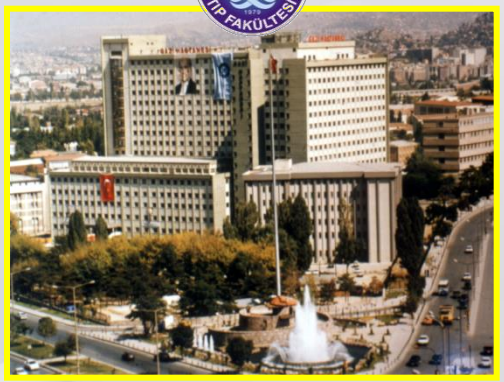
PROBİYOTİKLER-BİLMEMİZ GEREKENLER

Esin ŞENOL

G.Ü.T.F. Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji-AD



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19 Mayıs 2013

Her an Nobel bekliyorum! Mikrobun kadar konuş

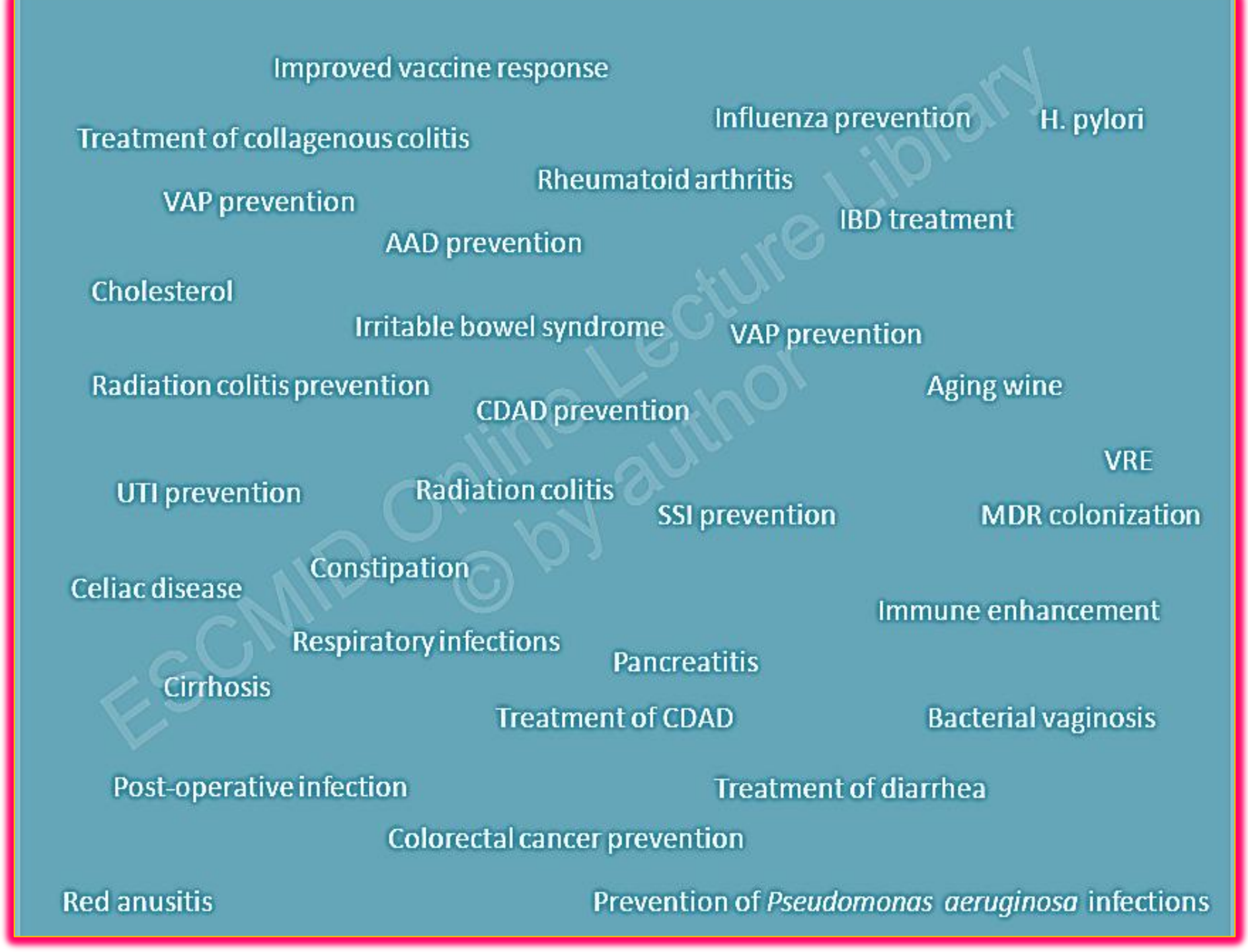
KİRLENMEK GÜZELDİR!

Yalnız galiba mikrop alanındaki çalışmalarım için biraz geç kaldım. Şu an tıp dünyası çalkalanıyor. **Son araştırmalara göre birkaç yüz farklı türden, trilyonlarca mikrop, vücudumuzda, cildimizde, dilimizde ve bağırsaklarımızda yaşıyor, üstelik bizi biz yapan, hastalıktan koruyan, bağışıklık sistemini güçlendiren, hatta neşimizi yerine getiren bile yine bu tipsizler!** İnsanoğlu, şehir hayatına geçip, ilaçlar ve yiyecekler yoluyla antibiyotik arttıkça vücuttaki mikrop çeşitliliği azalmış. Tıpkı doğada bazı bitki, böcek ve hayvanların neslinin tükenmesi ve dengenin bozulması gibi. Ortaçağ'da kediler uğursuz diye öldürülünce farelerin coşup çoğaldığı ve vebanın daha çabuk yayıldığı teorisi vardır ya... Onun gibi, antibiyotikli gıdalar ve ilaçlarla, enfeksiyon yapan kötü bakterilerin yanında, vücuttaki iyi mikropların bir kısmı telef olunca, dışarıdan gelen kötülerle savaşamamaya başlamışız. Batı insanının bedenindeki mikrop çeşitliliği, doğululardan daha az mesela. Yani onlar steril çevre, işlenmiş gıdalar ve ilaçlarla daha çok mikrobun neslini tüketmişler. **Amerikalı arkadaşınız ziyarete gelir, beraber dürüm yersiniz, siz mutlu mesut otururken zavallı gıda zehirlenmesi geçirir... Ondanmış işte!**

Çocuk 3 yaşına gelene kadar haşır neşir olduğu mikroplar onun mikrobiyal çeşitliliğini oluştururmuş. Reklam sloganı var ya 'Kirlenmek güzeldir', aynen öyleymiş yani. Sezaryenin bile bu açıdan zararı olduğu söyleniyor. Çocuk annesinden normal doğum yoluyla çıkarken, 'o yol üzerinde' bir sürü salgı, mikrop ve bakteriye maruz kalıyormuş cilt ve ağız yoluyla. Bunlar onun 'vücut ekosistemi'ni zenginleştirip, gelecekteki hayatında kötü mikropların bir kısmından koruyormuş. Sezaryen daha steril bir uygulama olduğundan, Amerika'da son trend, sezaryenle doğan çocukların cildine, annenin 'doğum yollarından' alınan salgıların pamuklu çubukla uygulanması!

"Mikropsuz büyütmeyin çocuğu, salın çayıra bayıra" diyorlar.

Balta girmemiş ormanlarda, hâlâ 2 bin yıl öncenin ilkelliğiyle yaşayan kabileler var Güney Amerika'da. Onların bünyelerindeki mikrop çeşitliliği bizi fena dövüyormuş! **Yani bizim mikrop sistemi belediye parkıysa, onlarınki, börtü böceğiyle, hayvanı bitkisiyle yağmur ormanı zenginliğindeymiş.** Bazı mikropların vücuttaki yokluğu, bağışıklık sisteminin kafasını karıştırırmış. Zararsız organizmaları bile zararlı sanıp onlarla savaşayım diye ortaya çıkan ve en çok gelişmiş ülkelerde görülen astım, alerji gibi hastalıkların sebebi buymuş!


Improved vaccine response
Influenza prevention
H. pylori
Treatment of collagenous colitis
Rheumatoid arthritis
VAP prevention
IBD treatment
AAD prevention
Cholesterol
Irritable bowel syndrome
VAP prevention
Radiation colitis prevention
Aging wine
CDAD prevention
VRE
UTI prevention
Radiation colitis
SSI prevention
MDR colonization
Constipation
Celiac disease
Immune enhancement
Respiratory infections
Pancreatitis
Cirrhosis
Treatment of CDAD
Bacterial vaginosis
Post-operative infection
Treatment of diarrhea
Colorectal cancer prevention
Red anusitis
Prevention of *Pseudomonas aeruginosa* infections
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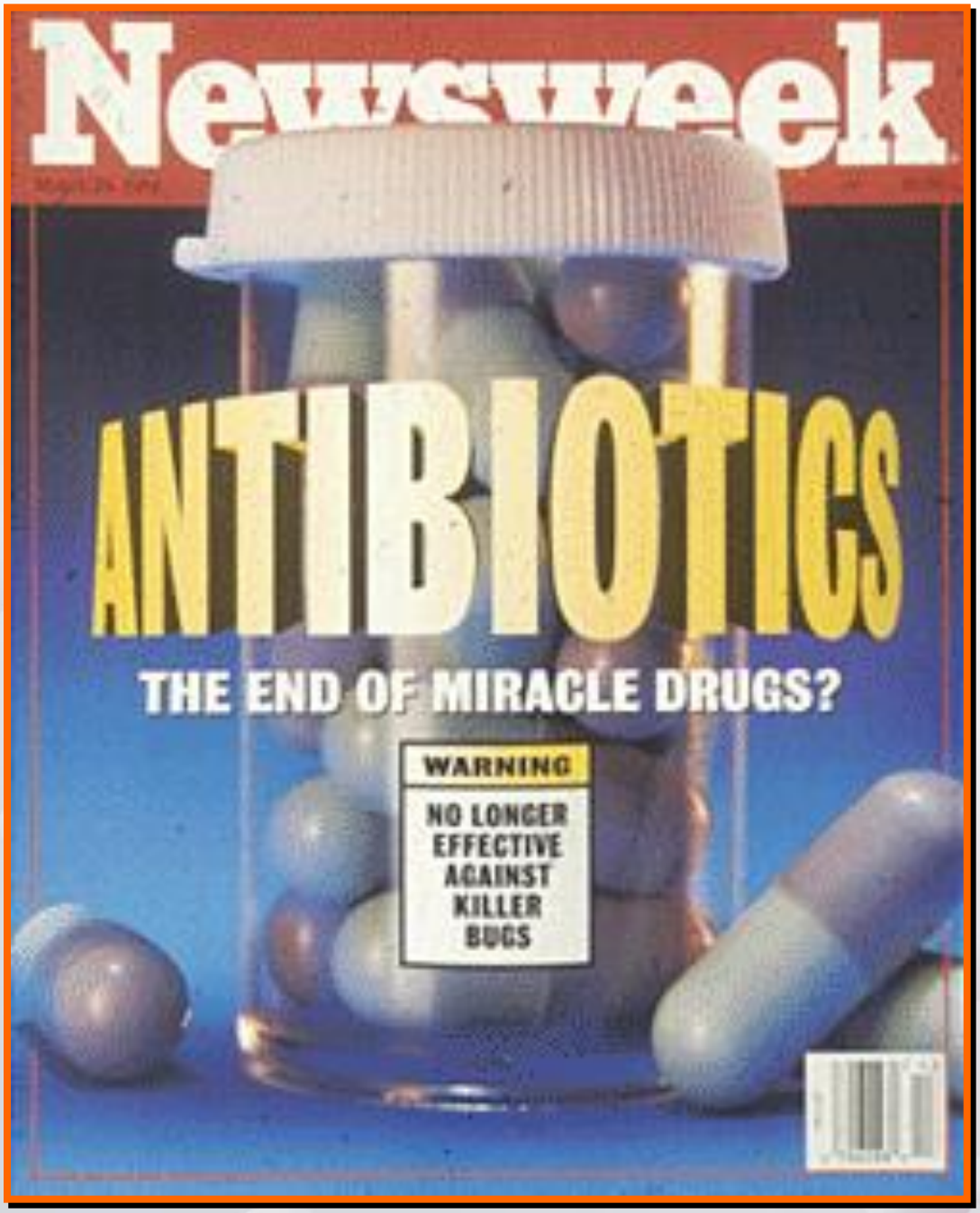
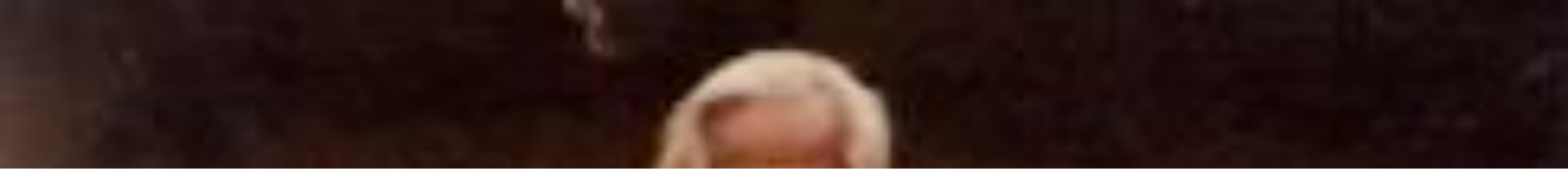

Newsweek
ANTIBIOTICS
THE END OF MIRACLE DRUGS?
WARNING
NO LONGER EFFECTIVE AGAINST KILLER BUGS

UZUN YAŞAMIN SIRRI- TESLİME TEYZE


YAŞLILIK HASTALIKLARIN
LİMANIDIR



GI EPİTEL

SEKRESYONLAR

BESİNLER

MİKROBİYOTA

METABOLOM:Hormonlar (steroid, eikosanoidler), Antimikrobiyel moleküller, Metabolitler

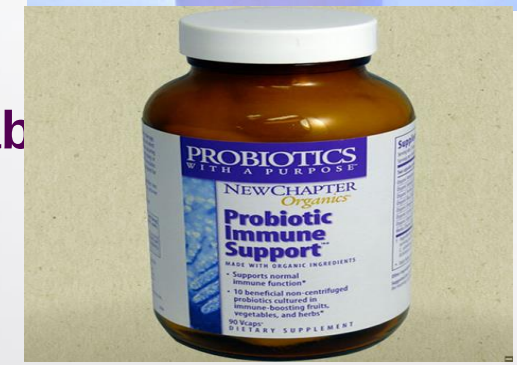
EKOSİSTEM

KENDİNİ SINIRLAYAN DOĞAL İNFLAMASYON

Probiyotik nedir?

- ✓ İnsan orijinli,detaylı tiplendirilmiş ve tanımlanmış
- ✓ Ptojenik özellikleri olmayan
- ✓ GİS'de canlı kalabilen
- ✓ Asit ve safraya dayanıklı
- ✓ İntestinal epitele tutunabilen, kolona kolonize olab
- ✓ Klinik olarak yararı gösterilmiş
- ✓ GÜVENLİ (GRAS)
- ✓ WHO, Birleşmiş Milletler ve FAO

(Food and Agriculture Organization) tanımı:



YETERLİ MİKTARDA VERİLDİĞİNDE SAĞLIK YÖNÜNDEN YARAR SAĞLAYAN CANLI MİKROORGANİZMALAR

EXPERT CONSENSUS DOCUMENT

The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic

Colin Hill, Francisco Guarner, Gregor Reid, Glenn R. Gibson, Daniel J. Merenstein, Bruno Pot, Lorenzo Morelli, Roberto Berni Canani, Harry J. Flint, Seppo Salminen, Philip C. Calder and Mary Ellen Sanders

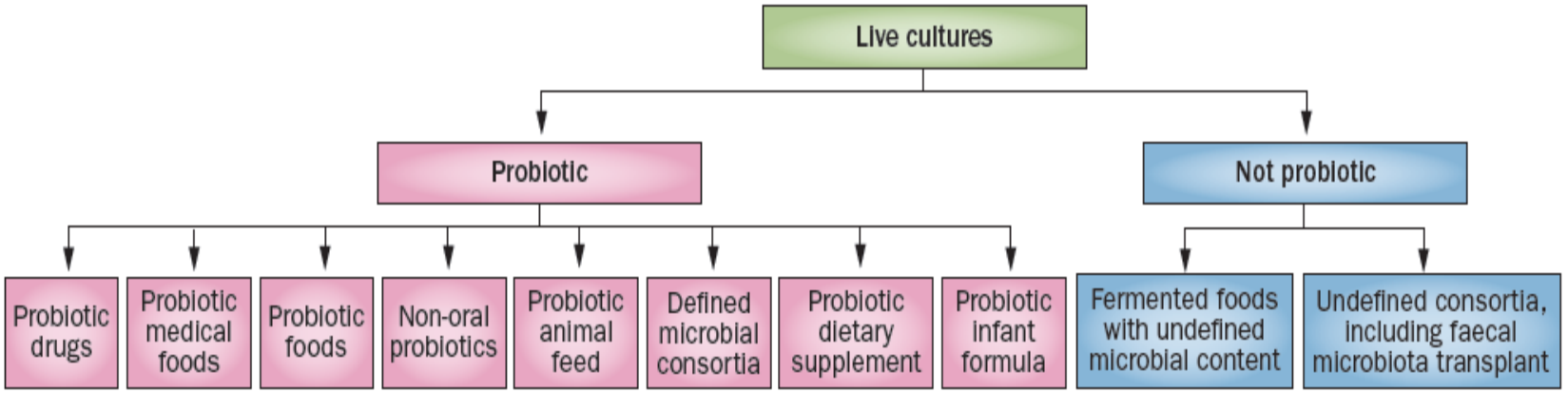
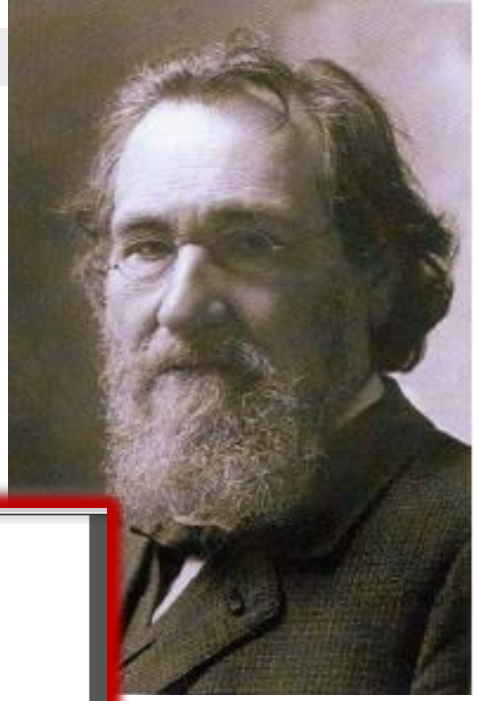


Figure 3 | Overall framework for probiotic products. Evidence of a health benefit is required for a probiotic, at either a strain-specific or group level, depending on the nature of the benefit. Probiotics can have different means of administration, target host species (humans and animals), target populations, target sites (gut and beyond), efficacy end points and regulatory categories. All probiotics must be safe for their intended use. Dead microbes, microbial products, microbial components do not come under the probiotic classification.

- Any specific claim beyond "contains probiotics" must be further substantiated
- Keep live cultures, traditionally associated with fermented foods and for which there is no evidence of a health benefit, outside the probiotic framework
- Keep undefined, faecal microbiota transplants outside the probiotic framework
- New commensals and consortia comprising defined strains from human samples, with adequate evidence of safety and efficacy, are 'probiotics'

Abbreviation: FAO, Food and Agriculture Organization of the United Nations.

Probiyotiklerin Tarihçesi



- Hz. İbrahim'in uzun yaşamını sağlayan ve

The history of probiotics: the untold story

M. Ozen[1*] and E.C. Dinleyici[2]

[1]Suleyman Demirel University, Department of Pediatrics, SDU Tip Fakultesi Hastanesi, Pediatri Bölümü, Çünür, 32100 Isparta, Turkey; [2]Eskisehir Osmangazi University, Faculty of Medicine, Department of Pediatrics, 26480 Eskisehir, Turkey; metehanoz@yahoo.com

Received: 20 July 2014 / Accepted: 26 September 2014

REVIEW ARTICLE

Abstract

Probiotic, a word derived from Latin, means 'for life'. A long time before the awareness of probiotic microorganisms, fermented products, such as beer, bread, wine, kefir, kumis and cheese had been very frequently used for nutritional and therapeutic purposes. It is widely believed that fermented products were probably found, or better to say, discovered spontaneously. The legend tells that yoghurt is most likely resulted from a fermentation process within the animal skin bags used for transportation of water and milk in regions with low humidity and high temperatures (Middle Asia and Middle East). The history of probiotics goes parallel with the evolution of human race and, thanks to the sophisticated techniques at the moment, can be traced back to the ancient times, nearly 10,000 years ago. The aims of this review are to highlight the important events for probiotic history, to correct the widely available anonymous misinformation in the literature and to remind to the readers important characters in its history.

Keywords: history of probiotics, fermented products, Henry Tissier, Stamen Grigorov, Elie Metchnikov

Mikrobiyal Flora Bozukluğu (Disbiyozis) eşlik eden hastalıklar

TABLE 1. Diseases and Disorders Associated with Human Gut Microbiome Aberrations (Adapted from[26])

Disease	Reference
Atopy and asthma	27
Celiac disease	28
Colon cancer	29
Type I diabetes	30
Type II diabetes	31
HIV infection	32
Inflammatory bowel disease	33–35
Irritable bowel syndrome	36–37
Gastroenteritis	38,39
Necrotizing enterocolitis	40
Obesity	41
Rheumatoid arthritis	42

J Clin Gastroenterol • Volume 45, Supp. 3, November/December 2011

Table 1 Microorganisms used as probiotics [17, 18]

Lactobacilli[a]	Bifidobacteria	Others
L. acidophilus-group	*B. longum* (BB536)	*Enterococcus faecalis*[b]
	B. longum (SP 07/3)	
L.acidophilus (LA-5)	*B. bifidum* (MF 20/5)	*Enterococcus faecium*[c]
L. crispatus (*L. acidophilus* "Gilliland")	*B. infantis*	*Lactococcus lactis*
L. johnsonii (LA1)	*B. animalis* (*B. animalis* ssp. *lactis* BB-12)	*Streptococcus thermophilus*
L. gasseri(PA 16/8)	*B. adolescentis*	*Propionibacteria*
L. casei- group	*B. breve*	*E. coli*[c] (*E. coli* "Nissle 1917")
L. (para)casei (*L. casei*) "shirota"		*Sporolactobac. Inulinus*[c]
L. casei "defensis")		
L. rhamnosus (LGG)		*Spores of Bacillus cereus* "toyoi"
L. reuteri		
L. plantarum (*299 and 299v*)		*Saccharomyces boulardii*[b]

TABLE 1. Mechanisms of Action of Probiotics

Antimicrobial Activity
Decrease luminal pH
Secrete antimicrobial peptides
Inhibit bacterial invasion
Block bacterial adhesion to epithelial cells
Enhancement of Barrier Function
Increase mucus production
Enhance barrier integrity
Immunomodulation
Effects on epithelial cells
Effects on dendritic cells
Effects on monocytes/macrophage
Effects on lymphocytes
- B lymphocytes
- NK cells
- T cells
- T cell redistribution

PROBİYOTİK-MİKROBİOTA

- İLİŞKİLİ FİLOTİPLERDE ↑-PATOJEN VE TOKSİNLERDE ↓
- MİKROBİOTA YAPISININ GÜÇLENDİRİLMESİ-BOZULMUŞSA ONARIM

- İnhibitörler (bakteriosin, H_2O_2, organik asitler)
- Çoğalmayı artıran salgılar
- İmmun cevaplar

❑ Genel mukozal immunite
❑ Dengeli T hc. Cevabı
❑ Polimerik IgA sentezi

- Müsin yapımı
- Epitel bariyere etki tight-junction-okludin,HsP "quarum sensing" moleküller
- NF-κβ inhibisyonu
- Apopitozu↓

İMMUN MODULASYON

Probiyotiklerin bozulmuş florayı düzeltmesi

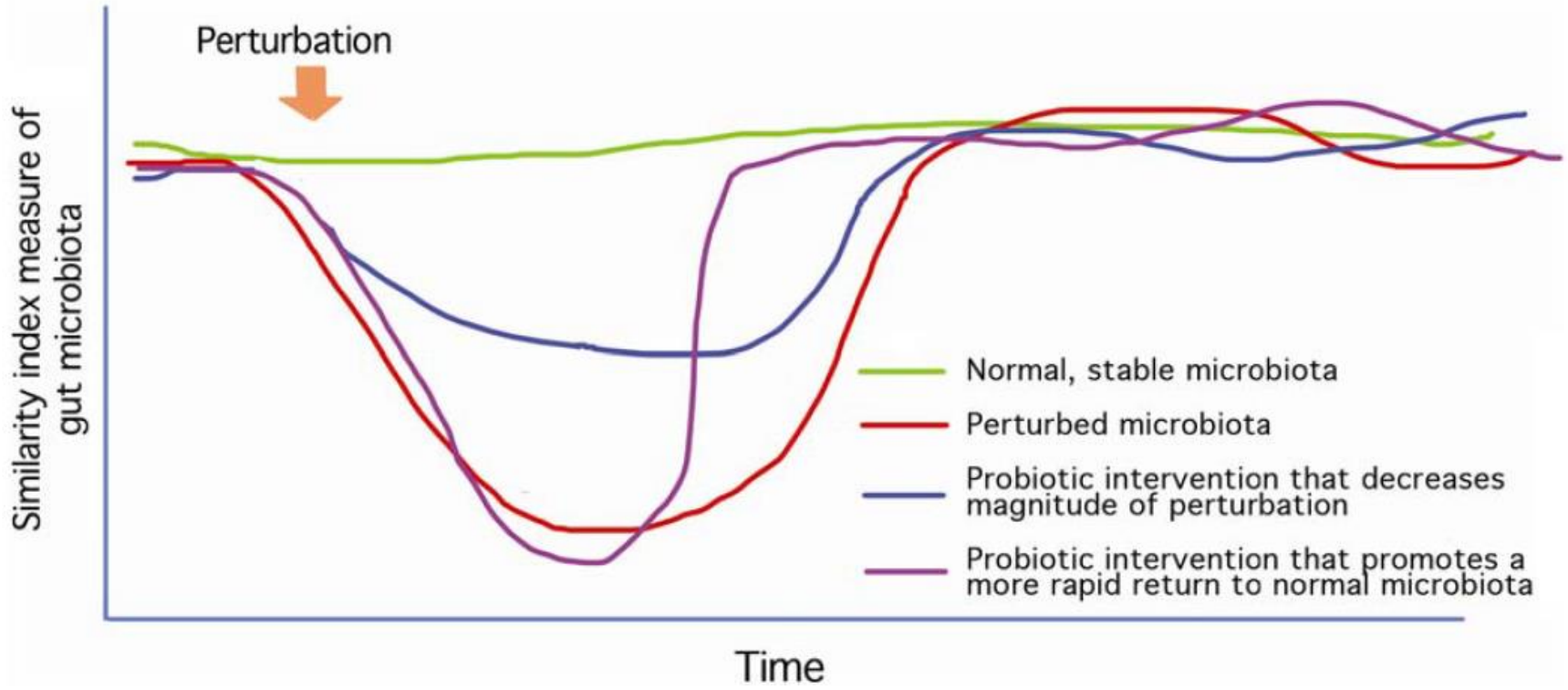


FIGURE 1. Probiotic intervention that decreases the magnitude of change or promotes a more rapid return to normal in a perturbed gut bacterial community. (Sanders et al. In Press). Reprinted with permission from Gut Microbes.

Probiyotik bakterilerin sentezlediği proteinlerin etkileri

Table 1. Probiotic extracellular proteins/peptides with a known role in the interaction of potential probiotic strains with mucosal cells

Protein	Micro-organism	Role	Reference
Serpin (AAN23973)	*B. longum* subsp. *longum* NCC2705	Inhibition of pancreatic and neutrophil elastases	Ivanov *et al.* (2006)
CHWPR peptide	*B. animalis* subsp. *lactis* BB-12	Upregulation of *c-myc* and *il-6* genes	Mitsuma *et al.* (2008)
Unidentified secreted proteins	*B. longum* subsp. *infantis*	Increase of the mucosal barrier function; attenuation of inflammation and colonic permeability in IL-10-deficient mice	Ewaschuk *et al.* (2008)
Unidentified secreted proteins	*B. breve* C50	Prolonged survival and maturation of DCs; increased IL-10 and IL-12 production by DCs	Hoarau *et al.* (2008)
Unidentified secreted proteins	*L. acidophilus* PZ 1138, *L. fermentum* PZ 1162, *L. paracasei* subsp. *paracasei* LMG P-17806	Induction of hBD2 production in epithelial cells	Schlee *et al.* (2008)
Peptides NPSRQERR and PDENK	*L. rhamnosus* GG	Antimicrobial activity	Lu *et al.* (2009)
Unidentified secreted proteins	*L. plantarum*, *L. acidophilus*, *L. casei* and *L. delbrueckii* subsp. *bulgaricus*	Induction of mucin secretion	Caballero-Franco *et al.* (2007)
Unidentified secreted proteins	*L. rhamnosus* GG	Increase of the production of HSP25 and HSP72 in YAMC cells	Tao *et al.* (2006)
Unidentified secreted proteins	*L. acidophilus* and *L. rhamnosus*	Increase of the chloride/hydroxyl exchange activity in Caco-2 cells	Borthakur *et al.* (2007)
p40 (homologous to gi|116493594)	*L. rhamnosus* GG	Growth promotion	Yan *et al.* (2007)
p75 (homologous to gi|116493849)	*L. rhamnosus* GG	Reduction of the injuries caused by TNF-α; attenuation of the TER decrease induced by hydrogen peroxide	Seth *et al.* (2008)
Supernatant containing P40 and p75?	*L. rhamnosus* GG	Decrease of IL-8 production in epithelial cells	Choi *et al.* (2008)
SlpA (YP_193101.1)	*L. acidophilus* NCFM	Induction of IL-10 production in DCs; DC immunomodulation	Konstantinov *et al.* (2008)
Unidentified secreted proteins	*E. coli* Nissle 1917	Inhibition of pathogen adhesion and colonization	Altenhoefer *et al.* (2004); Lasaro *et al.* (2009)
Flagellin	*E. coli* Nissle 1917	Increase of hBD2 and IL-8 production	Schlee *et al.* (2007)

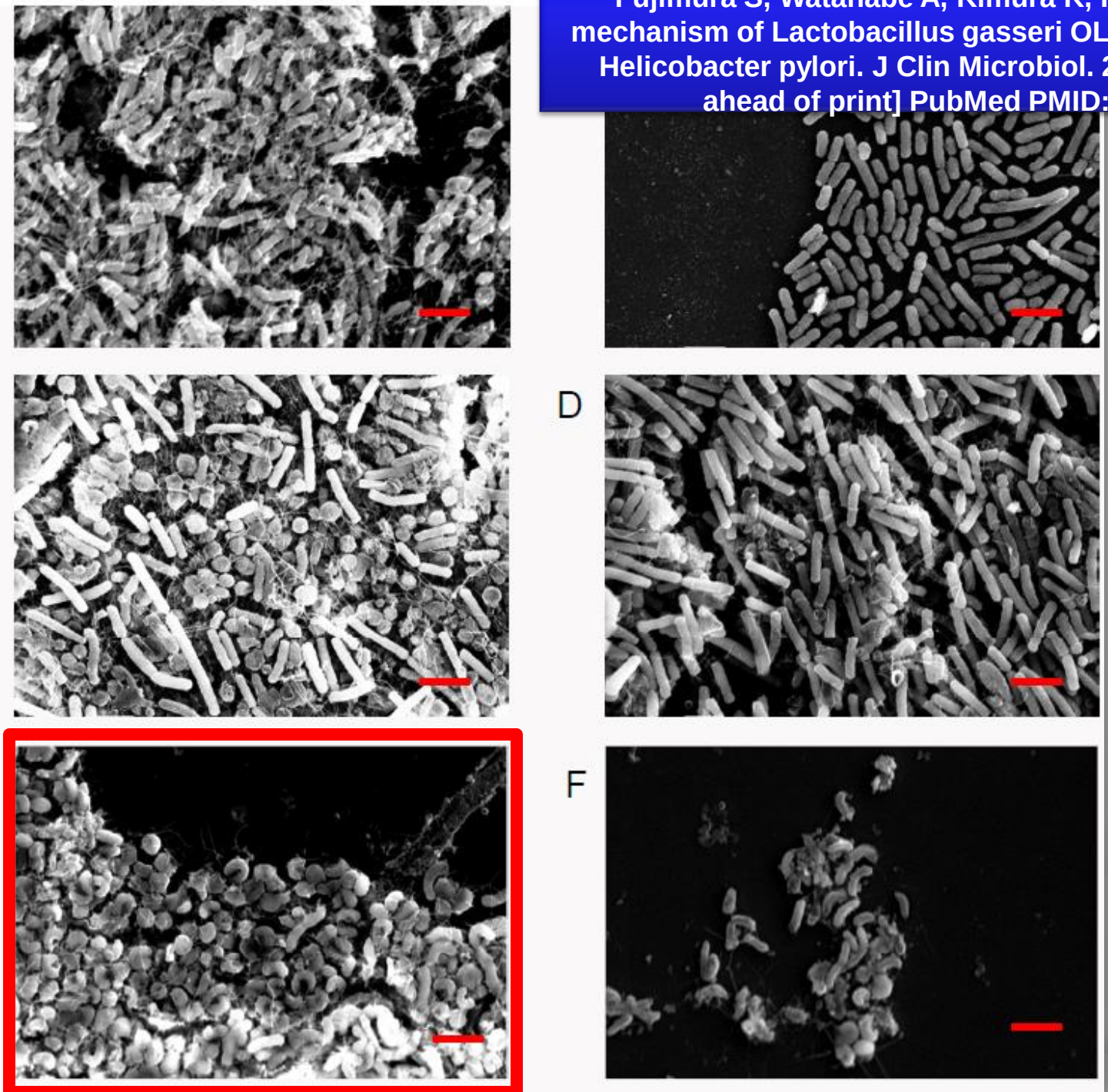
Curr Opin Clin Nutr Metab Care 2011 14:581

Table 1 **Summary of recent studies (2009–2010) on the effects of probiotics on systemic and mucosal immune function, barrier function, and metabolism.**

Type	Organism	Model system	Findings	Reference
Human clinical trials	*Lactobacillus delbrueckii bulgaricus* in yogurt	Healthy elderly	Increased NK cell activity Reduced risk of common cold	Ndagijimana et al. (2009)[15]
	Lactobacillus salivarius CECT5713	Phase 2 randomized, double-blind, placebo-controlled in 40 healthy adults	Increased frequency of defecation Increased % NK cells and monocytes Increased plasma IgM, IgA, IgG Increased plasma IL-10	Sierra et al. (2010)[16]
	Streptococcus thermophilus *Lactobacillus casei*	Double-blind, placebo-controlled trial in 162 children of low socioeconomic status for 4 months	No difference in response to vaccination No difference in days of fever or number of infections	Perez et al. (2010)[17]
	Lactobacillus gasseri CECT5714 *Lactobacillus coryniformis* CECT5711 in yogurt	Double-blind, randomized, placebo-controlled trial in 44 allergic children for 3 months	Decreased plasma IgE and increased Treg Increased gut sIgA Increased NK cells No difference in eosinophils, basophiles	Martinez-Canavate et al. (2009)[18]
	Bacillus coagulans GBI-30	10 healthy adults treated for 30 days, then exposed to adenovirus and influenza A	Probiotic treatment increased T cell production of TNF-α in response to virus exposure	Baron (2009)[19]
	Lactobacillus F19	Double-blind, placebo-controlled randomized trial in 179 infants from 4–13 months of age	Reduced incidence of eczema in probiotic group Increased IFNγ/IL-4 mRNA ratio in probiotic group	West et al. (2009)[20]
	Bifidobacterium lactis and long-chain fatty acids	Randomized, double-blind, controlled, parallel-group trial in 142 healthy infants for 7 months	No difference in growth between groups No difference in response to vaccines	Gibson et al. (2009)[21]
	Symbioflor 2 – *Escherichia coli*	Administered to 23 healthy adults for 3 weeks	Increased fecal beta-defensin2 in 78%	Mondel et al. (2009)[22]
	Lactobacillus sakei	Double-blind, placebo-controlled trial in 88 children with atopic eczema-dermatitis syndrome for 12 weeks	Probiotic group had decreased chemokine levels and clinical improvement	Woo et al. (2010)[23]
	VSL3	Ulcerative colitis patients	Treatment of UC patients with probiotic increased regulatory cytokines and lowered pro-inflammatory cytokine secretion from DC	Ng et al. (2010)[24]
	Bifidobacterium bifidum BGN4, *B. lactis* ADO11, *L. acidophilus* AD031	112 pregnant women treated from 4–8 weeks before delivery and until infants were 6 months old	Probiotic decreased prevalence of eczema 1 year No difference in serum total IgE	Kim et al. (2010)[25]
	Lactobacillus acidophilus, *Bifidobacterium longum*, fructooligosaccharides	16 healthy subjects studied after 1 month of treatment	Metabolic profiles in feces assessed by nuclear magnetic resonance	Ndagijimana et al. (2009)[15]
	B. longum, psyllium	120 ulcerative colitis patients treated for 4 weeks	Synbiotic therapy increased quality of life	Fujimori et al. (2010)[26]

Nutrition Reviews 2011; 69:392-403

Fujimura S, Watanabe A, Kimura K, Kaji M. Probiotics mechanism of Lactobacillus gasseri OLL2716 strain against Helicobacter pylori. J Clin Microbiol. 2012 Jan 11. [Epub ahead of print] PubMed PMID: 22205802.



Lactobacillus gasseri **eklenmesi kültürde H.P.'yi coccoid forma dönüştürüyor**

TABLE 2. Summary of Key Findings from Culture-dependent Assessments of the Impact of Probiotics on Colonizing Microbiota

Effects depend on strain, dose, and methods used
Transient increases in the genus, species, or strain of the fed probiotic strain are often observed in feces of patients
The fed probiotic is often not isolated 1 to 4 weeks after feeding has stopped (a few exceptions)
Changes in fecal populations of nonprobiotic species and genera are sometimes not observed and are not consistent among studies
Changes in biochemical parameters are sometimes observed, including changes in short chain fatty acid profiles, ammonia, amines, pH, phenols, p-cresol, and enzymatic activities
Reduction in numbers or virulence of pathogens or levels of toxins is sometimes observed

Hill, C. *et al. Nat. Rev. Gastroenterol. Hepatol.* **11**, 506–514 (2014); published online 10 June 2014; doi:10.1038/nrgastro.2014.66

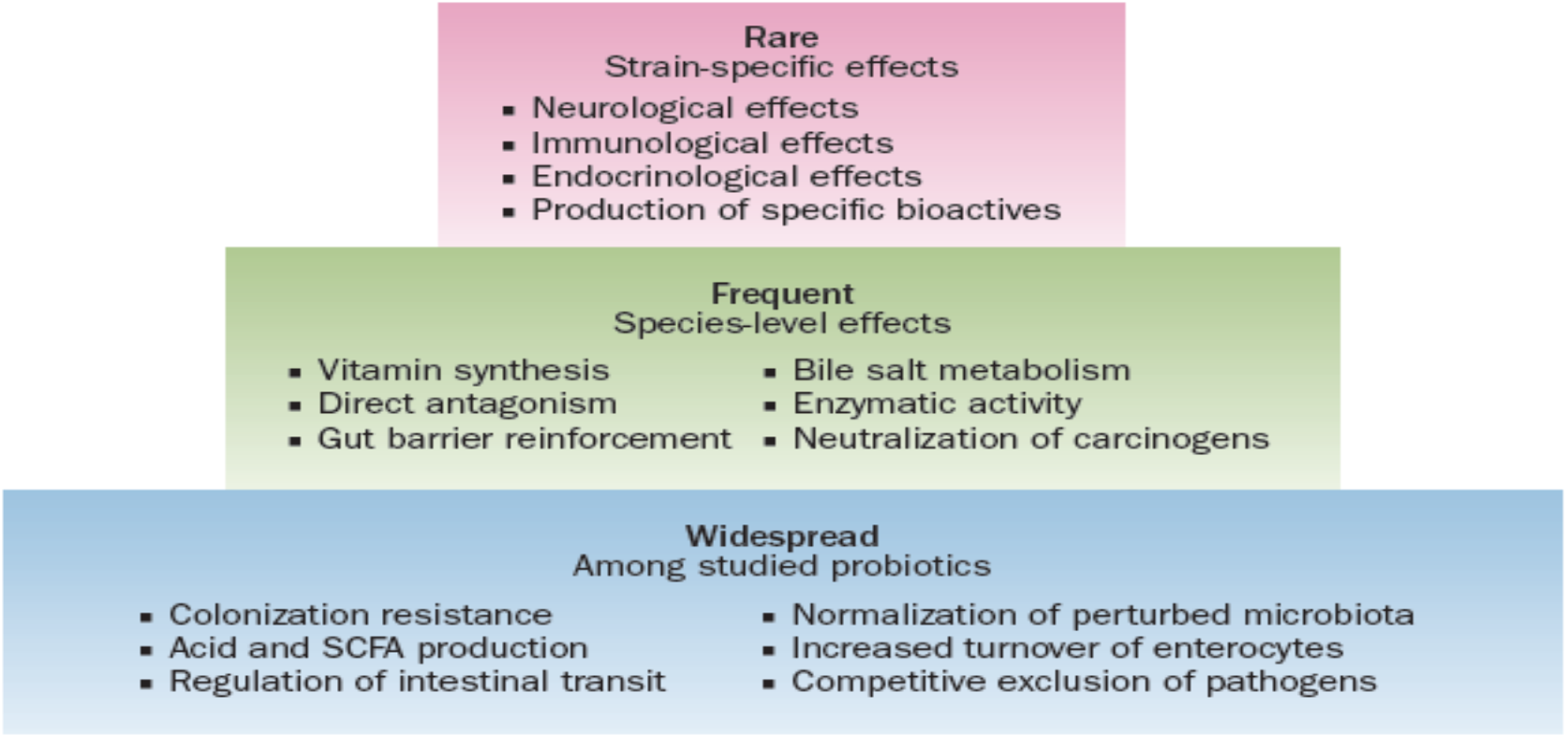


Figure 2 | Possible distribution of mechanisms among probiotics. Some mechanisms might be widespread among commonly studied probiotic genera; others might be frequently observed among most strains of a probiotic species; others may be rare and present in only a few strains of a given species. Evidence is accumulating on a cross-section of probiotic strains that suggest some generalizations can be made beyond strain-specific effects. Abbreviation: SCFA, short-chain fatty acid.

ÇALIŞMALAR

1973-2010; 4500

2002≥300, 2011≥1000

EN SIK ENTERİK İNFEKSİYONLAR

KRİTİK HASTALAR, YBÜ

KANIT-METAANALİZLER

REHBERLER

TABLE 11-3 Clinical Conditions or Settings Studied in Randomized, Controlled Clinical Trials to Evaluate Prebiotic, Probiotic, or Synbiotic Efficacy*

Prebiotics

Atopic dermatitis
Prevention of infections in infants or young children

Probiotics

Abdominal Conditions

Diarrheal diseases (infectious† and noninfectious‡)
Antibiotic-associated diarrhea
Necrotizing enterocolitis
Inflammatory bowel diseases (Crohn's disease, ulcerative colitis, pouchitis)
Collagenous colitis
Irritable bowel syndrome
Helicobacter pylori infection
Acute amebiasis
Acute severe pancreatitis
Diverticular colonic disease
Constipation
Hepatic encephalopathy
Colorectal neoplasia prevention

Oral and Respiratory Tract Conditions§

Gingivitis
Dental caries
Acute otitis media
Prevention of upper respiratory tract infections
Pulmonary exacerbations in cystic fibrosis

Urinary and Reproductive Tract Conditions

Prevention and treatment of bacterial vaginosis
Recurrent urinary tract infections
Recurrent bladder cancer

Allergic or Skin Conditions

Atopic dermatitis
Allergic rhinitis
Allergic asthma

Other

Prevention of infections in infants and young children
Prevention of nosocomial infections in intensive care units
Prevention of infections in the postoperative setting
Inhibition of nasal, oral, or fecal colonization with pathogenic bacteria¶
Mastitis
Hyperlipidemia
Hypertension
Spondyloarthropathy
Rheumatoid arthritis

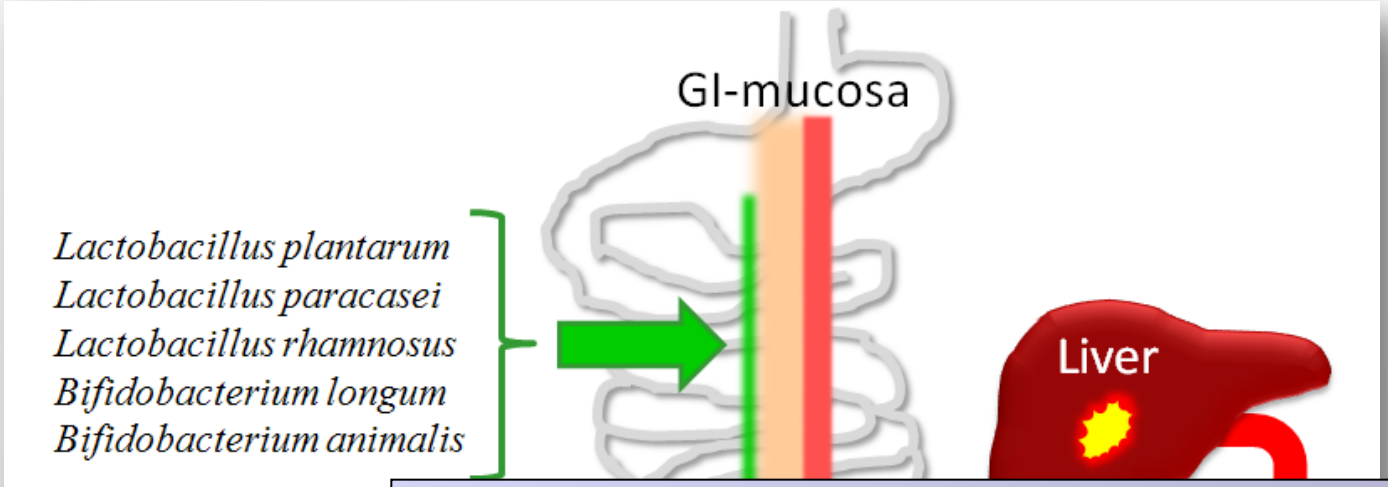
Synbiotics

Atopic dermatitis
Prophylaxis for diarrhea secondary to infant formula
Prevention of acute bacterial infections or respiratory tract infections
Impact on postoperative or trauma-associated infectious complications
Acute severe pancreatitis
Cirrhosis with hepatic encephalopathy

TABLE 11-4 Cochrane Database of Systematic Reviews: Efficacy of Probiotics

Goal of Prevention and Treatment	Author and Year	Number of Studies Included in Analysis of Probiotic Efficacy	Microbes in Probiotic	Conclusion
Gastrointestinal Diseases				
Treatment of infectious diarrhea	Allen et al.,[26] 2004	23 (5 adult studies; 18 pediatric studies)	*Lactobacillus* spp., *Saccharomyces boulardii*	Probiotics useful adjunct to rehydration therapy in adults and children; more research needed to identify specific probiotic regimen in specific patient groups
Prevention of pediatric antibiotic-associated diarrhea	Johnston et al.,[27] 2007	10 (pediatric studies)	*Lactobacillus* spp., *Bifidobacterium* spp., *Streptococcus* spp., *S. boulardii*	Trend toward better outcomes in probiotics group but not significant once intention-to-treat analysis was performed; future studies to focus on specific, more promising regimens and divide groups by age
Treatment of *Clostridium difficile*–associated colitis in	Pillai and Nelson,[28] 2008	4 (adult studies)	*Lactobacillus* spp., *S. boulardii*	Insufficient evidence; no evidence for probiotics by themselves; one of the four studies showed benefit for adjunct usage
Prevention of necrotizing enterocolitis in preterm infants	AlFaleh and Bassler,[29] 2008	9 (pediatric studies)	*Lactobacillus* spp., *Bifidobacterium* spp., *Streptococcus thermophilus*, *S. boulardii*	Probiotics reduced the risk of severe necrotizing enterocolitis and mortality in preterm infants weighing more than 1000 g; not enough data to conclude for infants with extremely low birth weight
Induction of remission in ulcerative colitis	Mallon et al.,[30] 2007	4 (adult studies)	*Escherichia coli* Nissle 1917, VSL #3, *Lactobacillus* GG, *Bifidobacterium* spp., prebiotics (fructo-oligosaccharide/inulin)	Probiotics did not improve overall remission rates in patients with mild to moderate ulcerative colitis; insufficient data to assess probiotics in moderate to severe ulcerative colitis
Induction of remission in Crohn's disease	Butterworth et al.,[31] 2008	1 (adult study)	*Lactobacillus* GG	Insufficient evidence to make any conclusions regarding efficacy of probiotics in inducing remission in Crohn's disease
Maintenance of remission in Crohn's disease	Rolfe et al.,[32] 2006	7 (6 adult studies; 1 pediatric study)	*E. coli* Nissle 1917, VSL #3, *Lactobacillus* GG, *S. boulardii*	No evidence that probiotics are beneficial for maintenance of remission in Crohn's disease; need for larger studies
Treatment for induction and maintenance of remission in pouchitis	Sandborn et al.,[33] 2000	1 (adult study)	VSL #3	Data limited, but probiotic therapy appears effective in maintaining remission in patients with chronic pouchitis
Treatment of collagenous colitis	Chande et al.,[34] 2008	1 (adult study)	*Bifidobacterium animalis* subsp, *lactis*	No evidence for effectiveness of probiotics in collagenous colitis
Interventions for recurrent abdominal pain and irritable bowel syndrome	Huertas-Ceballos et al.,[35] 2009	3 (pediatric studies)	*Lactobacillus* spp.	Insufficient evidence to support or refute efficacy of probiotics in recurrent abdominal pain and irritable bowel syndrome
Atopic Diseases				
Prevention of allergic disease and food hypersensitivity in infants	Osborn and Sinn,[36] 2007	12 (pediatric studies)	*Lactobacillus* spp., *Bifidobacterium* spp., *S. thermophilus*, *Propionibacterium freudenreichii*	Insufficient evidence; reduction in clinical eczema in infants but not consistent; need for further studies
Treatment of eczema	Boyle et al.,[37] 2008	12 (pediatric studies)	*Lactobacillus* spp., *Bifidobacterium* spp.	Not effective treatment for eczema; small risk of adverse events (case reports of infections and bowel ischemia) with probiotics
Miscellaneous Diseases				
Prevention of preterm labor	Othman et al.,[38] 2007	2 (adult studies)	*Lactobacillus johnsonii*, *Lactobacillus* spp. (vaginally)	In pregnancy, probiotics may have use for prevention and treatment of bacterial vaginosis; however, insufficient evidence to support or refute the use of probiotics in pregnancy to prevent preterm labor
Treatment of nonalcoholic fatty liver disease or steatohepatitis	Lirussi et al.,[39] 2007	2 (nonrandomized adult pilot studies)	*Lactobacilli* spp., VSL #3	Probiotics may improve conventional liver function test results and decrease markers of lipid peroxidation, but insufficient evidence to support or refute
Prevention of bacterial sepsis and wound complications for liver transplantation	Gurusamy et al.,[40] 2008	2 (adult studies)	*Lactobacilli* spp. and prebiotic (fiber)	Studies compared probiotics and prebiotics with selective bowel decontamination; the latter increased hospital stay and risk of infection compared with probiotics and prebiotics

TABLE 11-4 Cochrane Database of Systematic Reviews: Efficacy of Probiotics.



Lactobacillus plantarum
Lactobacillus paracasei
Lactobacillus rhamnosus
Bifidobacterium longum
Bifidobacterium animalis

Escherichia coli
Klebsiella pneumoniae
Sutterella wadsworthe
Bilophila wadsworthia
Acinetobacter lwoffii
Bacteroides fragilis
Prevotella melaninoge
Fusobacterium varium
Brachyspira aalborgi
Streptococcus anginos
Streptococcus pneumo
Peptostreptococcus an

Hepatolojide Barsak Florası ile ilgili alanlar

1. Hepatik Ensefalopati
2. NASH
3. Alkolik Hepatit
4. KC transplantasyonu
5. Kronik KC ve Siroz?

A Meta-Analysis of Probiotic Efficacy for Gastrointestinal Diseases

Marina L. Ritchie*, Tamara N. Romanuk

Department of Biology, Dalhousie University, Halifax, Nova Scotia, Canada

Abstract

Background: Meta-analyses on the effects of probiotics on specific gastrointestinal diseases have generally shown positive effects on disease prevention and treatment; however, the relative efficacy of probiotic use for treatment and prevention across different gastrointestinal diseases, with differing etiology and mechanisms of action, has not been addressed.

Methods/Principal Findings: We included randomized controlled trials in humans that used a specified probiotic in the treatment or prevention of Pouchitis, Infectious diarrhea, Irritable Bowel Syndrome, *Helicobacter pylori*, *Clostridium difficile* Disease, Antibiotic Associated Diarrhea, Traveler's Diarrhea, or Necrotizing Enterocolitis. Random effects models were used to evaluate efficacy as pooled relative risks across the eight diseases as well as across probiotic species, single vs. multiple species, patient ages, dosages, and length of treatment. Probiotics had a positive significant effect across all eight gastrointestinal diseases with a relative risk of 0.58 (95% (CI) 0.51–0.65). Six of the eight diseases: Pouchitis, Infectious diarrhea, Irritable Bowel Syndrome, *Helicobacter pylori*, *Clostridium difficile* Disease, and Antibiotic Associated Diarrhea, showed positive significant effects. Traveler's Diarrhea and Necrotizing Enterocolitis did not show significant effects of probiotcs. Of the 11 species and species mixtures, all showed positive significant effects except for *Lactobacillus acidophilus*, *Lactobacillus plantarum*, and *Bifidobacterium infantis*. Across all diseases and probiotic species, positive significant effects of probiotics were observed for all age groups, single vs. multiple species, and treatment lengths.

Conclusions/Significance: Probiotics are generally beneficial in treatment and prevention of gastrointestinal diseases. Efficacy was not observed for Traveler's Diarrhea or Necrotizing Enterocolitis or for the probiotic species *L. acidophilus*, *L. plantarum*, and *B. infantis*. When choosing to use probiotics in the treatment or prevention of gastrointestinal disease, the type of disease and probiotic species (strain) are the most important factors to take into consideration.

Citation: Ritchie ML, Romanuk TN (2012) A Meta-Analysis of Probiotic Efficacy for Gastrointestinal Diseases. PLoS ONE 7(4): e34938. doi:10.1371/journal.pone.0034938

Editor: Markus M. Heimesaat, Charité, Campus Benjamin Franklin, Germany

Received November 10, 2011; **Accepted** March 11, 2012; **Published** April 18, 2012

Probiotics for treating acute infectious diarrhoea (Review)

Allen SJ, Martinez EG, Gregorio GV, Dans L

63 çalışma
56'sı çocuklarda yapılmış
8014 kişi

İshal süresinde 24.7 saat azalma

2.günden itibaren günlük gayta sayısında azalma

4.Günden sonra halen ishali devam eden olgu sayısında azalma

The average of the effect was significant for mean duration of diarrhoea (mean difference 24.76 hours; 95% confidence interval 15.9 to 33.6 hours; n=4555, trials=35) diarrhoea lasting ≥4 days (risk ratio 0.41; 0.32 to 0.53; n=2853, trials=29) and stool frequency on day 2 (mean difference 0.80; 0.45 to 1.14; n=2751, trials=20).

The differences in effect size between studies was not explained by study quality, probiotic strain, the number of different strains, the viability of the organisms, dosage of organisms, the causes of diarrhoea, or the severity of the diarrhoea, or whether the studies were done in developed or developing countries.

Authors' conclusions

Used alongside rehydration therapy, probiotics appear to be safe and have clear beneficial effects in shortening the duration and reducing stool frequency in acute infectious diarrhoea. However, more research is needed to guide the use of particular probiotic regimens in specific patient groups.

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2010, Issue 11

World Journal of Gastroenterology

Online Submissions: http://www.wjgnet.com/1007-9327office
wjg@wjgnet.com
doi:10.3748/wjg.v16.i18.2202

World J Gastroenterol 2010 May 14; 16(18): 2202-2222
ISSN 1007-9327 (print)

EDITORIAL

Systematic review and meta-analysis of *Saccharomyces boulardii* in adult patients

31RKÇ;5029 olgu,1976-2009
AAD;RR:0.47

Lynne V McFarland

McFarland LV. *Saccharomyces boulardii* in adults

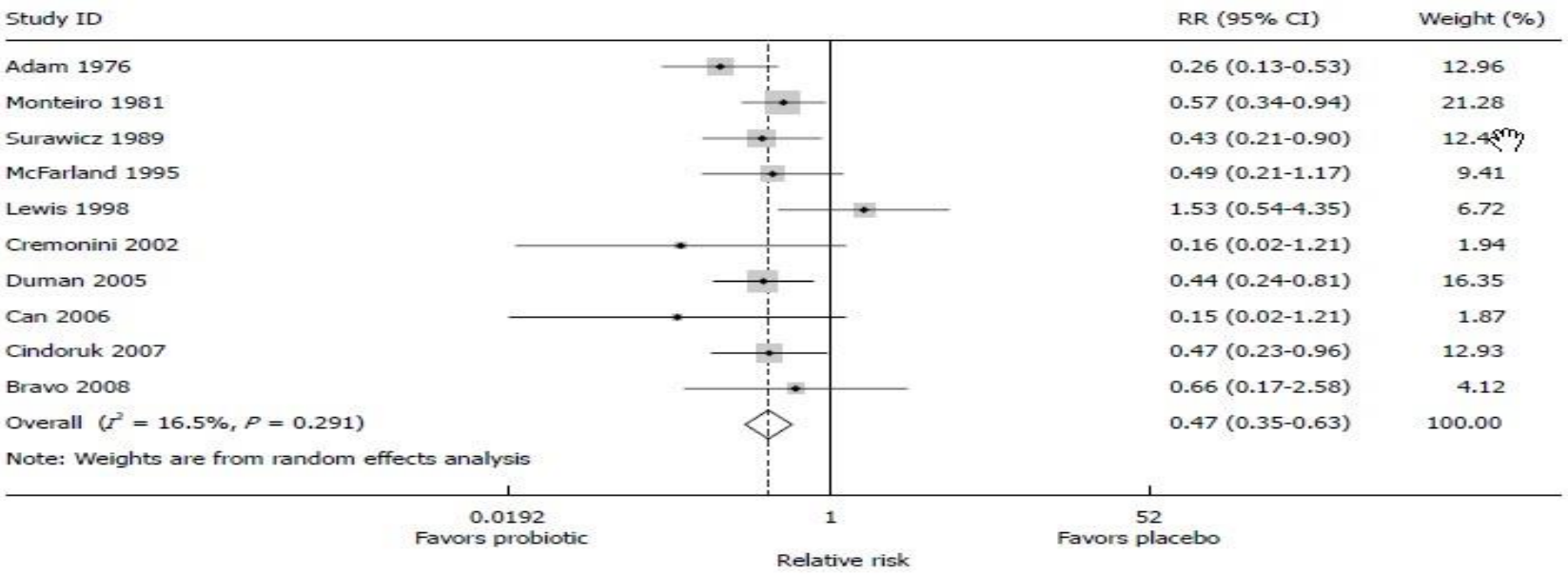


Table 3 Randomized controlled trials for the treatment of *C. difficile* disease using *S. boulardii*

Ref.	Treatment groups	Study population	Daily dose: cfu/d (mg/d)	Duration of treatment (wk)	Follow-up (wk)	*C. difficile* recurrence in probiotic group	*C. difficile* recurrence in placebo group
McFarland *et al*[55]	*S. boulardii* *vs* placebo	124 adult patients on varied doses of vancomycin or metronidazole; recurrent and initial CDAD cases; 3 referral sites, US	3×10^{10} (1000 mg)	4	4	15/57 (26.3%)*	30/67 (44.8%)
Surawicz *et al*[60]	*S. boulardii* *vs* placebo	168 adult patients recurrent CDAD; on vancomycin (2 g/d, $n = 32$) or V (500 mg/d, $n = 83$) or M (1 g/d, $n = 53$); 4 referral sites, US	2×10^{10} (1000 mg)	4	4	V (2 g/d) 3/18 (17%)*; V (500 mg/d) 23/45 (51%); M (1 g/d) 13/27 (48.1%)	V (2 g/d) 7/14 (50%); V (500 mg/d) 17/38 (44.7%); M (1 g/d) 13/26 (50%)

*$P < 0.05$, probiotic *vs* controls. V: Vancomycin; M: Metronidazole.

McFarland LV. *Saccharomyces boulardii* in adults

Table 6 Summary of recommendations for clinical use of *S. boulardii* in adults

Use for disease	Dose (mg/d)	Duration	Adjunct to	Strength of evidence[1]
Prevention of antibiotic associated diarrhea	500-1000	During antibiotics with additional 3 d to 2 wk after	Nothing	++++
Prevention of Traveler's diarrhea	250-1000	Duration of trip (3 wk)	Nothing	+++
Enteral nutrition-related diarrhea	2000	8-28 d	Nothing	++
H. pylori symptoms	1000	2 wk	Standard triple therapy	++
Treatment of *Clostridium difficile* infections	1000	4 wk	Vancomycin or metronidazole	+
Acute adult diarrhea	500-750	8-10 d	Nothing	+
Inflammatory bowel disease	750-1000	7 wk to 6 mo	Mesalamine	+
Irritable bowel syndrome	500	4 wk	Nothing	+
Giardiasis	500	4 wk	Metronidazole	+
HIV-related diarrhea	3000	7 d	Nothing	+

[1]Strength of evidence, + (weak, needs more randomized controlled trials) to ++++ (strong, efficacy and safety are evidence based from numerous large randomized controlled trials).

Probiotics for the Prevention and Treatment of Antibiotic-Associated Diarrhea

A Systematic Review and Meta-analysis

Susanne Hempel, PhD
Sydne J. Newberry, PhD
Alicia R. Maher, MD
Zhen Wang, PhD
Jeremy N. V. Miles, PhD
Roberta Shanman, MS
Breanne Johnsen, BS
Paul G. Shekelle, MD, PhD

Context Probiotics are live microorganisms intended to confer a health benefit when consumed. One condition for which probiotics have been advocated is the diarrhea that is a common adverse effect of antibiotic use.

Objective To evaluate the evidence for probiotic use in the prevention and treatment of antibiotic-associated diarrhea (AAD).

Data Sources Twelve electronic databases were searched (DARE, Cochrane Library of Systematic Reviews, CENTRAL, PubMed, EMBASE, CINAHL, AMED, MANTIS, TOXLINE, ToxFILE, NTIS, and AGRICOLA) and references of included studies and reviews were screened from database inception to February 2012, without language restriction.

Study Selection Two independent reviewers identified parallel randomized controlled trials (RCTs) of probiotics (*Lactobacillus, Bifidobacterium, Saccharomyces, Streptococcus, Enterococcus*, and/or *Bacillus*) for the prevention or treatment of AAD.

Data Extraction Two independent reviewers extracted the data and assessed trial quality.

Results A total of 82 RCTs met inclusion criteria. The majority used *Lactobacillus*-based interventions alone or in combination with other genera; strains were poorly documented. The pooled relative risk in a DerSimonian-Laird random-effects meta-analysis of 63 RCTs, which included 11 811 participants, indicated a statistically significant association of probiotic administration with reduction in AAD (relative risk, 0.58; 95% CI, 0.50 to 0.68; $P<.001$; I^2, 54%; [risk difference, –0.07; 95% CI, –0.10 to –0.05], [number needed to treat, 13; 95% CI, 10.3 to 19.1]) in trials reporting on the number of patients with AAD. This result was relatively insensitive to numerous subgroup analyses. However, there exists significant heterogeneity in pooled results and the evidence is insufficient to determine whether this association varies systematically by population, antibiotic characteristic, or probiotic preparation.

Conclusions The pooled evidence suggests that probiotics are associated with a reduction in AAD. More research is needed to determine which probiotics are associated with the greatest efficacy and for which patients receiving which specific antibiotics.

JAMA. 2012;307(18):1959-1969 www.jama.com

THE USE OF ANTIBIOTICS THAT DISturb the gastrointestinal flora is associated with clinical symptoms such as diarrhea, which occurs in as many as 30% of patients.[1,2] Symptoms range from mild and self-limiting to severe, particularly in *Clostridium difficile* infections, and antibiotic-associated diarrhea (AAD) is an important reason for nonadherence with antibiotic treatment.[3]

Probiotics are microorganisms intended to have a health benefit when consumed. Synbiotics refer to preparations in which probiotic organisms and prebiotics (nondigestible food ingredients that may benefit the host by selectively stimulating bacteria in the colon) are combined.

Potentially, probiotics maintain or re-

REVIEW | Annals of Internal Medicine

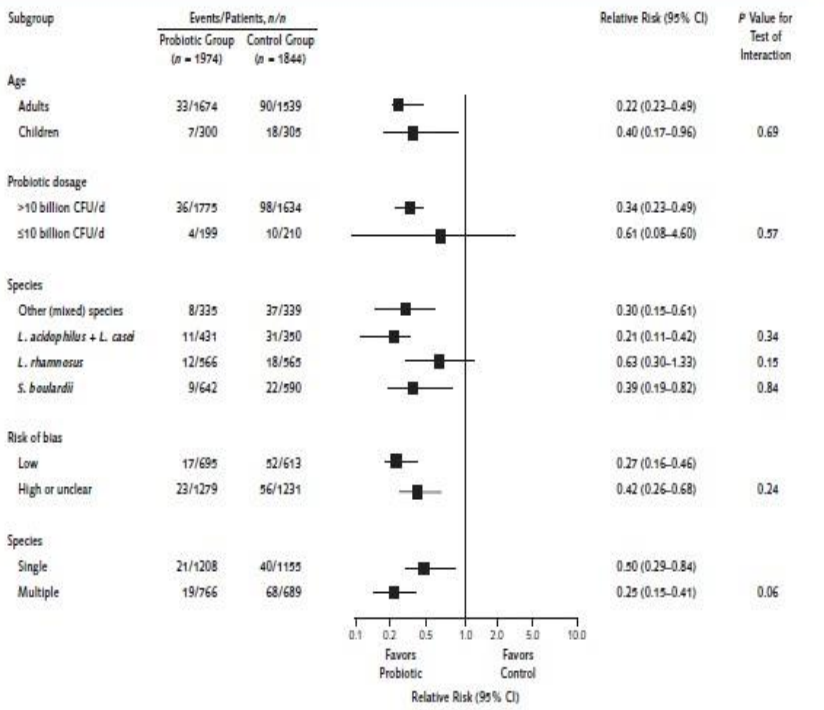
Probiotics for the Prevention of *Clostridium difficile*–Associated Diarrhea

A Systematic Review and Meta-analysis

Bradley C. Johnston, PhD; Stephanie S.Y. Ma, MD; Joshua Z. G
Mark Loeb, MD; and Gordon H. Guyatt, MD

- **20 randomize çalışma; 3818 hasta; CDİ azaltma insidansı %66**

Figure 4. Effect of probiotics on prevention of *Clostridium difficile*–associated diarrhea among subgroups.



CFU = colony-forming units.

Data Synthesis: Twenty trials including 3818 participants met the eligibility criteria. Probiotics reduced the incidence of CDAD by 66% (pooled relative risk, 0.34 [95% CI, 0.24 to 0.49]; I^2 = 0%). In a population with a 5% incidence of antibiotic-associated CDAD (median control group risk), probiotic prophylaxis would prevent 33 episodes (CI, 25 to 38 episodes) per 1000 persons. Of probiotic-treated patients, 9.3% experienced adverse events, compared with 12.6% of control patients (relative risk, 0.82 [CI, 0.65 to 1.05]; I^2 = 17%).

Limitations: In 13 trials, data on CDAD were missing for 5% to 45% of patients. The results were robust to worst-plausible assumptions regarding event rates in studies with missing outcome data.

Conclusion: Moderate-quality evidence suggests that probiotic prophylaxis results in a large reduction in CDAD without an increase in clinically important adverse events.

Primary Funding Source: None.

Ann Intern Med. 2012;157:878-888. www.annals.org
For author affiliations, see end of text.
This article was published at www.annals.org on 13 November 2012.

AP&T Alimentary Pharmacology and Therapeutics

Meta-analysis: probiotics in antibiotic-associated diarrhoea

E. J. Videlock* & F. Cremonini†

Results

A total of 34 studies were included with 4138 patients. The pooled relative risk (RR) for AAD in the probiotic group vs. placebo was 0.53 (95% CI 0.44–0.63), corresponding to a number needed to treat (NNT) of 8 (95% CI 7–11). The preventive effect of probiotics remained significant when grouped by probiotic species, population age group, relative duration of antibiotics and probiotics, study risk of bias and probiotic administered. The pooled RR for AAD during treatment for *Helicobacter pylori* (*H. pylori*) was 0.37 (95% CI 0.20–0.69), corresponding to a NNT of 5 (95% CI 4–10).

Lactobacillus GG;0.40
S.boulardii;0.46
Lactobacillus; 0.56
Bifidobacteria;0.56

Conclusions

This updated meta-analysis confirms earlier results supporting the preventive effects of probiotics in AAD.

Aliment Pharmacol Ther 2012; **35**: 1355–1369

17 Role of Probiotics in the Management of *Helicobacter pylori* Infection

Philip M. Sherman and Kathene C. Johnson-Henry

14 randomize :1671 olgu içeren klinik çalışmanın değerlendirildiği meta-analiz ;

H. pylori **tedavisine probiyotiklerin eklenmesi :74.8% → 83.6%**

Tedavi yan etkilerini ise :38.5% → 24.7%

Recommendations for Probiotic Use—2011 Update

Martin H. Floch, MD, W. Allan Walker, MD,† Karen Madsen, PhD,‡ Mary Ellen Sanders, PhD,§ George T. Macfarlane, PhD,‖ Harry J. Flint, PhD,¶ Levinus A. Dieleman, MD, PhD,‡ Yehuda Ringel, MD,# Stefano Guandalini, MD,** Ciaran P. Kelly, MD,†† and Lawrence J. Brandt, MD‡‡*

Abstract: This study describes the consensus opinion of the participants of the third Yale Workshop on probiotic use. There were 10 experts participating. The recommendations update those of the first 2 meetings that were published in 2005 and 2008. The workshop presentations and papers in this supplement relate to the involvement of normal microbiota involved in intestinal microecology, how the microbes interact with the intestine to affect our immunologic responses, the stability and natural history of probiotic organisms, and the role of the intestinal microbatome with regard to affecting cardiac risk factors and obesity. Recommendations for the use of probiotics in necrotizing enterocolitis, childhood diarrhea, inflammatory bowel disease, irritable bowel syndrome, and *Clostridium difficile* diarrhea are reviewed. As in previous publications, the recommendations are given as A, B, or C ratings. The recent positive experiences with bacteriotherapy (fecal microbiome transplant) are also discussed in detail and a positive recommendation is made for use in severe resistant *C. difficile* diarrhea.

Key Words: probiotics, recommendations, diarrhea

(*J Clin Gastroenterol* 2011;45:S168–S171)

The first Yale Workshop on Probiotics was convened in 2004. The clinical use of probiotics had gained worldwide attention of patients and health care delivery personnel, but although there was a growing literature on clinical trials, there were few clinical recommendations. Hence, we gathered thought leaders and investigators in the field and published the first workshop recommendations in 2005.[1] We held the second workshop with some of the original contributors but added others to broaden our view. The results of the second workshop were published in 2008.[2]

This paper[3] represents the work of 10 experts of the third Yale Workshop held in New Haven in April 2011.

Dr Walker and I designed this program in an effort

Recommendations for Probiotic Use—2011 Update

Martin H. Floch, MD. W. Allan Walker, MD.† Karen Madsen, PhD.‡ Mary Ellen Sanders, PhD.§ George T. Macfarlane, PhD.‖ Harry J. Flint, PhD.¶ Levinus A. Dieleman, MD, PhD.‡ Yehuda Ringel, MD.# Stefano Guandalini, MD.** Ciaran P. Kelly, MD.†† and Lawrence J. Brandt, MD.‡‡*

(*J Clin Gastroenterol* 2011;45:S168–S171)

Diarrhea			
Infectious childhood—treatment	A	*Saccharomyces boulardii*,[15] LGG,[16] *Lactobacillus reuteri* SD2112[17]	15–18
Prevention of infection	B	*S. boulardii*,[15] LGG[16]	15,16,18
Prevention of AAD	A	*S. boulardii*.[19] LGG,[20] combination of *Lactobacillus casei* DN114 G01, *Lactobacillus bulgaricus*, snf *Saccharomyces thermophilus*[21]	19–21
Prevention of recurrent CDAD	B/C	*S. boulardii*,[11] LGG,[22] bacteriotherapy[14]	11,12,14,22
Prevention of CDAD	B/C	LGG,[11] *S. boulardii*[22]	11,22
IBD			
Pouchitis			
Preventing and maintaining remission	A	VSL#3[23–25]	23–25
Induce remission	C	VSL#3[26]	26
Ulcerative colitis			
Inducing remission	B	*Escherichia coli* Nissle[27], VSL#3[28]	27–29
Maintenance	A	*E. coli* Nissle,[30] VSL#3[29]	28–30
Crohn's	C	*E. coli* Nissle,[31] *S. boulardii*,[32] LGG[33]	31–33
IBS			
	B	Bifidobacterium infantis B5624,[34,35] VSL#3[34–37,48]	34–37,48†
	C	*Bifidobacterium animalis*[38]	38
		Lactobacillus plantarum 299V[39]	39
Necrotizing Enterocolitis			
	B	*Lactobacillus acidophilus* NCDO1748[13] and *Bifidobacterium bifidium* NCDO1453[47]	13,47
Recommendations From 2008*			
Immune response			
	A	LGG, *Lactobacillus acidophilus* LAFT1, *Lactobacillus* plantarum, *Bifidobacterium lactis*, *Lactobacillus johnsonii*	40,41
Allergy			
Atopic eczema associated with cow's milk allergy			
Treatment	A	LGG, *Bifidobacterium lactis*[41]	41
Prevention	A	LGG, *B. lactis*[41]	41
Radiation enteritis			
	C	VSL#3,[42] *L. acidophilus*[43]	42,43
Vaginosis and vaginitis			
	C	*L. acidophilus*,[44] *Lactobacillus rhamnosus* GR-1,[45] *L. reuteri* RC14[46]	44–46

World Gastroenterology Organisation Global Guidelines

Probiotics and Prebiotics
October 2011

Review Team, Francisco Guarner, MD (Chair, Spain), Aamir G. Khan, MD (Pakistan), James Garisch, MD (South Africa), Rami Eliakim, MD (Israel), Alfred Gangl, MD (Austria), Alan Thomson, MD (Canada), Justus Krabshuis (France), Ton Lemair, MD (The Netherlands), Invited outside experts, Pedro Kaufmann, MD (Uruguay), Juan Andres de Paula, MD (Argentina), Richard Fedorak, MD (Canada), Fergus Shanahan, MD (Ireland), Mary Ellen Sanders, PhD (USA), Hania Szajewska, MD (Poland), Balakrishnan Siddartha Ramakrishna, MD (India), Tarkan Karakan, MD (Turkey), and Nayoung Kim, MD (South Korea)

Disorder, Action	Probiotic Strain/Prebiotic	Recommended Dose	Evidence Level	References	Comments
Treatment of acute infectious diarrhea	*Lactobacillus rhamnosus* GG	10^{10}-10^{11} cfu, twice daily	1a	1	Meta-analysis of RCTs; ESPGHAN/ESPID recommendation
	Saccharomyces boulardii, strain of *Saccharomyces cerevisiae*	200 mg, 3 times daily	1a	2	Meta-analysis of RCTs; ESPGHAN/ESPID recommendation
	Indian Dahi containing *Lactococcus lactis*, *Lactococcus lactis cremoris*, and *Leuconostoc mesenteroides cremoris*	10^{10} cfu of each strain, 2 or 3 times per day	2b	3	—
Prevention of antibiotic-associated diarrhea	*Saccharomyces boulardii*, strain of *Saccharomyces cerevisiae*	250 mg, twice daily	1a	4, 5	Meta-analysis of RCTs
	Lactobacillus rhamnosus GG	10^{10} cfu, once or twice daily	1b	6, 7	—
	Bifidobacterium lactis Bb-12 + *Streptococcus thermophilus*	10^{7} + 10^{6} cfu/g of formula	1b	8	—
	Lactobacillus rhamnosus (strains E/N, Oxy, and Pen)	2×10^{10} cfu, twice daily	1b	9	—
Prevention of nosocomial diarrhea	*Lactobacillus rhamnosus* GG	10^{10}-10^{11} cfu, twice daily	1b	10, 11	—
	Bifidobacterium lactis Bb-12 + *Streptococcus thermophilus*	10^{8} + 10^{7} cfu/g of formula	1b	12	—
Prevention of common gastrointestinal infections acquired in the community	*Lactobacillus casei* DN-114 001 in fermented milk	10^{10} cfu, once daily	1b	13, 14, 15	—
	Bifidobacterium lactis Bb-12 or *Lactobacillus reuteri* ATCC 55730	10^{7} cfu/g of formula powder	1b	16	—
	Lactobacillus casei Shirota in fermented milk	10^{10} cfu, once daily	1b	17	—
Adjuvant therapy for *H. pylori* eradication	*Lactobacillus casei* DN-114 001 in fermented milk	10^{10}-10^{12} cfu daily, for 14 days	1b	18	The probiotic was given together with a 7-d course of eradication triple therapy with omeprazole, amoxicillin, and clarithromycin

World Gastroenterology Organisation Global Guidelines

Probiotics and Prebiotics
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					and clarithromycin
Alleviates some symptoms of functional bowel disorders	*Lactobacillus rhamnosus* GG	10^{10}-10^{11} cfu, twice daily	1a	19	Meta-analysis of RCTs
	Lactobacillus reuteri DSM 17938	10^8 cfu, twice daily	1b	20, 21	—
Infantile colic	*Lactobacillus reuteri* DSM 17938	10^8 cfu/d	1b	22	—
Prevention of necrotizing enterocolitis in preterm infants	*Bifidobacterium bifidum* NCDO 1453, *Lactobacillus acidophilus* NCDO 1748	10^9 cfu each strain, twice daily	1b	23	Meta-analysis of pooled data from RCTs testing different probiotic preparations confirms significant benefits of probiotic supplements in reducing death and disease in preterm neonates [26]
	Infloran: *Lactobacillus acidophilus* + *Bifidobacterium infantis*	10^8 cfu each, twice daily	1b	24	—
	Bifidobacterium infantis, *Bifidobacterium bifidum*, *Streptococcus thermophilus*	10^9 cfu each, once daily	1b	25	—
Treatment of mildly active ulcerative colitis	VSL#3 mixture	4 to 9×10^{11} cfu, twice daily	1b	27	—

BMJ Open

Use of probiotics to correct dysbiosis of normal microbiota following disease or disruptive events: a systematic review

Lynne V McFarland

Strengths and limitations of this study

- A comprehensive review of the published literature from 1985—2013.
- Literature search unrestricted by language or country.
- Analysis of study designs resulted in novel strategy to limit bias and classify outcomes.
- Three types of outcomes of dysbiosis applied to evidence-based studies of specific probiotic strains.
- Author has over 30 years of research experience in the probiotic field.
- Pooled clinical trials using different study populations.
- Pooled probiotic doses and regimens.
- Indirect evidence linking probiotic strains and dysbiosis.
- Review performed by sole author.

Table 4 Comparison of the ability of probiotic to restore or improve dysbiosis with ranked clinical efficacy for various disease indications

Probiotic*	Restored normal microbiota*	Altered normal microbiota*	Ranked net evidence for efficacy†							
			AAD	CDI	IBD	IBS	TD	H pylori	Vaginitis/ BV	Acute paediatric diarrhoea
Restores microbiota										
Clostridium butyricum MIYAIRI	Yes	ND	–					–		
Lactobacillus. acidophilus+Bifido bifidum	Yes	ND	0	–						
L. acidophilus 1748+*Lactobacillus paracasei* F19+*Bifido lactis* Bb12	Yes	ND				–				
Bifido longum	Yes	No			–	+				
L. acidophilus+L. acidophilus+B. bifidum+B. animalis	Yes	ND								
L. acidophilus+L. paracasei+B. lactis (2)	Yes	No								
Saccharomyces boulardii lyo	Partial	Yes	++	++	++	0	+	–		++
L. rhamnosus GG	Partial	ND	–	–	–	0	0	–	0	++
L. acidophilus	Partial	No	++			++	–	–	+	
L. acidophilus+L. bifidus+L. rhamnosus	Partial	ND								
Alters microbiota										
Escherichia coli Nissle	ND	Yes			–					+
L. casei (DN114001 or Lcr35)	ND	Yes	+					0	+	++
L. rhamnosus GR1+*Lactobacillus fermentum* RC14	ND	Yes							++	
L. plantarum 8PA3+*B. bifidum*	ND	Yes								
Lactobacillus rhamnosus GG+*L. rhamnosus* Lc705+*P. freudenreichii shermanii* JS+*Bifido breve* Bb99	ND	Yes				++				
L. acidophilus+L. plantarum+L. rhamnosus+B bifidum	ND	Yes								
Lactobacillus brevis CD2+*Lactobacillus. salivarus* FV2+*L. plantarum* FV9	ND	Yes							+	
L. acidophilus+L. paracasei+Lactobacillus delbrueckii spp. bulgaricus+L. plantarum, Bifido longum, Bifido infantis, Bifido breve	ND	Yes	–		++	+				++
No effect on microbiota										
Bacillus clausii	ND	ND						–		–
L. plantarum 299v	ND	No	–	–		–				
B. lactis	ND	No	+							0
B. breve	No	No								
L. acidophilus+B. longum	No	ND								
L. rhamnosus 19070-2+*L. reuteri DSM*	ND	No								0
L. casei+B. breve	ND	No								
L. paracasei+L. acidophilus+B animalis	ND	No								
Pharmacokinetic only										
L. reuteri 55730	ND	ND								+
L. johnsonii La1	ND	ND			–			+		
L. salivarius UCC4331	ND	ND				–				
B. infantis 35624	ND	ND				0				
B. bifidum MIMBb75	ND	ND				+				
L. rhamnosus+B. longum	ND	ND								

*Including strain (when reported).
†Rank (bold values):++, ≥2 net randomised controlled trials (RCTs) with significant protective efficacy;+, only one net protective RCT; 0, equal number of significant and non-significant RCTs;–, ≥1 net non-significant RCT. Blank indicates no RCT performed for the disease indication.
AAD, antibiotic-associated diarrhoea; Acute Ped Diar, treatment of acute paediatric diarrhoea; BV, bacterial vaginosis; CDI, *Clostridium difficile* infections; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome;ND, not determined; TD, traveler's diarrhoea.

The Safety of Probiotics

Clinical Infectious Diseases 2008; 46:S104–11

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Table 1. Populations in whom *Lactobacillus* GG ha ied and has shown evidence of safety.

- Pregnant women
- Premature neonates
- Elderly individuals
- Children with rotavirus diarrhea
- Hospitalized children
- Hospitalized adults
- Finnish and other tourists
- Malnourished Peruvian children
- Patients with rheumatoid arthritis
- Adults with Crohn's disease
- Adults with *Helicobacter pylori* infection
- Adults with *Clostridium difficile*–associated diarrhea

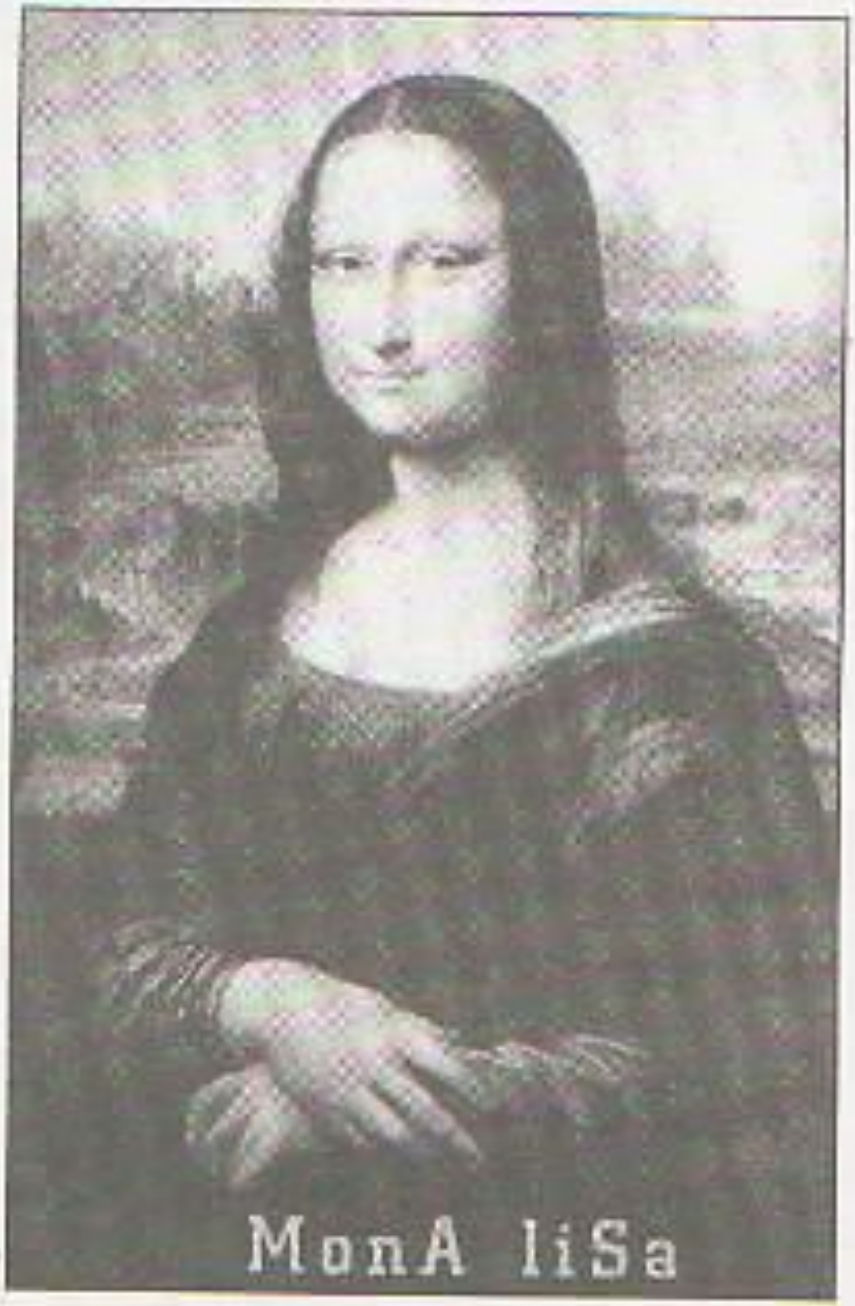
Table 2. Populations in whom safe use of other probiotics has been studied.

- Critically ill children (*Lactobacillus casei* Shirota)
- Patients with *Clostridium difficile*–associated diarrhea (*Lactobacillus plantarum, Saccharomyces boulardii,* and *Lactobacillus acidophilus* plus *Bifidobacterium*)
- Patients with Crohn's disease (*Lactobacillus johnsonii* LA 1, VSL#3)
- Adult women with urinary tract infections
- Children attending day care
- Liver transplant recipients (*L. plantarum* 299V)
- Adults in the intensive care unit (*L. plantarum* 299 V)
- Patients with liver failure (*L. plantarum* 299 V)
- Patients with rotavirus diarrhea (*Bifidobacterium lactis* BB-12, *Lactobacillus reuteri* SD 2222, and many others)
- Patients with necrotizing enterocolitis (*L. acidophilus, Bifidobacterium infantis*)
- Patients with HIV infection–associated diarrhea *(S. boulardii)*
- Adults with diarrhea *(S. boulardii, L. casei, Streptococcus thermophilus, Bacillus bulgaricus, L. acidophilus)*
- Adults with antibiotic-associated diarrhea *(L. plantarum, S. boulardii, L. acidophilus, B. bulgaricus)*
- Patients with bacterial vaginosis and candida vaginitis (*Lactobacillus fermentum* RC-14 plus *Lactobacillus rhamnosus* GR-1, *L. plantarum*)
- Patients with *Helicobacter pylori* infection (many)
- Patients with irritable bowel syndrome (many)

TABLE 11-1 Concerns about Marketed Probiotic Formulations

1. Marketed with taxonomically incorrect or fictitious microbial names
2. Lack of standards to define the number of viable organisms in available probiotics, the shelf life of the products, or appropriate storage conditions to maintain probiotic viability
3. Lack of clear labeling of many probiotic products on dosing or toxicity
4. No FDA or other oversight to provide minimal manufacturing standards for probiotics
5. Large number of different probiotic products without adequate scientific study to define the product efficacy, establish the biologic basis for proposed health benefit, or demonstrate product safety

TABLE 11-1 Concerns about Marketed Probiotic Formulations.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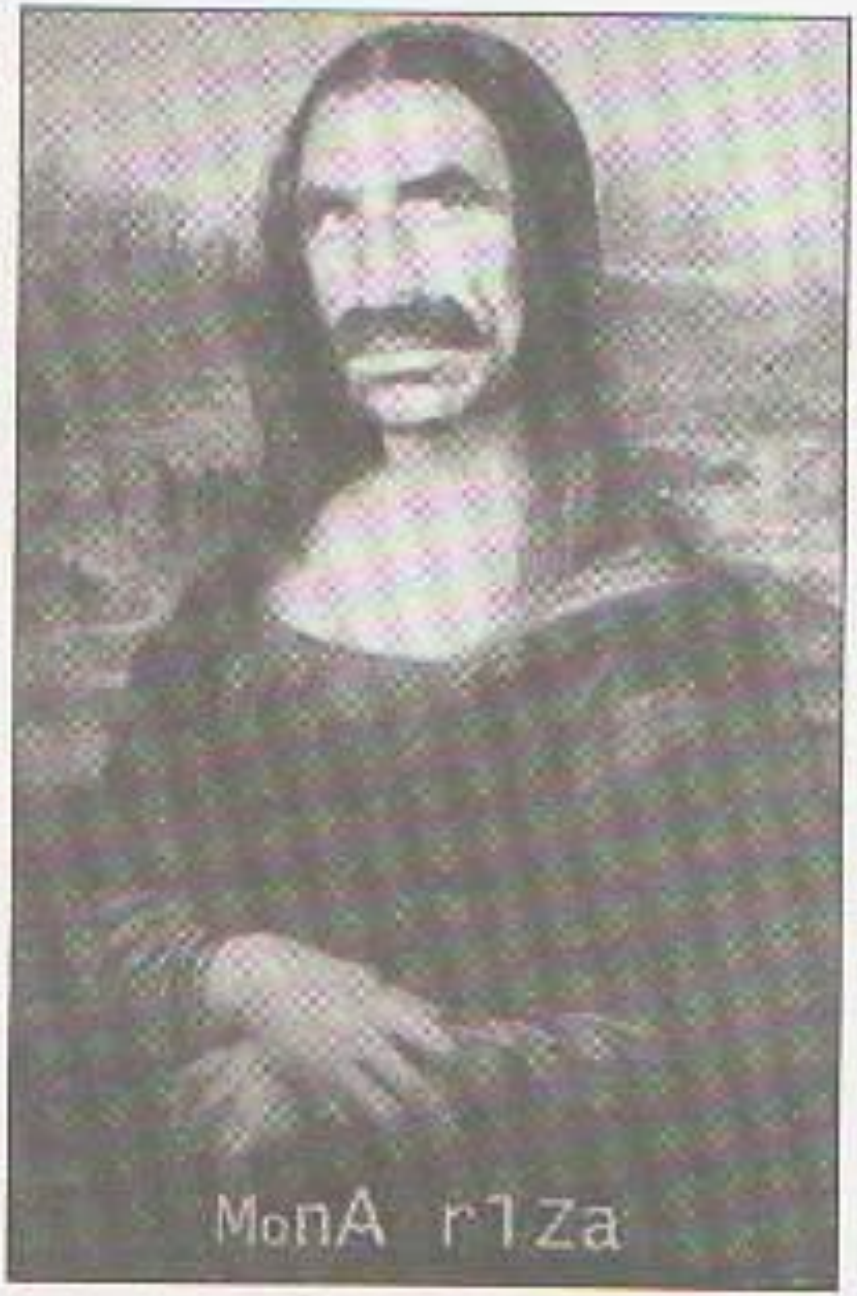
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INVITED ARTICLE HEALTHCARE EPIDEMIOLOGY

Robert A. Weinstein, Section Editor

Clinical Infectious Diseases 2012;54(5):707–13

Infection Control in the Multidrug-Resistant Era: Tending the Human Microbiome

Pritish K. Tosh[1,2] and L. Clifford McDonald[2]

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Increasing understanding of the normal commensal microorganisms in humans suggests that restoring and maintaining the microbiome may provide a key to preventing colonization and infection with multidrug-resistant organisms (MDROs). Intact communities of commensals can prevent colonization with MDROs through both competition for space and resources and the complex immunologic and biochemical interactions that have developed between commensal and host over millennia. Current antimicrobials, however, exert tremendous collateral damage to the human microbiome through overuse and broadening spectrum, which has likely been the driving force behind the introduction and proliferation of MDROs. The future direction of infection control and anti-infective therapy will likely capitalize on an expanding understanding of the protective role of the microbiome by (1) developing and using more microbiome-sparing antimicrobial therapy, (2) developing techniques to maintain and restore indigenous microbiota, and (3) discovering and exploiting host protective mechanisms normally afforded by an intact microbiome.


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BANA!!!"
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NA VURDUKÇA
MİZAH ANLAYIŞI
GELİŞİYO...

SON SÖZÜ MİKROPLAR SÖYLEYECEKTİR

Quorum sensing: the many languages of bacteria

Nicola C. Reading & Vanessa Sperandio

Review

Bench-to-bedside review: Quorum sensing and the role of cell-to-cell communication during invasive bacterial infection

Shadaba Asad and Steven M Opal