Welcome to the SRA 2017 Advancing the Science Webinar Series

Microbiota Informing Next-Generation Risks & Benefits

All SRA webinars are available to SRA members as videos after the webinars at SRA.org (with log-in as a member).
Preparing to Deliberate Evidence on Benefits and Risks Posed by the Microbiota of Milks

Peg Coleman, Warner North, and SRA RO Collaborators
Introduction
Warner North

➢ About the Society for Risk Analysis (SRA)
➢ Analytic-Deliberative Process - Dialogue in support of environmental/health risk assessment and decision making
The Society for Risk Analysis

➢ **Interdisciplinary:** physical sciences, biological sciences, social sciences, engineering - an “Open Forum” for discussion on risks.

➢ **Scope:**
  - **Risk assessment** - magnitude and likelihood of adverse consequences, such as to health and the environment;
  - **Risk management** - decision making on management of risk (engineering /normative support to those with decision responsibility)
  - **Risk perception and risk communication** - behavioral science on how people think about risk, communicate about risk, and act on risk.

➢ **International:** Parent Society plus Regional Organizations (25 = 14 outside USA; 11 in USA) and Specialty Groups (15). (Details on www.sra.org.)
Peg Coleman and Warner North

Peg Coleman    Website: http://www.colemanscientific.org/;
E-mail colemanmellen@gmail.com.
- Upstate New York State SRA President
- Member of Editorial Board for Risk Analysis, An International Journal
- Microbial Risk Assessment and Dose-Response Specialty Groups; Background in microbiology and microbial risk assessment

Warner North    Website: www.northworks.net;
E-mail: northworks@mindspring.com.
- SRA President 1991-1992
- Area Editor for decision sciences, Risk Analysis, An International Journal
- Background in physics, decision analysis, probabilistic modeling
Analytic - Deliberative Process

  [https://www.nap.edu/catalog/5138/](https://www.nap.edu/catalog/5138/)

- See also the 2008 NASEM Report, *Public Participation in Environmental Assessment and Decision Making* (2008)
  [https://www.nap.edu/catalog/12434/](https://www.nap.edu/catalog/12434/)

- FOCUS: Regulatory controversy in areas with complex emerging scientific information and diverse views among the interested and affected parties in the public - the “stakeholders.”

- Recent US application: 2013 NASEM workshops and subsequent publication, 2014 special issue in *Environmental Science and Technology*, on enhanced natural gas recovery from tight formations (“fracking”)

- Appropriate for “milk wars” - Risk management for microbiota of milks.
Stakeholder Involvement

- Many people have interpreted recommendations for stakeholder involvement as letting stakeholders speak, letting them write comments, and (perhaps) letting them have seats at the negotiating table.

- The main *Understanding Risk* recommendation is for involving stakeholders in an analytic-deliberative process. This means going beyond words and political negotiation. It means giving stakeholders opportunities to observe, learn, and comment in an iterative process of analysis and deliberation on policy alternatives.
FIGURE 1-2. A schematic representation of the risk decision process.
Five Key Points

➢ Getting the science right
➢ Getting the right science
➢ Getting the right participation
➢ Getting the participation right
➢ Developing an accurate, balanced, and informative synthesis.

(Understanding Risk, 1996; pages 6-7)
Now, over to Peg Coleman
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.
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, but change with context
  - Commensals can express mutualism or pathogenicity under certain conditions
As expected for ecosystems, microbial communities change over time and space.

Predicting risk of illness is complex and uncertain (e.g., age, doses of pathogens, environment, foods, health status, medications, nutrition, stress, water).

Perceptions of risk in the media often NOT supported by science.

Perceptions of bacteria as germs to be eradicated (germophobia) being replaced by awareness of fostering symbiotic partners in health (microbiomania).

In first decade of research, knowledge of roles of microbiota of milks is advancing.
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)
- Recent establishment of human donor milk banks (e.g., HMBANA established 1985; [https://www.hmbana.org/about-hmbana](https://www.hmbana.org/about-hmbana)) for care of at-risk infants (very low birth weight, premature, ill)
  - Early 20th century donor milk unprocessed, now pasteurized (WHO/UNICEF, 1980)

Non-human milks were produced and consumed for millennia, with domestication of cows ~8000 BC
- Industrialization and distribution to cities began to raise issues for safe milks in the US and around the world by the 19th century

Joint SRA Project: deliberating evidence, particularly from past decade, on benefits and risks associated with microbiota of milks
Failure of infants to thrive, significantly more infections
Reduced inhibition of pathogens
Inactivation or destruction of:
  • All immune cells
  • Immunoglobulins
    • Secretory IgA reduced <33%
    • IgG reduced ~70%
    • IgM completely inactivated
  • Lactoferrrin reduced 20%
  • Proteins (B-12 and folate-binder proteins) reduced/denatured 13%
  • Enzymes (e.g., lactoperoxidase, lysozyme) reduced 75%
  • Vitamins A, B-complex, C
  • Human milk oligosaccharides (HMOs)?
  • Microbiota, including commensal and beneficial (probiotic) strains

(Narayanan et al., 1984; Stein, 1986; Unger, 2010; Gyselet al., 2012; Koenig et al., 2015; McGuire et al., 2017)
Outline: Closing 2017 Webinar Series

➢ Microbiological discoveries (advancing knowledge of microbial ecology; Ed Yong, 2017)
  • Next-Gen risk assessment, risk communication, risk management

➢ ‘Milk wars’ around the globe
  • US history (Mendelson, 2011)
  • Australia history
  • New Zealand history
  • UK history

➢ Evidence considered in top-down and bottom-up approaches (bottom up considers microbial ecology of foods and gastrointestinal tract and dose-response relationships)
Early Microbiological Discoveries Impacting the Milk Wars

Ed Yong, 2017
Later Microbiological Discoveries Paving Path for Microbiome Studies

1960
- T. Rosebury
- R. Dubos, D. Savage, R. Schaedler
- Valued study of microbial symbionts
- Microorganisms Indigenous to Man (1962)

2007
- Human Microbiome Project
- True census of microbes, more powerful than traditional culture independent methods
- 16S rRNA transformed microbial taxonomy and ecology

Ed Yong, 2017
Path for Microbiome Studies

“history of warfare always proves more glamorous than accounts of cooperation... no one has made a success story of the useful role played by microbes in the intestine...”

R. Dubois (1948)

- Discovery of 16S rRNA as taxonomic tool, both descriptive and functional
- Genetics more powerful lens than physical traits (phenotype)
- Library for 30 microbes compiled by 1976
- True census of microbes, independent of ability to isolate and culture; birth of –omics disciplines

C. Woese (1970s)

- Metagenomics most important discovery since invention of microscope.
- Transformed microbial ecology from moribund science to sophisticated experimental discipline quantitating ecosystem relationships

N. Pace (~2000- present)
Recent Microbiological Discoveries Advancing Microbial Ecology

2007
- Human Microbiome Project Initiated
- Jaykus et al., 2009

First human milk microbiome paper (2011)

First bovine milk microbiome papers (2013)

2017
- R. Dietert, 2016
- M. McGuire et al.
- E. Yong

Microplia museum opened in Amsterdam, influenced by work of Delft School (2014)
Lotka-Volterra equations to model interspecies interactions (1925/1926) no longer apply just to Predator-Prey interactions. Eric Pamer and colleagues now apply Lotka-Volterra equations to describe the complex interactions of consortia of microbial communities in human and mouse ‘superorganisms’.

Similar patterns from inference modeling of subnetworks of metagenomic data from humans (on left) and mice (on right).

Blue lines mark resident microbiota predicted to inhibit opportunistic pathogen *Clostridium difficile* growth blooms in healthy hosts.

Red lines mark dysbiotic microbiota predicted to promote *C. difficile* growth blooms in ill (dysbiotic) hosts. *(Buffie et al., 2015)*
2017 Advancing the Science Webinar Series Concludes

Microbiota Informing Next-Generation Risks & Benefits

1. **Rodney Dietert** (Cornell University)
   *Protecting the Human Superorganism*

2. **Michelle McGuire** (Washington State University)
   *Human Milk Microbiota*

3. **Mark McGuire** (University of Idaho)
   *Bovine Milk Microbiota*

4. **Warner North and Peg Coleman** (NorthWorks and Coleman Scientific Consulting)
   *Preparing to Deliberate Evidence for Benefits and Risks for Microbiota of Milks*

Check [www.sra.org/upstateny/](http://www.sra.org/upstateny/) for updates on project and SRA round table panel symposium *(December 12, Arlington, VA)*
Learnings on Human Superorganism

Breast Milk Microbiota and Natural Childbirth as Preventative Measures of Immune-Microbiome Dysbiosis and Misregulated Inflammation

Dietert 2013

Microbial Partners in Human Superorganism Essential to Healthy Gut and Immune Systems
Learnings about Human Milk Microbiota

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

Results continue to challenge 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; McGuire et al., 2017)
Learnings about Human Milk Microbiota

Characterizing microbial communities in breast milk

Table 1. Genus assignments of the 9 OTUs identified in every sample (n = 47) and their relative abundance (%).

<table>
<thead>
<tr>
<th>Core OTU Genera</th>
<th>Relative abundance of OTU in total community (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus</td>
<td>15.8</td>
</tr>
<tr>
<td>Streptococcus</td>
<td>8.2</td>
</tr>
<tr>
<td>Stenotrophomonas</td>
<td>7.6</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>4.5</td>
</tr>
<tr>
<td>Corynebacterium</td>
<td>3.8</td>
</tr>
<tr>
<td>Rastronia</td>
<td>3.7</td>
</tr>
<tr>
<td>Propionibacterium</td>
<td>3.6</td>
</tr>
<tr>
<td>Sphingomonas</td>
<td>2.4</td>
</tr>
<tr>
<td>Bradyrhizobiales</td>
<td>1.9</td>
</tr>
<tr>
<td>Sum of all “core” OTUs</td>
<td>51.5</td>
</tr>
</tbody>
</table>

doi:10.1371/journal.pone.0021313.0001

“Stacked bar charts” – just look at color patterns

Practical implications (why should we care?)

Major warning: We need to conduct randomized controlled trials to assess correlation vs. causation!

Milk Living Food with Dense Diverse Bacterial Communities Linked with Development of Healthy GI Tract and Immune Systems in Offspring
Learnings about Bovine Milk Microbiota

- Bulk tank milk from 19 farms over 2 months

Similar genera dominate raw (e) and pasteurized (f) milk microbiota
Learnings about Bovine Milk Microbiota

Milk Living Food with Dense Diverse Bacterial Communities Linked with Development of Healthy G.I. Tract and Immune Systems in Offspring and Consumers?
Role/significance of Some Microorganisms in Raw Milk

**Food Technology**
- Lactococcus
- Lactobacillus
- Streptococcus
- Leuconostoc
- Enterococcus

**Health Promotion**
- Lactococcus
- Lactobacillus
- Streptococcus
- Leuconostoc
- Enterococcus

**Spoilage**
- Pseudomonas
- Acinetobacter
- Chryseobacterium
- Clostridium

**Illness**
- Listeria monocytogenes
- Staphylococcus
- Escherichia coli O157:H7
- Campylobacter
- Mycobacterium
- Salmonella

Soboleva, NZ IFST 2014
Compiling Evidence for Benefits and Risks

- Many epidemiologic and microbiota studies correlative, not causal; ambiguity, complexity, confounding factors, uncertain utility for prediction

- Joint SRA project will consider what we know, from both top-down and bottom-up data available, particularly
  - Evidence of pathogen presence and illnesses associated with certified raw milk from licensed farms over past decade or more
  - Evidence on microbial ecology of certified raw milk from licensed farms and pasteurized milks
  - Evidence on microbiota of human and bovine milks influencing healthy gut and immune systems (colonization resistance)
Microbiological discoveries impacting risk assessment, communication, and management

‘Milk wars’ around the globe

• US history (Mendelson, 2011)
• Australia history
• New Zealand history
• UK history

Evidence considered in top-down and bottom-up approaches
Early Highlights of the US Milk War

Ann Mendelson, 2011

1840
- Swill milk, sick cows, sick and dying kids
- Louis Pasteur

1890s
- First opponents of the milk war in the US
- Henry Cort’s American Association of Medical Milk Commissioners for certified pasteurized milk
- Nathan Straus’ Pasteurized Milk Laboratory and ‘milk depot’
Urban expansions brought challenges to distribute milk safely from farms to cities before refrigeration equipment and proper sanitation practices were developed.

‘The Milk Problem’ (1840s to 1920s)

Inner city confinement operations feeding already unhealthy cows brewery swill (spent grains) and distillery waste, producing unhealthy ‘swill milk’ associated with illness and deaths in up to 50% of children consuming it.
# Initial Opponents of the 20th Century Milk War

**Ann Mendelson, 2011**

## Nathan Straus
- New York City Philanthropist
- Son died from contaminated milk
- Had no medical or scientific training
- Founded *Straus Pasteurized Milk Laboratory* (1892) that provided milk to urban children

> “Raw Milk Kills”

## Henry L. Coit
- New Jersey Pediatrician
- Son died from contaminated milk
- Had physicians who were trained in dairy microbiology and sanitation supervise farm dairies
- Founded the **Association of American Medical Milk Commission** (1893)

> “Dirty Milk Kills”
The Continuing Milk Wars

Ann Mendelson, 2011
Coexistence of Pasteurized and Certified Raw Milk

Early arguments for pasteurization acknowledged that certified raw milk was also acceptable.

Pasteurized and raw milk coexisted for over 50 years, until mandatory pasteurization laws in cities and states beginning mid 20th century.

*The Common Sense of the Milk Question* by John Spargo (1908)

- Once dubbed pasteurization “a grave mistake” - implored both parties to reason together without “unnecessary vehemence”

*The Milk Question* by Milton J. Rosenau (1912)

- Pasteurization advocate
- Welcomed well-handled certified milk
- “It is self-evident that pasteurization is an expedient and not an ideal.”
Hearing from Organizations Challenging Pro-Pasteurization

- Sally Fallon Morell, founder of Weston A. Price Foundation
  Ted Beals, MD, WAPF board member
  • Real Milk Campaign, advocates meticulous documentation of scientific evidence for benefits and risks

- Mark McAfee, founder of Raw Milk Institute (RAWMI)
  • observes raw milk renaissance and advocates food safety plans, testing and Common Standards, and HACCP-style management to minimize risks on farm and at retail markets

- Ronnie Cummins, national director of the Organic Consumers Organization
  • Healthy Raw Milk Campaign; Buy Local, Organic, and Fair Made
Some Common Ground for Safe Milks

➢ Both sides of milk wars adopt similar technology-dependent principles of milk hygiene
  • thoroughly disinfecting all equipment at regular intervals
  • preventing it from coming in contact with surfaces other than stainless steel, glass, or inert plastics
  • milking via machine
  • promptly chilling and refrigerating during storage and transport
  • keeping milk sealed from exposure to the open air

➢ Use of coliform counts
  • hygienic quality indicator (not predictive of presence or counts of pathogens)

➢ Use of somatic cell count
  • indicator of animal health (not predictive of presence or counts of pathogens)

➢ (Specific pathogen testing? Presence or levels?)
Working towards Resolution of the Continuing Milk Wars

- Likelihood illness very low (2 per 10^5) per raw milk serving
- Raw Milk Institute (RAMMI) founded in 2011
- Stasiewicz listeriosis risk assessment (2014)
- Risk increases with pasteurization temperature
- UK CSA finding raw drinking milk safe

2007

2011

2014

2015

2017

Headlines on both sides of war: raw milk as 'hazardous poison' and safe food
SRA project gathers evidence on both sides of milk wars around the globe
States can license dairies for sale of fresh unprocessed (certified raw) milk at retail, licensed farm stores, or as ‘cow-/herd- share’ operations or prohibit sale.

NY State requires Quality Milk Production Services (QMPS) program and periodic testing for coliforms and specific pathogens.

Federal regulators advise raw milk is an inherently hazardous poison.
Microbiological discoveries impacting risk assessment, communication, and management

‘Milk wars’ around the globe
  - US history (Mendelson, 2011)
  - Australia history
  - New Zealand history
  - UK history

Evidence considered in top-down and bottom-up approaches
Australia

➢ Sale of raw milk illegal since 1940s
  • Potential presence of pathogenic bacteria
    • *Campylobacter*, pathogenic *E. coli*, and *Listeria, Salmonella, Staphylococcus aureus*

➢ Position from Victorian Department of Health and Human Services

➢ 2014 outbreak: 4 cases of serious illness (one fatality) in children who consumed cosmetic bath milk product

➢ Cow-/herd- shares illegal

➢ Some consumer organizations oppose prohibition
Outline: Closing 2017 Webinar Series

- Microbiological discoveries impacting risk assessment, communication, and management
- ‘Milk wars’ around the globe
  - US history (Mendelson, 2011)
  - Australia history
  - New Zealand history
  - UK history
- Evidence considered in top-down and bottom-up approaches
MPI notes concern about raw drinking milk and underground markets due to potential presence of pathogenic bacteria.

- Primary concern for *Campylobacter* and *STEC* (pathogenic *E. coli*)
- Lower concern for salmonellosis (less severe disease) and listeriosis (no observed milk-related illnesses)


Raw milk has been available under various regulations

- Food Act 1981 with limit 5 L/day for personal/family use
- Animal Products Act 1999 requiring Risk Management Programme
- Animal Products (Raw Milk Products Specifications) Notice 2009

Registered farms began selling raw milk via home delivery or from licensed farm stores and vending machines since 2016.

Regulators advise boiling raw milk before consumption.
Microbiological discoveries impacting risk assessment, communication, and management

‘Milk wars’ around the globe
  - US history (Mendelson, 2011)
  - Australia history
  - New Zealand history
  - UK history

Evidence considered in top-down and bottom-up approaches
United Kingdom

- Raw drinking milk safe for healthy people, compulsory warning label (UK FSA, 2015)
- Increasing numbers of licensed farms and consumers?

UK Food Standards Agency (FSA) Approaches

Government department run by independent board acting in public interest to assess, manage, and communicate risks using evidence-based methods (Paul Cook, 2016)

https://www.foodprotection.org/upl/downloads/meeting/program-overview/573f434f8bd893377a707.pdf

➢ Assess using best scientific advice and acknowledge uncertainties; re-assess in the light of new evidence (qualitative or quantitative)

• Top-Down from epidemiologic evidence from outbreaks to define scale and impact of sources

• Bottom-Up from data for microbiology, predictive microbiology, and dose-response relationships linked with human health/disease

➢ Manage: consistent, proportionate; not claim to eliminate risk (no foods ZERO risk)

➢ Communicate: consultation, openness, honesty, role of the media
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  - UK history
- Evidence considered in top-down and bottom-up approaches
Some Examples of Top-Down, Bottom-Up Assessments for US

- **Top-Down**, outbreaks reported from 1993-2014 associated with multiple dairy commodities and four pathogens
  - Langer et al. (2012; 1993-2006)
  - Mungai et al. (2015; 2007-2012)
  - Costard et al. (2017; 2009-2014)

- **Bottom-Up**, *Listeria monocytogenes*
  - FDA/FSIS (2003)
  - Latorre et al. (2011)
  - Stasiewicz (2014)

Additional assessments including those prepared by FSANZ, AFSCA, MPINZ will be considered in next phases of Joint SRA RO Project
Pathogens for Dairy Outbreaks

- *Bacillus* (pasteurized)
- *Brucella* (unpasteurized)
- *Campylobacter* (both)
- *Clostridium* (pasteurized)
- *Listeria* (both)
- Norovirus (pasteurized)
- *Salmonella* (unpasteurized)
- *Shigella* (both)
- *Staphylococcus* (both)
- STECs/VTECs (unpasteurized)

### Number of dairy associated outbreaks, 1993-2006 (Langer et al., 2012)

- Unpasteurized: 46 milk outbreaks, 930 cases, 71 hospitalized
- Pasteurized: 10 milk outbreaks, 2,098 cases, 20 hospitalized

### Uncertainties

- Any of the 46 outbreaks associated with unpasteurized milk representative of certified raw milk produced on licensed farms?
- Raw data not available from study authors
Correlative Evidence from Epidemiologic Studies

- Data from outbreaks may be poorly predictive of future outbreaks or the numbers of associated illnesses, hospitalizations, and deaths.

  Recent fatal listeriosis outbreak from commodity estimated by FDA/FSIS (2003) as very low risk: ice cream prepared from pasteurized milk served in hospital, no deaths for non-hospitalized consumers (Pouillot et al., 2016)

- Consider Solenne Costard’s analysis presented at SRA in 2014 and published this year in *Emerging Infectious Diseases*
  - Raw data provided by Solenne and her co-authors (Costard et al., 2017) raise questions about the analysis and its interpretation (details in backup slide)
  - For states regulating raw milk, claims for ‘unpasteurized dairy products’ not supported
    - cause 760 illnesses and 22 hospitalizations per year, mostly from *Salmonella* and *Campylobacter*
    - 840 (95% credibility interval 611-1,158) times more illnesses and 45 (95% credibility interval 34-59) times more hospitalizations than pasteurized products
NY State Outbreaks over 18 Years
(CDC FOOD Tool)

Data for all 18 years of surveillance currently available in CDC FOOD tool (July, 2017 download)

No outbreaks associated with *Listeria*, *Salmonella*, STEC, or *Staphylococcus* for nonpasteurized milk

All 10 outbreaks associated with *Campylobacter*

<table>
<thead>
<tr>
<th>Food vehicle</th>
<th>Number outbreaks</th>
<th>Number illnesses</th>
<th>Number hospitalizations</th>
<th>Number deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonpasteurized milk</td>
<td>10</td>
<td>100</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>All</td>
<td>1,036</td>
<td>29,772</td>
<td>3,151</td>
<td>337</td>
</tr>
<tr>
<td>Fraction relative to all sources</td>
<td>1%</td>
<td>&lt;1% (0.3%)</td>
<td>&lt;1% (0.1%)</td>
<td>&lt;1% (0/337)</td>
</tr>
</tbody>
</table>

Data for all 18 years of surveillance currently available in CDC FOOD tool (July, 2017 download)
No outbreaks associated with *Listeria*, *Salmonella*, STEC, or *Staphylococcus* for nonpasteurized milk
All 10 outbreaks associated with *Campylobacter*
**Bottom-Up Listeriosiss Predictions for Milks**

**Perception** that raw milk is **poison** is inconsistent with both FDA/FSIS (2003) and Latorre et al. (2011) **risk estimates**:

**Pasteurized Milk**
- 90.8 deaths per year *(high risk)*
- $10^{-9}$ per serving or 1 fatal case in 1,000,000,000 exposures at selected doses *(moderate risk)*

**Unpasteurized Milk**
- 3.1 deaths per year *(moderate risk)*
- $7 \times 10^{-9}$ per serving or 7 fatal cases in 1,000,000,000 exposures at selected doses *(high risk)*
- $\sim 2 \times 10^{-15}$ per serving or 2 cases in 1,000,000,000,000,000 exposures *(very low risk)*

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**Perception that raw milk is poison is inconsistent with both FDA/FSIS (2003) and Latorre et al. (2011) risk estimates:**
Research Supporting Evidence-Based Policies for Listeriosis?

Some governments regulate Ready to Eat Foods that…

- **support growth** as unsafe (adulterated) if 1 bacteria or colony forming unit (CFU)/mL *Listeria* is detected.

- **do not support growth** as adulterated only if $>100$ CFU/mL *Listeria* is detected.

- Evidence for growth/no growth of pathogens in certified raw milk at natural levels of contamination (1 to 10 CFU/mL)?
  If no growth for *Listeria*, raw milk at $<100$ CFU/mL could be considered unadulterated (acceptable or tolerable or ‘safe’)

- **Milk microbiota studies** could better characterize microbes associated with suppressive effects on *Listeria* and other pathogens
Difficulties of Communicating Scientific Information about Microbial Ecosystems

Dave Levitan’s List of Errors (2017)

- Oversimplification
- Cherry-pick
- Butter-up and undercut
- Demonizer
- Blame the blogger
- Ridicule and dismiss
- Literal nitpick
- Credit snatch
- Certain uncertainty
- Blind eye to follow-up
- Lost in translation
- Straight-up fabrication
- Conspicuous silence
Evidence Maps: Communicating Risk Assessments in Societal Controversies: The Case of Engineered Nanoparticles

Future: Compile and Map the Evidence, Deliberate ...

Risk Analysis
Back to Warner North
Five Key Points

➢ Getting the science right
➢ Getting the right science
➢ Getting the right participation
➢ Getting the participation right
➢ Developing an accurate, balanced, and informative synthesis.

Where Are We in This Process?

- Points 1 to 4: just beginning to assemble the science, participants - and get these “right.” We welcome further participation!

- Point 5: Synthesis is quite a distance away.
Where Are We in This Process?

- Points 1 to 4: just beginning to assemble the science, participants - and get these “right.” We welcome further participation!
- Point 5: Synthesis is quite a distance away.

But let us give you personal viewpoints, as of now.
Some Insights to Date:

- Microbial ecosystems are complicated to understand, model, and communicate about to stakeholders.

- Culture-independent methods used in first decade of microbiome research are transforming understanding of ‘superorganisms’, immunology, and microbial ecology of milks.

- Further research and further dialogue is needed for evidence-based regulation considering microbiota of milks.

- High value of further information likely based on high potential for better risk management to achieve benefits and balance, reduce risks.
Some Probiotic Examples - Clinical Trials


  Summary: elderly volunteers (65-80 years of age) treated twice daily with $10^{10}$ cfu of probiotic (*Lactobacillus rhamnosus*) for 28 days suffered no serious adverse events, and an inflammatory cytokine that could disrupt gut homeostasis and impact health decreased transiently.

➢ Donald G. MacNeil, Jr., “Protected From Bacteria by Bacteria” Source: New York Times, Health, August 21, 2017:


  Summary from *Nature*, August, 2017: sample ATCC-202195 of *Lactobacillus plantarum* from a healthy 11-month old Maryland child fed for one week reduced sepsis in babies in rural India by 40%; trial end early because it was judged unethical to deny treatment to placebo babies.

Last paragraph: “...getting the money to do such studies is hard experts say, because of prejudices against probiotics at many funding institutions, which view their use as naturopathy rather than evidence-based medicine.”
Paradigm Shifts Are Difficult Even in the Scientific Community

References:


Paradigm Shifts Are Difficult Even in the Scientific Community

References:


Risk Community has challenges to address for microbiota of milks!
Acknowledgments of Collaborators on Joint SRA Project

➢ SRA Webinar Series Speakers
  • Rodney Dietert, Cornell University
  • Michelle McGuire, Washington State University
  • Mark McGuire, University of Idaho

➢ Project Participants to Date
  • Heather Lynch, New England SRA
  • Steve Corin, Australia/New Zealand SRA
  • Stephen Cobb, New Zealand EPA
  • Naomi Cogger, Australia/New Zealand SRA
  • Paul Cook, UK Food Standards Agency
  • Tom Ross, University of Tasmania, Australia
  • Tanya Soboleva, Ministry for Primary Industries, New Zealand

➢ SRA Secretariat and Officers
  • Ann Bostrom, University of Washington, SRA Fellow
  • Christopher Clark, George Mason University, SRA Risk Communication Specialty Group Chair
  • Robin Dillon Merrill, Georgetown University, SRA Education Committee Chair
  • Michele Stephenson, Upstate NY SRA Webmaster
Questions?
More Information and Resources Appended
Back-up Slides
Free Resource for Consumers

(American Academy of Microbiology, 2014)
free download from American Society for Microbiology (ASM) at http://academy.asm.org/index.php/faq-series/ 5122-humanmicrobiome
Food Microbiology and Risk Resources

(Jaykus et al., 2009)

(Schmid, 2009)

(Working Towards Food We Can Trust; FSA, 2015, free download at food.gov.uk)

(McGuire et al., 2017)
Other Resources

(Dietert, 2016)

(Yong, 2017)

(Levitan, 2017)

(Alda, 2017)
Many excellent resources (books, reviews, and technical papers) available in published literature, some **free full text**

- National Academy of Sciences, the National Academies Press (more technical, but **free downloads** at [http://www.nap.edu/](http://www.nap.edu/))

- Technical journals (fees for online access without subscription)
Some Requirements for Selling Certified Raw Milk in NY State

- Brucellosis ring test
  - No longer required in NY and other validated brucellosis-free states; 9 CFR 78.43
- Tuberculosis test for each animal
  - No longer required in NY and other validated TB-free states
- Quality Milk Production Services (QMPS) program
  - Each animal tested for *E. coli* and pathogens including *Staphylococcus aureus*
- Monthly or quarterly milk sample tested for coliforms and pathogens including *Salmonella*, *Listeria*, *E. coli O157:H7*, *Campylobacter*, *Staphylococci*
- Satisfactory farm water test
- Farm inspections at least twice a year
  - Sanitary conditions
  - Health of cows
  - Health of individuals working on farm
Data NY State Outbreaks Associated with Nonpasteurized Milk (1998-2015)
Currently ~40 Licensed Dairies in NY State
No Salmonellosis, \textit{E. coli} enteritidis, Listeriosis, or \textit{Staphylococcus aureus} Illness Outbreaks

<table>
<thead>
<tr>
<th>Observed outbreaks</th>
<th>Year</th>
<th>Month</th>
<th>Number illnesses</th>
<th>Number hospitalizations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1998</td>
<td>7</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
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<td>0</td>
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<tr>
<td>4</td>
<td>2007</td>
<td>4</td>
<td>2</td>
<td>1</td>
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<tr>
<td>5</td>
<td>2010</td>
<td>1</td>
<td>20</td>
<td>1</td>
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<tr>
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<tr>
<td>10</td>
<td>2014</td>
<td>7</td>
<td>8</td>
<td>0</td>
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<tr>
<td><strong>Totals</strong></td>
<td></td>
<td></td>
<td><strong>100</strong></td>
<td><strong>4</strong></td>
</tr>
</tbody>
</table>

Data for all 18 years of surveillance currently available in CDC FOOD tool (July, 2017 download)
All 10 outbreaks attributed to \textit{Campylobacter}; no deaths reported for this 18-year period
Correlative Evidence from US Epidemiologic Studies

➢ Mungai et al. (2015; 2007-2012)
  • Data for pasteurized milk or total outbreak statistics not reported for context
  • ‘Black market’ milk, not certified raw milk from licensed farms, is associated with majority of illness outbreaks

➢ Costard et al. (2017; 2009-2014)
  • Pooling of milk and cheese for convenience of analysis problematic
  • Outbreaks associated with certified raw milk from licensed dairies not reported
  • Causality not demonstrated in this study
  • Generalizing from dairy outbreaks in the past invalid for predicting certified raw milk outbreaks, cases, and hospitalizations in the future
  • Model predictions most sensitive to the adjustment factors applied to the raw data
  • For states regulating raw milk, claims for ‘unpasteurized dairy products’ not supported
    - cause 760 illnesses and 22 hospitalizations per year, mostly from *Salmonella* and *Campylobacter*
    - 840 (95% credibility interval 611-1,158) times more illnesses and 45 (95% credibility interval 34-59) times more hospitalizations than pasteurized products
Bottom-Up: Listeriosis Relative Risks for Dairy Commodities Very Low to High

**FDA/FSIS, 2003**

**Very high and high risk foods** (upper left) **presumed** to support growth, including BOTH milks (pasteurized and unpasteurized)

**Very low and low risk foods** (lower right), including frozen foods and hard cheeses, **presumed to have intrinsic or extrinsic factors to prevent the growth** or are **processed** to alter the normal characteristics of food

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**Clusters A and B**
- **Very High Risk**
  - Deli Meats
  - Frankfurters (not reheated)

**Clusters C and D**
- **High Risk**
  - High Fat and Other Dairy Products
  - Pasteurized Fluid Milk
  - Soft Unripened Cheese

**Cluster E**
- **Moderate Risk**
  - No food categories

**Clusters 1**
- **Moderate Risk**
  - High Fat and Other Dairy Products
  - Pasteurized Fluid Milk
  - Soft Unripened Cheese

**Clusters 2**
- **Moderate Risk**
  - Deli-type Salads
  - Dry/Semi-dry Fermented Sausages
  - Frankfurters (reheated)
  - Fresh Soft Cheese
  - Fruits
  - Semi-soft Cheese
  - Soft Ripened Cheese
  - Vegetables

**Clusters 3**
- **Moderate Risk**
  - No food categories

**Clusters 4**
- **Low Risk**
  - Preserved Fish
  - Raw Seafood

**Clusters 5**
- **Very Low Risk**
  - Cultured Milk Products
  - Hard Cheese
  - Ice Cream and Other Frozen Dairy Products
  - Processed Cheese

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**Recent fatal outbreak** from commodity estimated **very low risk**: ice cream prepared from pasteurized milk served in hospitals, not consumed in general population (Pouillot et al., 2016)
Evidence for Updating Assumptions about *Listeria* Growth

At refrigeration temperatures of 41-43 °F:

- *Listeria* growth rate assumed by FDA/FSIS for both pasteurized and unpasteurized milk
  - 0.257 cfu/g/day

- *Listeria* growth rate increased with increasing pasteurization temperature for 25 seconds in recent university study
  - 0.503 cfu/mL/day for milk treated at 162°F
  - 0.562 cfu/mL/day for milk treated at 180°F

- Higher temperature also significantly decreased the time before *Listeria* growth began (shorter lag) and increased maximal growth (higher maximal density, $N_{\text{max}}$), causing higher growth of the pathogen at the higher pasteurization temperature

Exposure is underestimated for PASTEURIZED milk in FDA/FSIS assessment!

(FDA/FSIS, 2003; Stasiewicz et al, 2014)
Pasteurized (and Certified Raw) Milks **Not** Risk-Free

- Pasteurization reduces pathogen numbers but does **not** kill all bacteria present.
- Milk is a **better** growth medium for *Listeria* after heat treatment than before (Stasiewicz et al., 2014).
- The greater the volume of milk produced and distributed for consumption, the wider the effect when something goes wrong.
- **Sterile milk**, inside or outside the udder, is a myth now that the first decade of microbiome studies are published.
- The microbiome of post-pasteurization milk includes similar organisms and diversity as raw milk, but lower counts (Quigley et al., 2013a,b).
- Need for both sides of milk wars to consider all the evidence and address the true problem.
Milk Wars in Canada

- Economics: Milk Control Act/Milk Control Act intended to stabilize pricing (milk glut, falling prices; subsidies; limit supply)

- Sale of raw milk illegal since 1981 (Health Canada)
  - Potential presence of pathogenic bacteria
    - *Listeria*, pathogenic *E. coli*, and *Salmonella*

- Ontario law prohibits selling or giving away raw milk

- Dairy farmer Michael Schmidt (Glencolton Farm) awaiting decision in courts
  - Legality of farm-share, 200-member cooperative farm?
  - “It’s a total police state when it comes to raw milk here because there’s absolutely no leniency on any level. They are saying it’s the most dangerous substance you can think of and should never be allowed. There’s not even a proper scientific debate about it. It’s all on an emotional, fear-based level.”
  - Raw Milk Xenophobia?