

# Functional Gut Disorders in Infants

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## Disclosures

- Speaker fees - Nutricia Neocate, Merck Serono, AstraZeneca, Aspen Nutritionals
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- Research grant - AstraZeneca

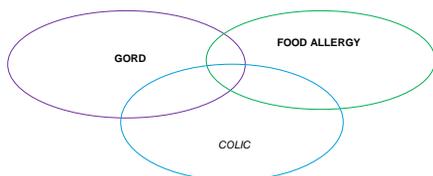


- Commonly asked questions
- What's changing and why might we be seeing more problems?
- Management and assessment of GOR and constipation
- The role of probiotics



## Commonly asked questions??

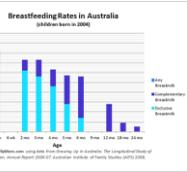
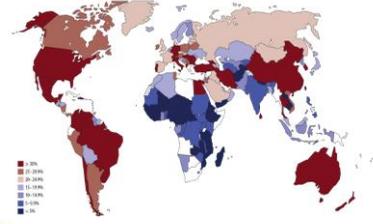
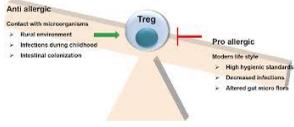
- I have/my husband has lactose intolerance – will it effect our choice of formula?
- I have/my husband has lactose intolerance – is this why my baby has diarrhoea?
- We are a very allergic family, will my new baby get allergies/how can I help?
- Why did my baby get constipated when she started solids-is there a serious problem/does she need tests?
- Does my baby have reflux and what treatments does she need?
- I think my baby has allergies, I'm breast feeding. Should she have allergy tests?
- I think my baby has allergies, I'm breast feeding. Should I try some dietary changes?



## The microbiota



## Why is this more and more relevant?



### Antibiotic Use in Children – A Cross-National Analysis of 6 Countries

See Neungjar, MD, MSc<sup>1</sup>, Jerry Aves, MD<sup>2</sup>, Valeria Bouboul, MD<sup>3</sup>, Anna Costantini, MD<sup>4</sup>, Jason Cho-Gongye, MD, PhD<sup>5</sup>, Usual Madruga, MD<sup>6</sup>, Binay Anand, MD, PhD<sup>7</sup>, Srikumar Pillai, MD, PhD<sup>8</sup>, Gabriel Garcia-Garcia, PharmD, PhD<sup>9</sup>, Howard Schorler, MD<sup>10</sup>, Kater Schwan, PhD<sup>11</sup>, Young Shin, PhD<sup>12</sup>, Sun B Kim, MD<sup>13</sup>, Ganesha Ram Srinivasan, MD<sup>14</sup>, Rajeev Sankaran, MD, PhD<sup>15</sup>, Angela Tang, MD<sup>16</sup>, Gaurav Tripathi, MD, PhD<sup>17</sup>, Tamer Zu-Darab, PhD<sup>18</sup>, and Seoyoung C. Kim, MD, ScD, MSc<sup>19</sup>

Table 11. Antibiotic courses per child/year in participating countries (2008-2012)

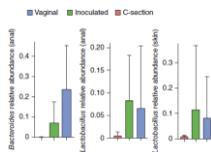
Age group	Country	No. of children	Prescribed antibiotic courses per child/year
0-7 years	Spain	1,102,045	1.06
	Italy	9,689,252	1.41
	Italy PD	3,078,331	1.28
	Italy PV	452,869	1.28
	Germany	2,416,200	1.02
	Spain	217,120	1.02
8-17 years	Spain	1,867,282	1.02
	Italy	4,024,226	2.20
	Italy PD	862,289	1.02
	Italy PV	3,241,937	1.08
	Germany	1,512,283	1.02
	Spain	675,006	0.68
18-19 years	Spain	11,021,021	0.78
	Italy	1,623,049	0.78
	Italy PD	508,249	0.78
	Germany	8,130,205	0.62
	Spain	2,129,722	0.52
	Italy	177,120	0.52
10-19 years	Spain	2,482,215	0.67
	Italy	6,572,044	0.52
	Italy PD	2,019,219	0.52
	Italy PV	4,552,825	0.58
	Germany	1,442,202	0.58
	Spain	1,442,202	0.58

-The 'average' toddler in South Korea has 3.41 courses of antibiotics/year -Italy/Spain have more than x3 the rate of antibiotic use than Norway

## The future?

### Partial restoration of the microbiota of cesarean-born infants via vaginal microbial transfer

Maria G Dominguez-Bello<sup>1,2</sup>, Kassandra M De Jesus-Labory<sup>3</sup>, Nani Shera<sup>4</sup>, Laura M Cox<sup>4</sup>, Amnon Amir<sup>4</sup>, Antonia Gonzalez<sup>4</sup>, Nicholas A Bokulich<sup>5</sup>, Se Jin Song<sup>4,5</sup>, Marina Hoashi<sup>1,6</sup>, Juana I Rivera-Vinas<sup>7</sup>, Keimari Mendez<sup>7</sup>, Rob Knight<sup>4,8</sup> & Jose C Clemente<sup>1,8</sup>



## Gastro-oesophageal reflux

- Gastro-oesophageal reflux (GOR) occurs in approximately 50% of infants but typically resolves at around 12-18 months without the need for intervention
- GOR is termed gastro-oesophageal reflux disease (GORD) when reflux-associated symptoms occur
- GORD needs treating, GOR does not...



## Symptoms of GORD in infancy

- Vomiting/ regurgitation
- Sleep disturbance
- Irritability, typically post prandial
- Respiratory symptoms – recurrent chest infections/evidence of aspiration
- Evolving food aversion
- Failure to thrive

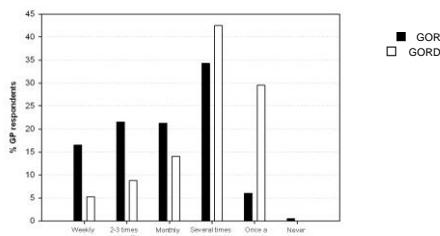
### ORIGINAL ARTICLE

#### Infant gastro-oesophageal reflux disease (GORD): Australian GP attitudes and practices

Catherine N Kirby,<sup>1</sup> Ahuva Y Segal,<sup>1</sup> Rupert Hinds,<sup>2</sup> Kay M Jones<sup>1</sup> and Leon Pitterman<sup>1</sup>

<sup>1</sup>Office of the Pro Vice-Chancellor, Berwick and Peninsula Campuses, Monash University and <sup>2</sup>Department of Paediatrics, Monash University, Melbourne, Victoria, Australia

## Frequency of GOR and GORD case presentations



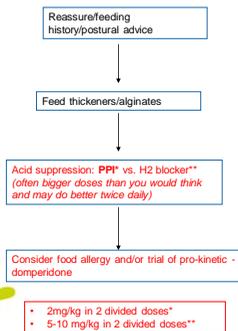
## Investigations are rarely helpful to confirm reflux but may help to exclude other diagnoses

- Bloods
- Barium follow through
- Ultrasound



If you think the baby needs investigating because of concerning or atypical features, then referral to paediatrician is probably needed

## Hierarchy of GOR(D) treatment in infants



## Summary

- Most babies who reflux do not require treatment
- Most reflux will get better towards the end of the first year of life
- Most of our treatment options are not very good for turning off 'simple/physiological' reflux
- Infants with secondary negative consequences do need treatment/referral

## Food allergy and 'reflux'

- Lack of improvement with good acid suppression **may** indicate cow's milk allergy
- Family history of atopy/food allergy, eczema or lower gastrointestinal symptoms (**Allergic colitis**) are supportive but not always present
- Allergy tests are hopeless (very likely to be negative even in confirmed allergy) for this indication at this age – **DON'T BOTHER**
- A trial of prescribed formula may be needed, in breast feeding mums trial exclusions first – **IT WON'T BE LACTOSE INTOLERANCE**



"It has nothing to do with you, Bessie. It's just that I'm lactose intolerant."

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## Food allergy ( $\pm$ reflux)

- Symptoms may start during breast feeding...consider maternal cow's milk and soya exclusions (make sure mum is getting enough calcium)
- PBS requirements include discussion with specialist...even if the feed has been started and worked, good time for referral
- Not like a peanut allergy! Will be likely to improve with age from 12 months onwards...



## Constipation



- Around 3% of paediatric outpatients and up to 30% of paediatric gastroenterology outpatients appointments relate to constipation
- Around 30% of school age children suffer with constipation at some time during childhood
- Less than 5% of children have an underlying organic diagnosis**
- Less medications are available in infancy – the most safe/well studied is lactulose

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## Red flags

- Constipation starting <1 month
- Passage of meconium >48 hours
- Failure to thrive/systemic symptoms
- Blood in the absence of a fissure
- Abdominal distension/bilious vomiting
- Abnormal position of anus
- Abnormal lower limb neurology/sacral dimples
- FH of Hirschsprung disease



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## The '5%' and the big clue(s)

- Hirschsprung disease: delayed passage of meconium  $\pm$  family history  $\pm$  chromosomal issue (Trisomy 21/Down's syndrome)
- Coeliac disease: FTT  $\pm$  abdomen more distended than degree of constipation  $\pm$  family history  $\pm$  nutritional deficiencies
- Cow's milk allergy: personal/family history of atopy/eczema  $\pm$  time of onset  $\pm$  reasonable diet with very poor response to laxatives (good doses)
- Spinal cord anomalies: abnormal spinal examination/lower limb neurology  $\pm$  urinary symptoms



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## Summary

- Very common in children, but very uncommonly 'pathological'
- Common times for constipation to occur...introduction of solids, toilet training
- No tests needed in most cases
- Encourage fluid intake
- Ensure good doses of osmotic laxatives (stool softeners) – Osmolax/Movicol in > 1 years are demonstrably the best...start on generous doses "top-down"; bit less certain in < 1 years...Lactulose is certainly safe and moderately effective

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## Probiotics and prebiotics

### • Probiotics

Live micro-organisms which, when administered in adequate amounts, confer a health benefit on the host

### • Prebiotics

A selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the gastrointestinal microflora that confers benefits upon host well-being and health



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## Can prebiotics/probiotics...

- Reduce the severity of infantile colic?
- Reduce the incidence of gastrointestinal disease/allergy or eczema in children?



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## Probiotics enter the mainstream!

ARTICLES

### Probiotics in primary prevention of atopic disease: a randomised placebo-controlled trial

Marko Hailtoni, Seppo Salminen, Heikki Anttonen, Pentti Kero, Pentti Koskinen, Erka Isolauri

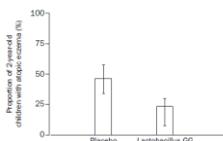


Figure 2: Treatment effect of Lactobacillus GG on atopic disease. Bars are 95% CI.

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## Lancet 2001

- Lactobacillus GG
- Prenatal to mothers (at risk); postnatal for 6/12 to babies
- 50% less atopic eczema in probiotic arm

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## Probiotics for colic

Research

Original Investigation

### Prophylactic Use of a Probiotic in the Prevention of Colic, Regurgitation, and Functional Constipation: A Randomized Clinical Trial

Flavia B. de Souza, MD, Antonio Di Marco, MD, Giuseppe Rizzuto, MD, Elza Caveri, MD, Cristina Vitale, MD, Luigi Orsiello, MD, Elza Marcolino, MD, Rosanna Bergato, MD, Maria Crocetti, MD, Emanuela Razzolini, MD, Antonio Dal Vecchio, MD, Silvio Stefan, MD, PhD, Ruggero Francavilla, MD, PhD

### Treating infant colic with the probiotic *Lactobacillus reuteri*: double blind, placebo controlled randomised trial

OPEN ACCESS

Valerie Tang, paediatrician<sup>1,2</sup>, Hannah Rees, associate professor<sup>1,2</sup>, Miles L. K. Tang, professor<sup>1,2</sup>, Frank A. O'Keefe, gastroenterologist<sup>1,2</sup>, Antonio L. Nunes, gastroenterologist<sup>1,2</sup>, Catherine Sibley, research fellow<sup>1</sup>, Paul G. Heaney, paediatric gastroenterologist<sup>1,2,3,4</sup>, Amanda Black, paediatrician<sup>1</sup>, Rosalind E. Barr, paediatrician<sup>1</sup>, Andrew Wake, paediatrician<sup>1,2</sup>

<sup>1</sup>Royal Children's Hospital, Parkville, Victoria, Australia; <sup>2</sup>Monash Children's Research Institute, Clayton, Australia; <sup>3</sup>The University of Melbourne, Parkville, Victoria, Australia; <sup>4</sup>Department of Paediatrics and Child Health, City and Health, Bristol, England; <sup>5</sup>University of Cambridge, Cambridge, England

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## Probiotics summary



- Accumulating evidence for benefits of probiotics in eczema reduction, when given to mums in last trimester and babies after birth
- Probiotics should be considered in the management of infantile colic, when other causes of irritability have been excluded
- The question of which probiotic for which indication remains unclear, but most studies use lactobacillus reuteri

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## Conclusion



- Gastrointestinal problems are very common in infants, but very rarely represent significant underlying pathology
- Gut immaturity/allergy/GOR will improve with or without our help
- Probiotics can have a role
- **Always keep an eye open for the red flags**

## Questions?

