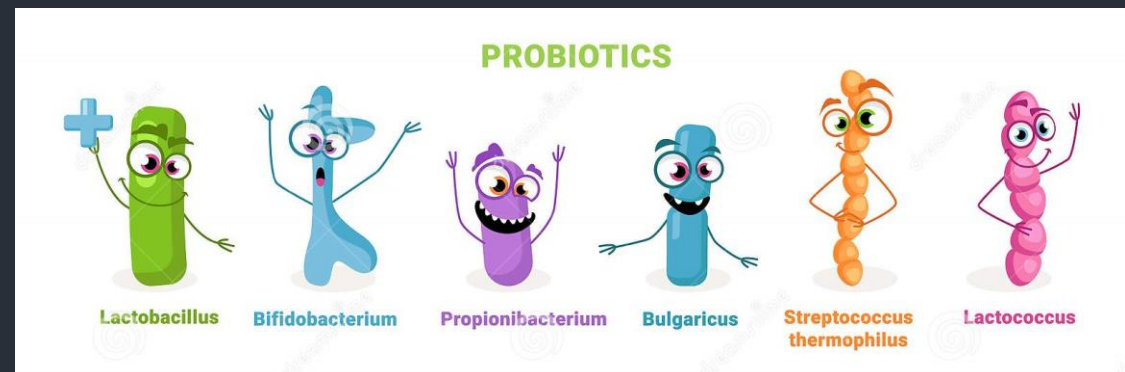


Probiotics in pediatric GI disorders

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Background:

Probiotics:

- Live microorganisms
- When administered in adequate amounts,
- Confer a health benefit on the host
- Widely used
- Uncertainty regarding their efficacy
- Discordant recommendations about their use.

Probiotic History:

- **Hippocrates** declared, 2000 years earlier, that “death sits in the bowels.”
- At the beginning of 1900s **Louis Pasteur** identified the microorganisms responsible for the process of fermentation
- **E. Metchnikoff** associated the enhanced longevity of Bulgarian rural people to the regular consumption of fermented dairy products such as yogurt.

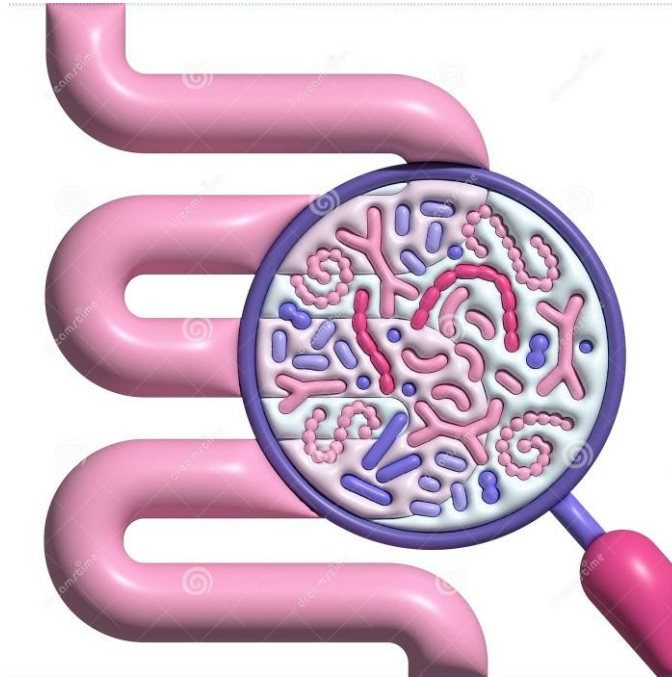
Probiotic History:

- The history of **probiotics** is as old as the **human** history
- It is closely related to the use of fermented food.
- It should be hypothesized that as farming started to replace hunting and gathering around **10,000 years ago**, man began to produce fermented food and beverages

TABLE 1. History and Origin of Some Fermented Foods**History of Some Fermented Foods**

Food Origin	Approximate Year of Introduction	Region
Mushrooms	4000 BC	China
Soy sauce	3000 BC	China, Korea, Japan
Wine	3000 BC	North Africa, Europe, Middle East
Fermented milk	10,000 BC	Middle East
Fermented milk products	7000-5000 BC	Egypt, Greece, Italy
Fermented rice	2000 BC	China, Asia
Fermented honey (mead)	2000 BC	North Africa, Middle East
Cheese	2000 BC	Middle East, China
Fermented malted cereals: beer	2000 BC	North Africa, China, Middle East
Bread	1500 BC	Egypt, Europe
Fermented meats	1500 BC	Middle East
Sourdough bread	1000 BC	Europe
Fish sauce	1000 BC	Southeast Asia, North Africa
Garum (from fish guts)	400 BC	Greece, Italy (Rome)
Pickled vegetables	1000 BC	China, Europe
Tea	200 BC	China

Gut microbiota promotes healthy effects on the host and prevents diseases.



Probiotics:

What Is Known:

- Probiotics are increasingly being used in the pediatric population.
- Uncertainty about how to appropriately use.
- The effects: strain specific.

What Is New:

- Indications for the use of probiotics for selected GI disorders in children covered in earlier documents are updated.
- Indications not covered in earlier documents are included.

Other indications?

- Autoimmune conditions: MS, lupus, rheumatoid arthritis
- During and post antibiotic use
- Post chemotherapy
- Post radiation
- Food allergies
- Chronic fatigue syndrome
- Surgical site infections
- Total cholesterol and LDL-cholesterol lowering
- Blood glucose and A_{1C} levels in type II diabetes mellitus
- Halitosis
- Hepatic encephalopathy
- Infection risk in the critically ill
- Late-onset sepsis in preterm infants

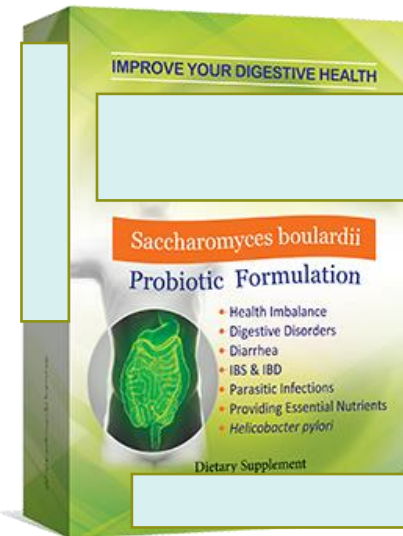
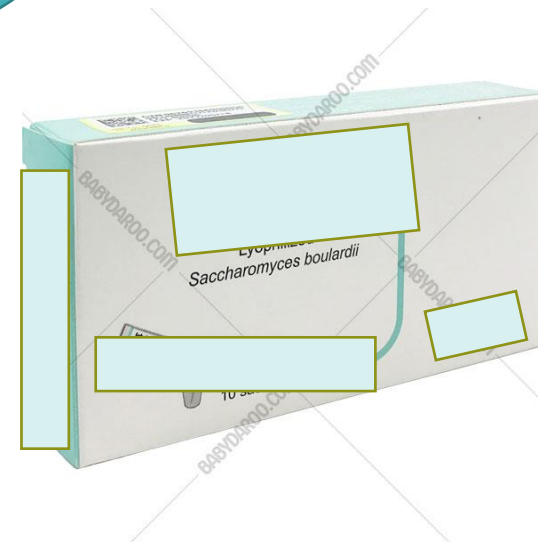
Acute Gastroenteritis:

- Lacticaseibacillus rhamnosus (L rhamnosus) GG [at a dose of $\geq 10^{10}$ CFU/day, for 5–7 days]
 - reduced duration of diarrhea
 - length of hospitalization
 - stool output
- Saccharomyces (S) boulardii (at a dose of 250–750mg/day, for 5–7 days)
 - reduced duration of diarrhea
- Limosilactobacillus reuteri (L reuteri) (at daily doses 1×10^8 to 4×10^8 CFU, for 5 days)
 - reduced duration of diarrhea
- Combination of L rhamnosus and L reuteri (at a dose of 2×10^{10} CFU for each strain, for 5 days)
 - reduced duration of diarrhea
- **Not** recommend the combination of Lactobacillus helveticus and L rhamnosus
- **Not** recommend Bacillus clausii

Each 10 drops contains
 5×10^{10} CFU
Lactobacillus
rhamnosus



250mg
Saccharomyces
Boulardii



Each sachet contains
Lactobacillus reuteri
(8×10^8 CFU).

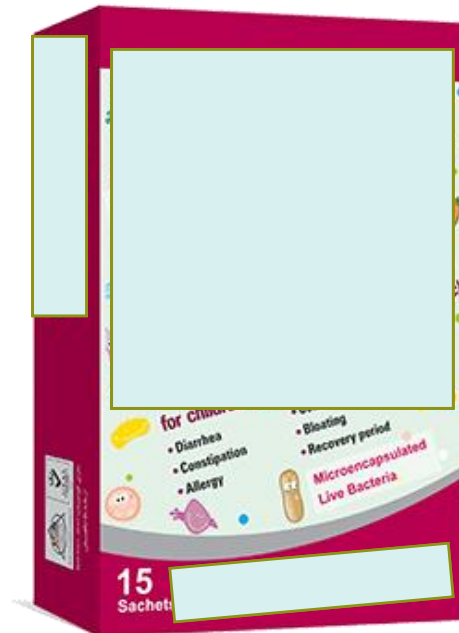
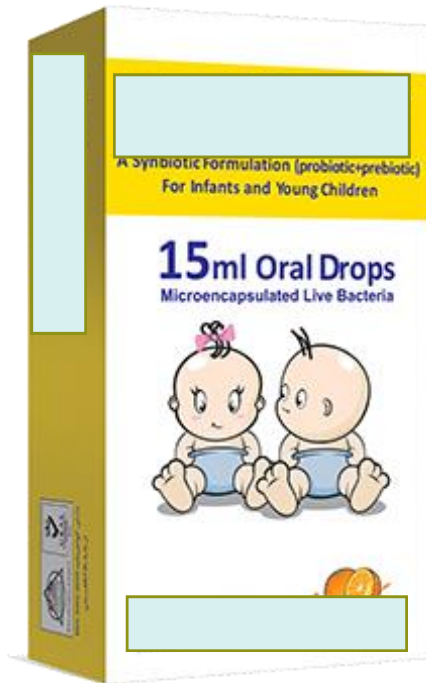
1×10^9
L.reuteri/1
cc

Each 5 drops
contains 8×10^8
CFU Lactobacillus
reuteri.



L.Ramnosus
GG+ L.ruteri+
B.infantis
10⁹

- L.Ramnosus GG+....
- Bifidobacterium infantis
 - Lactobacillus casei
 - Bifidobacterium breve
 - Lactobacillus acidophilus
 - Lactobacillus bulgaricus
 - Streptococcus thermophilus
- 10⁹



Prevention of Antibiotic-Associated Diarrhea:

- AAD: a common and challenging complication
- ambulatory and hospital settings alike that occurs in up to a third of all patients treated with antibiotics
- may occur after a few weeks and even up to a few months after the administration of the antibiotics
- **The risk is higher with aminopenicillins without/with clavulanate, cephalosporins, clindamycin**
- Any antibiotic that is active against anaerobes
- Almost any oral and intravenous antibiotic treatment can cause AAD
- Clinically: mild diarrhea.....fulminant pseudomembranous colitis. Usually, no pathogen is identified.
- In the most severe forms and in an increasing number of patients with chronic conditions such as those with inflammatory bowel diseases, cystic fibrosis, and cancer, however, the causative agent is often identified as *Clostridium difficile*

Prevention of Antibiotic-Associated Diarrhea:

- If the use of probiotics for preventing antibiotic-associated diarrhea (AAD) is considered because of the existence of risk factors:
 - class of antibiotic(s)
 - duration of antibiotic treatment
 - Age
 - need for hospitalization
 - Comorbidities
 - previous episodes of AAD:
- high doses (≥ 5 billion CFU/day) of *S. boulardii** or *L. rhamnosus* GG started simultaneously with antibiotic treatment to prevent AAD in outpatients and hospitalized children

Prevention of Nosocomial Diarrhea:

- L rhamnosus GG (at least 10⁹ CFU/day) for the duration of the hospital stay for the prevention of nosocomial diarrhea in children
- **Not** recommend L reuteri

Prevention of Necrotizing Enterocolitis:



For reducing the risk of necrotizing enterocolitis in preterm infants, provided all safety issues are met

- L rhamnosus GG (at a dose ranging from 1×10^9 CFU to 6×10^9 CFU)
- Combination of Bifidobacterium (B) infantis, B lactis, and Streptococcus thermophilus at 3.0 to 3.5×10^8 CFU (of each strain)
- **No** recommendation for or against L reuteri or the combination of B bifidum & Lactobacillus acidophilus
- **Not** recommend B breve or S boulardii

Prevention of Necrotizing Enterocolitis:



Probiotics may theoretically be responsible for at least 5 types of side effects:

- systemic infections
- deleterious metabolic activities
- excessive immune stimulation
- antibiotic resistance gene transfer
- gastrointestinal side effects: intestinal gas formation

Prevention of Necrotizing Enterocolitis:



- Probiotic sepsis in premature infants could be particularly important
- Immunocompromised patient group.
- Probiotic bacteraemia may be hard to detect with classic culture methods
- Multiple case reports have described single or multiple cases of bacteraemia (sometimes in conjunction with NEC) in premature infants
 - B infantis
 - L rhamnosus GG

Helicobacter pylori Infection:

- In children with H pylori infection, along with H pylori therapy, **S boulardii** for increasing the eradication rates and decreasing gastrointestinal adverse effects

Inflammatory Bowel Disease:

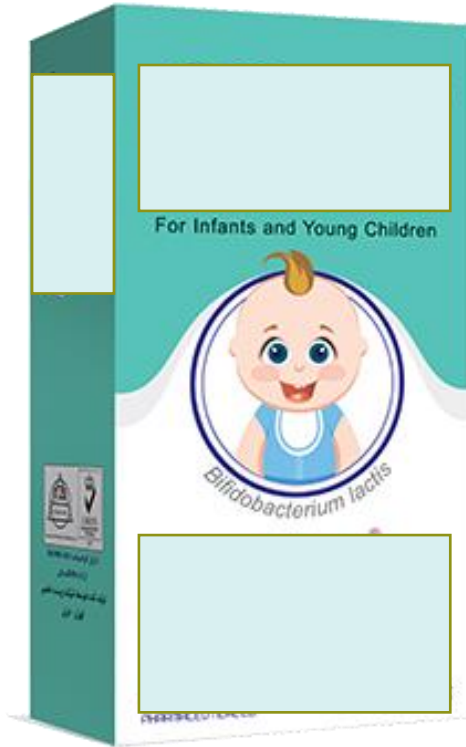
- **No** recommendation can be made for or against the use of probiotics studied so far in the management of children with **ulcerative colitis** due to insufficient evidence.
- **No** recommendation can be made for or against the use of probiotics studied so far in the treatment of children with **Crohn disease** due to insufficient evidence

Infant Colic:



- L reuteri (108 CFU/ day for **at least 21 days**) for the management of infant colic in breastfed infants
 - No recommendation for or against in formula-fed infants
- B lactis (108 CFU/day, for 21–28 days) for the management of infant colic in breastfed infants
- **No** recommendation can be made for or against the use of any of the probiotics studied so far for **preventing** infant colic due to insufficient evidence.

1×10^9
B.lactis



Functional Abdominal Pain Disorders:

- *L reuteri* (at a dose of 10^8 CFU to 2×10^8 CFU/day) for pain intensity reduction in children with functional abdominal pain disorders
- *L rhamnosus GG* (at a dose of 10^9 CFU to 3×10^9 CFU twice daily) for the reduction of pain frequency and intensity in children with irritable bowel syndrome

NO recommendation:

- **Functional Constipation:**
 - not recommend the use of probiotics as a single or adjuvant therapy
- **Celiac Disease:**
 - No recommendation can be made for or against the use of probiotics
- **Small Intestinal Bacterial Overgrowth:**
 - No recommendation can be made for or against the use of probiotics in the treatment or prevention of small intestinal bacterial overgrowth
- **Pancreatitis:**
 - As no randomized controlled trial on the use of probiotics for pancreatitis in children was identified, no recommendation can be made for or against the use of probiotics for the management of pancreatitis.

2022

Probiotics for the Management of Pediatric Gastrointestinal Disorders: Position Paper of the ESPGHAN Special Interest Group on Gut Microbiota and Modifications

**Hania Szajewska, MD, †Roberto Berni Canani, MD, ‡Magnus Domellöf, MD, †Alfredo Guarino, MD, §Iva Hojsak, MD, ¶Flavia Indrio, MD, †Andrea Lo Vecchio, MD, ¶Walter A. Mihatsch, MD, #Alexis Mosca, MD, **Rok Orel, MD, ††Silvia Salvatore, MD, ††Raanan Shamir, MD, §§Chris H. P. van den Akker, MD, §§Johannes B. van Goudoever, MD, ¶¶Yvan Vandenplas, MD, ¶¶Zvi Weizman, MD, on behalf of the ESPGHAN Special Interest Group on Gut Microbiota and Modifications*

2020

Use of Probiotics for the Management of Acute Gastroenteritis in Children: An Update

**Hania Szajewska, †Alfredo Guarino, ‡Iva Hojsak, §Flavia Indrio, ‡Sanja Kolacek, ¶¶Rok Orel, ¶¶Silvia Salvatore, #Raanan Shamir, **Johannes B. van Goudoever, ††Yvan Vandenplas, ††Zvi Weizman, and *Bartłomiej M. Zalewski, on behalf of the Working Group on Probiotics and Prebiotics of the European Society for Paediatric Gastroenterology, Hepatology and Nutrition*

2020

Probiotics and Preterm Infants: A Position Paper by the European Society for Paediatric Gastroenterology Hepatology and Nutrition Committee on Nutrition and the European Society for Paediatric Gastroenterology Hepatology and Nutrition Working Group for Probiotics and Prebiotics

**Chris H.P. van den Akker, *Johannes B. van Goudoever, †Raanan Shamir, ‡Magnus Domellöf, §Nicholas D. Embleton, ¶Iva Hojsak, ¶Alexandre Lapillonne, **Walter A. Mihatsch, ††Roberto Berni Canani, ††Jiri Bronsky, §§Cristina Campoy, ¶¶¶Mary S. Fewtrell, ¶¶Nataša Fidler Mis, ††Alfredo Guarino, ¶¶¶Jessie M. Hulst, ¶¶¶Flavia Indrio, ¶¶Sanja Kolaček, ¶¶¶Rok Orel, †††Yvan Vandenplas, †††Zvi Weizman, and ¶¶¶¶Hania Szajewska*



خوشسیراز و وضع بی‌مثالش
خداوندانکه دار از زوالش