Communicating Evidence for Benefits and Risks of Raw Milks

What do we know about **benefits and risks of pasteurization** of milks from **humans** and **cows**?

Photo by Leandro Cesar Santana on Unsplash

Facebook Promotion: **Holistic Approaches to Microbiota and Immunology for Neonates**, Upstate NY SRA event Oct 23rd at Cornell University

Print by Ithaca artist Mary Beth Ihnken for SRA Whole Truth, Whole Milk Campaign

Society for Risk Analysis (SRA) Symposium, New Orleans, LA December 5, 2018
1. Summary of first two years of joint RO project
   • 2017 webinar series, bibliographies
   • 2018 Upstate NY SRA event at Cornell University
   • 2018 UK SRA event at Institute for Risk and Uncertainty, University of Liverpool

2. Questions posed

3. Shaping the future direction of the project
   • Building interest using traditional and social media strategies
   • Engaging in a third round of RO activities for 2019 (local symposia)
   • Brainstorming next steps for 2020 and beyond (international workshop)
1. Summary of first two years of joint RO project
Bacteria are all around (and inside) us!

- **Microbiota** are **symbiotic**, commensal or mutualistic partners, with few pathogens that may cause disease with disturbance of ecosystems (dysbiosis).

- **Homo sapiens** + microbiota = human ‘superorganism’, holobiont, ‘supraorganism’

- Earth’s ecosystems are full of ‘superorganisms’ containing ‘multitudes’ of microbiota. New medical landscape emerging in 21st century, with microbial ecology challenging assumptions about health and disease.
Joint SRA Project on Microbiota of Milks

http://www.sra.org/upstateny/; https://www.colemanscientific.org/blog/

Working Bibliographies on Unfamiliar Topics

- **Benefits** and risks of *microbiota of milks*; note conflicting studies on US milk outbreak data (Costard et al., 2015 vs Whitehead and Lake, 2018)

- **Colonization resistance**, innate protection against pathogens by normally dense, diverse gut microbiota influenced by environment

Britton and Young Gastroenterology, 2014; Dietert, 2017
2017 Advancing the Science Webinar Series
Microbiota Informing Next-Generation Risks & Benefits
slide sets posted at http://www.sra.org/upstateny/

1. Rodney Dietert (Cornell University),
Protecting the Human Superorganism (January 24)

2. Michelle McGuire (Washington State U),
Human Milk: Mother Nature’s Prototypical Probiotic Food (March 21)

3. Mark McGuire (University of Idaho),
Bovine Milk Microbiota (May 23)

4. Warner North & Peg Coleman (Northworks, Coleman Scientific Consulting)
Preparing to Deliberate Evidence on Benefits and Risks Posed by the Microbiota of Milks (August 28)
Immunology in 21st Century

- Classical portrait:
  - Surveillance and destruction of pathogens

- Emerging insights for ‘superorganisms’:
  - ‘Microimmunosome’ includes dense and diverse microbiota that synergistically and cooperatively protects against pathogens
  - Joint management of our relationships with our resident microbes, particularly at mucosal epithelia
    - Thousands of commensals (Firmicutes, Bacteriodetes, Actinobacteria, Proteobacteria phyla) contribute to mucosal immune homeostasis in the gut
  - Alliances NOT fixed by microbial or human genetics, but change with context, interactions
    - commensals can express mutualism or pathogenicity under different conditions

Rod Dietert, 2017 SRA webinar
Human milk

- Emphasis on human milk waxed and waned over recent centuries, but now maternal milk recommended from birth and for two years or more
- Wet nursing ancient practice in many cultures (Code of Hammurabi from 2250 BC)

Breastfeeding reduces **frequency AND duration** of **respiratory** and **diarrheal** illness in infants <6 months age (Lopez-Alarcon et al., 1997)

**Exclusive breastfeeding** protects against common infections during infancy and lessens the **frequency AND severity** of infectious episodes (Ladomenou et al., 2010)
Learnings about Human Milk Microbiota

Human Microbiome Project (HMP): nine body sites initially examined (NOT breast)

Results in first decade continue to challenge established theories (dogma):

- Breast tissue expected to be sterile, now known to be FALSE assumption! (Urbaniak et al., 2014)
- Milk microbiota NOT contaminants! (Hunt et al., 2011; Rodriguez, 2014; Addis et al., 2016)

Cho and Blaser, 2012
2018: Question for Cornell Event

What do we know about benefits and risks of *pasteurization* of breastmilk?

Divergent Perceptions on Risk Communication

1. Potential *presence* of pathogens in breastmilk is *certainly* a risk for infants, perhaps *fatal*

2. Infants need *large doses of microbes*, including *small doses of potential pathogens*, to develop healthy gut and immune systems

*SRA risk practitioners* are considering how to *communicate* with technical audiences and the public about the complexity of the *human superorganism* and *dose-response* relationships.
2018 Event: Holistic Approaches to Microbiota and Immunology for Neonates


Join distinguished Cornell Professors in dialogue about scientific advances in neonatology and controversial impacts of new evidence for maximizing benefits of the breastmilk microbiota!

WHEN: Tuesday, October 23rd from 4:30 to 6:15 pm

WHERE: Lecture Hall 2, College of Veterinary Medicine

- Rodney Dietert presented on 2018 NeoReviews paper.
- SRA President-Elect Katherine McComas, served as rapporteur considering impacts of new evidence on assessing, communicating, and managing benefits and risks to neonates.
- Together, participants deliberated implications of evidence from neonates in NICUs who lose benefits of the breastmilk microbiota when human milk banks pasteurize donor milk.

Event Sponsored by Upstate NY SRA (http://www.sra.org/upstateny)
Video available at https://www.colemanscientific.org/blog/
The Human Superorganism in Early Life

Rodney Dietert
Professor of Immunotoxicology
Cornell University

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Colonization Resistance
(Dietert, 2016, 2018)

- Microbiota of healthy people can effectively inhibit colonization and overgrowth by invading pathogens. First observed in 1954 and termed colonization resistance in 1971, current methods of the 21st century are revealing mechanisms.

  - associated with a stable and diverse gut microbiota that do not trigger inflammation (homeostasis)
  - involves specific interactions between the immune system and the microbiota

A Focus on Microbiome Completeness and Optimized Colonization Resistance in Neonatology
Rodney R. Dietert
NeoReviews 2018;19:e78
DOI: 10.1542/neo.19-2-e78
Rodney’s Predictions

• In the near future, the **highest priority** of both **preventive and therapeutic medicine** will be… managing or ‘**Minding our Microbes**’ (theme of World Microbiome Day 2018).

• Holistic medicine will support us in becoming ‘**microbial gardeners**’ or shepherds watching over our microbial flocks or consortia to maintain health and minimize illness.
Earth Microbial Planet, Higher Organisms w Microbiome

Microbial layer in upper atmosphere

Personal microbial bubble

Image from NASA.gov

Our Depleted Microbiome

Same country, shift to urban environment lowers microbiome diversity 35-40%.

Six Factors Leading to Microbiome Depletion, Modern Epidemic of Non-Communicable Diseases (NCDs), Loss of Colonization Resistance to Infectious Pathogens

1. Antibiotic overreach (over-prescription and agric. uses)

2. The food revolution and diet (including reduced infant breastfeeding)

3. Urbanization

4. Birth delivery mode (e.g., increased elective Cesarean)

5. Misdirected efforts at human safety (drugs, food additives, and chemicals were never vetted for the microbiome)

6. 20th century paradigm for mammalian-only human medicine, ignoring microbiome as partners in health

Adapted from Dietert, R.: The Human Superorganism, 2016
Microbiome Destruction – What Next?

Elective Cesarean delivery

- Altered infant cytokine production
- Elevated risk for several diseases associated with the mucosal immune system

Prophylactic use of antibiotics for growth promotion in food-producing animals

- More hospital-associated microbes seeding the neonatal gut
- Increased antimicrobial resistance and zoonotic risk from pathogens (e.g., Campylobacter spp., Salmonella spp., Escherichia coli and Staphylococcus aureus)

Howler monkeys

- Captivity (Food and lifestyle restricted)
- Reduced microbiota diversity
- Humanized microbiome - from animal handlers

Cumulative Environmental Health Risks: Increased Incompleteness of Microbiome in Infants Can Cause Increased Lifetime Risks

Pre-Existing NCDs
- Medications (e.g., Diabetes, Obesity)
- Maternal stress
- F1 immune programming
- Reduced Tregs

Environmental tobacco smoke
- PAHs, others
- Air pollution/urbanization

Bereavement

Cesarean delivery
- Antibiotics administered
- Reduced microbial seeding
- Elevated risk of allergy, autoimmunity, obesity, CVD

Formula feeding
- Missing prebiotics and microbes
- Altered metabolites & Immune development

BPA, heavy metals, certain food additives

Adapted from: Dietert, R. NeoReviews 2018 19(2):e78-e88.
Katherine McComas: Am I Dooming My Child to Present and Future Suffering by My Decisions?

• Message so far, and some slides with highly technical details, could be very frightening to mothers and families!

• Relieved that Rodney offered practical advice that could alleviate blame, fear, emotional responses that all is lost!

• Communications and infrastructural supports for nursing mothers dramatically different in past decade

• breastfeeding pods in airports with promotional materials about benefits of breastfeeding!
Katherine McComas: Who Cares about Microbiota and their genes, the Microbiome?

- Google Trends tell us, expanding audience from unexpected places: Vermont and Massachusetts!
  - Interested in exploring reasons?
<table>
<thead>
<tr>
<th>Immunological activity</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maturation of local and systemic immune system</td>
<td>Houghteling and Walker, 2015</td>
</tr>
<tr>
<td>Implementation of mucosal newborns’ defense</td>
<td>Smith et al., 2007; Sekirov et al., 2008</td>
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<tr>
<td>Stimulation of specific cytokines that create a balanced microenvironment</td>
<td>Walker and Iyengar, 2015</td>
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<td>Correct development of B cells</td>
<td>Martin et al., 2010</td>
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<td>Stimulation of cytotoxic Th1 cells</td>
<td>M’Rabet et al., 2008</td>
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<td>Correct balancing between Th1 and Th2 response</td>
<td>Walker and Iyengar, 2015</td>
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<tr>
<td>Development of oral tolerance</td>
<td>Vhasselt, 2010</td>
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<td>Stimulation of Peyer’s patches</td>
<td>Gross, 2007</td>
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Breastfeeding: Protection Against NCDs

- **26% reduced risk** of obesity (meta analysis of 113 studies) (Horta et al. Acta Paediatr Suppl 104:30-37, 2015)


- *Exclusive breastfeeding at 4-6 weeks after birth is associated with increased telomere length (chromosomes) in the child at 4 years of age, an indication of reduced aging effect* (Wojcicki et al. Am J Clin Nutr 104(2):397-405, 2016)

- **19% reduced risk** of childhood leukemia, most prevalent childhood cancer (review of 18 studies) (Amitay et al. JAMA Pediatr 169: e151025, 2015)

Highlights from Rodney Dietert

- Failure to self-complete to **newborn superorganisms** with **dense, diverse microbiota** may be the single greatest health risk **across a life time**. Management of the “second genome” (i.e., seed, feed, protect microbiota) is most effective in early life.

- The neonatal **immune system** and the **microbiome** need to **co-mature** to: i) avoid persistent inflammation and immune dysfunction; ii) reduce risk of NCDs; and iii) enhance colonization resistance (reduce the risk of infections).

- **Safety** needs to be based on the **whole human superorganism**. *Protect superorganism ecology.*

- **Benefit-risk determinations** must include the **human microbiome**.
Human Milk Banks provide pasteurized human donor milk to hospitalized preterm infants and sick/high risk infants based on fear of microbes. Holder pasteurization (heating to 62.5°C for 30 minutes) is required due to perception: possible presence of potential pathogens perceived as ‘risky’.

Yet LOSS of Benefits for Pasteurized Milks Demonstrated in Clinical Studies Conducted around the World!

- Squires, 2017 : 302 low birth weight infants (US, WA)
- Cossey et al., 2013 : 303 very low birth weight infants (Belgium)
- Strand et al., 2012 : 335 infants and toddlers (Nepal)
- Montjaux-Regis et al., 2011 : 55 premature infants (France)
- Schanler et al., 2005 : 243 extremely low birth weight infants (US, TX)
- Narayanan et al., 1984 : 226 high risk, low birth weight infants (India)
General View for Human Milk Banks: Risk Minimization

- Rigorous donor screening methods similar to blood donation

- Some process (pasteurize, freeze) donor milk to reduce risks

- Some screen donor milk for other potential pathogens and indicators of contamination

- Some limits for pathogens/indicators (counts per mL) in donor milks (Omarsdottir et al., 2008)
  
  - <100,000 *Staphylococcus aureus*
  
  - <100 Enterobacteriaceae
  
  - 0 (below limit of detection) for potential pathogens

*Listeria monocytogenes, Salmonella, Group B/α-hemolytic Streptococcus, coagulase-negative Staphylococcus*
More Decision Context: Conclusions about Pathogen Presence in Breastmilk and Value for Prediction

• ‘Results of initial milk cultures do not predict subsequent culture results.

• Random milk cultures, even if obtained at any time during hospitalization, are not predictive of infection in premature infants.

• The sporadic nature of the appearance of certain isolates, however, suggests common exposure of both mother and infant.

• Routine milk cultures do not provide sufficient data to be useful in clinical management.’

Schanler et al., 2011
2018 Event in the UK
2. Questions Posed
Questions Posed

1. What did you learn about the microbiome? About adult and neonatal superorganisms?

2. What evidence surprised you as you consider applying new information to assessing, communicating or managing risks and benefits of pasteurization of human and bovine milks?

3. What would you like to learn more about regarding the microbiota and immunology throughout life?
Some Responses to Question 1

• The gut microbiome affects brain function!

• Ingested microbes don’t have to colonize the gut to provide metabolic benefits in the lumen of the gut.

• Transient strains can effect metabolism, physiology, and immune function in the gut, even without persistence in feces! Early studies that judged ineffectiveness of some probiotic strains merit further study; failure to demonstrate persistence of administered strains in feces does not prove that the strains are not beneficial.
Questions Posed

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Some Responses to Question 2

- Breastmilk microbiota affects not just acute infectious disease, but also chronic and non-communicable diseases (e.g., asthma, inflammatory diseases, obesity).

- Failure to self-complete (form a dense, diverse microbiome) may be the single greatest health risk across a lifetime.

- Incorporating benefits may be different from considering benefits as prevention of illness.

- What metrics of health could we measure?
Figure from Microbiota and Dose-Response: Evolving Paradigm of Health Triangle

- Acknowledgement of ecosystem effects, superorganism and modulators
- More complex than interactions of host, pathogen, and environmental factors
- Wider environmental influences than considered for most microbial dose-response models
  - Diet (and exercise)
  - Occupation
  - Stress
  - Travel
  - Indoor and outdoor environments
Questions Posed

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A Response to Question 3

- What is the frequency and abundance of key pathogens in raw milks that are causing illness in:
  - Neonates?
    - Bacteria causing fatal necrotizing enterocolitis and sepsis NOT typical foodborne pathogens
  - Children?
  - Adults?
  - Elderly?
  - Immunocompromized?
Another Response to Question 3

- Is it time to consider **Recommended Daily Allowances** not just for vitamins, for also for **microbes**, as Colin Hill of University College Cork, Ireland suggests?

Many studies demonstrate **strains**, groups/**consortia** of strains, and **fecal microbiome transplants** that promote healthy gut and immune systems and protect against pathogens.

Should consumers be permitted to choose raw milks as a dietary source enriched in commensal bacteria?
3. Shaping the Future Directions of the Project
Shaping the Future Directions of the Joint RO Project

1. Building interest with diverse stakeholders using traditional and social media strategies

2. Engaging in a third round of RO activities for 2019 (local symposia, pilot crowdfunding campaign, manuscript)

3. Brainstorming next steps for 2020 and beyond (international workshop)
Updating Long-Term Goals for Joint RO Project?

• Build a shared understanding of microbial benefits and risks with stakeholders (21st century science);

• Facilitate a paradigm shift for an expanded framework for microbial benefit-risk assessment that incorporates the ‘superorganism’, food microbiota, and their roles in contributing to health and disease, particularly ‘colonization resistance’;

• More?