In the Name of God

Probiotics for the Management of Fussiness and Gastroesophageal Reflux in Children

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Can Probiotics Help with Acid Reflux?

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GERD

- The most common gastrointestinal disorder that leads to referral to a pediatric gastroenterologist during infancy.
- The passage of gastric contents into the esophagus (GER) is a normal physiologic process that occurs in healthy infants, children and adults.
- Most episodes are brief and don’t cause symptoms.

GERD

- The distinction between physiologic and pathologic GER is determined by :
- Number, severity & complications(FTT, esophagitis, esophageal stricture & chronic respiratory disease).
- In pediatric population immaturity of lower esophageal sphincter function results in its frequent transient relaxation.
- Gastroesophageal reflux is common in young infants, particularly those born prematurely or with a history of medical complexity.

Physiologic vs Pathologic

- Physiologic GERD
- Postprandial
- Short lived
- Asymptomatic
- No nocturnal sx

- Pathologic GERD
- Symptoms
- Mucosal injury
- Nocturnal sx

Prevalence

GER:

- <3 mo : 50%
- at 4 mo : 40%
- at 12mo: 5%

GERD:

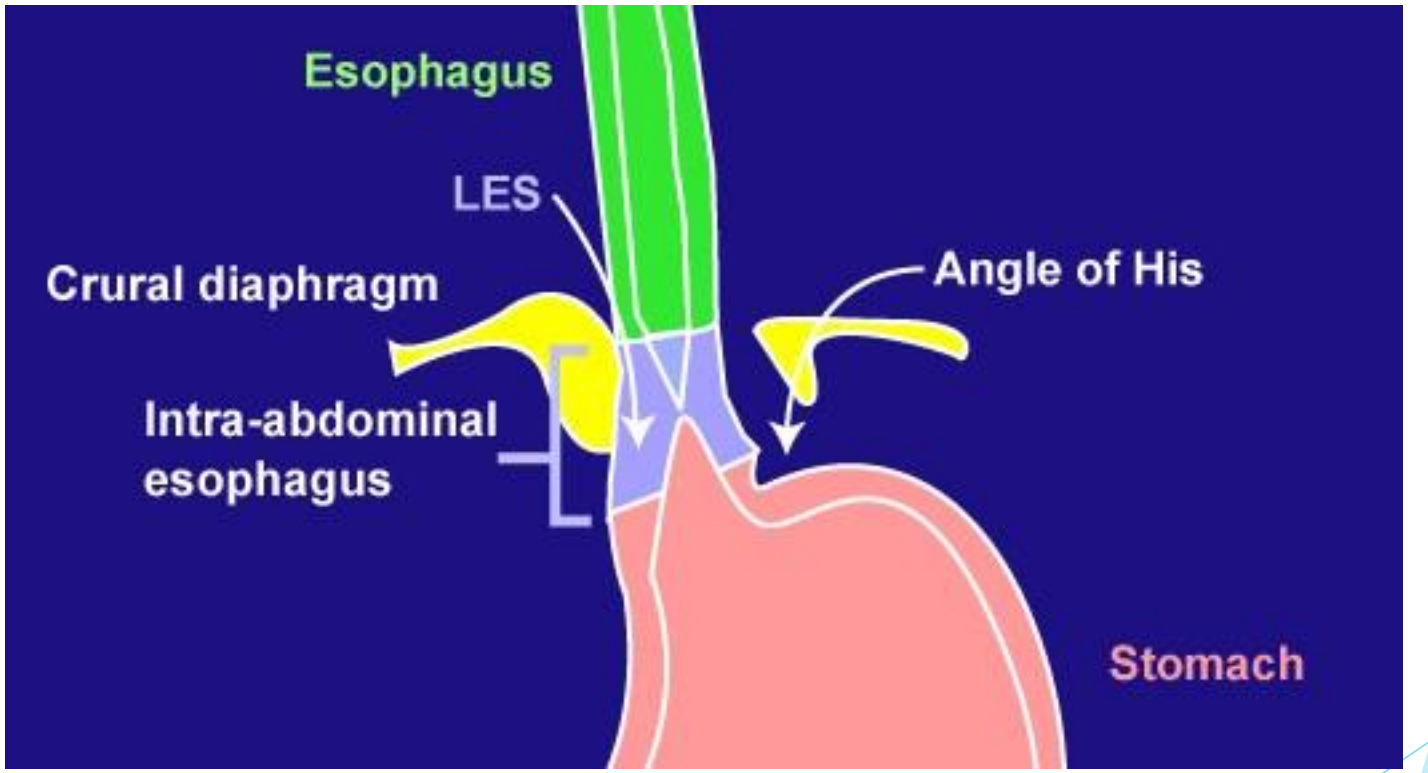
- infancy: 5-9%
- 3-9 years: 1.8%
- 10-17 years: 3-5%
  Adult: 4-30%

Contributing factors

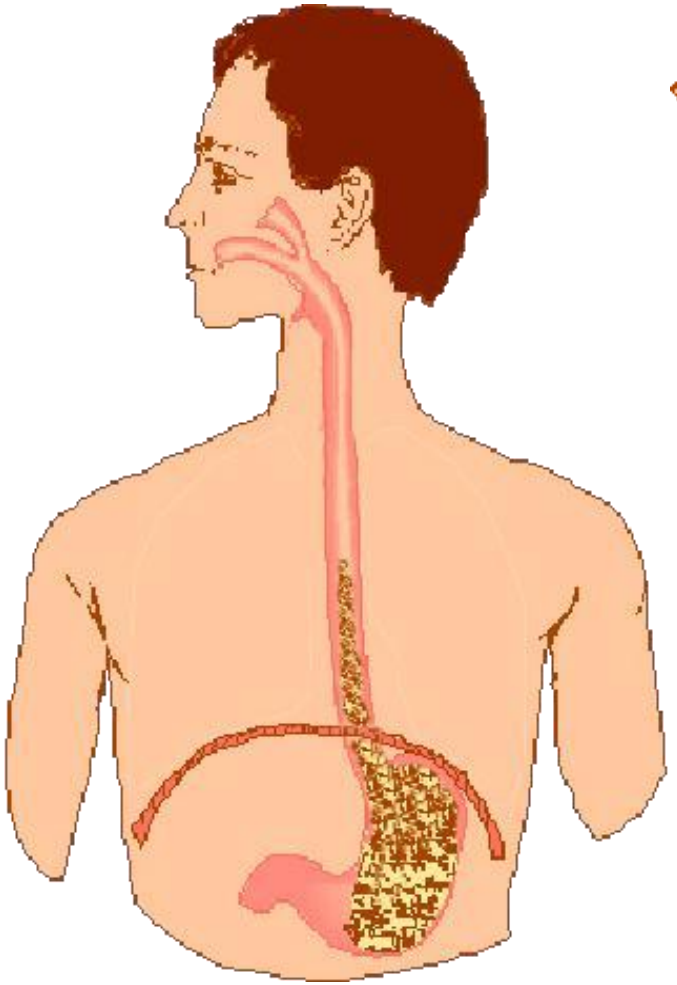
- Race ,sex ,body mass index, hiatal hernia,
- Possible gen: on chromosome 9,13
  - An AD syndrome with otolaryngeal manifestations.13q14: GERD1

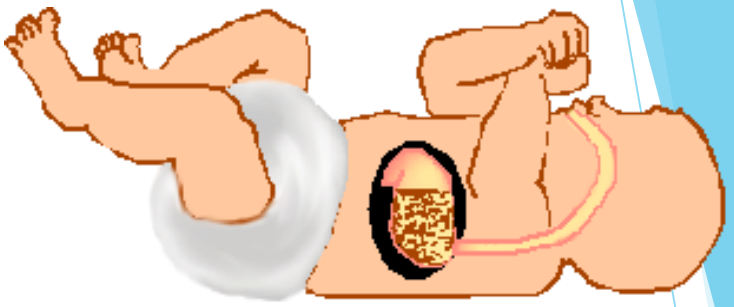
Others : environment ,diet ,smoking

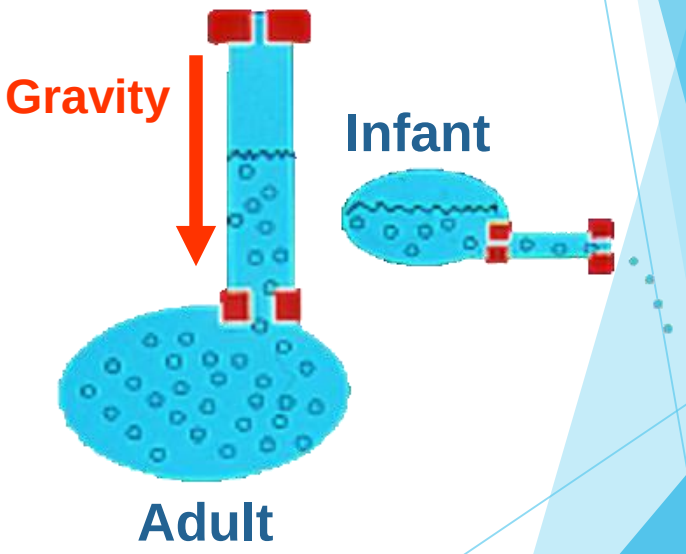
The Antireflux Barrier



Esophageal Capacitance






Gravity
Infant
Adult

Three important part of defense

- 1-Anti reflux barrier: LES, crura, his angle.
- 2-Esophgeal clearance: gravity, esophageal peristalsis
- 3-Mucosal resistance: epithelium Bicarbonate, mucin, prostaglandin E2,epidermal growth factor, transforming growth factor, Epithelial tight junction ,inter cellular glycoprotein

Mechanisms of GER

- Transient LES relaxation
- Intra-abdominal pressure
- Gastric compliance
- Delayed gastric emptying
- Stress,
- **Dysbiosis**,
- Food intolerances

Mechanisms of Esophageal Complications

- **Impaired esophageal clearance**
- **Defective tissue resistance**

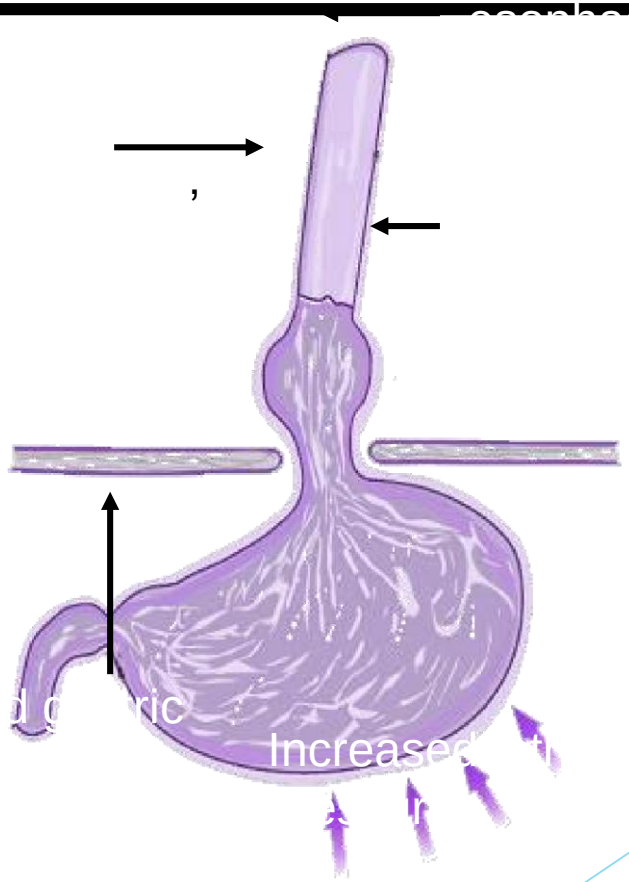
- **Noxious composition of refluxate**

TLESR

- Transient relaxation of lower esophageal sphincter: spontaneous, abrupt, prolonged and complete relaxation of LES.
- It is most frequent mechanism causing GER.

- In normal infants GER is a self limited problem starting at first months of life with a peak at 4 mo and resolving at 12-24mo.

Causes of increased exposure of the esophagus to gastric refluxate



Katzka & DiMarino 1995

Other condition associated with GERD

- Abnormal GI motility (enteric neural or muscle function)
- Gastric outlet obstruction (gastric ulcer, pyloric, duodenal ulcer) may cause GERD.
- 1/3 of infants with sever psychomotor retardation have significant GER.
- Large hiatal hernias, chronic B.P.D
- GER occurs in CF, CP, ICP, Down syndrome.
- Acid exposure of distal esophagus induce dysmotility vicious cycle GER

Can Probiotics Help with Acid reflux?

- A probiotic is a dose of live bacteria similar to those found naturally in the body.
- The U.S. Food and Drug Administration (FDA) has not yet approved any health benefit claim associated with probiotics.
- **Excessive gas formation in the stomach leads to acid reflux.**
- Unwanted bacteria in the stomach disrupt the digestion process and get the undigested food fermented.
- Fermentation results in release of excess gas.
- The gas in turn will give pressure to the LES muscles and make the diaphragm open.
- The acids will then pass to the esophagus.

Can Probiotics Help with Acid Reflux?

- The process of fermentation can be prevented by pro-bacteria reducing the growth of bad bacteria in the stomach.

- The healthy balance of bacteria will be regained and the digestion will occur smoothly.
- Probiotics, sometimes called “good bacteria,” can suppress the growth of “bad bacteria” like *E. coli.*
- Adding probiotics to diet is easy.
- There are certain foods containing probiotics and these foods are found easily.
- Some of these food items are: Yogurts, Fermented soft cheese, sourdough bread, Kefir.
- Natural probiotics can be found as an oral supplement. Such can also be taken to cure acid reflux.

Maternal & Child Nutrition

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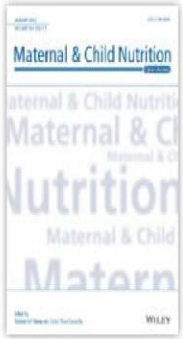

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REVIEW ARTICLE | Open Access

Probiotics for preventing and treating infant regurgitation: A systematic review and meta-analysis

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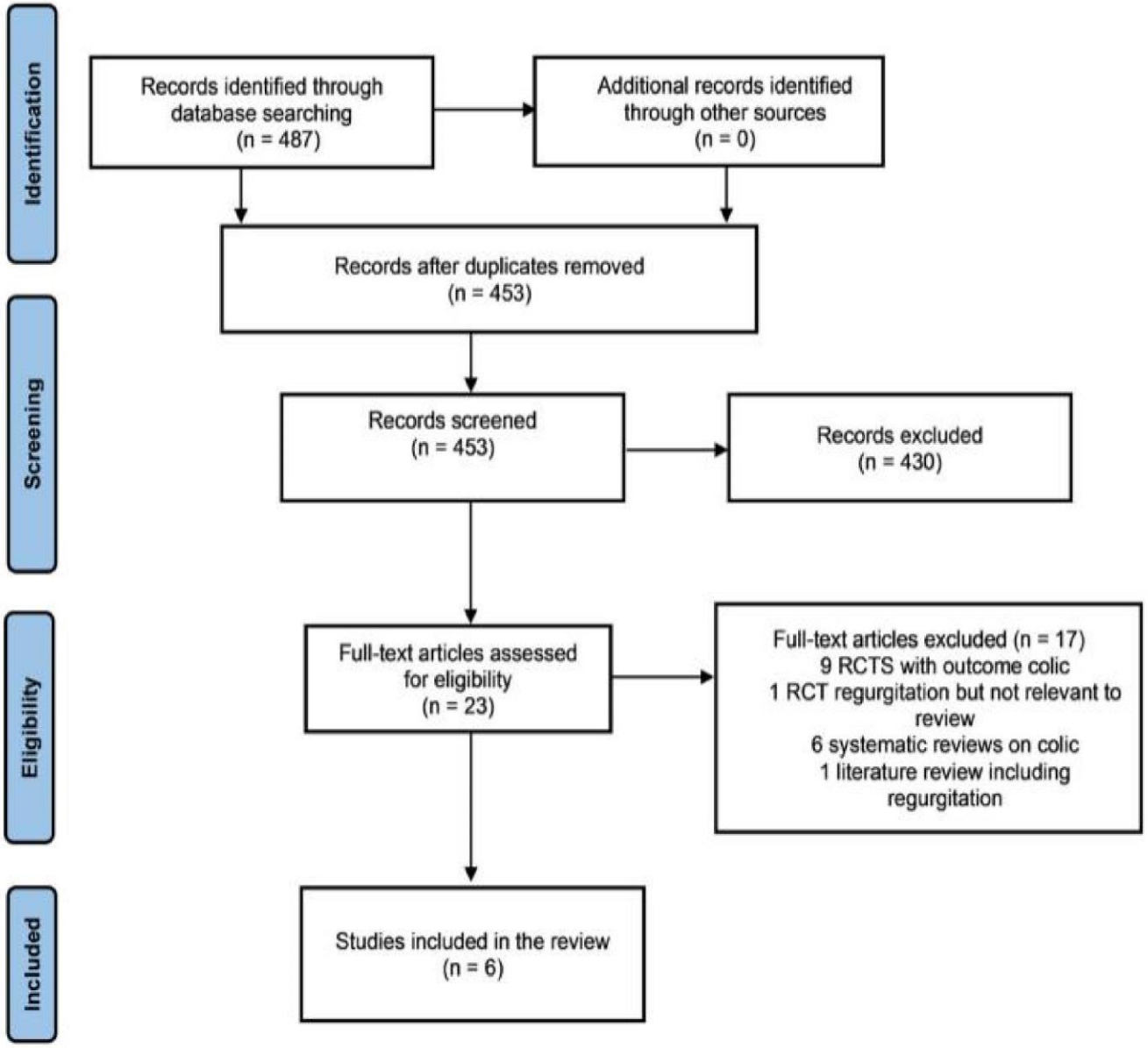
Abstract


Identification
Screening
Eligibility
Included
Records identified through database searching (n = 487)
Additional records identified through other sources (n = 0)
Records after duplicates removed (n = 453)
Records screened (n = 453)
Records excluded (n = 430)
Full-text articles assessed for eligibility (n = 23)
Full-text articles excluded (n = 17)
9 RCTS with outcome colic
1 RCT regurgitation but not relevant to review
6 systematic reviews on colic
1 literature review including regurgitation
Studies included in the review (n = 6)

Infant regurgitation

- Six trials examined the effect of probiotics on episodes of regurgitation per day following 1 month of intervention.
- Three studies were included in the meta- analysis (Indrioet al.2008,2014,2017).
- Meta- analysis showed a statistically significant reduction in regurgitation in the probiotic group compared to the placebo group.
- They were unable to include the remaining three studies due to the method of reporting.
- Garofoli et al.(2014) reported for infants receiving the probiotic(L. reuteri DSM 17938 administered 5 drops), a significant reduction was shown in the average daily number of regurgitations (p= 0.02) from baseline to Day 28 of the study period.
- Baldassarre et al. (2016) reported that the onset of regurgitation was significantly reduced in the probiotic group compared to the placebo group when administered to women 4 weeks before the expected delivery date until 4 weeks after delivery.

- Indrio et al. (2014) was the only study to report regurgitation after 3 months of the commencement of the intervention and found a statistically significant reduction in regurgitation for infants receiving the probiotic compared to the placebo.

Gastric emptying time

- Due to the method of reporting for gastric emptying time, they were unable to perform meta- analysis.
- Indrio et al. (2008) reported that gastric emptying rate (%) was statistically significantly faster in the newborns receiving probiotics compared with a placebo (25% vs.50%,$p < 0.001$).
- Indrio et al. (2011) reported the change in gastric emptying rate (%) before and after the intervention and found a statistically significantly increased gastric emptying rate in infant sreceiving probiotics compared to placebo.($p = 0.01$).
- Indrio et al. (2017) also reported a significantly increased gastric emptying rate percentage change for infants receiving probiotics compared to placebo($p < 0.01$)

Conclusion

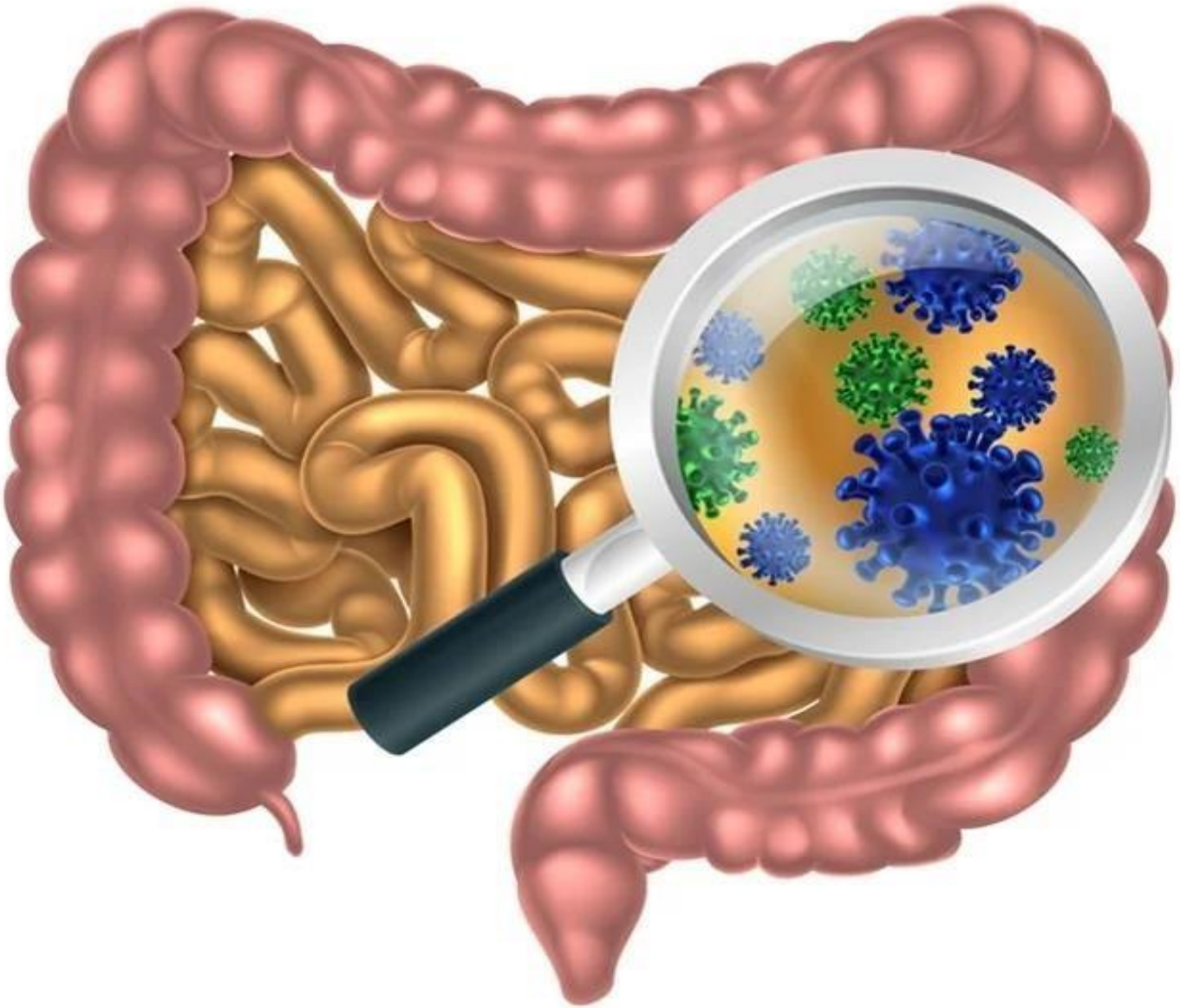
- The currently available evidence does not support or refute the efficacy of probiotics for the prevention and treatment of infant regurgitation.
  - However, data from the individual trials and are promising.
- There are no indications from the available data that probiotics have any adverse effects.
- The use of probiotics could potentially be a noninvasive, safe, cost effective and preventative positive health management strategy for both women and their babies.
- Further well- controlled RCTs are warranted to investigate the efficacy of various strains and species, dosage, and combinations of probiotics.
- In addition, further research is required to determine the effectiveness of administering probiotics to women antenatally and/or postnatally to prevent regurgitation in breastfed infants.

Other Studies

- In one of study published in **JAMA Pediatr**, the researchers at an Italian university reported that giving infants a probiotic during their first three months of life can help prevent stomach problems like colic.
- This study found that administering five drops of the probiotic *lactobacillus reuteri* results in much shorter crying episodes, less spitting up, and less constipation.
- These conditions often cause numerous visits to the pediatrician, changes in feeding patterns, parental anxiety, and loss of parental working days with important socioeconomic consequences.

Other Studies

- In his book "Fast Tract Digestion," Norman Robillard, Ph.D., makes a case that small intestine bacterial overgrowth (SIBO) may be the real cause of gastroesophageal reflux disease (GERD).
- SIBO is a health condition in which there are too many bacteria in the upper part of the small intestine, a place where these microorganisms really shouldn't be.
- GERD is a disease in which stomach acid burns the lining of the esophagus (acid reflux), causing the symptoms of heartburn.



How might SIBO and GERD be connected?

- Dr. Robillard's theory is that the gas produced by the bacteria residing in the small intestine puts enough pressure on the small intestine and stomach that it can push the acid into the esophagus.
- In addition to identifying a new mechanism of GERD, Dr. Robillard also offers a new look at treatment.
- He does not endorse the use of acid-reducing medications, particularly the use of proton pump inhibitors(PPIs) , which is currently the standard treatment for GERD.
  - His theory is that the reduced stomach acid contributes to the bacterial overgrowth in the small intestine, as stomach acid serves a preventative role in keeping bacteria from populating the small intestine.

How might SIBO and GERD be connected?

- What Dr. Robillard recommends is that GERD patients follow a diet that is low in what he calls "difficult to digest" carbohydrates.
- It is his belief that a diet high in these carbohydrates contributes to both the overgrowth of these bacteria and the increased gas output that is causing reflux.
  - Interestingly, his list of carbohydrates to avoid is very similar to those of the low fermentable oligosaccharides, disaccharides, monosaccharides and polyols(lowFODMAP) diet for IBS.
  - **A crucial difference is those foods that are high in resistant starch, such as unripe bananas and corn, which are encouraged on the low-**

FODMAP diet but discouraged by Dr. Robillard in terms of treating GERD.

How might SIBO and GERD be connected?

- There is not yet a lot of supporting research for this compelling theory.
- One small study involved having GERD patients swallow a solution of either fructooligosaccharides (FOS) or placebo after meals for one week each. FOS are non-digestible and, therefore, fermentable by intestinal bacteria. Interestingly, FOS is a type of FODMAP, found in foods like **onions, garlic, and asparagus.**
- The researchers found that the FOS increased the times of relaxation of the esophageal sphincter muscles, as well as increased the amount of acid reflux and GERD symptoms.

- In this study the researchers concluded that it was fermentation within the colon that caused the increase in GERD symptoms.
- Another very small study found that a low-carbohydrate diet significantly improved GERD symptoms in eight obese GERD patients.

Probiotics, Colic & fussiness

- As any exhausted parent knows, having a colicky baby with inconsolable crying,, fussiness and screams of pain is both distressing and worrying.
- A growing area of interest is the role of the gut microbiome, and many parents and carers are considering the use of probiotics for colic.
- The exact reason why some babies develop colic and reflux remains unknown.
- Growing evidence suggests that gut bacteria could play a role.
- Babies with colic may have lower levels of beneficial bacteria and higher levels of inflammation that cause digestive issues, including colic and reflux.
- Having lots of the right bacteria in your baby's gut is very important.
- The prenatal environment, delivery method and genetics can shape the baby's gut.

Recent researches suggest that certain strains of beneficial bacteria particularly

Bifidobacterium, have been shown to reduce the symptoms associated with colic.

How can probiotics help with colic and reflux?

- The diversity of baby's gut health (**child microbiome**) is instrumental in having a happy and healthy baby.
- Probiotics are microorganisms which are beneficial to health and help support digestive issues which can cause crying and fussing.
- Not all probiotics are the same.
- There are specific probiotics designed for babies with evidence suggesting they can help relieve symptoms of colic and reflux by:
  - 1)Supporting the diversity of baby's gut (the more diverse the less colicky)
  - 2)Reducing susceptibility to pathogens (harmful microbes), such as *E. coli* and *Klebsiella* spp.
  - 3)Having an anti-inflammatory effect on the gut, which may decrease symptoms associated with colic and reflux

- When babies are given the correct strain of probiotic, it helps to create a diverse and healthy microbiome which help to develop the digestive and immune system.

Which are the best probiotic strains for colic and reflux?

- Some of the best probiotics for babies include:
- *Bifidobacterium breve* M-16V® is shown to discourage the growth of pathogens associated with colic, help colonization of infant's gut with healthy bacteria and reduce gastrointestinal symptoms such as colic and reflux.
- *Lactobacillus rhamnosus* GG® is shown to reduce crying associated with colic and reflux symptoms whilst also helping with gastrointestinal infections.
- Some researches suggest *Lactobacillus reuteri* DSM 17938[8] showed mixed results when looking at an improvement of symptoms relating to colic.

- The microbiome of adults and babies are significantly different.
- When babies are born one of the first natural bacterial colonisers is Bifidobacterium, evidence suggest that babies suffering from colic and reflux often have lower levels of this bacteria in their gut.

Recommendations

- Pick a short course(2-6 weeks) of strains that have been featured in gold-standard trials and demonstrated to be safe and effective for use in infants and children.
- Choose liquid probiotic drops, they are easier to administer to an unsettled baby not needing the fridge. They are safe for use, suitable for formula-fed or breastfed babies and can also, be used alongside medicines for colic.
- Continue breastfeeding
- Formula or breastmilk thickening
- Burp your baby after every 1 to 2 ounces of formula

- Avoid overfeeding; give the baby the amount of formula or breast milk recommended.
- Hold the baby upright for 30 minutes after feedings
- Acid reducing drugs, prokinetic drugs

Esophageal ulceration endoscopic appearance

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Thanks for
Your Attention