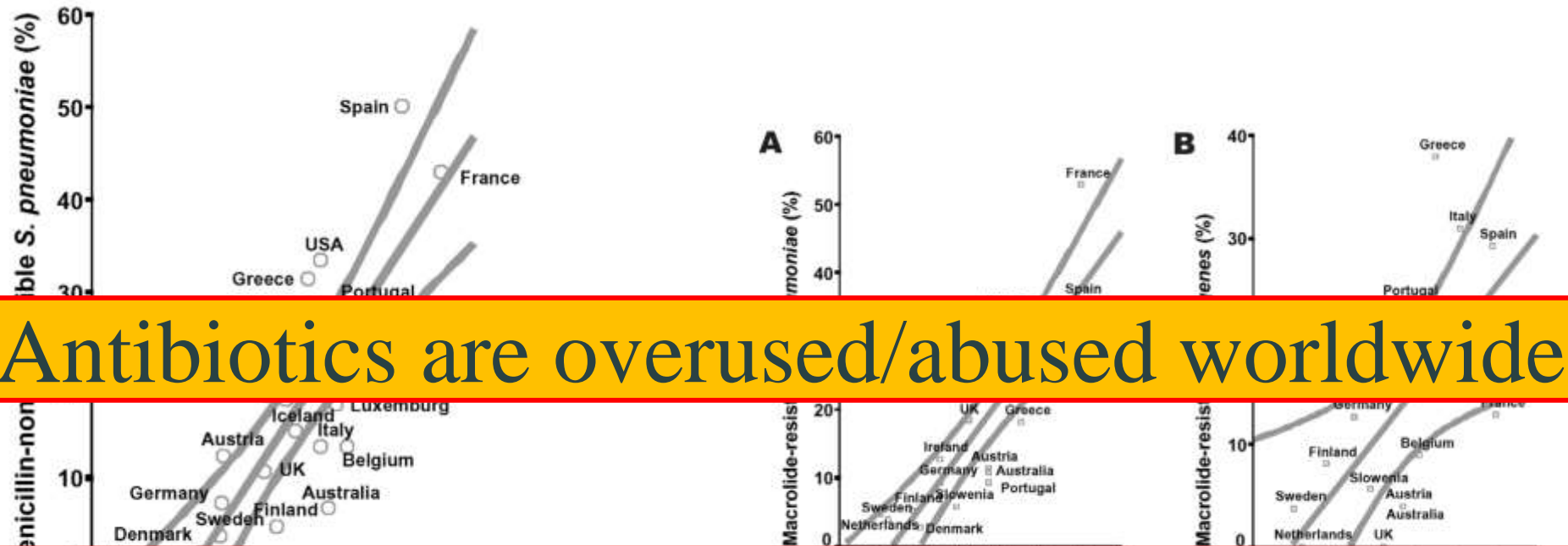
**Antibiotic
Selection Pressure
and Resistance in
*Streptococcus
pneumoniae* and
*Streptococcus
pyogenes***

Werner C. Albrich,* Dominique L. Monnet,†
and Stephan Harbarth‡

EMERGING INFECTIOUS DISEASES®



Volume 10, Number 3—March 2004



Antibiotics are overused/abused worldwide

MDR pathogens – „global crisis”

Rationalizing antimicrobial therapy in the ICU: a narrative review

Jean-François Timsit^{1,2*}, Matteo Bassetti³, Olaf Cremer⁴, George Daikos⁵, Jan de Waele⁶, Andre Kallil⁷, Eric Kipnis⁸, Marin Kollef⁹, Kevin Laupland¹⁰, Jose-Artur Paiva¹¹, Jesús Rodríguez-Baño¹², Étienne Ruppé^{2,13}, Jorge Salluh¹⁴, Fabio Silvio Taccone¹⁵, Emmanuel Weiss^{16,17} and François Barbier¹⁸

Intensive Care Med (2019) 45:172–189

<https://doi.org/10.1007/s00134-019-05520-5>

Table 1 Determinants of increased risk of MDRB infection at ICU admission and during the ICU stay

Predictors of MDRB infection	At ICU admission	During the ICU stay
Patient features	Co-morbid illness/immunosuppression/recent hospital and/or ICU stay	Higher severity of acute illness/Invasive interventions
Type of infection	Hospital-acquired > healthcare-associated > community-acquired	ICU-acquired > others
Antimicrobial selection pressure	Prior antibiotics*/antifungals	Antibiotics*/antifungals in the ICU
Colonization status	Previously documented colonization with MDRB	In-ICU acquisition of MDRB

3-szor több AB az ITO-n mint osztályon

MDRB multidrug-resistant bacteria, ICU intensive care unit

*Especially if agents with broad-spectrum and/or potent activity against intestinal anaerobes

Az ITO-n 70% kap AB

Szervkárosodás

Wright J, Paauw DS. Complications of antibiotic therapy. *Med Clin North Am* 2013;97:667–679, xi.

Mitochondriális diszfunkció

Singh R, Sripada L, Singh R. Side effects of antibiotics during bacterial infection: mitochondria, the main target in host cell. *Mitochondrion* 2014;16:50–54.

Microbiom, Gomba infekció

Alverdy JC, Krezalek MA. Collapse of the microbiome, emergence of the pathobiome, and the immunopathology of sepsis. *Crit Care Med* 2017;45:337–347.

Clostridium difficile

Kalghatgi S, Spina CS, Costello JC, Liesa M, Morones-Ramirez JR, Slomovic S, Molina A, Shirihai OS, Collins JJ. Bactericidal antibiotics induce mitochondrial dysfunction and oxidative damage in mammalian cells. *Sci Transl Med* 2013;5:192ra85.

Akkor most mitévők legyünk?!

International guidelines...

American Thoracic Society Documents

Clinical Practice Guidelines for the Diagnosis and Management of Intravascular Catheter-Related Infection: 2009 Update by the Infectious Diseases Society of America

Leonard A. Mermel,¹ Michael Allon,² Emilio Bouza,⁹ Donald E. Craven,³ Patricia Flynn,⁴ Naomi P. O'Grady,⁵ Issam I. Raad,⁶ Bart J. A. Rijnders,¹⁰ Robert J. Sherertz,⁷ and David K. Warren⁸

Joseph S. Solomkin,¹ John E. Mazuski,² John S. Bradley,³ Keith A. Rodvold,^{7,8} Ellie J. C. Goldstein,⁵ Ellen J. Baron,⁶ Patrick J. O'Neill,⁹ Anthony W. Chow,¹⁶ E. Patchen Dellinger,¹⁰ Soumitra R. Eachempati,¹¹ Sherwood Gorbach,¹² Mary Hilfiker,⁴ Addison K. May,¹³ Avery B. Nathens,¹⁷ Robert G. Sawyer,¹⁴ and John G. Bartlett¹⁵

Empirical use of antibiotics and adjustment of empirical antibiotic therapies in a university hospital: a prospective observational study

Julian Mettler¹, Mathew Simcock^{1,2}, Pedram Sendi^{1,2}, Andreas F Widmer¹, Roland Bingisser³, Manuel Battegay¹, Ursula Fluckiger¹ and Stefano Bassetti^{*1,4}

BMC Infectious Diseases 2007, 7:21

Table 4: Characteristics of patients receiving adequate or inadequate empirical antibiotic treatment (univariate analysis).

Characteristic	Patients (n) receiving adequate empirical antibiotic treatment	Patients (n) receiving inadequate empirical antibiotic treatment	p-value	OR (95% CI) for adequate therapy
Number of patients	418 (77.6%)	121 (22.4%)		
Women	170 (70.3%)	72 (29.8%)	< 0.001	0.47 (0.31–0.70)
41 – 60 yr.	91 (87.5%)	13 (12.5%)	0.007	2.31 (1.12–4.30)
> 60 years	253 (74.6%)	86 (25.4%)	0.034	0.62 (0.40–0.97)
Ward:				
Medicine/Geriatrics	281 (78.3%)	78 (21.7%)	0.399	1.19 (0.80–1.76)
Surgery	135 (78.9%)	36 (21.1%)	0.733	1.09 (0.70–1.65)
Medical and surgical intensive care	25 (71.4%)	10 (28.6%)	0.408	0.73 (0.34–1.55)
Neurology	1 (25.0%)	3 (75.0%)	0.040†	0.10 (0.01–0.94)
Died in hospital	25 (80.6%)	6 (19.4%)	0.671	1.22 (0.49–3.04)

Van-e egyáltalán bakteriális infekció?!

28%

Van infekció?

Infection = ABs

No infection = No ABs

Az infekció jelei

- Clinical signs:
 - Most important
- Fever ($>38^{\circ}\text{C}$), WBC ($>12\ 000$):
 - Low sensitivity (~50%)
Galicier L and Richet H. *Infect Control Hosp*
- Microbiology:
 - Results: 24 hours or more

Not good
enough

Pooooor!

Very late!

We need biomarkers!

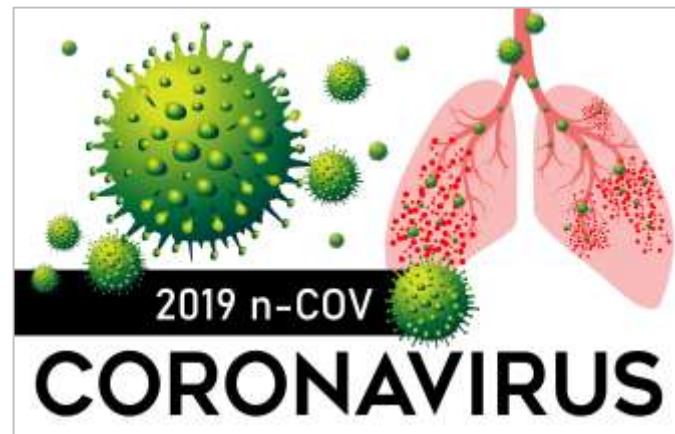
Pierrakos and Vincent *Critical Care* 2010, **14**:R15
<http://ccforum.com/content/14/1/R15>



WARNING!
Using biomarkers is not easy



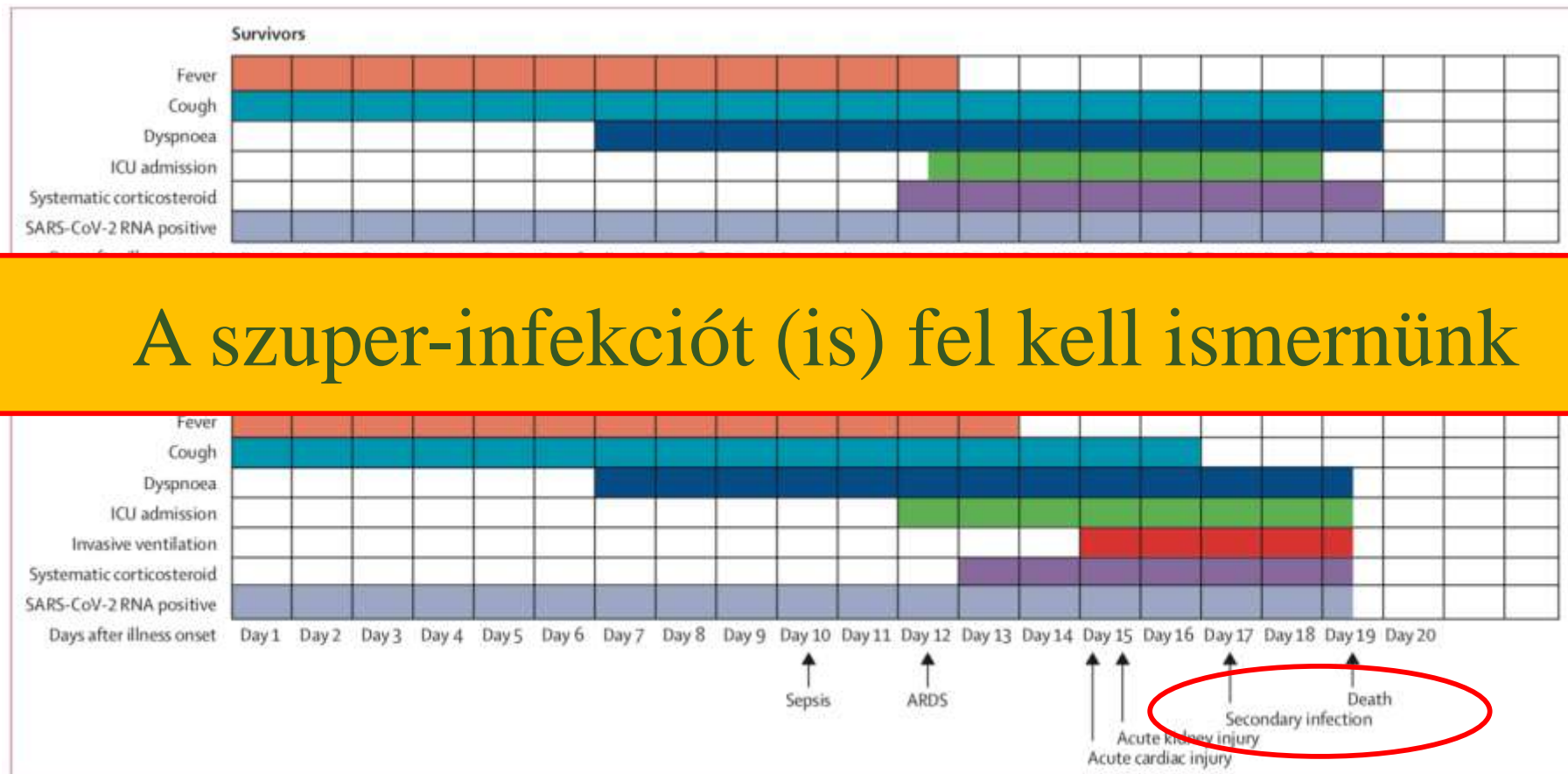
COVID-19



Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study

Fei Zhou*, Ting Yu*, Ronghui Du*, Guohui Fan*, Ying Liu*, Zhibo Liu*, Jie Xiang*, Yeming Wang, Bin Song, Xiaoying Gu, Lulu Guan, Yuan Wei, Hui Li, Xudong Wu, Jiuyang Xu, Shengjin Tu, Yi Zhang, Hua Chen, Bin Cao

Lancet 2020; 395: 1054-62



A szuper-infekciót (is) fel kell ismernünk

Hemophagocytic lymphohistiocytosis in adults: collaborative analysis of 137 cases of a nationwide German registry

Sebastian Birndt¹ · Thomas Schenk¹ · Babett Heinevetter¹ · Frank M. Brunkhorst² · Georg Maschmeyer³ · Frank Rothmann³ · Thomas Weber⁴ · Markus Müller⁵ · Jens Panse⁶ · Olaf Penack⁷ · Roland Schroers⁸ · Jan Braess⁹ · Norbert Frickhofen¹⁰ · Stephan Ehl¹¹ · Gritta Janka¹² · Kai Lehmborg¹² · Mathias W. Pletz¹³ · Andreas Hochhaus¹ · Thomas Ernst¹ · Paul La Rosée¹⁴

Journal of Cancer Research and Clinical Oncology (2020) 146:1065–1077
<https://doi.org/10.1007/s00432-020-03139-4>

Infections	61 (44.5)
Viral	39 (28.5)

Csak vírus infekció is okozhat diszregulált gyulladáshoz vezető választ („hyperinflammáció”, „citokin vihar”)

Virális pneumonia és bakteriális szuper-infekció

Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study

Xiaobo Yang*, Yuan Yu*, Jiqian Xu*, Huaqing Shu*, Jia'an Xia*, Hong Liu*, Yongran Wu, Lu Zhang, Zhui Yu, Minghao Fang, Ting Yu, Yaxin Wang, Shangwen Pan, Xiaojing Zou, Shiyong Yuan, You Shang

Lancet Respir Med 2020

	Survivors (n=20)	Non-survivors (n=32)	All patients (n=52)
Hospital-acquired pneumonia	4 (20%)	2 (6%)	6 (11.5%)
Bacteraemia	0	1 (3%)	1 (2%)
Urinary tract infection	0	1 (3%)	1 (2%)

Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study

Fei Zhou*, Ting Yu*, Ronghui Du*, Guohui Fan*, Ying Liu*, Zhibo Liu*, Jie Xiang*, Yeming Wang, Bin Song, Xiaoying Gu, Lulu Guan, Yuan Wei, Hui Li, Xudong Wu, Jiuyang Xu, Shengjin Tu, Yi Zhang, Hua Chen, Bin Cao

Lancet 2020; 395: 1054-62

	Total (n=191)	Non-survivor (n=54)	Survivor (n=137)	p value
Treatments*				
Antibiotics	181 (95%)	53 (98%)	128 (93%)	0.15
Secondary infection	28 (15%)	27 (50%)	1 (1%)	<0.0001

Baktérium miatt,
vagy baktériummal?

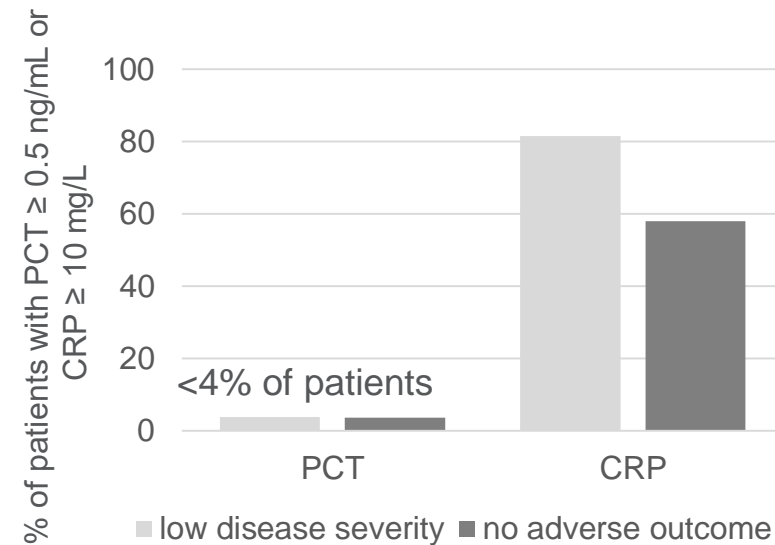
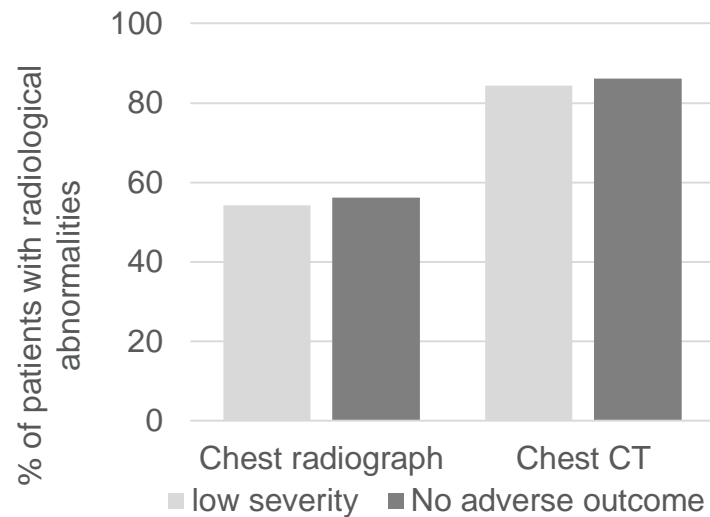
Bakteriális szuperinfekció: ~15%

Clinical Characteristics of Coronavirus Disease 2019 in China

W. Guan, Z. Ni, Yu Hu, W. Liang, C. Ou, J. He, L. Liu, H. Shan, C. Lei, D.S.C. Hui, B. Du, L. Li, G. Zeng, K.-Y. Yuen, R. Chen, C. Tang, T. Wang, P. Chen, J. Xiang, S. Li, Jin-lin Wang, Z. Liang, Y. Peng, L. Wei, Y. Liu, Ya-hua Hu, P. Peng, Jian-ming Wang, J. Liu, Z. Chen, G. Li, Z. Zheng, S. Qiu, J. Luo, C. Ye, S. Zhu, and N. Zhong, for the China Medical Treatment Expert Group for Covid-19*

DOI: 10.1056/NEJMoa2002032

1099 pts

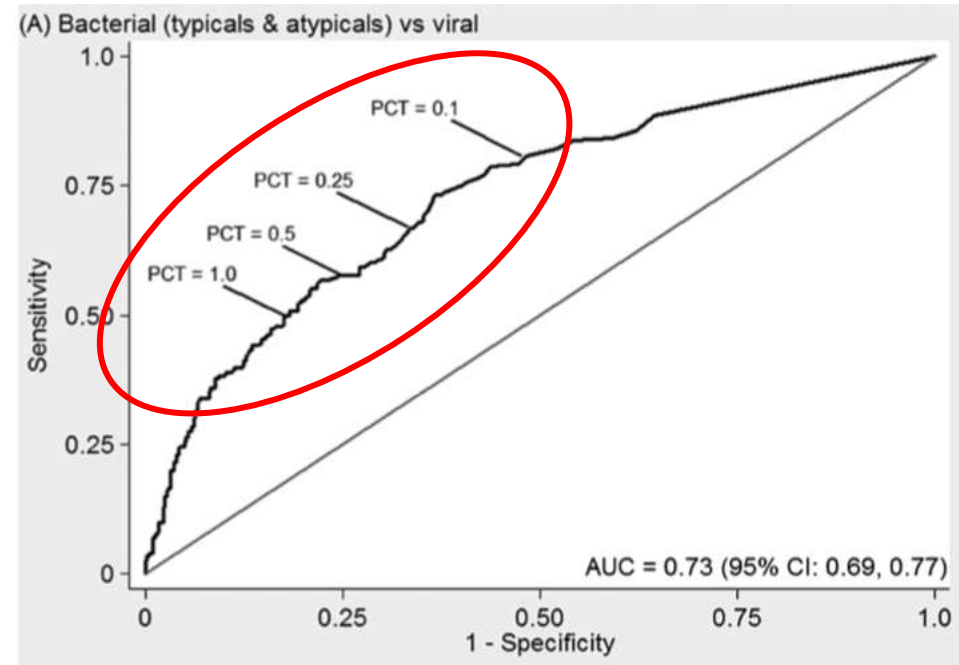
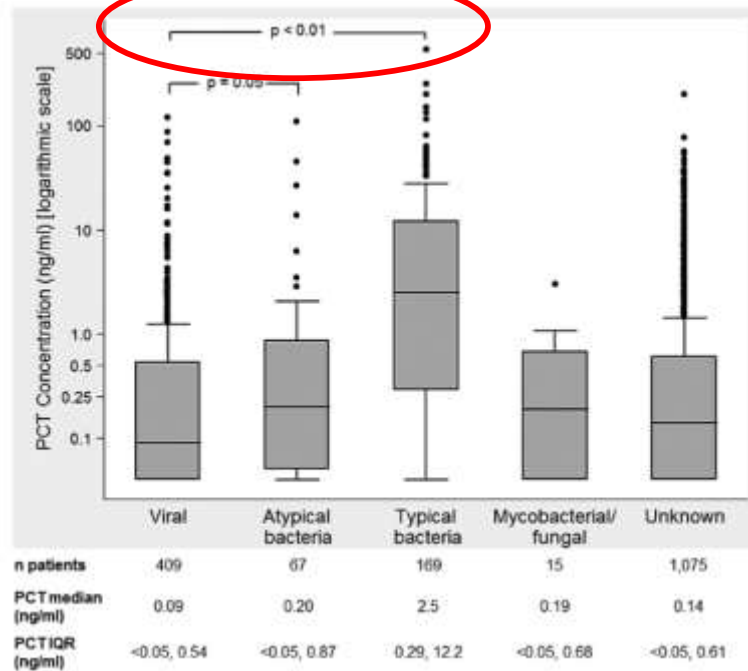


A radiológia, CRP nem segít – PCT talán

Procalcitonin as a Marker of Etiology in Adults Hospitalized With Community-Acquired Pneumonia

Wesley H. Self,¹ Robert A. Balk,² Carlos G. Grijalva,¹ Derek J. Williams,¹ Yuwei Zhu,¹ Evan J. Anderson,³ Grant W. Waterer,^{4,5} D. Mark Courtney,⁵ Anna M. Bramley,⁶ Christopher Trabue,⁷ Sherene Fakhran,⁸ Anne J. Blaschke,⁹ Seema Jain,⁶ Kathryn M. Edwards,¹ and Richard G. Wunderink⁵

Clinical Infectious Diseases® 2017;65(2):183–90



Conclusions. No procalcitonin threshold perfectly discriminated between viral and bacterial pathogens, but higher procalcitonin strongly correlated with increased probability of bacterial pathogens, particularly typical bacteria.

COVID-19

Mit tudunk a
PCT-ről COVID-19 betegekben?

Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study

Nanshan Chen*, Min Zhou*, Xuan Dong*, Jieming Qu*, Fengyun Gong, Yang Han, Yang Qiu, Jingli Wang, Ying Liu, Yuan Wei, Jia'an Xia, Ting Yu, Xinxin Zhang, Li Zhang

Lancet 2020; 395: 507-13

Patients (n=99)

(Continued from previous column)

Infection-related biomarkers

Procalcitonin (ng/mL; normal range 0.0–5.0)	0.5 (1.1)
Increased	6 (6%)
Interleukin-6 (pg/mL; normal range 0.0–7.0)	7.9 (6.1–10.6)
Increased	51 (52%)
Erythrocyte sedimentation rate (mm/h; normal range 0.0–15.0)	49.9 (23.4)
Increased	84 (85%)
Serum ferritin (ng/mL; normal range 21.0–274.7)	808.7 (490.7)
Increased	62 (63%)
C-reactive protein (mg/L; normal range 0.0–5.0)*	51.4 (41.8)
Increased	63/73 (86%)

Co-infection

Other viruses	0
Bacteria	1 (1%)
Fungus	4 (4%)

- 71% received ABs
- 1% bacterial infection
- 4% on invasive MV
- 23% admitted to ICU – no subgroup data on PCT

Kétségeim vannak...

Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China

Chaolin Huang*, Yeming Wang*, Xingwang Li*, Lili Ren*, Jianping Zhao*, Yi Hu*, Li Zhang, Guohui Fan, Jiuyang Xu, Xiaoying Gu, Zhenshun Cheng, Ting Yu, Jiaan Xia, Yuan Wei, Wenjuan Wu, Xuelei Xie, Wen Yin, Hui Li, Min Liu, Yan Xiao, Hong Gao, Li Guo, Jungang Xie, Guangfa Wang, Rongmeng Jiang, Zhancheng Gao, Qi Jin, Jianwei Wang†, Bin Cao†

Lancet 2020; 395: 497-506

	All patients (n=41)	ICU care (n=13)	No ICU care (n=28)	p value
Procalcitonin, ng/mL	0.1 (0.1-0.1)	0.1 (0.1-0.4)	0.1 (0.1-0.1)	0.031
<0.1	27/39 (69%)	6/12 (50%)	21/27 (78%)	0.029
≥0.1 to <0.25	7/39 (18%)	3/12 (25%)	4/27 (15%)	..
≥0.25 to <0.5	2/39 (5%)	0/12	2/27 (7%)	..
≥0.5	3/39 (8%)	3/12 (25%)*	0/27	..

- Általánosságban a PCT <0.1ng/mL felvételkor
- 4-ből 3 betegnél alakult ki szuper-infekció, PCT emelkedéssel: 0.69μg/L, 1.46μg/L and 6.48μg/L

Delta Procalcitonin Is a Better Indicator of Infection Than Absolute Procalcitonin Values in Critically Ill Patients: A Prospective Observational Study

Domonkos Trásy,¹ Krisztián Tócsos,¹ Márton Németh,¹ Péter Hankovszky,¹ András Lovas,¹ András Mikor,² Edit Hajdú,² Angelika Osztrólczki,¹ János Fazakas,³ and Zsolt Molnár¹

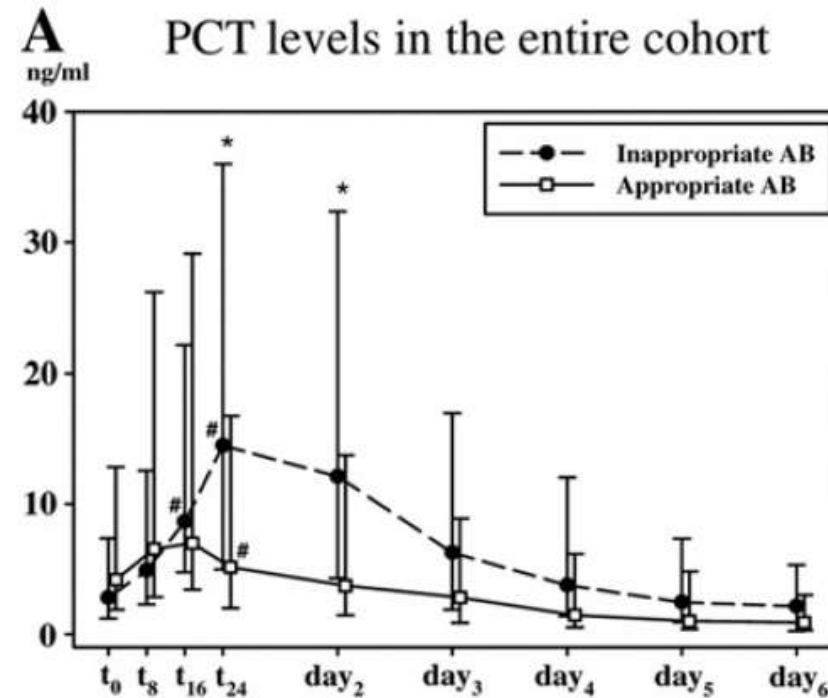
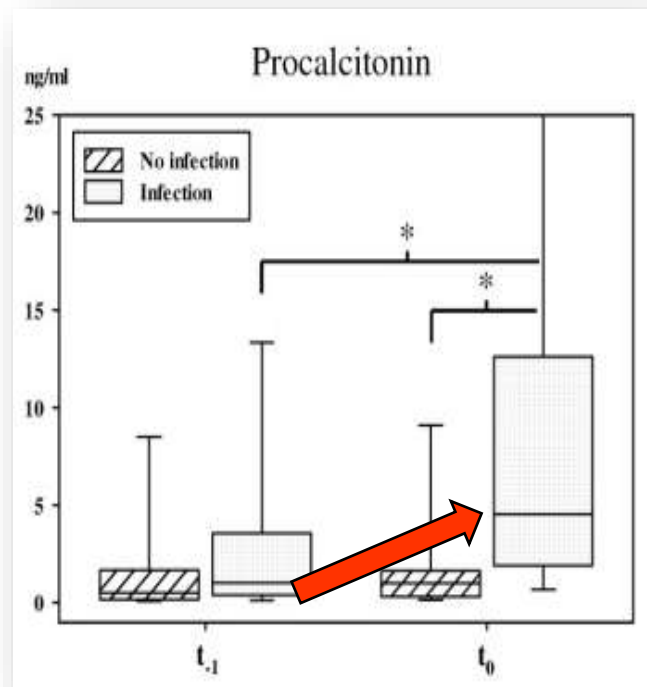
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Early procalcitonin kinetics and appropriateness of empirical antimicrobial therapy in critically ill patients A prospective observational study

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Kinetika vs. abszolút értékek

COVID-19

Recommendations/Guidelines

Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with Coronavirus Disease 2019 (COVID-19)

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Recommendation:

43. In mechanically ventilated patients with COVID-19 and respiratory failure, we **suggest** using empiric antimicrobials/antibacterial agents, over no antimicrobials (Weak recommendation, low quality evidence).

Remark: if the treating team initiates empiric antimicrobials, they should assess for de-escalation daily, and re-evaluate the duration of therapy and spectrum of coverage based on the microbiology results and the patient's clinical status.

COVID-19: a synthesis of clinical experience in UK intensive care settings

Antibiotics

Antibiotic usage should be judicious. There are some reports of later aspergillosis and candida infections.

- *Stopping antibiotics in COVID patients unless clearly indicated, using procalcitonin (PCT) and other inflammatory markers to monitor for bacterial infection and restarting as required**
- *Using procalcitonin as a 'stop' signal to guide when to stop antibiotic use**

**False negative PCTs seem less of an issue than false positives in determining antibiotic use – anecdotally, rising procalcitonin has also been seen in patients without evidence of bacterial infection, perhaps in relation to 'cytokine storm', and so a low PCT may be more helpful (true negative) than a high PCT (false positive)*

Felveszel egy COVID-19 beteget, súlyos hipoxiás légzési elégtelenség, gépi lélegeztetés miatt az ITO-ra, az SBO-ról. Elindítanál-e empirikus AB-t a felvételt követő 1 órán belül, ha a PCT: 0.1 ng/mL?

- Mindenképpen
- Nem tudom eldönteni
- Nem

- **Bakteriális fertőzés COVID-ban alapvetően ritka**
- **Bakteriális szuperinfekcióval viszont számolni kell (~ 15%)**
- **A COVID-19 betegek 70-95%-uk kap AB-t már felvételkor**
- **Alacsony PCT (0.1 ng/mL):**
- **Klinikai kép+biomarkerek (kinetika) \cong racionalizált + személyre szabott AB terápia**