Unità di Pediatria ad Alta Intensità di Cura
Università degli Studi di Milano
Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico

34 Congresso Nazionale di
ANTIBIOTICOTERAPIA
in età pediatrica

Probiotici nella gravida per prevenire la patologia allergica e infettiva nei primi anni di vita

S. Esposito, Milano

PROBIOTICI NELLA GRAVIDA PER PREVENIRE LA PATOLOGIA INFETTIVA E ALLERGICA NEI PRIMI ANNI DI VITA

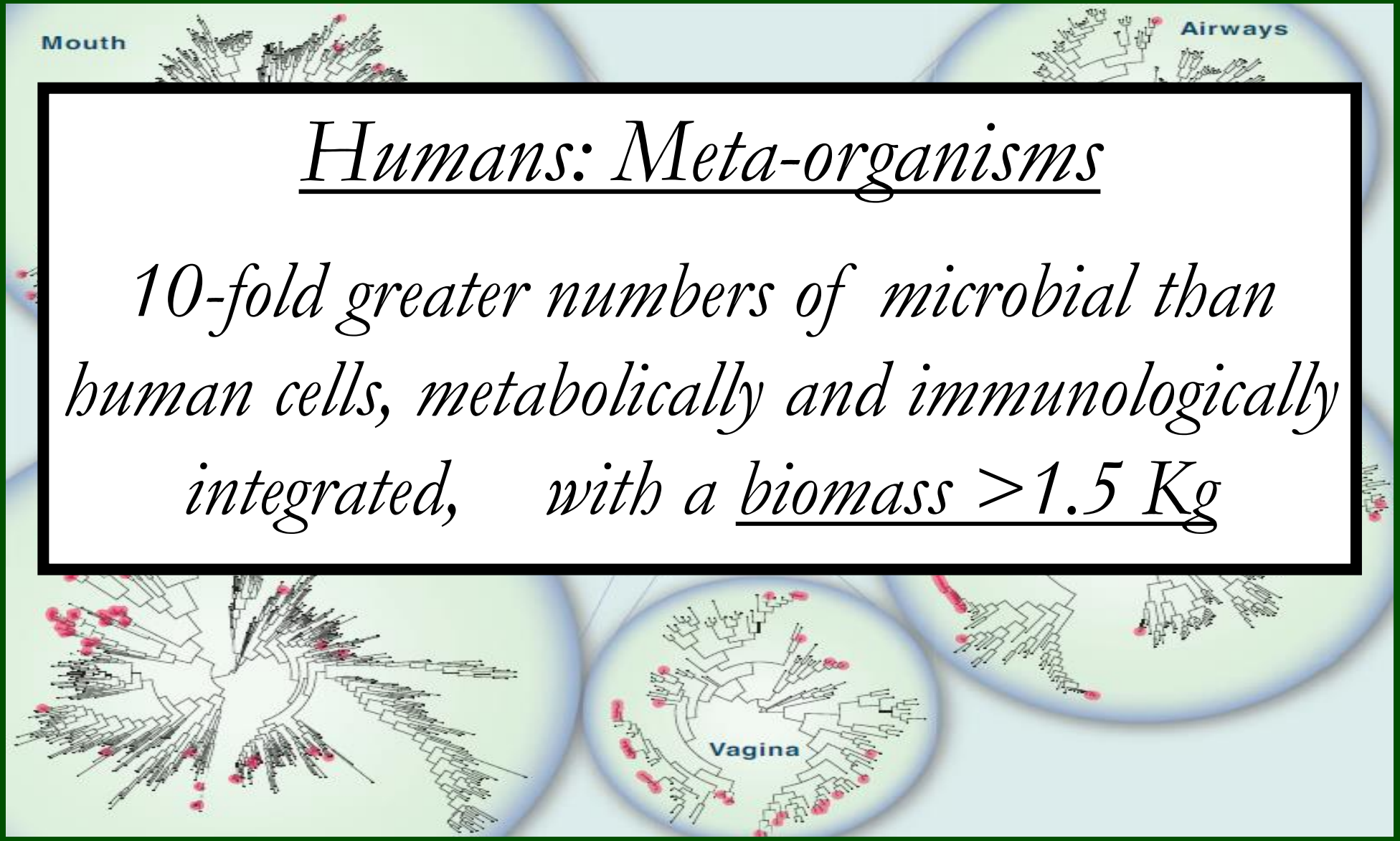
Susanna Esposito
Unità di Pediatria ad Alta Intensità di Cura, Università degli Studi di Milano, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano

AGENDA

- Overall role of microbiota
- Microbiota and pregnancy
- *Enterococcus faecium* L3
- *Lactobacillus casei* R0215
- *Lactococcus lactis* subsp *lactis* SP 38
- *Bifidobacterium animalis subsp. lactis* BB12

Human Microbiota:
an old-new frontier of research?

Human microbiota



Humans: Meta-organisms

10-fold greater numbers of microbial than human cells, metabolically and immunologically integrated, with a biomass >1.5 Kg

Lee YKL, Science 2010

Pediatric RESEARCH Volume 76 | Number 1 | July 2014

nature publishing group

Review

The human gut microbiota: a dynamic interplay with the host from birth to senescence settled during childhood

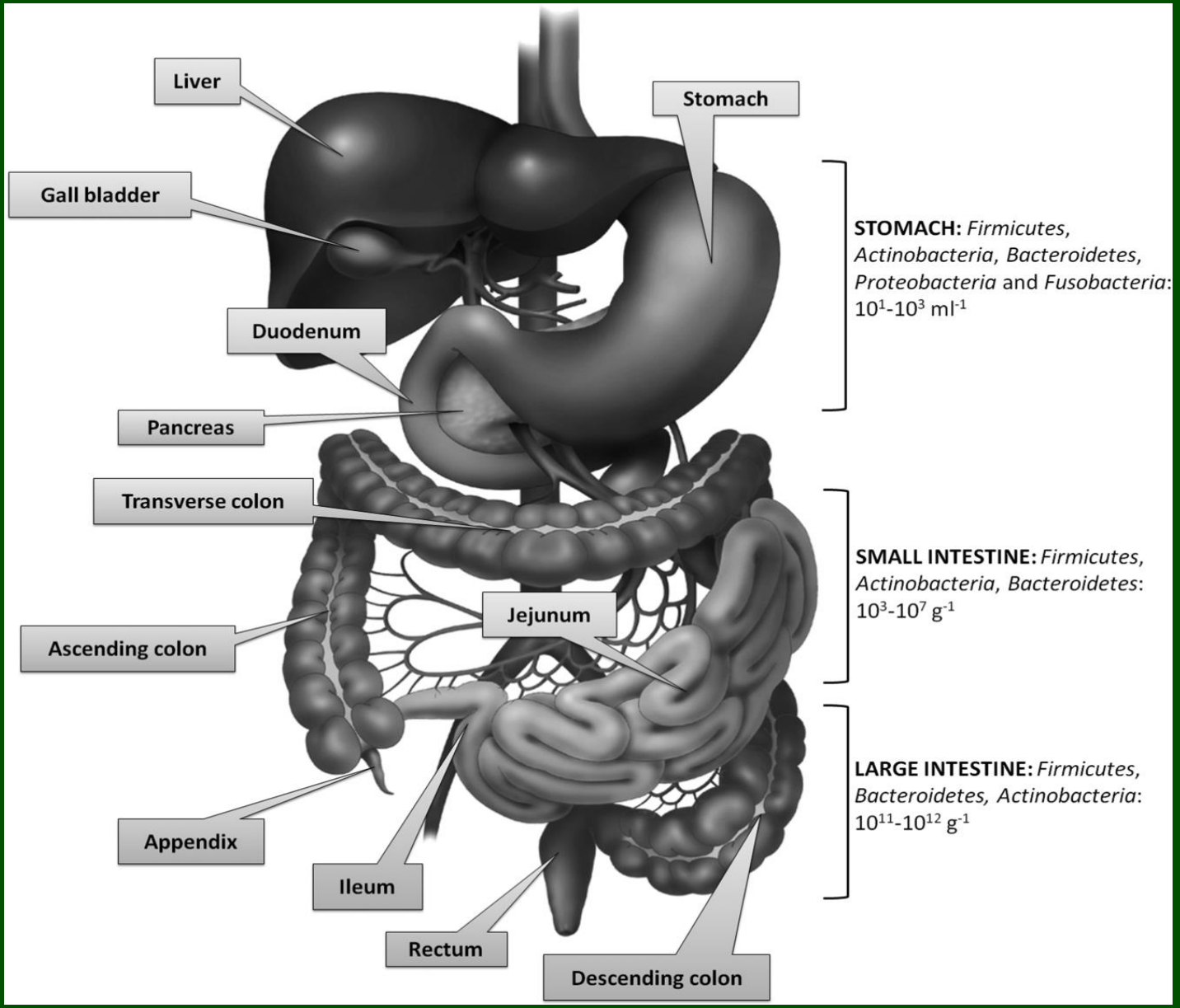
Lorenza Putignani[1], Federica Del Chierico[2], Andrea Petrucca[2,3], Pamela Vernocchi[2,4] and Bruno Dallapiccola[5]

The microbiota "organ" is the central bioreactor of the gastrointestinal tract, populated by a total of 10^{14} bacteria and characterized by a genomic content (microbiome), which represents more than 100 times the human genome. The microbiota plays an important role in child health by acting as a barrier against pathogens and their invasion with a highly dynamic

producing immunological memory (2). Indeed, the intestinal epithelium at the interface between microbiota and lymphoid tissue plays a crucial role in the mucosa immune response (2). The IS ability to coevolve with the microbiota during the perinatal life allows the host and the microbiota to coexist in a relationship of mutual benefit, which consists in dispensing, in

***Homo sapiens sapiens*: 30.000 geni**

Gut microbiota



$< 10^3$ CFU/mL

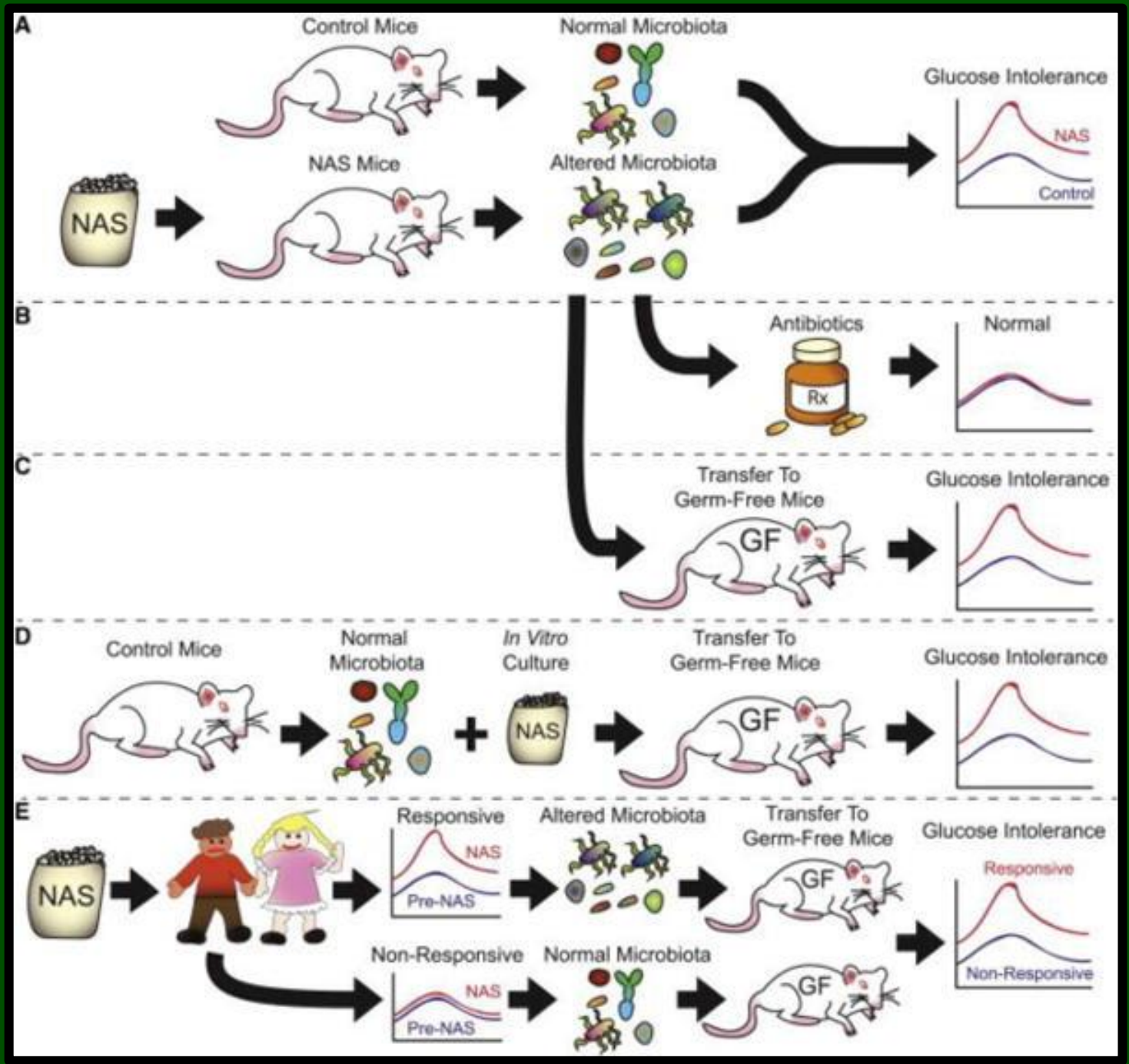
10^3-10^7 CFU/mL

10^{11}-10^{12} CFU/mL

***Firmicutes* + *Bacteroidetes*: 90%**

Proteobacteria → fenotipo obeso (pediatria)

Actinobacteria (bifidi) → bimbi/adolescenti a fenotipo magro con bassa incidenza di infezioni respiratorie e manifestazioni allergiche


A
Control Mice
Normal Microbiota
Glucose Intolerance
NAS
NAS Mice
Altered Microbiota
NAS
Control
B
Antibiotics
Normal
Rx
C
Transfer To
Germ-Free Mice
Glucose Intolerance
GF
D
Control Mice
Normal
Microbiota
In Vitro
Culture
Transfer To
Germ-Free Mice
Glucose Intolerance
NAS
GF
E
Responsive
Altered Microbiota
Transfer To
Germ-Free Mice
Glucose Intolerance
NAS
Pre-NAS
GF
Responsive
NAS
Non-Responsive
Normal Microbiota
Pre-NAS
GF
Non-Responsive

Preliminary Communication

Oral, Capsulized, Frozen Fecal Microbiota Transplantation for Relapsing *Clostridium difficile* Infection

Ilan Youngster, MD, MMSc; George H. Russell, MD, MSc; Christina Pindar, BA; Tomer Ziv-Baran, PhD; Jenny Sauk, MD; Elizabeth L. Hohmann, MD

IMPORTANCE Fecal microbiota transplantation (FMT) has been shown to be effective in treating relapsing or refractory *Clostridium difficile* infection, but practical barriers and safety concerns have prevented its widespread use.

OBJECTIVE To evaluate the safety and rate of resolution of diarrhea following administration of frozen FMT capsules from prescreened unrelated donors to patients with recurrent *C difficile* infection.

Author Audio Interview at jama.com

JAMA Patient Page page 1818

Supplemental content at jama.com

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT01914731

JAMA. 2014;312(17):1772-1778. doi:10.1001/jama.2014.13875
Published online October 11, 2014.

At birth the human body is sterile

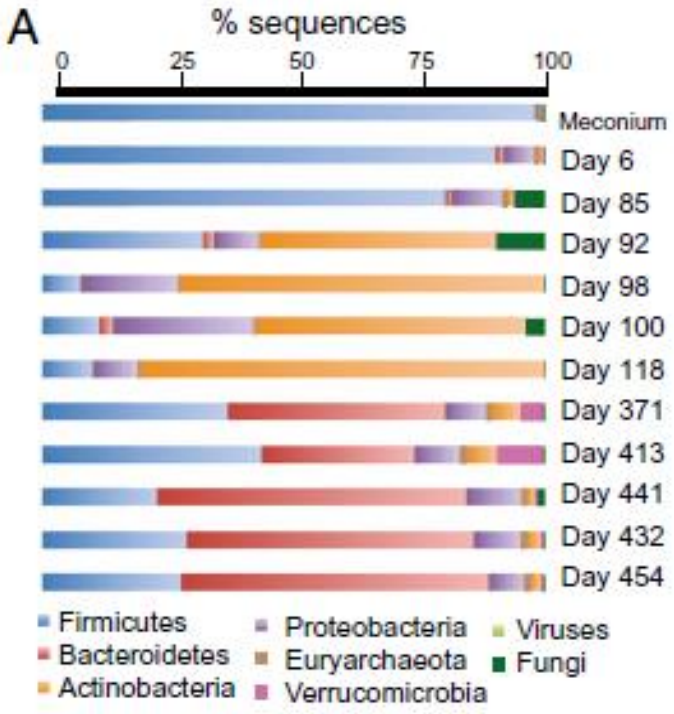
Vaginal microbiota (mother)

Fecal microbiota (mother)

Oral and Skin microbiota
(mother/father/relatives/babysitter)

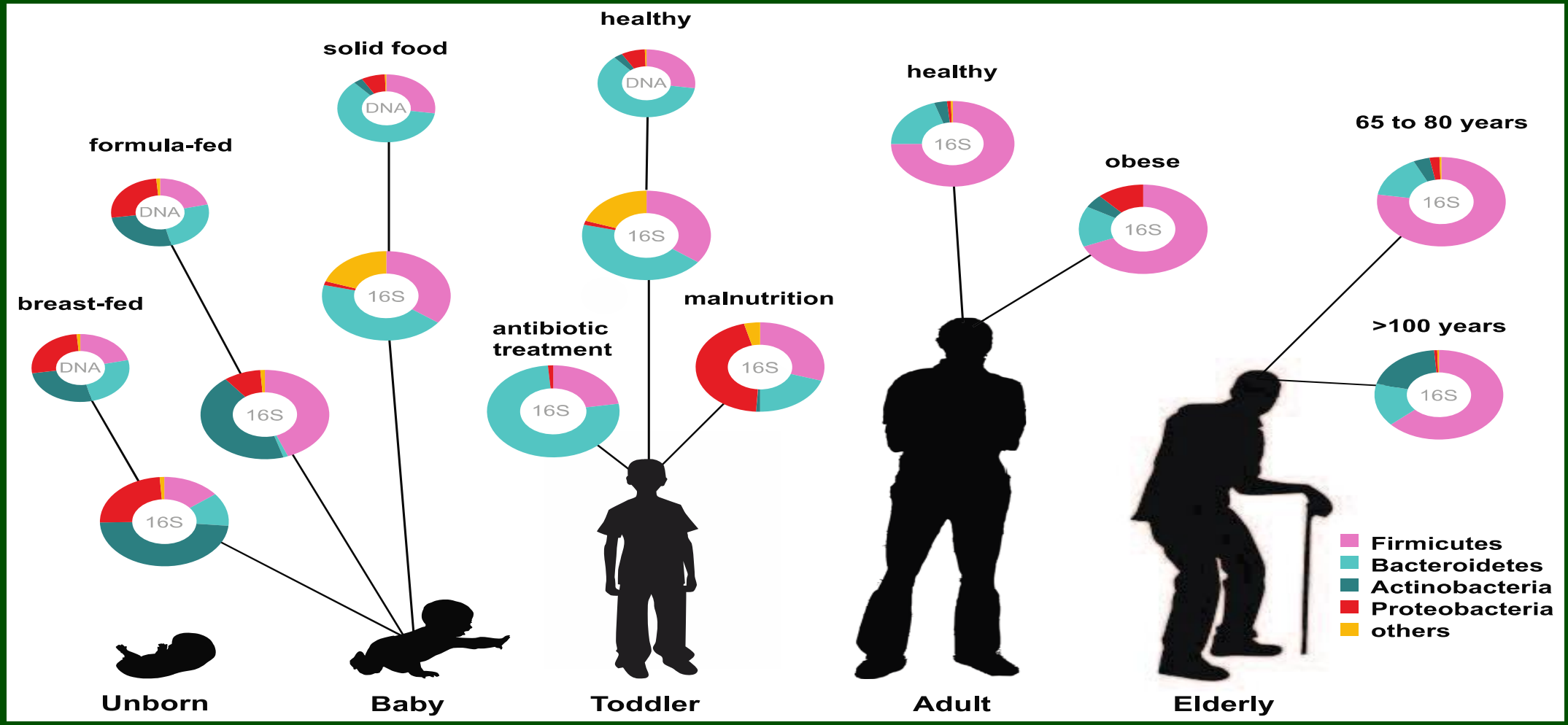
Diet

Enviroment



Native CORE microbiota
(8-36 months of life)

Human Microbiota: Alterations During Human Life Cycle



Relative abundance of key phyla of the human microbiota composition.
Misured by either 16S RNA or metagenomic approaches (DNA)

From: Frontiers in Cellular and Infection Microbiology August 2012/vol.1/ art. 104

Journal of the Royal Society of Medicine Volume 73 February 1980

Genital flora during pregnancy and colonization of the newborn[1]

Jean M Ross MB DObstRCOG
J R Needham FILMS LIBiol
Divisions of Perinatal Medicine and Comparative Medicine
Clinical Research Centre, Northwick Park Hospital
Watford Road, Harrow HA1 3UJ

Summary: A longitudinal study of the cervical and vaginal microflora of 131 pregnant women showed a similar range of organisms at first visit (up to 16 weeks), at 28 weeks and at 36 weeks of pregnancy. Twenty different groups or genera of microorganisms were recovered, predominantly lactobacilli. There was a fall in the isolation rate of organisms in the mothers 6 to 8 weeks after delivery. Lactobacilli and yeasts including *Candida albicans* were recovered less frequently whereas the incidence of *Escherichia coli* and group B streptococci increased.

Infants born to these mothers were swabbed within 24 hours of delivery and yielded organisms from the umbilicus, ear and mouth in 24%, 33% and 38% of cases respectively. Alpha haemolytic streptococci and *Staphylococcus aureus* were the predominant organisms. Sixteen different groups or genera were isolated.

The isolation rates in non-pregnant women attending a 'well-women' clinic were similar to those in the postnatal mothers; few women of 60 years or more were colonized.

Discussion

This survey demonstrates the normal microbial flora of the lower genital tract in antenatal patients during the three trimesters of pregnancy and postnatally, and the transfer of microorganisms to their newborn. The patients attending the 'well-women' clinic could not be used strictly as controls to the postnatal women because they were unmatched for age and

Biol Neonate. 1996;69(1):30-5.

Transmission of mother's microflora to the newborn at birth.

Mändar R, Mikelsaar M.

Our aim was to study the initial microbial colonization of the newborns by comparing it with their mothers' vaginal microflora. Nineteen mother-newborn pairs were examined at delivery. We found a close association, both qualitative and quantitative, between the individually different microflora of a mother's vagina and that of her newborn. The degree of contamination of the newborn significantly correlated with the counts of microorganisms found in the vagina of mothers. **In 85% of investigated individual mother-newborn pairs we revealed similar predominant microorganisms**. There were no cases of the mothers and their newborns harbouring similar potentially pathogenic prevailing microorganisms.

QUESITO:

E se volontariamente somministrassimo ceppi alla partoriente
con l’intento di determinarne la presenza
anche nell’intestino del neonato?

J Pediatr Gastroenterol Nutr. 2004 Mar;38(3):293-7.

Administration of oral probiotic bacteria to pregnant women causes temporary infantile colonization.

Schultz M, Göttl C, Young RJ, Iwen P, Vanderhoof JA.

It is difficult to permanently change the composition of the complex intestinal microflora of the adult. Orally administered probiotic bacteria produce only temporary colonization of the intestine in patients with a fully developed gut microflora. The gastrointestinal tract of a healthy fetus is sterile. During the birth process and rapidly thereafter, microbes from the mother and the surrounding environment colonize the gastrointestinal tract until a dense, complex microflora develops. Probiotic bacteria have been shown to beneficially influence the intestinal and systemic immune system and mediate protection against nosocomial infections affecting the neonate. The purpose of this study was to determine whether oral administration of the probiotic micro-organism Lactobacillus rhamnosus strain GG (L. GG) to the pregnant woman leads to colonization of the newborn infant. The authors identified six women who were taking L. GG during late pregnancy. None of the children received L. GG after birth, and their mothers discontinued its consumption at the time of delivery. L. GG concentration in fecal samples was determined by colony morphology and molecular analysis. In all four children delivered vaginally and in one of two children delivered by cesarean section, L. GG was present in fecal samples at 1 and 6 months of age. Three children remained colonized for at least 12 months, and in two children L. GG was detected in fecal samples at 24 months of age. Three mothers were tested 1 month post partum and no L. GG was present in fecal samples. No L. GG was found in one of these women 24 months post partum. There was no L. GG detectable in stools of the siblings of two children at the 2-year and 3-years after birth of the index child. L. GG was not isolated from the stools of children whose mothers were not taking L. GG. **Temporary colonization of an infant may be possible by colonizing the pregnant mother before delivery. Colonization is stable for as long as 6 months, and in unexplained circumstances may persist for as long as 24 months.**

Diabetes Obes Metab. 2015 Apr 16.

Probiotics in Reducing the Risk of Gestational Diabetes.

Isolauri E, Rautava S, Carmen Collado M, Salminen S.

Overweight and obesity currently constitute a major threat to human wellbeing. Almost half of the female population are currently overweight. Pregnant overweight women are at risk of gestational diabetes impacting the health of the mother and the child, both short- and long-term. Notwithstanding the extensive scientific interest centered on the problem, research efforts have thus far been unable to devise preventive strategies. Recent scientific advances point to a gut microbiota dysbiosis, with ensuing low-grade inflammation as a contributing element, in obesity and its comorbidities. Such findings would suggest a role for specific probiotics in the search for preventive and therapeutic adjunct applications in gestational diabetes. The aim of this paper is to critically review recent demonstrations of the role of intestinal microbes in immune and metabolic regulation, which could be exploited in nutritional management of pregnant women by probiotic bacteria. By modulating specific target functions, probiotic dietary intervention may exert clinical effects beyond the nutritional impact of food. As this approach in pregnancy is new, an overview of the gut microbiota in shaping host metabolism together with the definition of probiotics are presented, and finally, specific targets and potential mechanisms for probiotics in pregnancy are discussed. Pregnancy appears to be the most critical stage for interventions aiming to reduce the risk of non-communicable disease in future generations, beyond the immediate dangers attributable to the health of the mother, labour and the neonate. **Specific probiotic interventions during pregnancy thus provide an opportunity to promote the health not only of the mother but also of the child.**

J Allergy Clin Immunol. 2012 Dec;130(6):1355-60.

Maternal probiotic supplementation during pregnancy and breast-feeding reduces the risk of eczema in the infant.

Rautava S et al.

Probiotics have shown promising potential in reducing the risk of eczema in infants. Optimal probiotic intervention regimen remains to be determined. We investigated whether maternal probiotic supplementation during pregnancy and breast-feeding reduces the risk of developing eczema in high-risk infants.
This was a parallel, **double-blind placebo-controlled trial of 241 mother-infant pairs**. Mothers with allergic disease and atopic sensitization were randomly assigned to receive (1) Lactobacillus rhamnosus LPR and Bifidobacterium longum BL999 (LPR+BL999), (2) L paracasei ST11 and B longum BL999 (ST11+BL999), or (3) placebo, beginning 2 months before delivery and during the first 2 months of breast-feeding. The infants were followed until the age of 24 months. **Skin prick tests were performed at the ages of 6, 12, and 24 months.**
Altogether 205 infants completed the follow-up and were included in the analyses. The risk of developing eczema during the first 24 months of life was significantly reduced in infants of mothers receiving LPR+BL999 (odds ratio [OR], 0.17; 95% CI, 0.08-0.35; P < .001) and ST11+BL999 (OR, 0.16; 95% CI, 0.08-0.35; P < .001). The respective ORs for chronically persistent eczema were 0.30 (95% CI, 0.12-0.80; P = .016) and 0.17 (95% CI, 0.05-0.56; P = .003). Probiotics had no effect on the risk of atopic sensitization in the infants. No adverse effects were related to the use of probiotics. **Prevention regimen with specific probiotics administered to the pregnant and breast-feeding mother, that is, prenatally and postnatally, is safe and effective in reducing the risk of eczema in infants with allergic mothers positive for skin prick test.**

Quali sono i comuni «problemi» del neonato?

Infezioni respiratorie

Diarrea/enterocolite/infezioni intestinali

} *Enterococcus faecium* L3

Coliche (mal di pancia, risvegli notturno con pianti)
Lactobacillus casei R0215

Scarsa digeribilità del latte (lattosio e proteine)
Lactococcus lactis subsp *lactis* SP 38

Sistema immunitario debole e sbilanciato vs allergie
Bifidobacterium animalis subsp. lactis BB12

Enterococcus faecium L3 LMG P-27496

depositato il 25 marzo 2013
c/o BCCM/LMG Bacteria Collection, Gent, Belgio.

Clinical features

Features tested	Group 1 (placebo)		Group 2 (L3)		Pearson χ^2	p-level
	no	yes	no	yes		
Feeding brakeage	61,5%	38,5%	79,3%	20,7%	1,88	n.s.
Internal infection	76,9%	23,1%	89,7%	10,3%	1,62	n.s.
Amniotic infection	73,1%	26,9%	89,7%	10,3%	2,53	n.s
Necrotizing enterocolitis	92,3%	7,7%	100%	0%	2,08	**<0,05**
Complications with infection	46,2%	53,8%	79,3%	20,7%	6,51	**<0,05**

Body weight dynamics

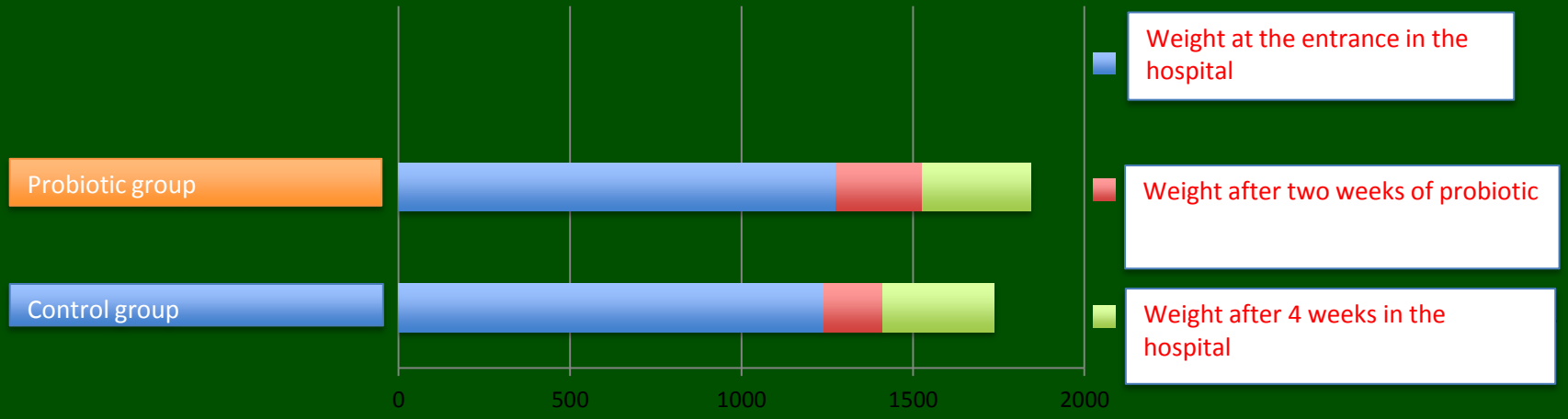
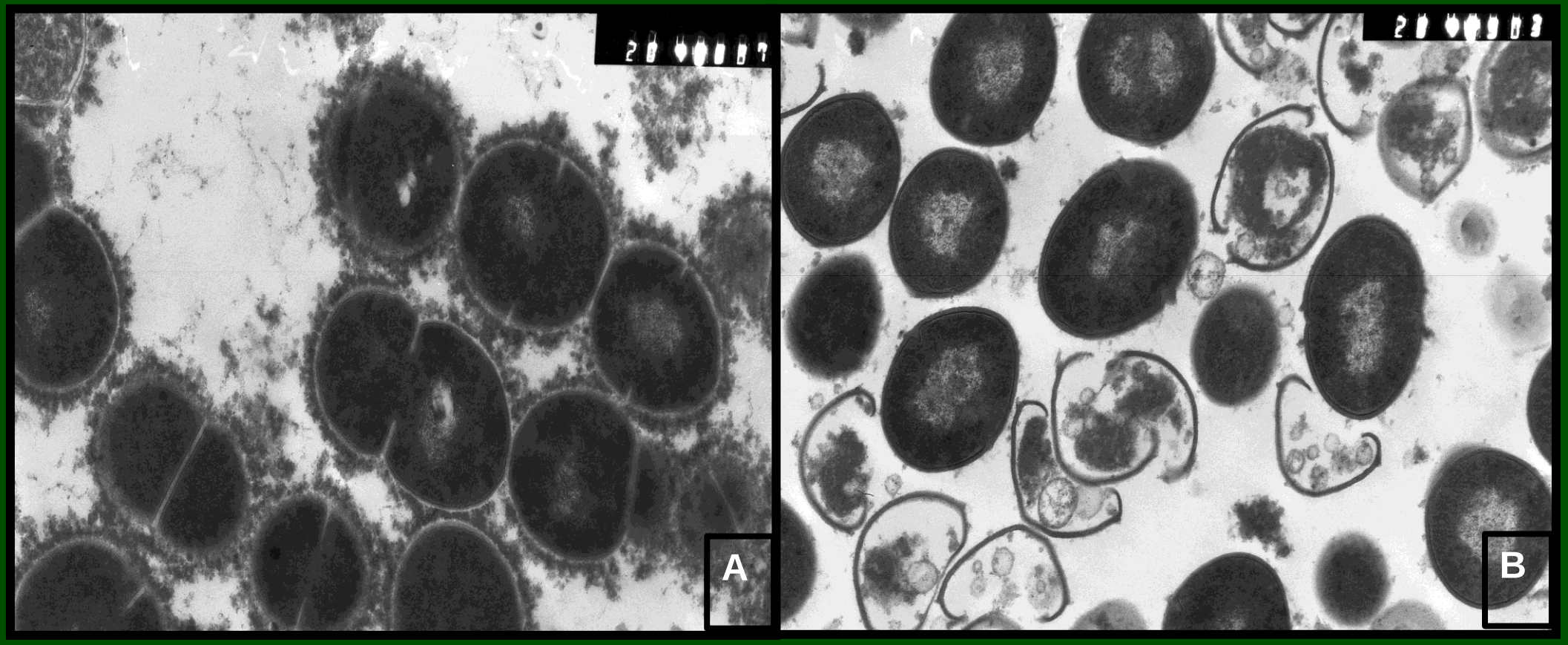


Tabella 1 Somministrazione di *Enterococcus faecium* L3 nel terzo trimestre di gravidanza in donne con positività al tampone per streptococco e/o candida

Ceppo	positività prima del trattamento	positività dopo il trattamento	efficacia
Candida (albicans)	44/112	7/112	84%
Streptococco (Gruppo B)	24/112	5/112	79.5%
Streptococco (Gruppo D)	10/112	6/112	40%
Streptococco + Candida	20/112	0/112	100%
Gardnerella + Candida	14/112	0/112	100%



Streptococchi in coltura (A) e streptococchi in coltura in presenza delle enterocine rilasciate dal ceppo L3 (B) osservati in microscopia elettronica (1:30.000)

Quali sono i comuni «problemi» del neonato?

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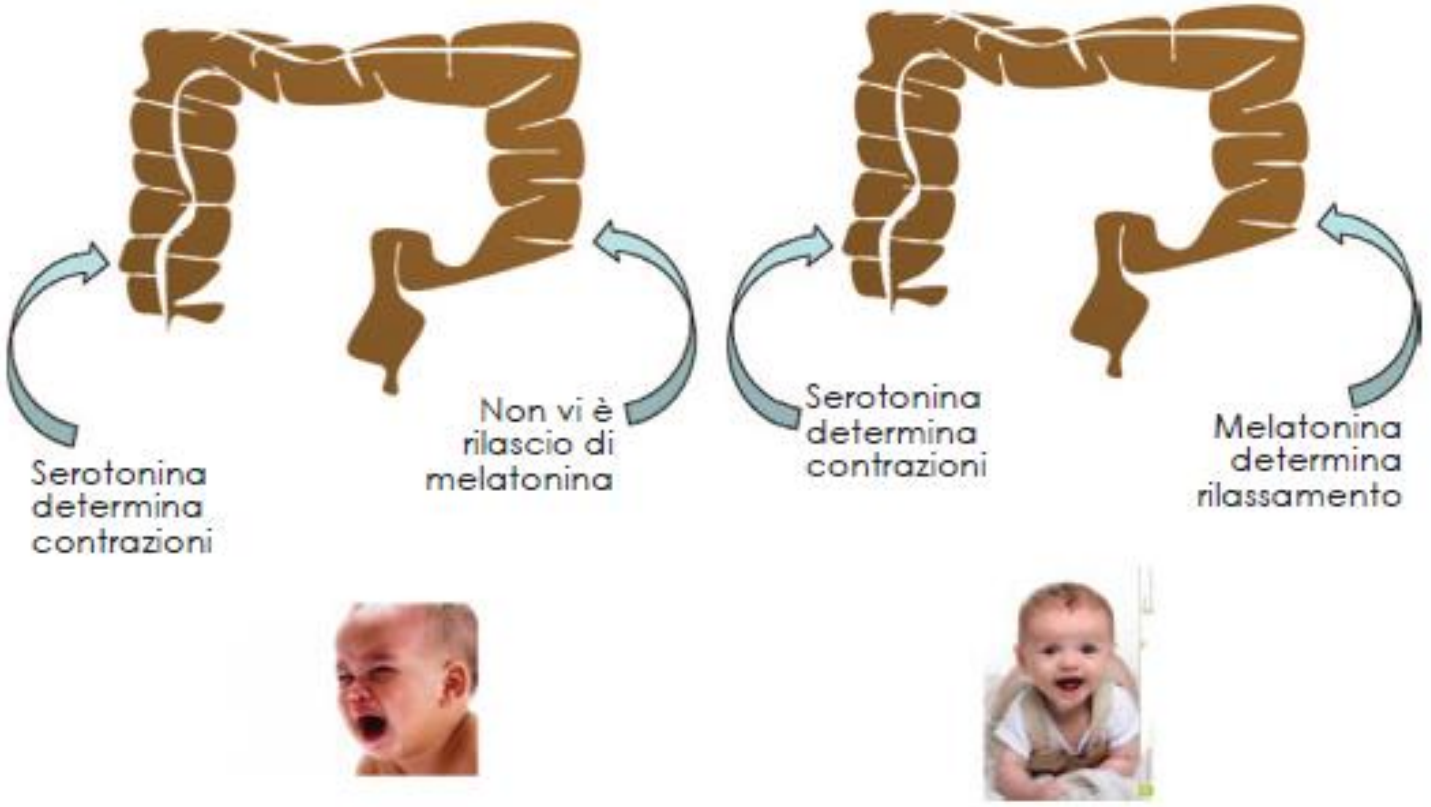
Lactococcus lactis subsp *lactis* SP 38

Sistema immunitario debole e sbilanciato vs allergie
Bifidobacterium animalis subsp. lactis BB12

Figura 3 Antagonismo 'neonatale' tra serotonina e melatonina intestinale



Tra 0 e 3 mesi le cellule enterocromaffini del neonato rilasciano solo serotonina e questa è responsabile di gran parte delle contrazioni intestinali; dopo il 3° mese le medesime cellule iniziano a produrre melatonina ad azione antagonista

Am J Perinatol. 2015 Mar 4.

Oxidative Stress-Mediated Damage in Newborns with Necrotizing Enterocolitis: A Possible Role of Melatonin.

Marseglia L, D'Angelo G1, Manti S, Aversa S, Reiter RJ, Antonuccio P, Centorrino A, Romeo C, Impellizzeri P, Gitto E.

Necrotizing enterocolitis is a gastrointestinal surgical emergency in premature neonates. Free radicals have been linked to the development of the disease in infants. Ischemia, hypoxia-reperfusion, infection, and inflammation produce elevated levels of reactive oxygen species, impairing the redox balance and shifting cells into a state of oxidative stress. Melatonin, an effective direct free-radical scavenger and indirect antioxidant agent, exerts pleiotropic action on the human body. Several studies have tested the efficacy of melatonin in counteracting oxidative injury in diseases of newborns. Melatonin has been widely used in newborns including cases of asphyxia, respiratory distress syndrome, and sepsis, and no significant toxicity or treatment-related side effects with long-term melatonin therapy have been reported. **Therefore, melatonin, besides standard therapies, could be considered as a potentially safe approach to prevent and treat necrotizing enterocolitis in premature infants.** This review summarizes what is known about the role of oxidative stress, and potentially beneficial effects of antioxidants, such as melatonin, in necrotizing enterocolitis.

Kandil *et al. BMC Gastroenterology* 2010, **10**:7
http://www.biomedcentral.com/1471-230X/10/7

BMC Gastroenterology

RESEARCH ARTICLE Open Access

The potential therapeutic effect of melatonin in gastro-esophageal reflux disease

Tharwat S Kandil[1*], Amany A Mousa[2], Ahmed A El-Gendy[3], Amr M Abbas[3]

World Journal of Gastroenterology

Online Submissions: http://www.wjgnet.com/esps/
bpgoffice@wjgnet.com
doi:10.3748/wjg.v20.i10.2492

World J Gastroenterol 2014 March 14; 20(10): 2492-2498
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

TOPIC HIGHLIGHT

WJG 20th Anniversary Special Issues (4): Irritable bowel syndrome

Melatonin for the treatment of irritable bowel syndrome

Kewin Tien Ho Siah, Reuben Kong Min Wong, Khek Yu Ho

J Physiol Pharmacol. 2012 Dec;63(6):613-21.

Conversion L-tryptophan to melatonin in the gastrointestinal tract.

Zagajewski J et al.

Melatonin is a major biosynthetic product of pineal gland exerting a potent antioxidant and the reactive oxygen metabolites scavenging activities but the mechanism of formation of this indole at extrapineal sources has not been fully elucidated. It is known that the gastrointestinal (GI)-tract plays an important role as a source of melatonin synthesis but the conversion of L-tryptophan into melatonin in the GI-tract of experimental animals and humans should be further examined. In this study, the conversion of L-tryptophan to melatonin was determined in the serum collected from rats administered intragastrically with this amino acid acting as melatonin precursor. For this purpose, a simple, sensitive and reliable method was developed for simultaneous determination of six L-tryptophan metabolites in rat serum, namely, 5-hydroxytryptamnie (5-HT), 5-hydroksytryptophan (5-HTR), kynurenin (KYN), antranilic acid (AA), indole-3-acetic acid (IAA) and melatonin that were analyzed in one chromatographic run by high-performance liquid chromatography (HPLC) with UV and native fluorimetric detection with multiple wavelengths. We used nucleosil Supelco C18 5 μm 4.6 mm x 250 nm column with the standard mobile phase consisting of solvent A (water/0.1% trifluoroacetic acid (TFA) and solvent B (methanol/0.1% TFA) in gradient elution. Fifty five rats received vehicle (saline) of L-tryptophan (50 mg/kg) or melatonin (50 mg/kg) by means of intragastric gavage and they were anesthetized and sacrificed at 0, 10, 20, 30, 60, 120 or 240 min upon L-tryptophan or melatonin administration for the venous blood withdrawal. The serum collected samples were kept on ice for the HPLC determination. The average recovery of 5-HT, 5-HRT, KYN, AA, TRP, IAA, and melatonin were 99±3%, 97±1.5%, 94±2.5%, 99±2.46, 98±1.5 and 98±2%, respectively. **We conclude that 1) L-tryptophan is converted to melatonin in the GI-tract during the day when the pineal gland synthesis is inhibited,** and 2) the reverse phase high performance liquid chromatography (RP-HPLC) is a new sensitive and reliable method that could be successfully applied to the study of kinetics and metabolism of L-tryptophan in GI-tract.

Protocol

The conversion of amino acids into biogenic amines was tested for several strains in a non-growing system. The strains were incubated to an OD_{600} of 1.0 on CDM without a carbon source. For lactobacilli, the pH was set at 4.0 and for the bifidobacteria and the *Bacillus* strain the pH was at 5.0. Cells were incubated for 7 days at 37°C. Non-inoculated medium was used as a control. The amino acid and biogenic amine analysis were performed at Ansynth (Berkel and Rooderijs, the Netherlands).

Results

	Level of tryptophan produced during incubation
Lactobacillus casei R0215	29.8 mg/L
Lactobacillus rhamnosus R0011	29.3 mg/L
Bifidobacterium longum R0175	16 mg/L
Bacillus subtilis R0179	10.9 mg/L

Quali sono i comuni «problemi» del neonato?

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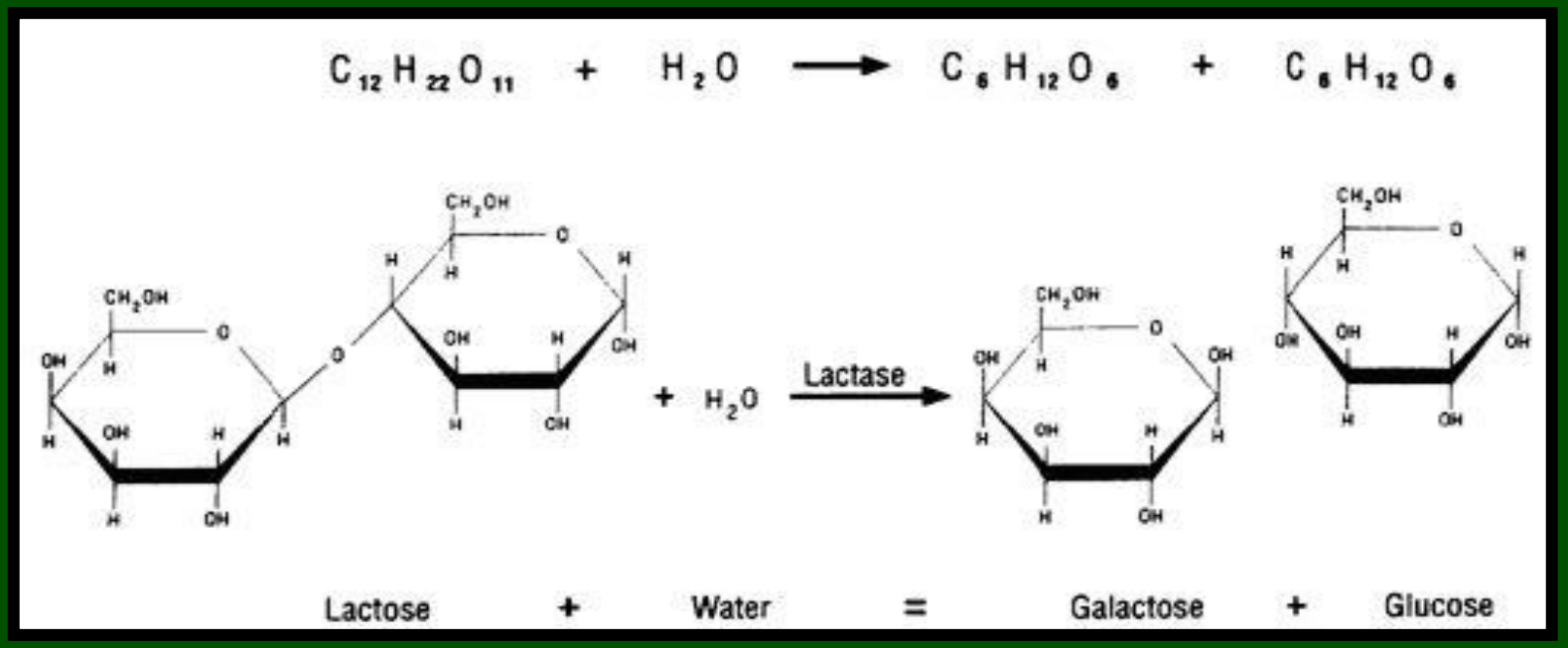

Beta-galattosidasi

Appl Environ Microbiol. 1976 Jul;32(1):38-44.

Plasmids in Streptococcus lactis: evidence that lactose metabolism and proteinase activity are plasmid linked.

Efstathiou JD, McKay LL.

Populations of lactose positive (Lac+) and proteinase positive (Prt+) cells from Streptococcus lactis M18, C10, and ML3 grown at 39 degrees C gave rise to increasing proportions of Lac- Prt- clones. The deficiencies did not appear until after a number of generations at the elevated temperature, and the rate depended on the strain.Lac- Prt+ and Lac+ Prt- mutants were isolated after treatment with ethidium bromide. Plasmid deoxyribonucleic acid was isolated by cesium chloride-ethidium bromide equilibrium density gradient centrifugation from the parent cultures as well as from their Lac- Prt-, Lac- Prt+, and Lac+ Prt- mutants. Five distinct plasmid sizes of approximate molecular weights of 2,4, 8, 21, and 27 million were found in S. lactis C10, whereas the Lac- Prt- derivative lacked the 8- and 21-million-dalton plasmids, but the 8-million-dalton plasmid was present in the Lac-Att mutant. In S. lactis m18 five plasmids possessing molecular weights of about 2, 4, 10, 18 and 27 million were observed. The 10- and 18-million-dalton plasmids were not detected in the Lac- Prt- mutants, whereas the Lac- Prt+ derivative lacked only the 18-million-dalton plasmid and the Lac+ Prt- mutant lacked only the 10-million-dalton plasmid. In S. lactis ML3 five distinct plasmids, with approximate molecular weights of 2, 4, 8, 22, and 30 million, were present. The 8- and 22-million-dalton plasmids were not detected in the Lac- Prt- derivative, but the 8-million-dalton plasmid was present in the Lac- Prt+ mutant. **The evidence suggests that lactose-fermenting ability and proteinase activity in these organisms are mediated through two distinct plasmids** having molecular weights of 8 x 10(6) to 10 x 10(6) for proteinase activity and 18 x 10(6) to 22 x 10(6) for lactose metabolism.

Quali sono i comuni «problemi» del neonato?

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Bifidobacterium animalis subsp. lactis BB12

Bifidobacterium animalis subsp. *lactis*, BB-12®*

Review delle evidenze scientifiche

Mikkel Jungersen, Dorte Eskesen
Affari scientifici, Chr. Hansen A / S, Hørsholm DK-2970, Danimarca
dkmkj@chr-hansen.com

Parole chiave Probiotici, *Bifidobacterium*, BB-12®

Efficacia

Il BB-12® è il più documentato probiotico *Bifidobacterium* al mondo, con più di 300 pubblicazioni scientifiche delle quali oltre 130 sono pubblicazioni di studi clinici (**2**).
Da più di 25 anni il BB-12® è stato testato in studi clinici, condotti su diversi soggetti, da neonati nati prematuri fino ad anziani, ed è stato somministrato in dosi fino a 100 miliardi di CFU/giorno.

Figura 2 Risposta di anticorpi specifici dell'influenza (IgG) nel plasma in soggetti vaccinati, dopo somministrazione di BB-12® o placebo per 6 settimane

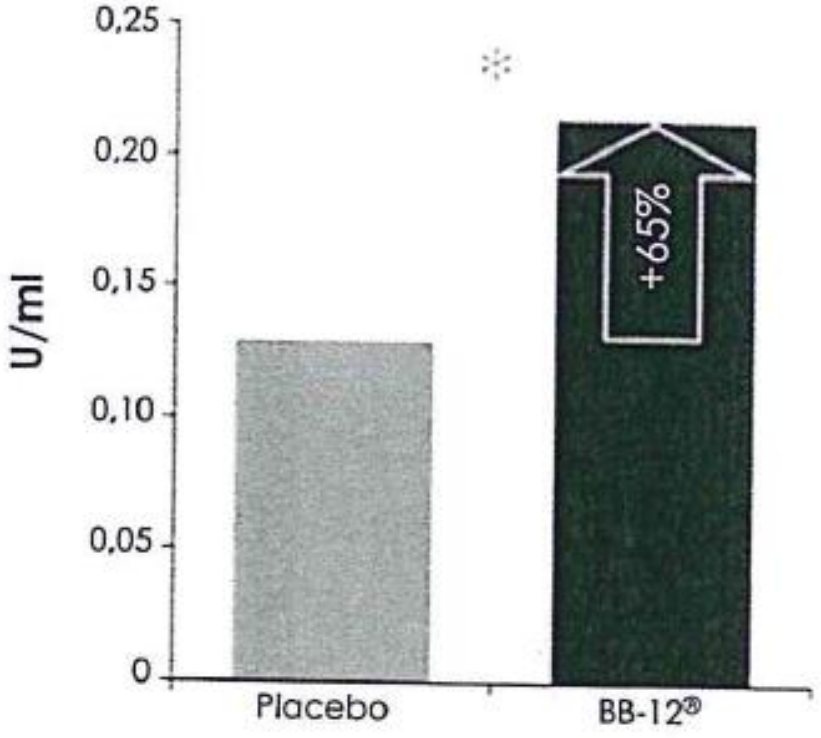
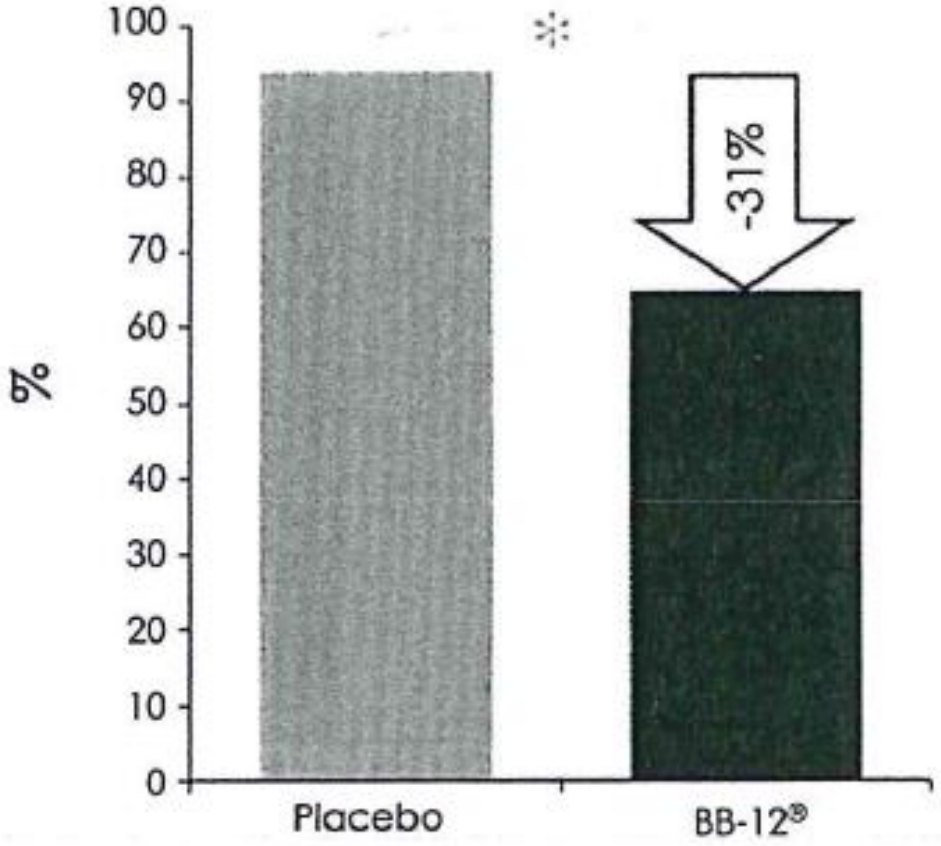


Figura 3 Incidenza % di infezioni del tratto respiratorio in bambini che hanno ricevuto placebo o BB-12® (una compressa a lento rilascio in un succhiotto)



J Immunol. 2013 Sep 1;191(5):2446-56.

Divergent immunomodulating effects of probiotics on T cell responses to oral attenuated human rotavirus vaccine and virulent human rotavirus infection in a neonatal gnotobiotic piglet disease model.

Chattha KS et al.

Rotaviruses (RVs) are a leading cause of childhood diarrhea. Current oral vaccines are not effective in impoverished countries where the vaccine is needed most. Therefore, alternative affordable strategies are urgently needed. Probiotics can alleviate diarrhea in children and enhance specific systemic and mucosal Ab responses, but the T cell responses are undefined. In this study, we elucidated the T cell and cytokine responses to attenuated human RV (AttHRV) and virulent human RV (HRV) in gnotobiotic pigs colonized with probiotic **Bifidobacterium lactis Bb12** [Bb12]), mimicking gut commensals in breastfed infants. Neonatal gnotobiotic pigs are the only animal model susceptible to HRV diarrhea. Probiotic colonized and nonvaccinated (Probiotic) pigs had lower diarrhea and reduced virus shedding postchallenge compared with noncolonized and nonvaccinated pigs (Control). Higher protection in the Probiotic group coincided with higher ileal T regulatory cells (Tregs) before and after challenge, and higher serum TGF-β and lower serum and biliary proinflammatory cytokines postchallenge. Probiotic colonization in vaccinated pigs **enhanced innate serum IFN-α, splenic and circulatory IFN-γ-producing T cells, and serum Th1 cytokines, but reduced serum Th2 cytokines** compared with noncolonized vaccinated pigs (Vac). Thus, Bb12 induced systemic Th1 immunostimulatory effects on oral AttHRV vaccine that coincided with lower diarrhea severity and reduced virus shedding postchallenge in Vac+Pro compared with Vac pigs. Previously unreported intestinal CD8 Tregs were induced in vaccinated groups postchallenge. Thus, probiotics Bb12 exert divergent immunomodulating effects, with enhanced Th1 responses to oral AttHRV vaccine, whereas inducing Treg responses to virulent HRV.

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Br J Nutr. 2009 Jun;101(11):1679-87.

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256 donne trattate in gravidanza con BB12 o placebo per 1 trimestre

Riduzione della glicemia basale e aumento degli acidi grassi polinsaturi

TAKE HOME MESSAGES

Madre

Nascituro

Madre		Nascituro
Anti-microbico	*Enterococcus faecium* L3 5 MILARDI ufc	Anti-microbico Migliora peso (pre-termine)
Digestione Lattosio	*Lactococcus lactis* SP38 3 MILARDI ufc	Digestione Lattosio & Proteine latte
Anti-colon irritabile	*Lactobacillus casei* R0215 3 MILARDI ufc	Anti-coliche
Riduce glicemia Aumenta PUFA Regolarizza intestino Potenzia immunità	*Bifidobacterium animalis s. Lactis* 3 MILARDI ufc	Potenzia vaccini Riduce UTRI Riduce allergie

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18-20 February

MILAN MARRIOTT HOTEL Milan, Italy

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