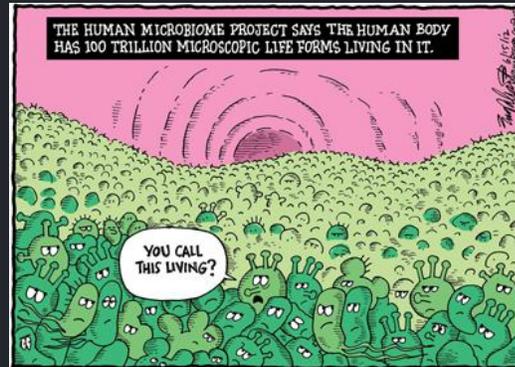


Overcoming the obstacle of scientific knowledge: What do we know about milk immunity and microbiomes?

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University of South Florida

I have no conflicts of interest to disclose.



Hyping the immune system

"...a 'made-to-order' immune-support meal"¹

"The importance of breastfeeding cannot be overstated in building a strong immune system."⁴

"...breastfeeding boosts a baby's immune system..."⁵

"...a child's immune response does not reach its full strength until age five or so"²



"Breastmilk is liquid gold, and it's yours to give!"⁶

"Mother's milk is the Rosetta Stone for all food"³

"...a baby's immune system is at its weakest right after birth"⁷

Quotes from:

- <https://www.babble.com/parenting/study-suggests-pumped-breast-milk-not-be-as-protective-as-nursing/>
- https://kellymom.com/pregnancy/bf-prep/how_breastmilk_protects_newborns/
- <https://www.ucdavis.edu/news/breast-milk-reveals-clues-health/>
- <https://www.healthychild.com/breastfeeding-for-a-strong-immune-system/>
- <http://www.lllii.org/nb/nbiss3-09p28.html>
- <http://www.lllii.org/faq/prevention.html>
- <https://www.thescientificparent.org/passive-immunity-101-will-breast-milk-protect-my-baby-from-getting-sick/>

Hyping the microbiome

"The Miracle of the Infant Microbiome"¹

**Infant Gut
Microbiome
Associated
With
Cognitive Development³**

"It might be possible to remodel a baby's microbiome"²

"...microscopic happenings can have lifelong consequences, both for ourselves, our children – and our species as a whole"⁴



Quotes from:

1. <https://www.hyperbiotics.com/blogs/recent-articles/the-miracle-of-the-infant-microbiome>
2. <https://www.popscl.com/gut-bacteria-babies-probiotics>
3. [http://www.biologicalpsychiatryjournal.com/article/S0006-3223\(17\)31720-1/fulltext](http://www.biologicalpsychiatryjournal.com/article/S0006-3223(17)31720-1/fulltext)
4. https://www.barnesandnoble.com/w/the-microbiome-effect-toni-harman/1124091847?ean=9781780662701&st=PLA&sid=BNB_DRS_New+Core+Shopping+Books_0000000&2sid=Google_&sourceId=PLGoP164972&gclid=CjwKCAIAksvTBRBFiEiwADSBZFhs8DVR6r2buXGk_1vp2sWLy1z0QWnAR3wkphdneJeCbHOcdvzQHIBoCkCAQAVD_BwE

Who knows what?

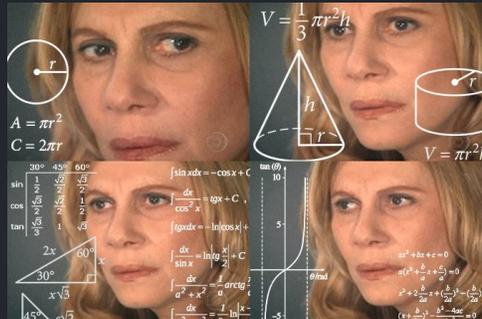
- Stakeholders:
 - Researchers/scientists
 - Science journalists
 - Health policymakers
 - Informed professionals
 - Uninformed professionals!!
 - Parents
 - The public/society



And, the infants themselves

What is the truth?

- Infant immune systems: weak or not?
- How does milk immunity work?
- How does birth and milk affect infant microbiomes?



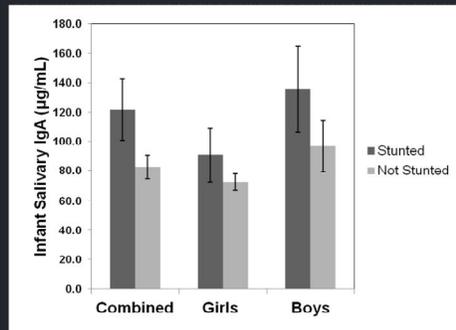
1. Are infant immune systems weak?

- Infant immune systems are functional but naïve before birth
 - This means they work, but they're immature
- Begin maturation upon contact with microbes
 - Birth, skin, kissing, other people, households, pets, crawling, weaning foods
- Risk of harm depends on how virulent the microbe is



1. Are infant immune systems weak?

Other factors can modify how the immune system works



Miller and McConnell (2012). *American Journal of Physical Anthropology*, 149, 136-141.

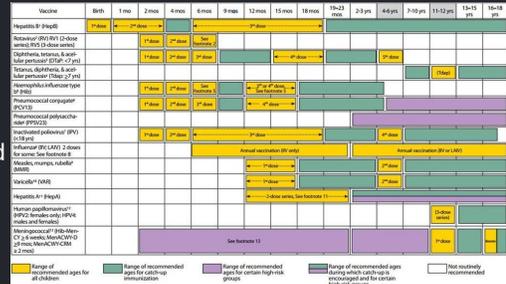
1. Are infant immune systems weak?

- Infants are protected by what scientists call “passive immunity” from their mothers
- Maternal IgG is transferred to fetus – extends protection through 6 months
- Also protected via IgA in milk



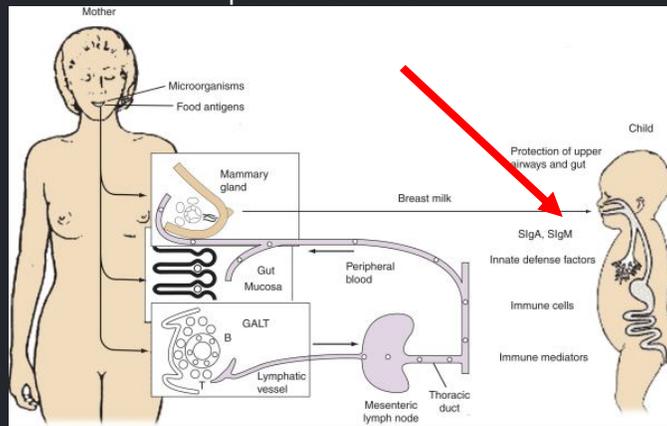
1. Are infant immune systems weak?

- “Weak/strong” is the wrong terminology to use!
- “So? Who cares?”
 - Can lead laypeople to the wrong conclusions about how immune systems work (“strong” immune responses have their own set of problems)
 - Lead them to think that exposure to any microbe is a positive, when actually the virulence/harm associated with exposure is not equally distributed among microbes
 - Can lead them to think that multiple vaccinations at one time can “overload” an infant immune system – the infant is exposed to many new microorganisms and can handle them, provided they do not cause harm in the form of infection!



2. How does milk immunity work?

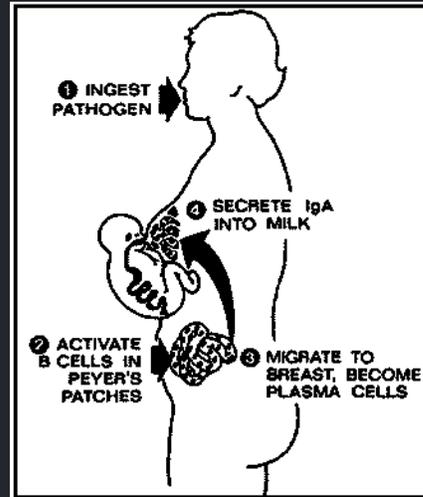
“Passive” immunity: The transfer of active antibodies from one person to another



From: Brantzaeg, P (2003). Mucosal immunity: Integration between mother and the breast-fed infant. *Vaccine* 21:3382-3388.

2. How does milk immunity work?

- IgA produced by breasts
- IgA provides specific information about mother's disease environment to infant
- Concentration of breastmilk IgA is associated with higher protection

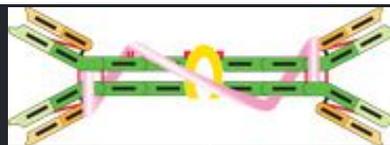


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2. How does milk immunity work?

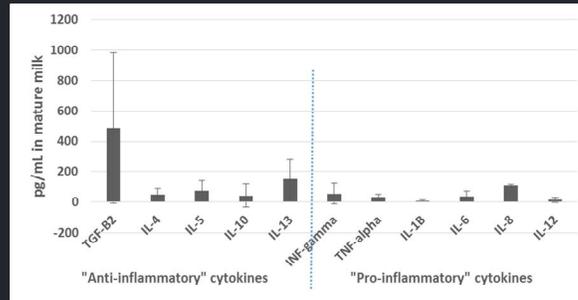
- Immunoglobulin A (~10% total protein)
- Lactoferrin – binds to iron
- Lysozyme – anti-bacterial enzyme

	Human Milk (g/l)	Bovine Milk (g/l)
Casein	2.5	27.3
Whey protein	6.4	5.8
α -Lactalbumin	2.6	1.1
Lactoferrin	1.7	trace
β -Lactoglobulin	-	3.6
Lysozyme	0.5	trace
Serum albumin	0.5	0.4
Immunoglobulin A	1.0	0.03
Immunoglobulin G	0.03	0.6
Immunoglobulin M	0.02	0.03



2. How does milk immunity work?

- Wide range of cytokines, chemokines, cytokine receptors, cytokine receptor antagonists
- Give sense of activity of cells
- Generally anti-inflammatory in milk



Values from Agarwal et al. 2011 *J Hum Lact*, 27.
Mature mil, ELISA values only

13

2. How does milk immunity work?

- Values vary wildly between populations
- Little is known about their effects, short term or long term

	U.S. Mean (S.D.) or % (n = 74)	Kenya Mean (S.D.) or % (n = 233)	T-value (p)
Foremilk fat (g/dL)	3.6 (1.6)	2.7 (1.4)	4.3 (<0.0001)
TGF-β2 (pg/mL)	736.4 (48.0)	74.8 (16.8) ¹	13.9 (<0.0001)
sTNF-αRI (pg/mL)	685.0 (27.5)	831.9 (15.6)	2.7 (0.008)
sTNF-αRII (pg/mL)	839.1 (21.1)	1151.4 (15.7)	6.8 (<0.0001)
IL-1ra (pg/mL)	532.4 (100.1)	192.6 (17.0) ²	4.2 (<0.0001)

2. How does milk immunity work?

- So what?
 - We know that the basic mechanisms of “passive immunity” only last as long as an infant is nursing
 - Dose-response of breastfeeding is established, but not dose of milk immunity (subtle difference)
 - The long-term effects are likely, but not clear
 - Immunological messengers called cytokines may play a longer-term role, but their function in infant bodies are not well-established

3. Birth, milk, and infant microbiomes

- Common wisdom: vaginal versus C-section delivery creates drastically different microbiomes in infants
- Delivery differences found at birth only in mouth and skin
- “We conclude that within the first 6 weeks of life, the infant microbiota undergoes substantial reorganization, which is primarily driven by body site and not by mode of delivery.”

Maturation of the infant microbiome community structure and function across multiple body sites and in relation to mode of delivery

Derrick M Chu, Jun Ma, Amanda L Prince, Kathleen M Antony, Maxim D Seferovic & Kjersti M Aagaard 

Nature Medicine **23**, 314–326 (2017)

doi:10.1038/nm.4272

[Download Citation](#)

Received: 22 August 2016

Accepted: 19 December 2016

Published online: 23 January 2017

3. Birth, milk, and infant microbiomes

- Probiotic use in adults is transient
- In infants, one strain can potentially persist in the microbiome
- The supplemented bacteria use human milk oligosaccharides to survive

Note: study was funded by company manufacturing this supplement

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Persistence of Supplemented *Bifidobacterium longum* subsp. *infantis* EVC001 in Breastfed Infants

Steven A. Fresse, Andra A. Hutton, Lindsey N. Contreras, Claire A. Shaw, Michelle C. Palumbo, Giorgio Casaburi, Gege Xu, Jasmine C. C. Davis, Carifto B. Lebrilla, Bethany M. Henrick, Samara L. Freeman, Daniela Barile, J. Bruce German, David A. Mills, Jennifer T. Smilowitz, Mark A. Underwood
Rosa Krajmalnik-Brown, Editor

DOI: 10.1128/mSphere.00501-17

3. Birth, milk, and infant microbiomes

- Does milk “seed” infant microbiomes?
- “During the first 30 days of life, infants who breastfed to obtain 75% or more of their daily milk intake received a mean (SD) of 27.7% (15.2%) of the bacteria from breast milk and 10.3% (6.0%) from areolar skin.”

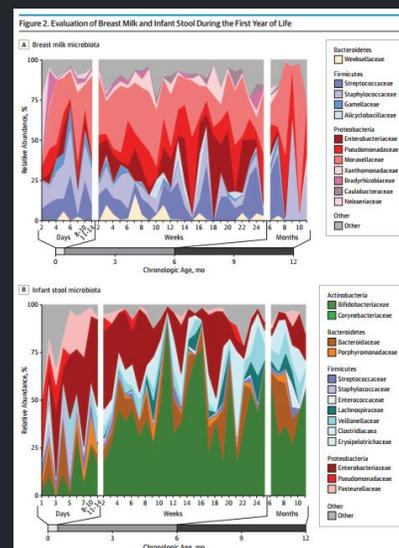
July 2017

Association Between Breast Milk Bacterial Communities and Establishment and Development of the Infant Gut Microbiome

Pia S. Pannaraj, MD, MPH^{1,2}; Fan Li, PhD¹; Chiara Cerini, MD¹; et al

Author Affiliations

JAMA Pediatr. 2017;171(7):647-654. doi:10.1001/jamapediatrics.2017.0378



3. Birth, milk, and infant microbiomes

- Do infants “order” their milk immunity?
- Original idea based on paper that showed (via ultrasound) that saliva might make its way into the breast via reversal of milk flow
- People ran with this, suggesting that microbes in saliva might stimulate immune cells in mammary glands and produce milk

Pediatrics
February 2004, VOLUME 113 / ISSUE 2

Ultrasound Imaging of Milk Ejection in the Breast of Lactating Women

Donna T. Ramsay, Jacqueline C. Kent, Robyn A. Owens, Peter E. Hartmann

3. Birth, milk, and infant microbiomes

- Very little information exists using next generation sequencing (NGS)
- One paper has sequenced 10 infant saliva samples vs. 10 mothers' milk samples.
- “No statistically significant relationships were observed between maternal and child microbiomes”— but, were methods adequate?

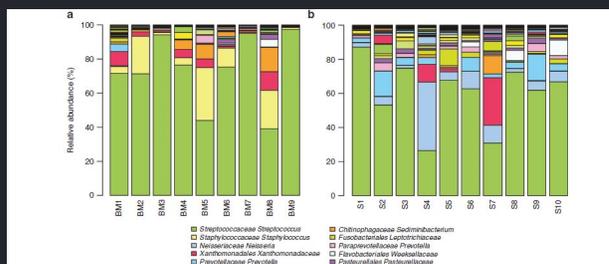


Figure 1. Relative abundances of bacterial taxa in CHAMACOS samples. (a) Relative abundances of taxa found in maternal milk samples. (b) Relative abundances of taxa found in child saliva samples. *Streptococcus* was the most abundant taxon in the majority of samples from both groups. CHAMACOS, Center for the Health Assessment of Mothers and Children of Salinas, CA.

Bacterial microbiome of breast milk and child saliva from low-income Mexican-American women and children

Veronica Davé¹, Kelly Street¹, Stephen Francis¹, Asa Bradman^{1,2}, Lee Riley¹, Brenda Eskenazi^{1,2} and Nina Holland^{1,2}

3. Birth, milk, and infant microbiomes

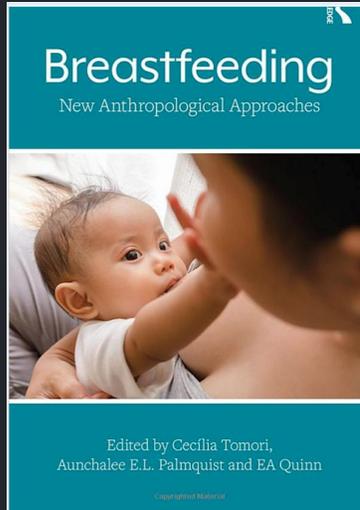
- Sequencing is ongoing: ~250 infant salivary microbiomes with some matching milk samples from rural Kenya (age 2 weeks – 25 months)
- Initial investigations show salivary *Streptococcus* abundance in line with Dave et al. 2016
- Unlike other studies, we have found very low levels of bacterial DNA in milk
- Next steps: apply new methods for comparison

3. Birth, milk, and infant microbiomes

- Takeaway: we do not know 100% what a healthy infant microbiome is!
- Attempts to modify it are based on adult science on probiotics
- Breastfeeding from the nipple is the best “default” recommendation based on available science

Questions?

- What questions have you gotten from parents/the public?
- What questions do you have?
- What kinds of misinformation have you heard?



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