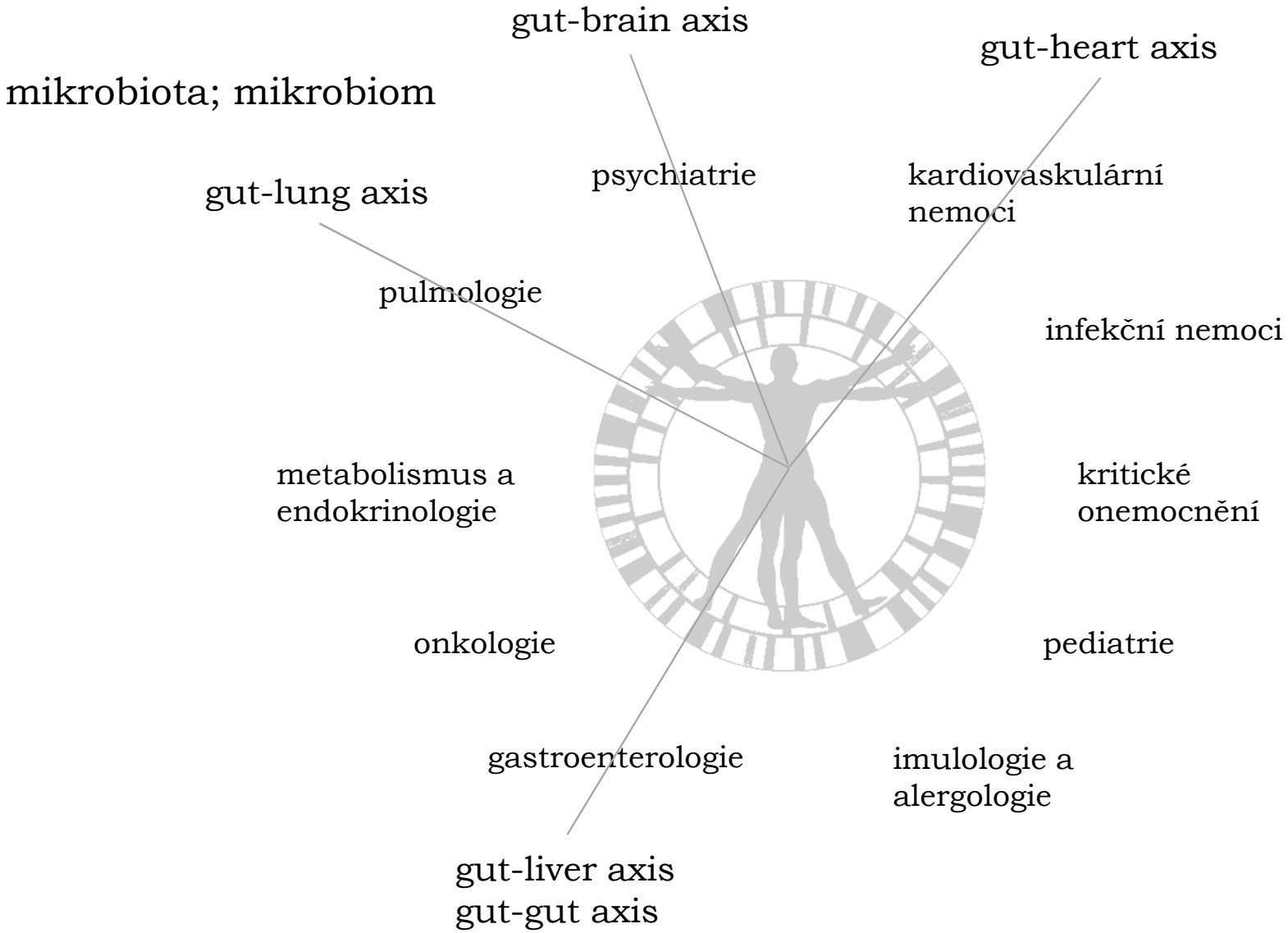
FAKULNÍ NEMOCNICE PLZEŇ
I. INTERNÍ KLINIKA

BIOMEDICÍNSKÉ CENTRUM

Dysbióza v kritickém onemocnění
Cesta na dno a zase zpět?

Jaroslav Raděj
I. interní klinika – JIP, Fakultní nemocnice v Plzni, Lékařská fakulta v Plzni, Univerzita Karlova
XV. kongres České společnosti intenzivní medicíny; červen 2022


gut-brain axis
gut-heart axis
mikrobiota; mikrobiom
psychiatrie
kardiovaskulární nemoci
gut-lung axis
pulmologie
infekční nemoci
metabolismus a endokrinologie
kritické onemocnění
onkologie
pediatrie
gastroenterologie
imulologie a alergologie
gut-liver axis
gut-gut axis

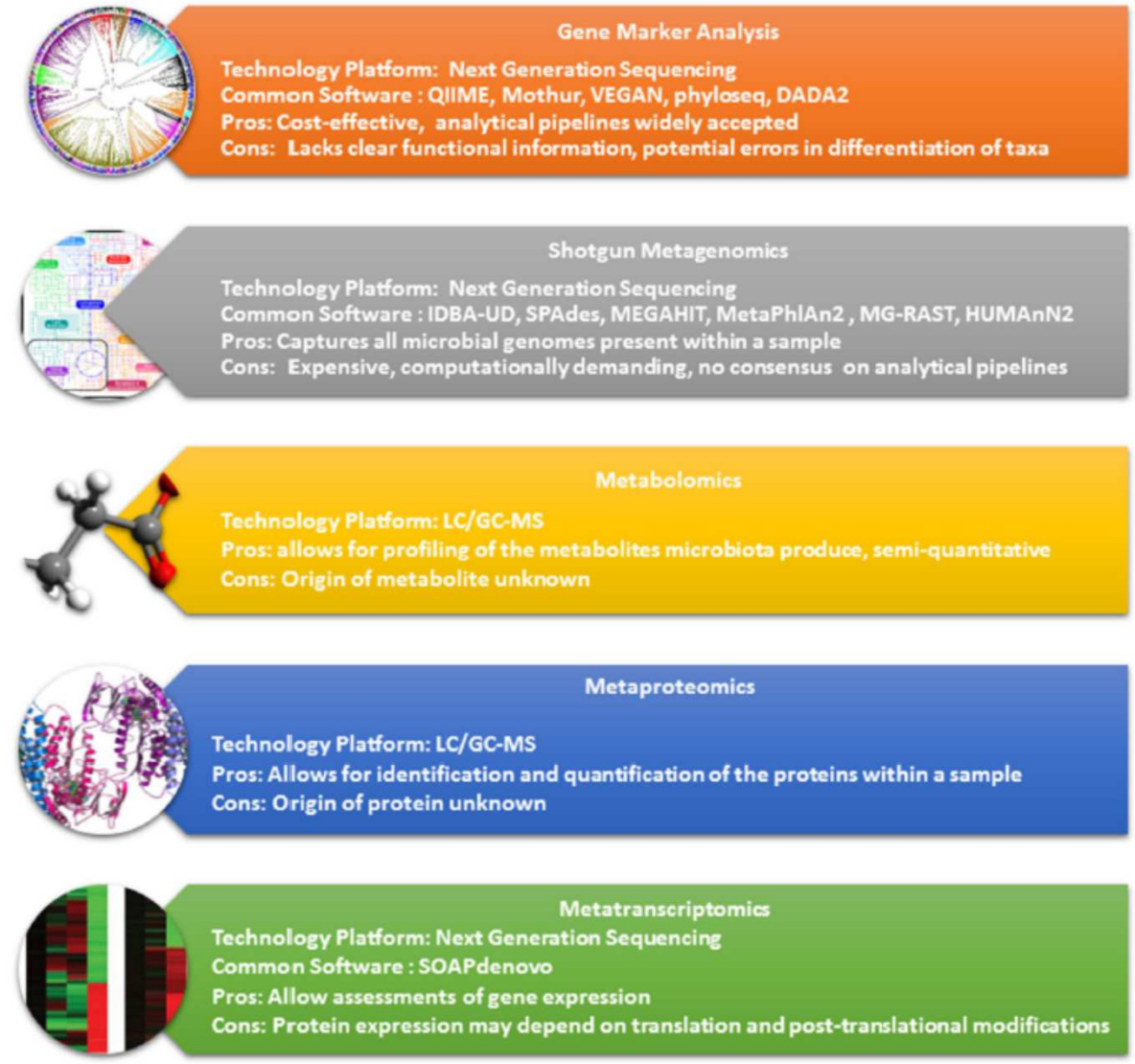


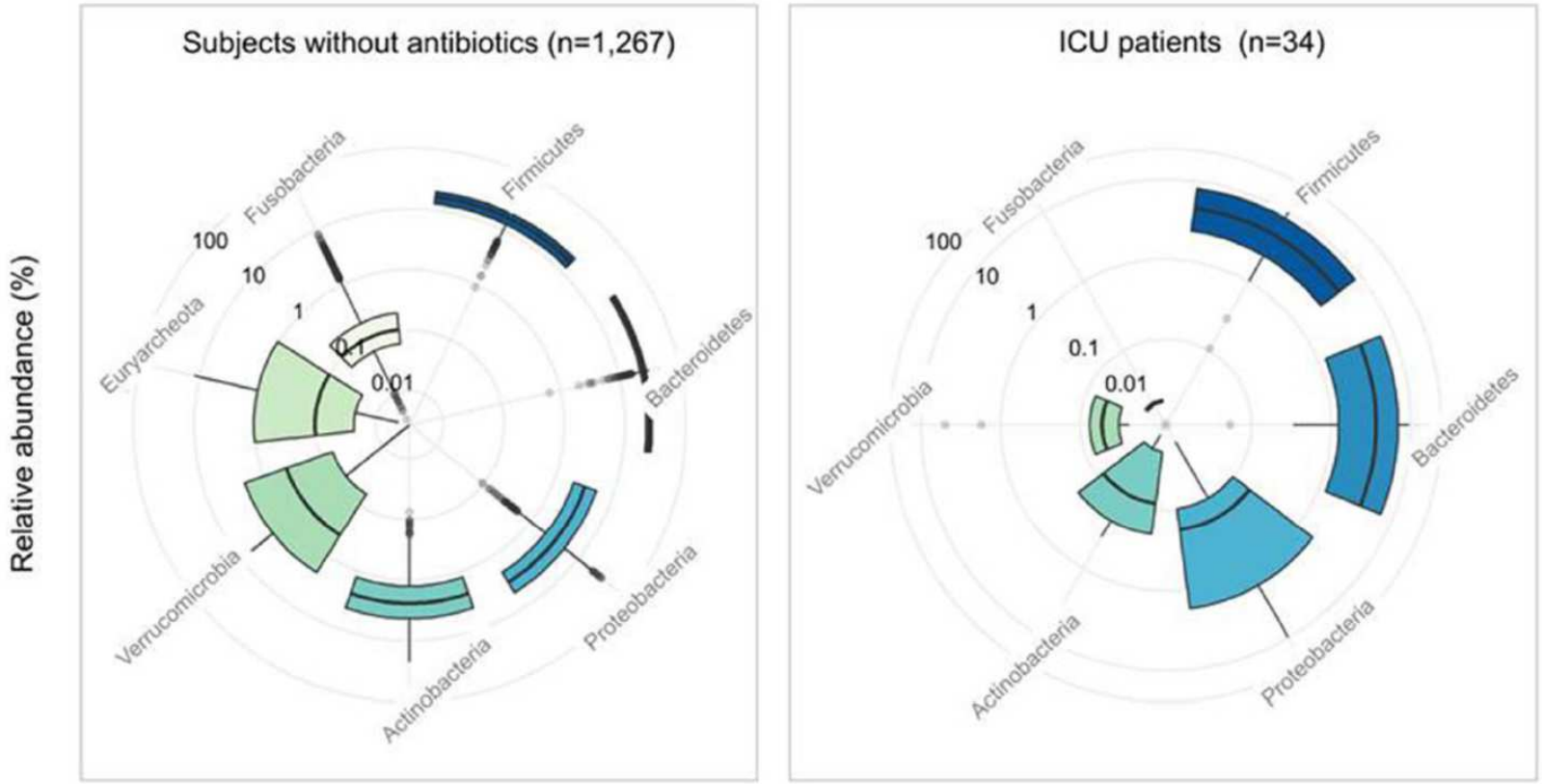
Fig. 1 Technologies for studying the microbiome

16S ribosomal RNA
Internal Transcribed Spacer ITS

plný genom včetně viromu, mykobiomu,...
geny pro MDR

J Galloway-Peña, B Hanson. Digestive Diseases and Sciences 2020

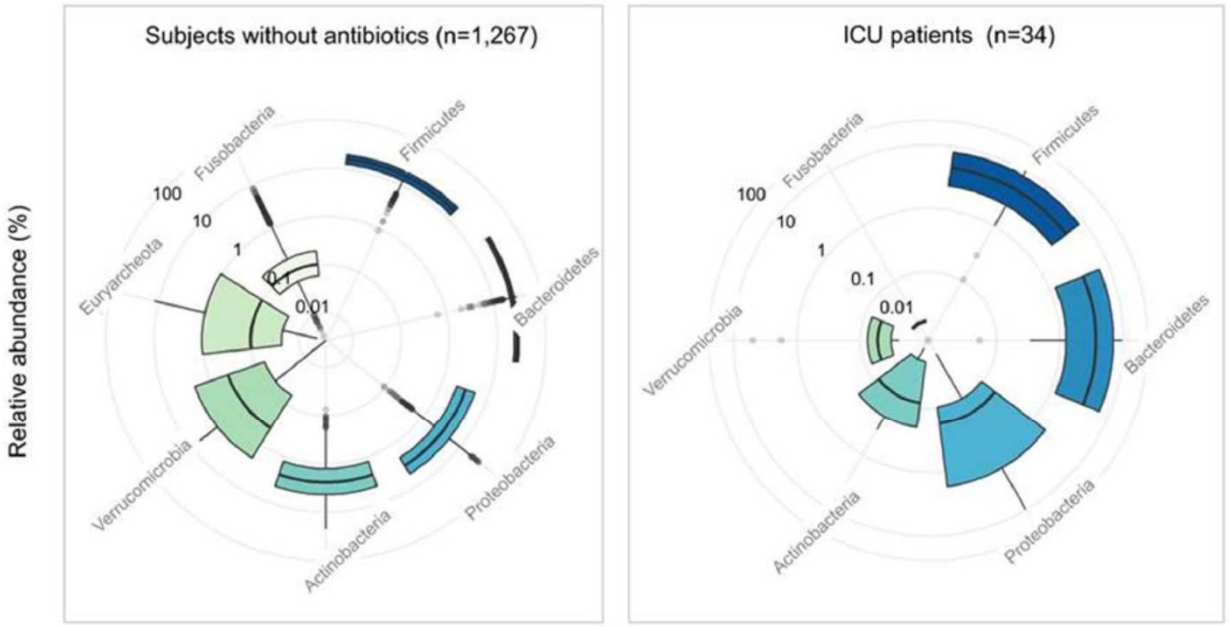
Intensive Care Med (2018) 44:1561–1564
https://doi.org/10.1007/s00134-018-5309-3



Firmicutes: *Clostridium, Lactobacillus, Enterococcus, Streptococcus*
Bacteroidetes: *Bacteroides, Prevotella*
Proteobacteria: *Enterobacteriaceae, Pseudomonas, Acinetobacter*
Actinobacteria: *Corynebacterium, Actinomyces, Bifidobacterium*
Verrucomicrobia: *Akkermansia*
Euryarcheota: not bacteria but Archeae .
Fusobacteria: *Fusobacterium*

*Correspondence: francois.barbier@chr-orleans.fr

than a mere surrogate marker of severity or prolonged



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Verrucomicrobia: *Akkermansia*
Euryarcheota: not bacteria but Archeae .
Fusobacteria: *Fusobacterium*

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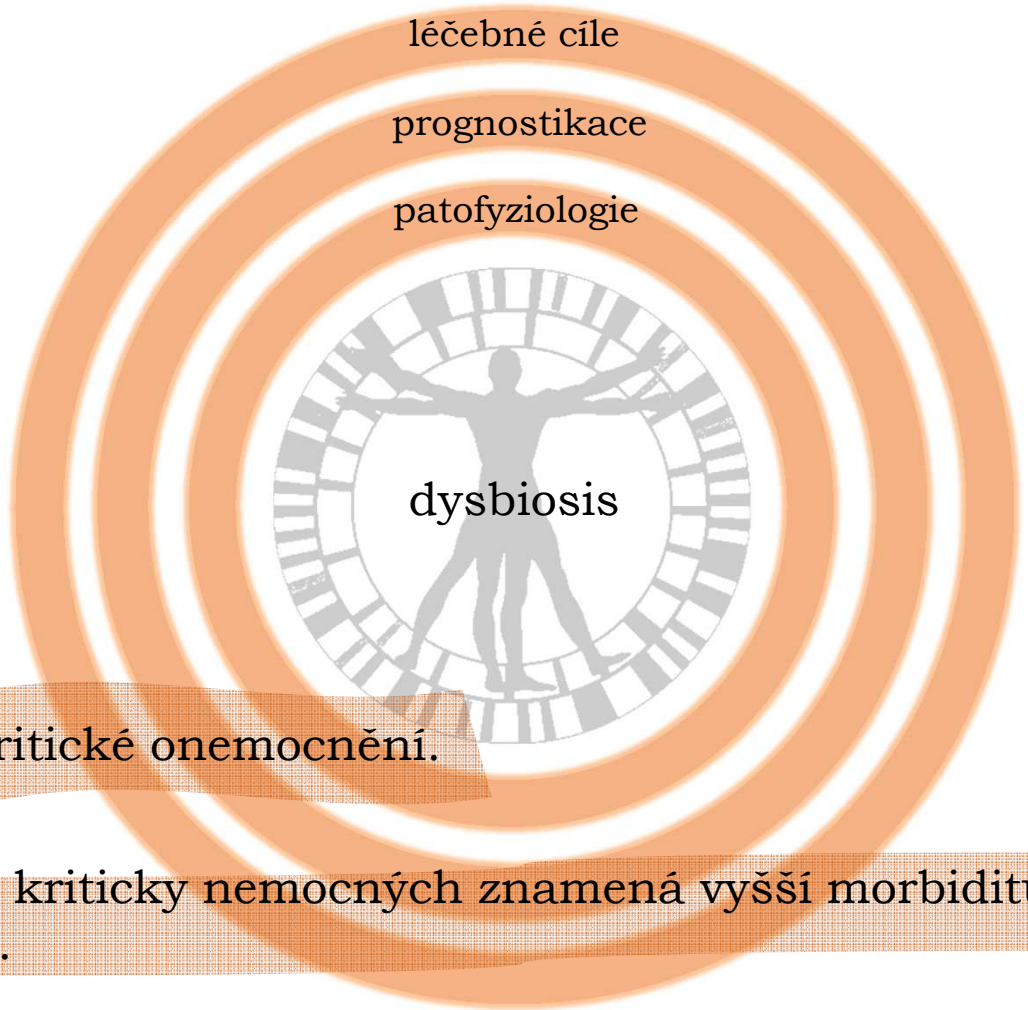
loss of diversity
loss of site specificity
shift forward dominant pathogen
enhancement of virulence and resistence



Dysbioza provází kritické onemocnění.

Extrémní dysbioza u kriticky nemocných znamená vyšší morbiditu a mortalitu, riziko další infekce a sepse.

Dig Dis Sci (2011) 56:2361–2365
DOI 10.1007/s10620-011-1649-3

ORIGINAL ARTICLE

Dramatic Changes of the Gut Flora Immediately After Severe and Sudden Insults

Mineji Hayakawa · Takashi Asahara · Naomi Henzan · Hiromoto Murakami · Hiroshi Yamamoto · Nobutaka Mukai · Yousuke Minami · Masahiro Sugano · Nobuhiko Kubota · Shinji Uegaki · Hisako Kamoshida · Atsushi Sawamura · Koji Nomoto · Satoshi Gando

Table 2 Fecal flora on day 0

Flora	Control subjects ($n = 12$)	Patients ($n = 15$)	P value
Total bacteria	10.1 (9.8–10.4)	7.5 (6.7–8.0)	<0.001
Obligate anaerobes			
Clostridium coccoides group	9.4 (9.0–9.7)	6.1 (5.4–7.0)	<0.001
Clostridium leptum subgroup	9.2 (9.0–9.7)	6.5 (6.1–7.3)	<0.001
Bacteroides fragilis group			
Bifidobacterium			
Atopobium cluster			
Prevotella			
Clostridium perfringens			
Facultative anaerobes			
Lactobacillus			
Enterobacteriaceae			
Enterococcus			
Staphylococcus			
Obligate aerobes			
Pseudomonas	<3.0	<3.0	ns

ns not significant

All measurements were presented as log10 counts/g and median (interquartile range 25–75%)

Table 3 Fecal organic acid concentrations on day 0

Organic acids	Control subjects ($n = 12$)	Patients ($n = 15$)	P value
Total organic acids(μmol/g)	90.1 (83.1–94.2)	41.3 (16.2–65.6)	<0.001
Acetic acid (μmol/g)	64.4 (60.4–67.6)	35.7 (12.1–58.4)	0.002
Propionic acid (μmol/g)	11.7 (9.6–14.8)	1.4 (0.5–6.1)	<0.001
Butyric acid (μmol/g)	10.3 (7.6–10.5)	<0.55 (<0.55–4.4)	<0.001
Succinic acid (μmol/g)	0.5 (<0.075–1.9)	<0.075	ns
Formic acid (μmol/g)	0.4 (<0.05–1.27)	0.4 (<0.05–0.8)	ns
Lactic acid (μmol/g)	<0.2 (<0.2–<0.2)	<0.2 (<0.2–<0.2)	ns
Isovareric acid (μmol/g)	<0.8	<0.8	ns
Valeric acid (μmol/g)	<0.65	<0.65	ns

ns not significant

All measurements were presented as median (interquartile range 25–75%)

Prevel et al. Critical Care (2022) 26:105
https://doi.org/10.1186/s13054-022-03980-8

Critical Care

RESEARCH Open Access

Gut bacteriobiota and mycobiota are both associated with Day-28 mortality among critically ill patients

Renaud Prevel[1,2*], Raphaël Enaud[2,3], Arthur Orieux[1], Adrian Camino[2], Patrick Berger[2], Alexandre Boyer[1,2], Laurence Delhaes[2,4] and Didier Gruson[1,2]

Table 2 Factors associated with Day-28 mortality in critically ill patients

Variables	Multivariate analysis OR	97.5 CI	*p* value
Shannon 16S rDNA	**0.19**	**[0.04–0.60]**	**< 0.01**
SAPSII	**1.08**	**[1.01–1.17]**	**0.04**
Sex (male)	**14.4**	**[1.45–516]**	**0.05**
Atrial fibrillation	5.03	[0.76–41.1]	0.10
Variables	**Multivariate analysis OR**	**97.5CI**	***p* value**
Shannon ITS2	**0.29**	**[0.09–0.75]**	**0.02**
SAPSII	**1.08**	**[1.02–1.17]**	**0.02**
Sex (male)	**18.8**	**[1.84–582]**	**0.04**
Atrial fibrillation	4.53	[0.07–33.4]	0.11

Conclusion: The gut bacteriobiota and mycobiota *α* diversities are independently associated with Day-28 mortality in critically ill patients. The causal nature of this interference and, if so, the underlying mechanisms should be further investigated to assess if gut microbiota modulation could be a future therapeutic approach.

Keywords: Microbiota, Mycobiota, Intensive care unit

Am J Transl Res 2021;13(3):1548-1557
www.ajtr.org /ISSN:1943-8141/AJTR0121238

Original Article

Dysbiosis of intestinal microbiota in critically ill patients and risk of in-hospital mortality

Ru Wei[1*], Xu Chen[2*], Linhui Hu[3*], Zhimei He[4], Xin Ouyang[4], Silin Liang[5], Shixue Dai[6], Weihong Sha[6], Chunbo Chen[5,7]

Table 3. Predictive characteristics of admission indicator and their combinations for ICU mortality

Logistic regression model	AUROC (95% CI)	Youden index	Cut-off	OR (95% CI)	*P*
Univariate models					
APACHE II	0.724 (0.595-0.831)	0.5714	27.00	1.261 (1.091-1.458)	0.002
SOFA	0.649 (0.516-0.767)	0.3452	10.00	1.436 (1.159-1.777)	0.001
Bifidobacterium	0.718 (0.588-0.826)	0.4677	0.0041	0.800 (0.622-1.029)	0.082
Multivariate models					
APACHE II plus *Bifidobacterium*	0.876 (0.766-0.946)	0.6514	1.82	2.716 (1.435-5.141)	0.002
SOFA plus *Bifidobacterium*	0.882 (0.774-0.950)	0.6071	1.07	2.720 (1.488-4.973)	0.001

Chanderraj et al. Microbiome (2022) 10:2
https://doi.org/10.1186/s40168-021-01190-y

Microbiome

RESEARCH Open Access

The bacterial density of clinical rectal swabs is highly variable, correlates with sequencing contamination, and predicts patient risk of extraintestinal infection

Rishi Chanderraj[1,2], Christopher A. Brown[2,3], Kevin Hinkle[2], Nicole Falkowski[2], Robert J. Woods[1,4] and Robert P. Dickson[2,5,6,7*]

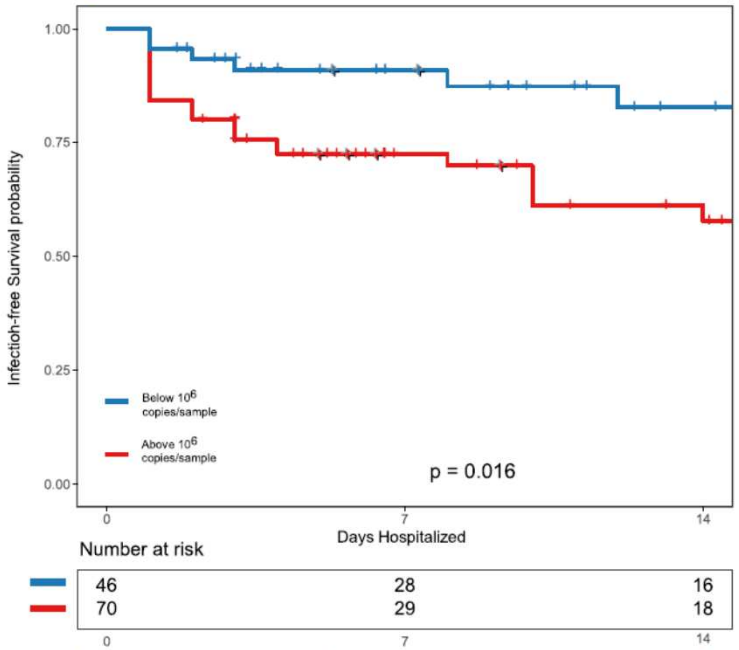


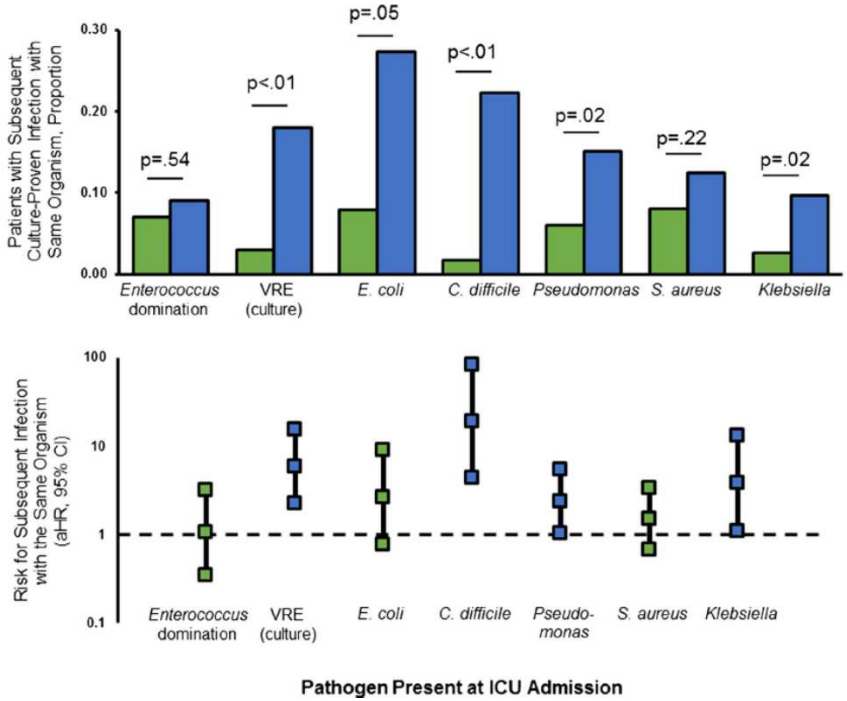
Fig. 5 The bacterial density of rectal swabs at the time of hospital admission is predictive of subsequent extra-intestinal infections. Kaplan-Meier curves of infection-free survival in our cohort of hospitalized patients. Cross tick-marks represent censored patients. Using a threshold of 10^6 16S rRNA gene copies/specimen, we found that patients with high bacterial density were more likely to have extraintestinal infections at 7 and 14 days following sampling ($p = 0.016$ with stratified log-rank)

Intensive Care Med (2018) 44:1203–1211
https://doi.org/10.1007/s00134-018-5268-8

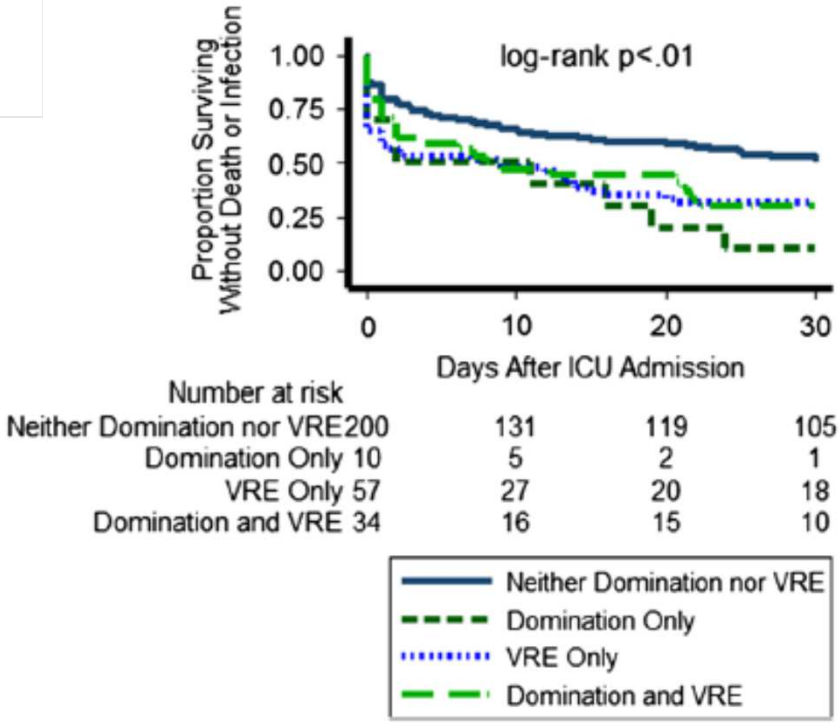
ORIGINAL

Pathogen colonization of the gastrointestinal microbiome at intensive care unit admission and risk for subsequent death or infection

Daniel E. Freedberg[1*], Margaret J. Zhou[2], Margot E. Cohen[3], Medini K. Annavajhala[4], Sabrina Khan[4], Dagmara I. Moscoso[1], Christian Brooks[1], Susan Whittier[5], David H. Chong[6], Anne-Catrin Uhlemann[4,7] and Julian A. Abrams[1,8]



dominantní enterokokus ≥ 30% 16S RNA



Crit Care Med 2016

Significance of Prior Digestive Colonization With Extended-Spectrum β-Lactamase-Producing Enterobacteriaceae in Patients With Ventilator-Associated Pneumonia.

Bruyère R1, Vigneron C, Bador J, Aho S, Toitot A, Quenot JP, Prin S, Charles PE.

pozitivní prediktivní hodnota 41.5%
negativní prediktivní hodnota 99,4%

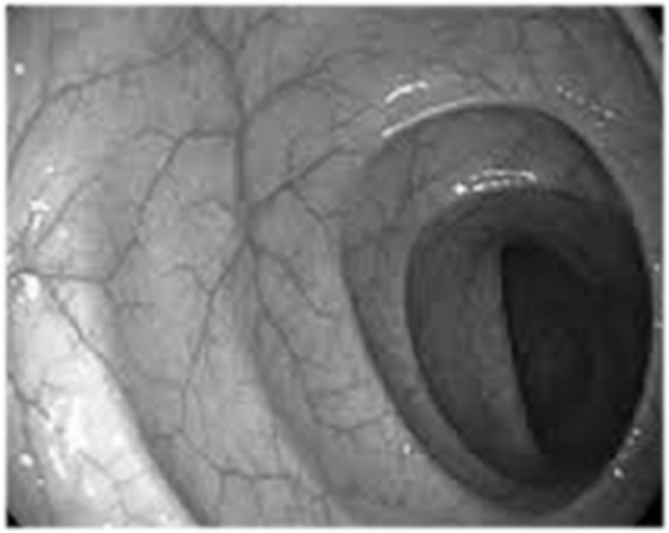
PLoS One 2018

Relationship between digestive tract colonization and subsequent ventilator-associated pneumonia related to ESBL-producing Enterobacteriaceae.

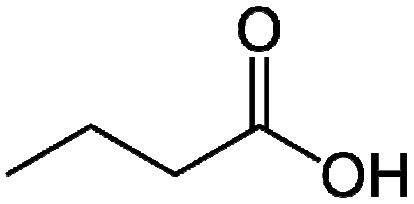
Houard M, Rouzé A, Ledoux G, Six S, Jaillette E, Poissy J, Préau S, Wallet F, Labreuche J, Nseir S, Voisin B.

pozitivní prediktivní hodnota 43,6%
negativní prediktivní hodnota 97,3%
median doby od GIT kolonizace do VAP 8 dní

90 % v tlustém střevě
99% jde o bakterie



- ✓ metabolismus, hormonální produkce,…
- ✓ trofika a integrita střeva
- ✓ kolonizační rezistence
- ✓ imunitní interakce a modulace

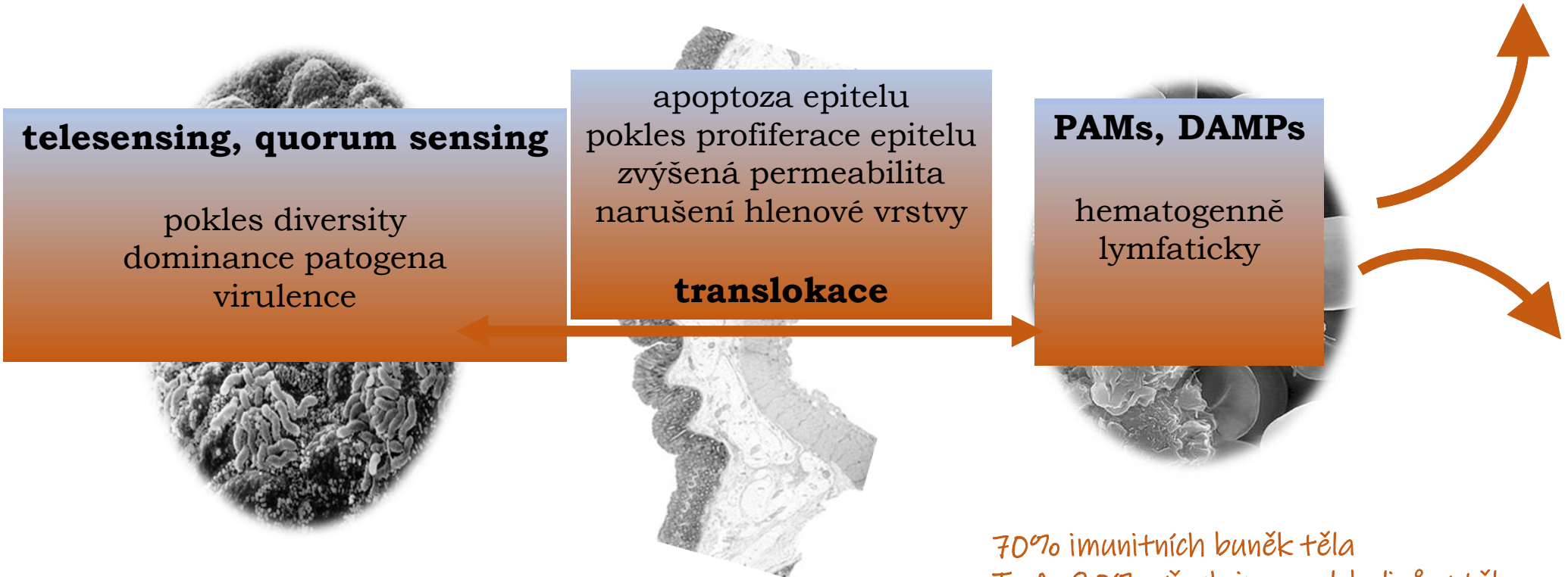


gen → transcript → metabol

omics

gen → transcript → metabol

omics



telesensing, quorum sensing

pokles diversity
dominance patogena
virulence

apoptoza epitelu
pokles profiferace epitelu
zvýšená permeabilita
narušení hlenové vrstvy

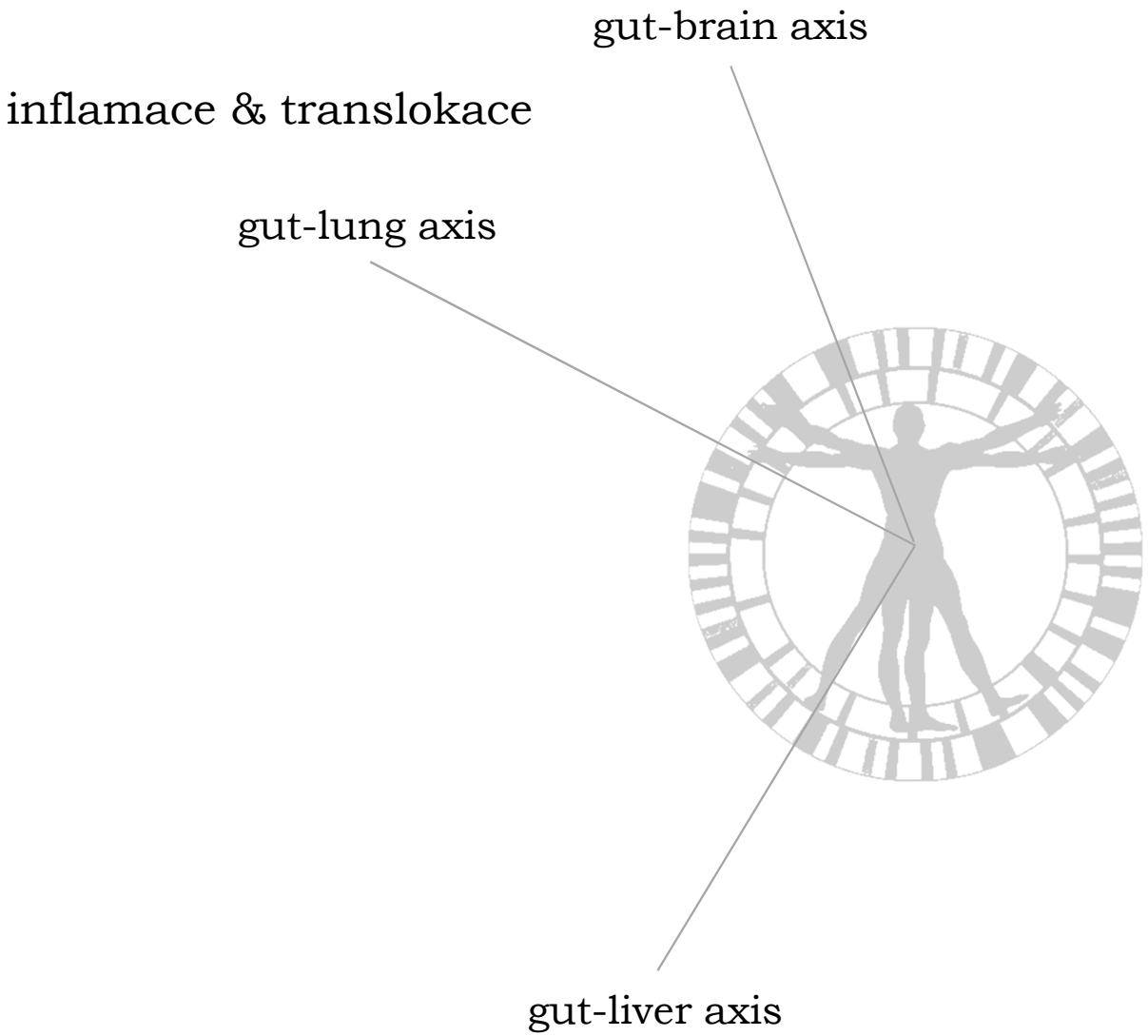
translokace

PAMs, DAMPs

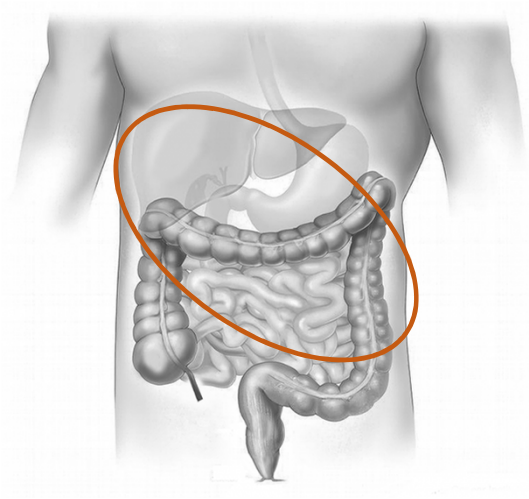
hematogenně
lymfaticky

MAMPs vs PRRs

70% imunitních buněk těla
IgA...80% všech imunoglobulinů v těle


gut-brain axis
inflamace & translokace
gut-lung axis
gut-liver axis

gut-liver axis



Dysbioza, inflamace, akutní jaterní postižení, MODS

Dysbioza, inflamace, chronická jaterní postižení

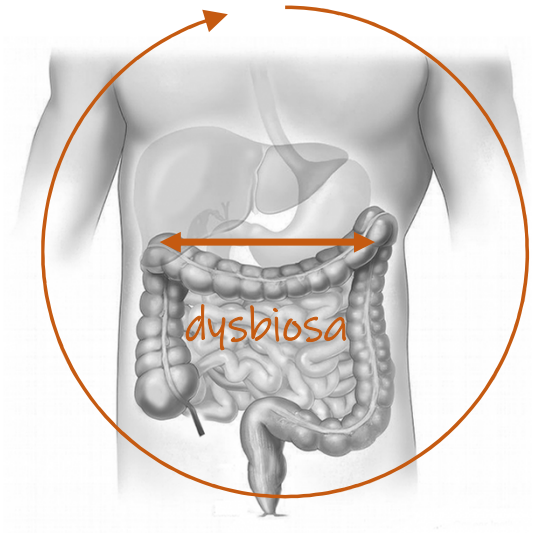
Dysbioza, inflamace, akutní dekompenzace chronické jaterní choroby, sekundární sklerozující cholangitis u kriticky nemocných

gut-liver axis

MODS

játra

proteiny akutní fáze, cytokiny
clearance bakterií a toxinů
produkce žlučových kyselin



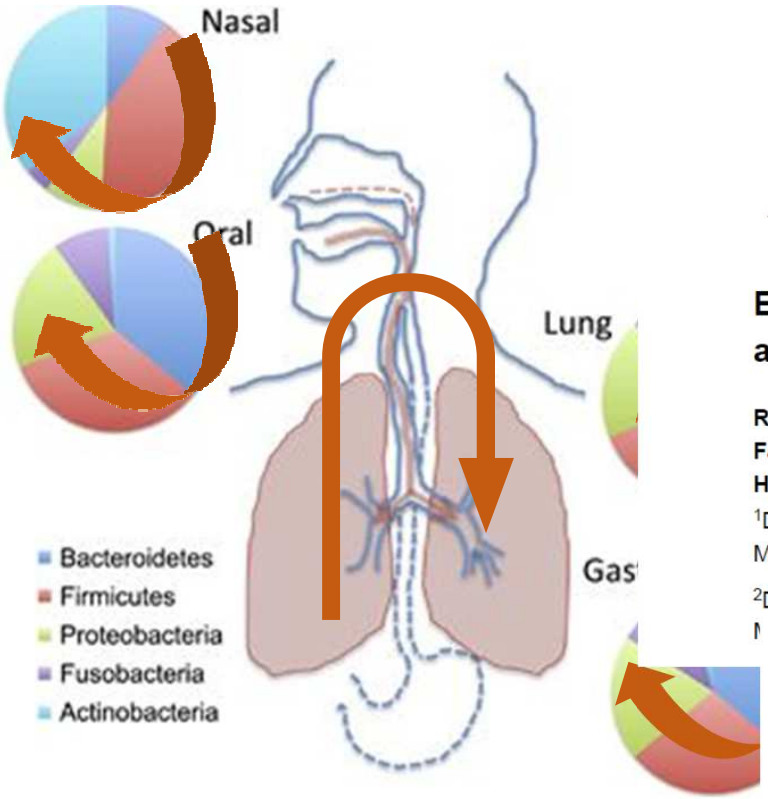
střevo

permeabilita a traslokace
inflamace

portální řečiště
lymfatický systém
žlučové kyseliny

- trávení a metabolismus
- baktericidní ve střevě, stimulují produkci antimicrob. peptidů
- redukují střevní permeabilitu
- DMAPs, inflamace a oxidativní stres, poškození jater

gut-lung axis



imigrace

eliminace

biofyzikální a biochemické vlivy

Nat Microbiol. ; 1(10): 16113. doi:10.1038/nmicrobiol.2016.113.

Enrichment of the Lung Microbiome with Gut Bacteria in Sepsis and the Acute Respiratory Distress Syndrome

Robert P. Dickson, MD[1], **Benjamin H. Singer, MD, PhD**[1], **Michael W. Newstead**[1], **Nicole R. Falkowski**[1], **John R. Erb-Downward, PhD**[1], **Theodore J. Standiford, MD**[1,3], and **Gary B. Huffnagle, PhD**[1,2,3]

[1]Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, University of Michigan Medical School, Ann Arbor, Michigan

[2]Department of Microbiology and Immunology, University of Michigan Medical School, Ann Arbor,

Gut microbiota

OPEN ACCESS

ORIGINAL ARTICLE

The gut microbiota plays a protective role in the host defence against pneumococcal pneumonia

Tim J Schuijt,[1,2,3] Jacqueline M Lankelma,[1] Brendon P Scicluna,[1] Felipe de Sousa e Melo,[1] Joris J T H Roelofs,[4] J Daan de Boer,[1] Arjan J Hoogendijk,[1] Regina de Beer,[1] Alex de Vos,[1] Clara Belzer,[5] Willem M de Vos,[5,6] Tom van der Poll,[1,2] W Joost Wiersinga[1,2]

Gut 2016;**65**:575–583

G.B. Huffnagle. Mucosal Immunology 2017

anti-biotics

AMERICAN SOCIETY FOR MICROBIOLOGY | mSystems®

Integrative Transkingdom Analysis of Antibiotic Perturbation and Critical Illn

Bastiaan W. Haak,[a] Ricard Argelaguet,[b] Cormac M. Kinsella,[c] Robert F. J. Michelle Klein,[c] Maarten F. Jebbink,[c] Floor Hugenholtz,[a] Sarantos Kostidis,[d] Wouter J. de Jonge,[e] Marcus J. Schultz,[f] Tom van Gool,[g] Tom van der Poll,[a,i] W. Joost Wiersinga[a,j]

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[c]Laboratory of Experimental Virology, Department of Medical Microbiology, Amsterdam UMC, Lo
[d]Center for Proteomics and Metabolomics, Leiden University Medical Center, Leiden, The Netherl
[e]Tytgat Institute for Liver and Intestinal Research, Amsterdam UMC, Location AMC, Amsterdam, T
[f]Department of Intensive Care, Amsterdam UMC, Location AMC, Amsterdam, The Netherlands
[g]Department of Parasitology, Amsterdam UMC, Location AMC, Amsterdam, The Netherlands
[h]Laboratory of Microbiology, Wageningen University, Wageningen, The Netherlands
[i]Research Programs Unit Immunobiology, Department of Bacteriology and Immunology, Helsini
[j]Department of Medicine, Division of Infectious Diseases, Amsterdam UMC, Location AMC, Amst

Bastiaan W. Haak and Ricard Argelaguet contributed equally. Author order was determined by role in

ABSTRACT Bacterial microbiota play a critical role in mediating local a immunity, and shifts in these microbial communities have been linked outcomes in critical illness. Emerging data indicate that other intestina including bacteriophages, viruses of eukaryotes, fungi, and protozoa, interlinked with the bacterial microbiota and their host, yet their collec ing antibiotic perturbation and critical illness remains to be elucidated. V multi-omics factor analysis (MOFA) to systematically integrate the k rRNA), fungal (intergenic transcribed spacer 1 rRNA), and viral (virus di generation sequencing) components of the intestinal microbiota of 3 patients with and without sepsis and 13 healthy volunteers. In additio fied the absolute abundances of bacteria and fungi using 16S and 1 and characterized the short-chain fatty acids (SCFAs) butyrate, acetate nate using nuclear magnetic resonance spectroscopy. We observe tha anaerobic intestinal environment is directly correlated with an overgro pathobionts and their corresponding bacteriophages as well as an al ment of opportunistic yeasts capable of causing invasive disease. We a strong depletion of SCFAs in both disease states, which was asso increased absolute abundance of fungi with respect to bacteria. T findings illustrate the complexity of transkingdom changes followin the intestinal bacterial microbiome.

IMPORTANCE While numerous studies have characterized antibiotic- tions of the bacterial microbiome, few studies describe how these dis the composition of other kingdoms such as viruses, fungi, and proto this knowledge gap, we employed MOFA to systematically integr and bacterial sequence data from critically ill patients (with and both prior to and following exposure to

Clinical Infectious Diseases

MAJOR ARTICLE

Risk of Subsequent Sepsis Within 90 Stay by Type of Antibiotic Exposure

James Baggs, John A. Jernigan, Alison Laufer Halpin, Lauren Epstein, Kelly M. Hatfield, and L

Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia

Background. We examined the risk of sepsis within 90 days after discharg received during the previous stay.

Methods. We retrospectively identified a cohort of hospitalized patients Database. We examined the association between the use of certain antibiotics and the risk of postdischarge sepsis controlling for potential confounding fac primary exposure was receipt of antibiotics more strongly associated with clini outcome was a hospital stay within 90 days of the index stay that included an *Clinical Modification* (*ICD-9-CM*) discharge diagnosis of severe sepsis (*ICD-9*

Results. Among 516 hospitals, we randomly selected a single stay for eli septic shock developed within 90 days after discharge. The risk of sepsis ass 65% higher than in those without antibiotic exposure.

Conclusions. Our study identified an increased risk of sepsis within high-risk antibiotics or increased quantities of antibiotics during hospitali antimicrobial use may be unnecessary, this study builds on previous evider pitals may not only prevent antimicrobial resistance, *Clostridium difficile* i unwanted outcomes potentially related to disruption of the microbiota, inc

Keywords. sepsis; septic shock; anti-bacterial agents; administrative d

Sepsis is a life-threatening clinical syndrome characterized by acute organ dysfunction resulting from infection and a major contributor to excess morbidity, mortality, and healthcare costs [1]. Nearly one-quarter of sepsis cases have suspected gastrointestinal or an unknown source of infection [2–4]. In addition, there is a long-recognized role for the middle and lower gastrointestinal tract microbiota in the regulation of the immune response, specifically in sepsis [5–7]. Emerging evidence shows that major disruptive forces, such as antibiotics, can lead to shifts in the microbiota that have greater pathogenic potential [8, 9], possibly leading to bacterial translocation [10, 11], a dysregulated immune response [5], or both.

Antibiotics are essential treatments for many hospitalized patients. More than half of hospitalized patients receive an antibiotic [12, 13], but an estimated 30%–50% of antibiotic use in hospitals is inappropriate [13, 14]. Widespread use of antibiotics not only leads to selection for drug resistance and increases risk

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Correspondence: J. Baggs, 1600 Clifton Rd, Mail Stop A31, Atlanta, GA 30333 (tbaggs@cdc.gov).

Clinical Infectious Diseases® 2018;66(7):1004–12

DOI: 10.1093/cid/cix947

www.nature.com/scientificreports

scientific reports

OPEN

Third generation cephalosporins and piperacillin/tazobactam have distinct impacts on the microbiota of critically ill patients

Hasinika K. A. H. Gamage[1,9], Carola Venturini[2,9], Sasha G. Tetu[1], Masrura Kabir[2,8], Vineet Nayyar[3], Andrew N. Ginn[2,4], Belinda Roychoudhry[2], Lee Thomas[2], Mitchell Brown[4], Andrew Holmes[5], Sally R. Partridge[2], Ian Seppelt[6,7], Ian T. Paulsen[1]✉ & Jonathan R. Iredell[2]✉

Effective implementation of antibiotic stewardship, especially in critical care, is limited by a lack of direct comparative investigations on how different antibiotics impact the microbiota and antibiotic resistance rates. We investigated the impact of two commonly used antibiotics, third-generation cephalosporins (3GC) and piperacillin/tazobactam (TZP) on the endotracheal, perineal and faecal microbiota of intensive care patients in Australia. Patients exposed to either 3GC, TZP, or no β-lactams (control group) were sampled over time and 16S rRNA amplicon sequencing was performed to examine microbiota diversity and composition. While neither treatment significantly affected diversity, numerous changes to microbiota composition were associated with each treatment. The shifts in microbiota composition associated with 3GC exposure differed from those observed with TZP, consistent with previous reports in animal models. This included a significant increase in *Enterobacteriaceae* and *Enterococcaceae* abundance in endotracheal and perineal microbiota for those administered 3GC compared to the control group. Culture-based analyses did not identify any significant changes in the prevalence of specific pathogenic or antibiotic-resistant bacteria. Exposure to clinical antibiotics has previously been linked to reduced microbiota diversity and increased antimicrobial resistance, but our results indicate that these effects may not be immediately apparent after short-term real-world exposures.

The human gut microbiota plays an integral role in host metabolic functions and immunity. Intensive care has been associated with substantial changes in the intestinal microbiota of patients, including reduced microbial diversity, altered composition with a propensity for expansion of pathobionts such as Proteobacteria, and increased levels of antibiotic resistance[1–3]. However, the magnitude of these changes is not uniform among individuals due to large interpersonal variation in baseline microbiota composition[4,5]. Antibiotics are heavily used in intensive care units (ICUs) and timely antibiotic intervention, immediately upon presentation, saves lives[6]. Antimicrobial exposure, however, can have long-lasting detrimental impacts on gut microbiota health, including reduced resistance against subsequent infections[7–9], with recovery from dysbiosis dependent on the type of antibiotic treatment received[4,10–12]. There is therefore urgent need to define ways to preserve microbiota integrity in ICU patients, including the use of probiotics and selective digestive tract decontamination to reduce microbiota dysbiosis[13–15].

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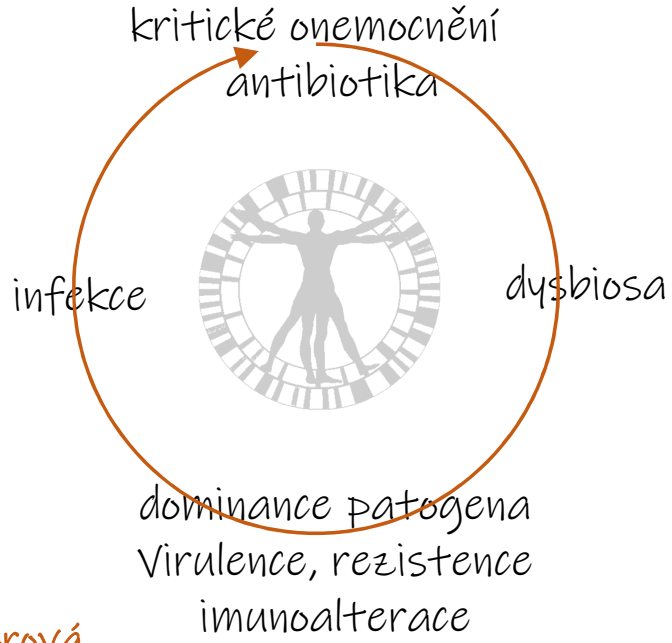
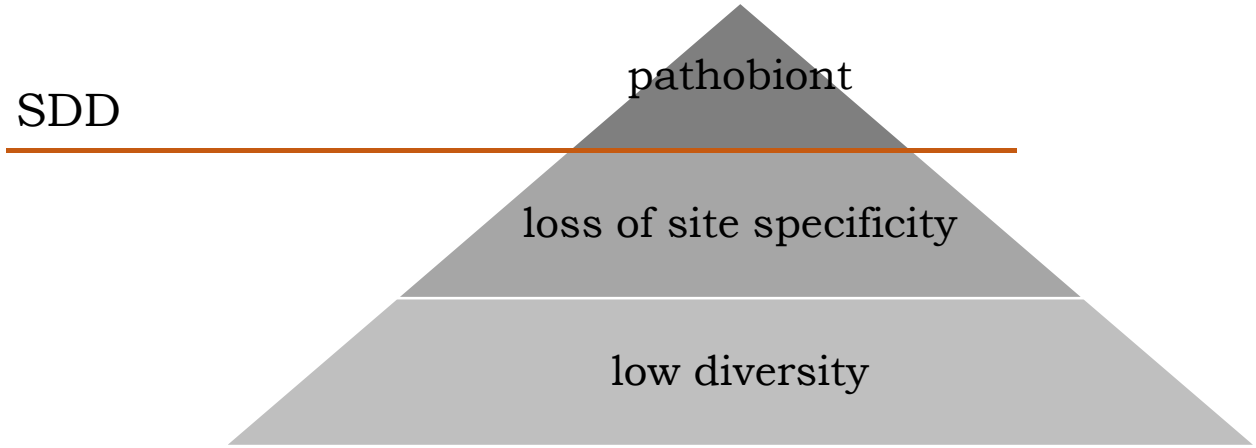
- ✓ minimalizace expozice (GIT) antibiotikům
  biliární exkrece, anaerobní spektrum
- ✓ antimicrobial stewardship
- ? GIT intraluminární betalaktamáza
  aktivní uhlí
- ? alternativní antimikrobiální efekt
  snížení virulence



- ✓ katecholaminy, PPI, H2B...dysbiosa
- ✓ opiáty... dysbiosa, imunoalterace, bariérová disintegrita, virulence



antimicrobial stewardship vs. EBM (pokles VAP a mortality v nízkém epid. riziku bakt. rezistence bez systémové léčby cef. III. gen.)

riziko bakteriální rezistence?...následné?

SDD vs. SOD…CHX…mortalita?....náhrada??

good oral care

eubiotikum rifaximin

- ✓ redukce bakt. translokace a virulence
- ✓ anti-inflamace
- ✓ pozitivní modulace mikrobioty

World Journal of Gastroenterology

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DOI: 10.3748/wjg.v23.i25.4491

World J Gastroenterol 2017 July 7; 23(25): 4491-4499
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REVIEW

Table 1 Studies investigating the effects of rifaximin on gut microbiota composition

Ref.	Patients/model	Technique	Rifaximin dose	Changes in gut microbiota after rifaximin
Brigidi *et al*[77], 2002	12 pts UC	Standard bacteriological procedures	1800 mg/d, 3 cycles of 10 d followed by 25 d of wash-out	*Enterococci*: < *Coliform*: = *Bifidobacteria*: > *Lactobacilli*: < *Clostridium perfrigens*: > than < *Bacteroides*: unpredictable variations *Candida*: = Overall composition: not explored
Maccaferri *et al*[78], 2010	4 pts colonic active CD	Continuous culture colonic model system, FISH, quantitative PCR, PCR-denaturing gradient gel electrophoresis	1800 mg/d	Bifidobacterium: > Atopobium: > *Faecalibacterium prausnitzii*: > Overall composition: =
Bajaj *et al*[76], 2013	20 pts HE	454 pyrosequencing	1100 mg/d	Overall composition: =
Xu *et al*[79], 2014	Rat model of visceral hyperalgesia	Quantitative PCR, 454 pyrosequencing	150 mg/kg, twice daily	*Lactobacillus*: > Clostridiaceae, Erysipelotrichaceae, and Peptostreptococcaceae: < Overall composition: 84% reduction in bacterial load
Soldi *et al*[80], 2015	15 pts non-C IBS	Real-time PCR, Illumina pyrosequencing	1650 mg/d for 14 d	Faecalibacterium prausnitzii: > Clostridiaceae, Streptococcaceae: < Bacteroidaceae, Prevotellaceae: > Overall composition: =
Ponziani *et al*[81], 2016	20 pts CD, UC, non-C IBS, DD, HE	454 pyrosequencing	1200 mg/d for 14 d	*Lactobacillus*: > *Roseburia, Haemophilus, Veillonella* and *Streptococcus*: < Overall composition: =

Pts: Patients; UC: Ulcerative colitis; CD: Crohn's disease; FISH: Fluorescence in situ hybridization; PCR: Polymerase chain reaction; HE: Cirrhosis with hepatic encephalopathy; non-C IBS: Irritable bowel syndrome without constipation; DD: Diverticular disease.

pro-biotika

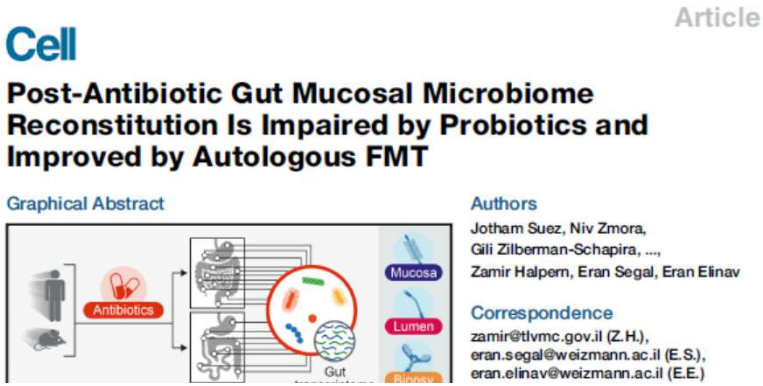
- ✓ kompetice
- ✓ imunomodulace
- ✓ antimikrobiální peptidy
- ✓ stimulace tvorba hlenu
- ✓ stimulace produkce IgA
- ✓ integrita střevní stěny

? prolongace rekonstituce post-ATB MCB

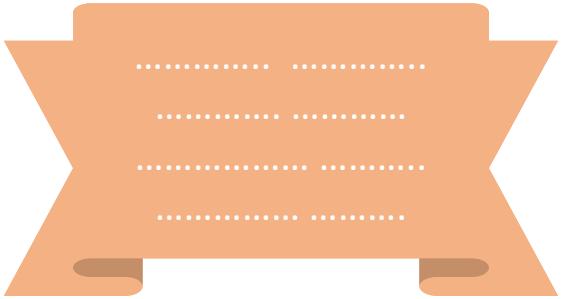
?! translokace, bakteriémie, infekce

VAP; mortalita a morbidita; infekce; průjem

Lactobacillus rhamnosus X PROSPECT trial, JAMA 2021
Lactobacillus plantarum X ROCIT trial, ICM 2021



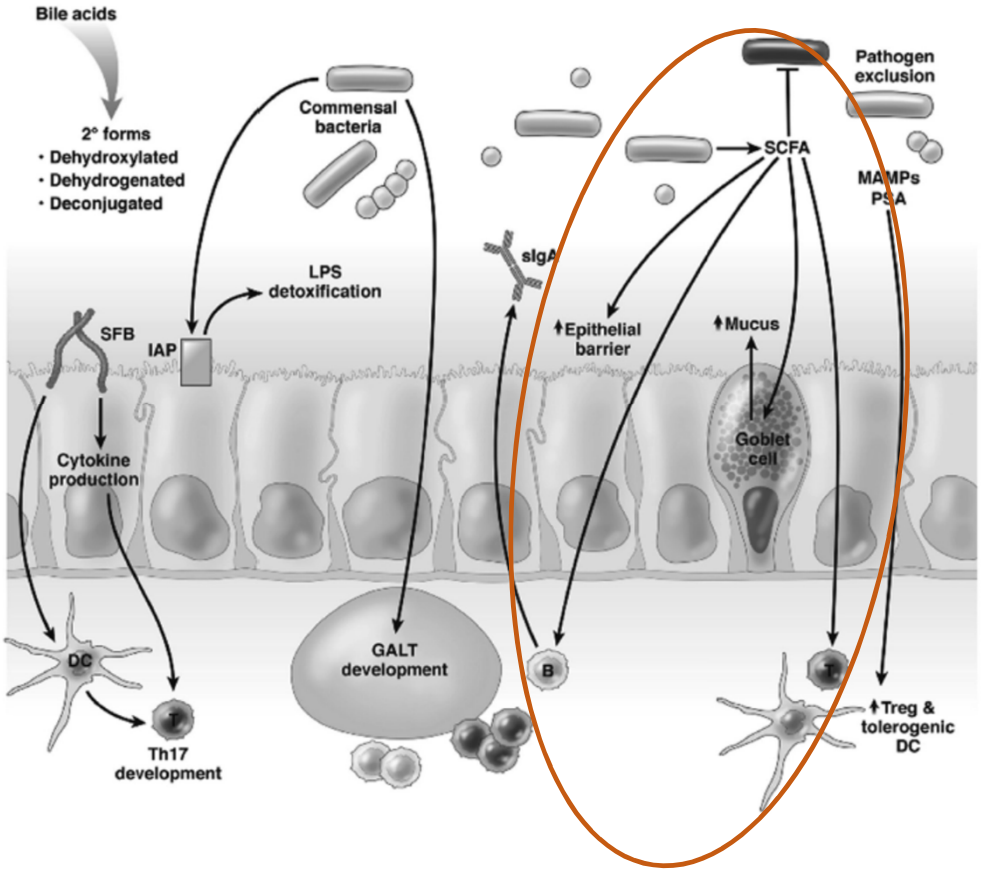
pro-biotika



next generation probiotika
producenti SCFAs, směs, spory anaerobů
pacient a dysbiosa specifická
množství

SCFAs
butirát, acetát, propionát

- ✓ podpora komensální MCB
- ✓ zvyšuje kolonizační rezistenci
- ✓ přímý antimikrobiální efekt (C. alb)
- ✓ trofika střevního epitelu, hlen
- ✓ podpora barierové funkce
- ✓ imunomodulační efekt



McClave SA, Lowen CC, Martindale RG. The 2016 ESPEN Arvid Wretlind lecture: The gut in stress. Clin Nutr 2018

vláknina

anaerobní MCB; fermentace; SCFAs

starvace	vs.	výživa
parenterální	vs.	enterální
no fibre	vs.	fibre
low fibre	vs.	high fibre
klinická výživa	vs.	mixovaná, přirozená strava

Crit Care Explor. 2020

Impact of Fiber-Based Enteral Nutrition on the Gut Microbiome of ICU Patients Receiving Broad-Spectrum Antibiotics: A Randomized Pilot Trial

Daniel E Freedberg, Megan Messina, Elissa Lynch, Monika Tess, Elizabeth Miracle, David H Chong, Romina Wahab, Julian A Abrams, Harris H Wang, Christian Munck

+ 61% SCFAs producenti vs. -46%
6x SCFAs ve stolici

high fat vyživa…dysbiosa, inflamace
low phosphate nutrice….přechod do virulence

DOI: 10.1002/jpen.2319

ORIGINAL RESEARCH

Effect of dietary fiber on gut barrier function, gut microbiota, short-chain fatty acids, inflammation, and clinical outcomes in critically ill patients: A systematic review and meta-analysis

Ting Liu MD[1] | Can Wang BD[1] | Yu-yu Wang BD[1] | Li-li Wang MD[2] | Omorogieva Ojo PhD[3] | Qian-qian Feng MD[4] | Xiao-song Jiang BD[1] | Xiao-Hua Wang PhD[5]

TABLE 3 Results of subgroup analysis of the duration of hospital stay by outcomes

Group	Reference no.	Studies, *n*	MD (95% CI)	*P*-value	I^2, % (*P*)
Total	8,22,24,26,28,29,30,35,37	9	−3.16 (−5.82 to −0.49)	0.02*	53 (0.03)
Type of supplement					
Fiber	22,24,26,29,30,37,	6	−3.61 (−7.66 to 0.45)	0.08	69 (<0.01)
Probiotic	8,28,35	3	−3.12 (−6.18 to −0.07)	0.04*	0 (0.58)
Supplementary fiber dose, g/day					
<20	24,28,30,35,37	5	−0.41 (−3.03 to 2.21)	0.76	15 (0.32)
≥20	22,26,29,8	4	−5.62 (−8.04 to −3.21)	<0.001*	0 (0.43)
Intervention time, days					
≤7	26,29,23,24	3	−3.90 (−10.19 to 2.40)	0.22	79 (<0.01)
>7	22,28,30,23,35,37,8	6	−2.12 (−4.47 to 0.24)	0.08	13 (0.33)
Type of ICU					
Medical	8,29	2	−4.77 (−7.48 to −2.07)	< 0.001*	0 (0.86)
Surgical	22	1	−5.20 (−20.26 to 9.86)	0.50	–
General	24,26,28,30,35,37	6	−2.47 (−6.34 to 1.39)	0.21	63 (0.02)

Abbreviations: ICU, intensive care unit; MD, mean difference.
*$P < 0.05$.

TABLE 4 Results of subgroup analyses of mortality by outcomes

Group	Reference no.	Studies, *n*	OR (95% CI)	*P*-value	*I2*, % (*P*)
Total	22,24,25,28–32,34–36,38	12	0.87 (0.68–1.11)	0.28	8 (0.37)
Type of supplement					
Fiber	2,24,29,31,34,38	6	0.89 (0.66–1.21)	0.46	8 (0.37)
Probiotics	25,28,34–36	5	0.91 (0.59–1.40)	0.67	35 (0.20)
Fiber + probiotics	32	1	0.39 (0.11–1.33)	0.13	–
Supplementary fiber dose, g/day					
<20	24,25,28,30–32,34,35	8	0.95 (0.74–1.23)	0.72	0 (0.74)
≥20	22,29,36,38	4	0.18 (0.06–0.57)	0.004*	0 (0.83)
Intervention time, days					
≤7	24,28,29	3	0.78 (0.47–1.30)	0.34	21 (0.28)
>7	22,25,30–32,34–36,38	9	0.89 (0.68–1.18)	0.43	23 (0.25)
Type of ICU					
Medical	29,36	2	0.13 (0.03–0.65)	0.01*	0 (0.66)
Surgical	22,25,32	3	0.40 (0.13–1.22)	0.11	0 (0.90)
General	24,28,30,31,34,35,38	7	0.97 (0.75–1.25)	0.81	0 (0.71)

Abbreviations: ICU, intensive care unit; OR, odds ratio.
*$P < 0.05$.

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DOI: 10.1002/jpen.2210

REVIEW

Safety of Using Enteral Nutrition Formulations Containing Dietary Fiber in Hospitalized Critical Care Patients: A Systematic Review and Meta-Analysis

Kelly Copeland Cara MS[1,2] | Andrew R. Beauchesne MD, MS[3] | Taylor C. Wallace PhD[4,5] | Mei Chung PhD, MPH[1,2]

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Abstract

Enteral nutrition (EN) is the preferred route of nutrition support for patients with critical illness undergoing intensive care. Experts in the field caution against using fiber during EN because of perceived adverse patient outcomes; however, a comprehensive

Random-effects meta-analysis models showed significantly lower diarrhea scores for fiber groups compared with nonfiber groups (pooled mean difference: −2.78; 95% CI, −4.10 to −1.47) but mixed results for risk of diarrhea between groups, depending on

Random-effects meta-analysis models showed significantly lower diarrhea scores for fiber groups compared with nonfiber groups (pooled mean difference: −2.78; 95% CI, −4.10 to −1.47) but mixed results for risk of diarrhea between groups, depending on

39% lower risk of gastrointestinal (GI) complications overall for fiber compared with nonfiber groups (pooled RR: 0.61; 95% CI, 0.47–0.79) but no group differences for indi-

nonfiber groups (pooled RR: 0.61; 95% CI, 0.47–0.79) but no group differences for individual GI complications, mortality, and intensive care unit or hospital length of stay. Analyses stratified by soluble- or mixed-fiber interventions reduced heterogeneity in models but showed identical conclusions. EN formulas with fiber may help reduce incidence and severity of diarrhea and GI complications overall in critically ill patients, without increased risk of other adverse events. Bias among specific GI measures indicates more high-quality studies are needed to verify these conclusions.

KEYWORDS
adverse event, critical care, diarrhea, dietary fiber, enteral nutrition, treatment outcome

FMT
Fecal Microbial Transplantation

- ✓ kompletní microbiota
- ✓ metabolity
- ✓ antimikrobiální peptidy
- ✓ imunoglobuliny
- ✓ žlučové kyseliny
- ? současně atb
- ? in
- alo vs. auto
- horní vs. dolní GIT, kapsle
- ? rizika krátko a dlouhodobá

➢ těžká a fulminatní CDI...FMT snižuje mortalitu a potřebu kolektomie (retrospektivní studie)

směřování u kriticky nemocných:

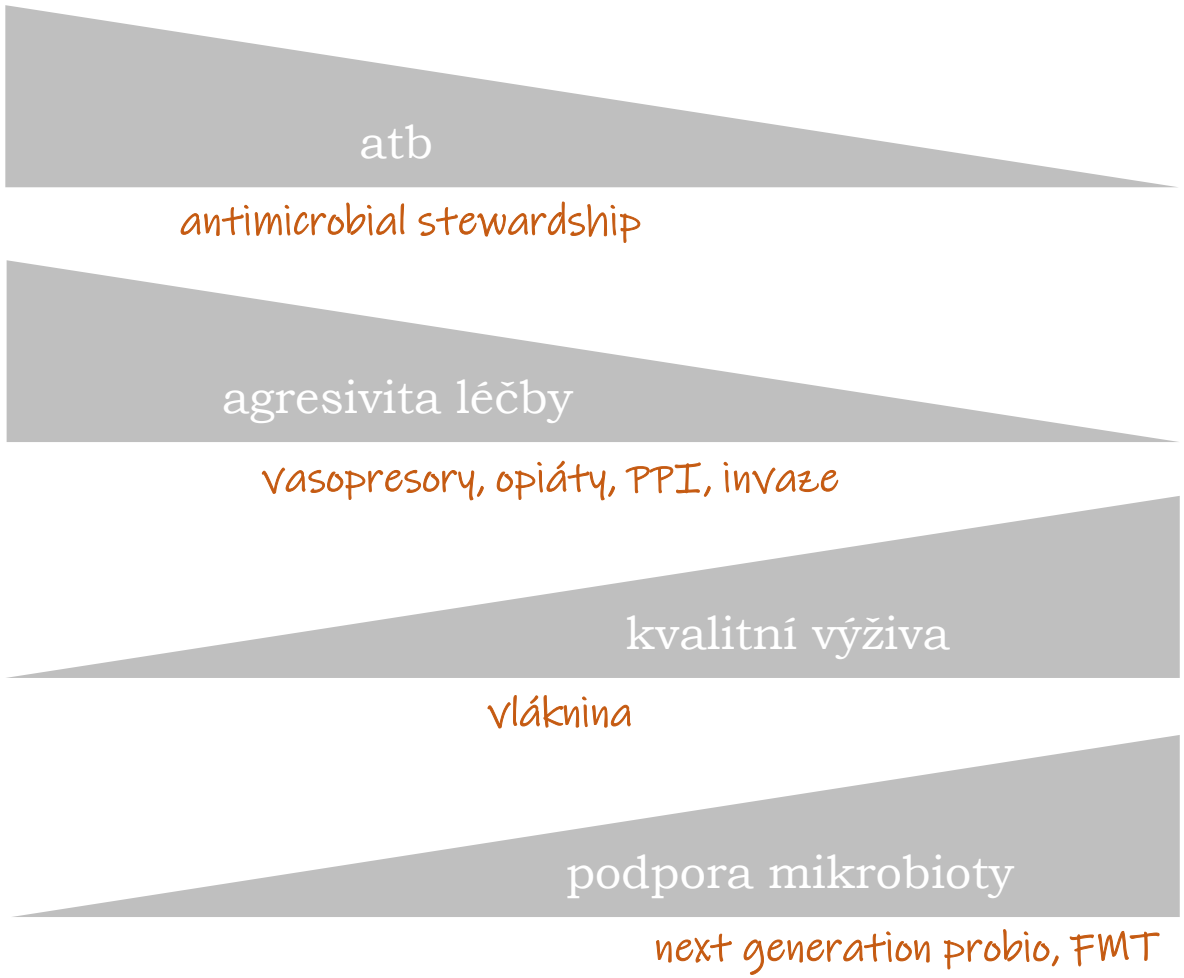
- ➢ těžká a fulminatní CDI
- ➢ postantibiotický průjem, AAD
- ➢ sepse
- ➢ recidivující infekce rezistentními kmeny
- ➢ protrahované kritické onemocnění

11. We suggest fecal microbiota transplantation (FMT) be considered for patients with severe and fulminant CDI refractory to antibiotic therapy, particularly, when patients are deemed poor surgical candidates (strong recommendation, low quality of evidence). ACG 2021

dtto ESMID 2021

ultimum refugium SIL ČLS JEP 2018

microbiota targeted…



nODS
CCI
PICS

FIND - Centrum výzkumu infekčních onemocnění CZ.02.1.01/0.0/0.0/16_019/0000787

obrázky a fotografie :
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