Effects of supplementation with *Bifidobacterium infantis* in combination with bioactive milk components on gastrointestinal symptoms in children with autism

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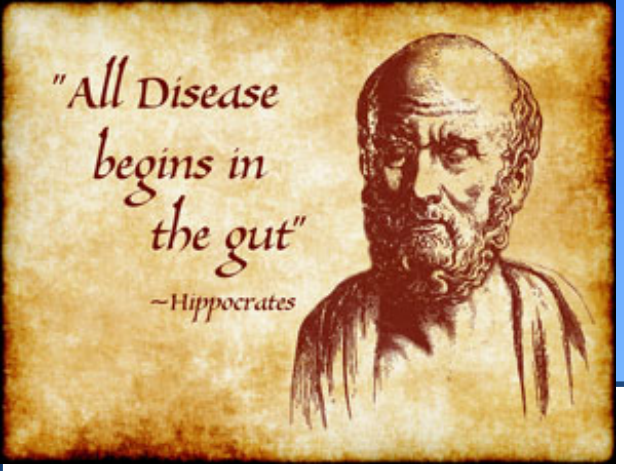


Introducing the Milk Oriented Microbiota

The Gut Brain Axis in Autism

Therefore, an effective intervention may be to supplement children with autism with GI symptoms with a probiotic (*Bifidobacterium infantis*) + prebiotic (bovine colostrum product – BCP) combination (synbiotic) compared to a prebiotic alone.

- Gastrointestinal symptoms:
  - Chronic constipation, diarrhea, IBS, excessive vomiting, acid reflux[3]
  - Associated with autism severity[4]

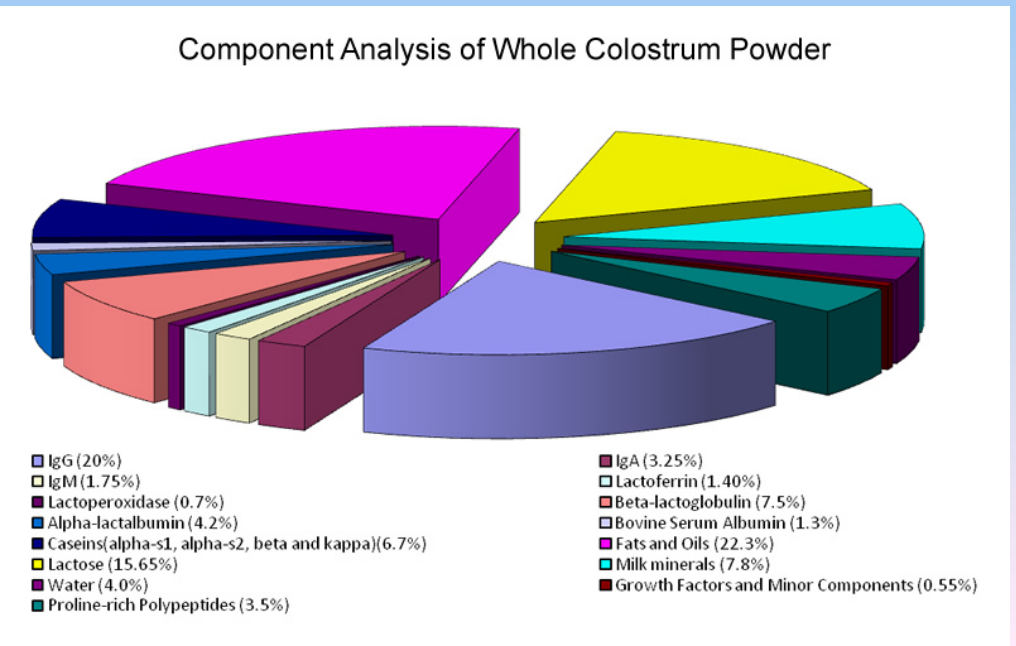
Study Aims

- **Aim 1:** Assess tolerability
  - *Hypothesis* – Both synbiotic and prebiotic will be well tolerated with limited/mild side effects
- **Aim 2:** Alter gut microbial composition
  - *Hypothesis* – Synbiotic administration will result in increased commensal *Bifidobacteria* and decreased pathogenic bacteria compared to prebiotic alone
- **Aim 3:** Improve GI symptom frequency and severity
  - *Hypothesis* – GI symptoms (constipation, diarrhea) will improve in frequency and severity in relation to changes in stool microbiota

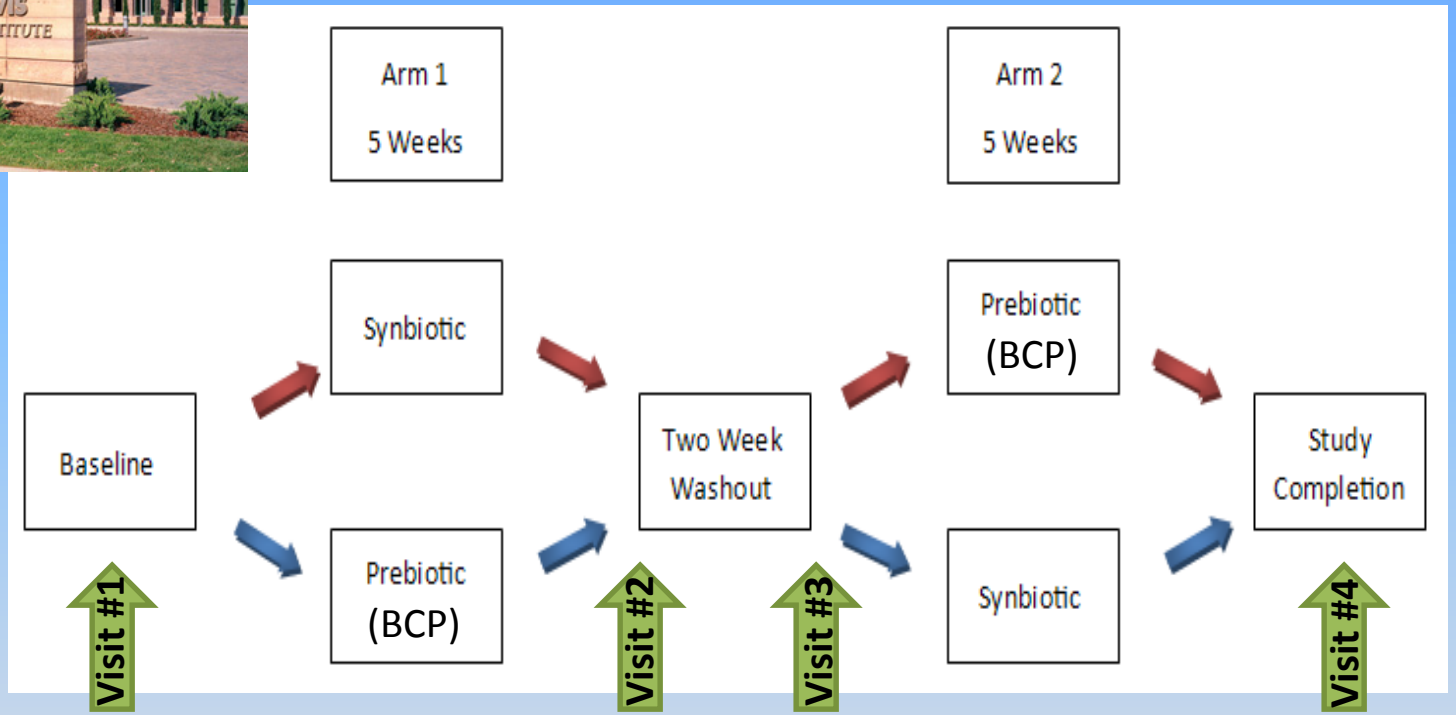
Why *B. infantis* and BCP?

- *Bifidobacterium longum* spp. *infantis*
  - Abundant in breastfed infants[5] and low in children with autism[1]
  - Beneficial in IBS[6] and NEC[7]
- Bovine Colostrum Product
  - Bovine milk oligosaccharides[8]
  - Immune factors[9]

Immucon Oligosaccharides (liquid)	
3 and 6 sialyllactose	5.2g/L
3 and 6 sialyllactosamine	4.2g/L
Free sialic acid	1.6g/L
LNnT and other HexNAc BMO	1.8g/L
Trioses	1.0g/L



Study Design



- Synbiotic = Probiotic + Prebiotic
- Probiotic – 20 billion CFU/day; Prebiotic – 0.15g/lb/day (12.5% of daily fiber)
- Parental reporting of GI symptom and behavioral changes as well as collection of blood, urine and stool at each of the four visits

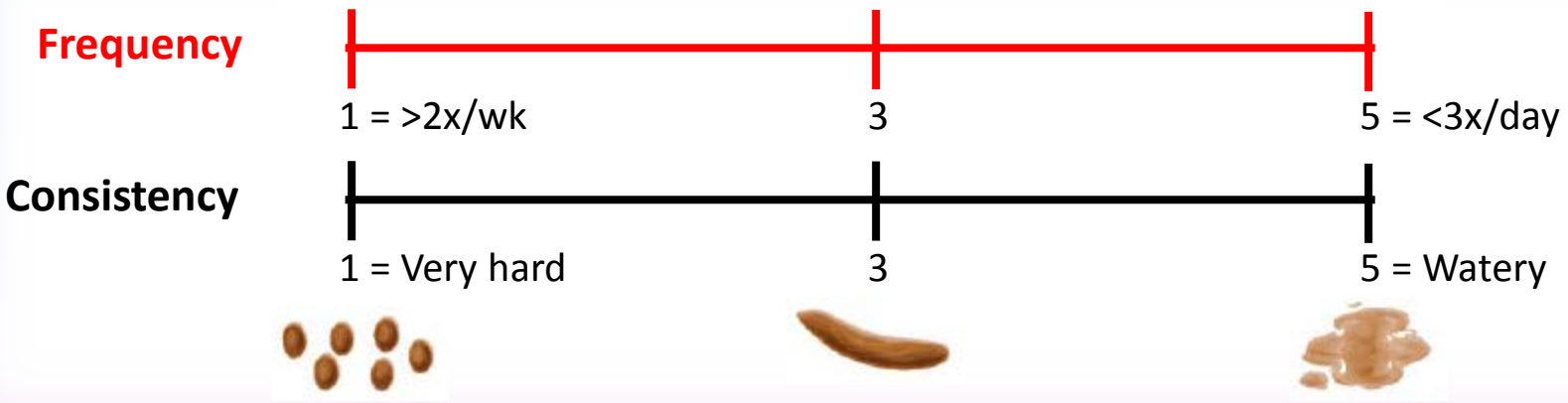
Subject Details

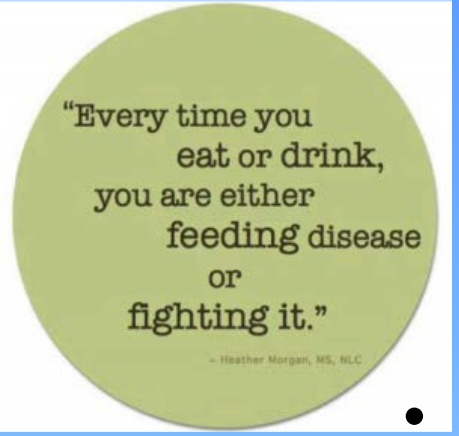
Subject Demographics	
Total Enrolled (n)	11
Male:female	6:4
Age Range (years)	3 - 9
Constipation/Diarrhea/ Mixed	3/4/4
IBS	7
Vomiting	5
Gas/boating	10

- Inclusion Criteria:
  - Age 2-11 years
  - Previous ASD Dx
  - Functional Constipation, Functional Diarrhea, IBS Dx based on RomeIII
- Exclusion Criteria:
  - History of milk allergy
  - Compromised immunity
  - GI disease
  - Use of steroids, antifungals, antibiotics in past month
  - Medically prescribed diet
  - Other co-morbid medical/genetic conditions
  - Use of medications affecting GI mobility
  - IQ < 40

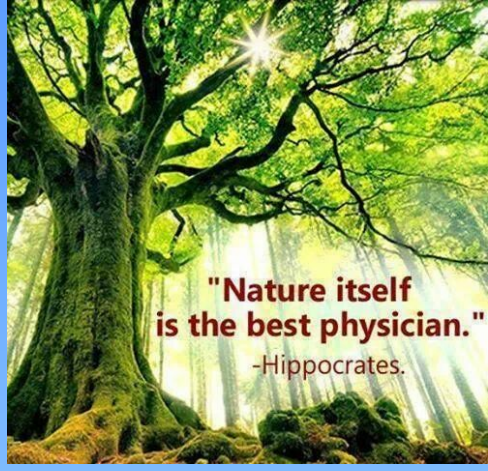
Interesting Trends

- GI symptom alterations were robust and readily assessed by parents in some but not all children studied, especially in children with an initial diagnosis of functional diarrhea
- Willingness to try new foods is an important bias in all studies of foods in these children
- Increased weight gain was observed in some children who had previously experienced difficulty with weight gain and had low initial BMI and thus BMI is an important dependent variable
- Most common side effects included gassiness and lethargy





Future Directions



- Short term:
  - Study is ongoing
  - Plasma cytokine analysis
  - Metabolomic analysis of plasma, urine and stool
  - Look for changes in intestinal permeability markers
  - Compare responders to non-responders
- Long term:
  - Larger trial with objective measures of GI and behavioral changes
  - Sensory studies to improve palatability
- Stay tuned in 2016!

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