THE PEW CHARITABLE TRUSTS

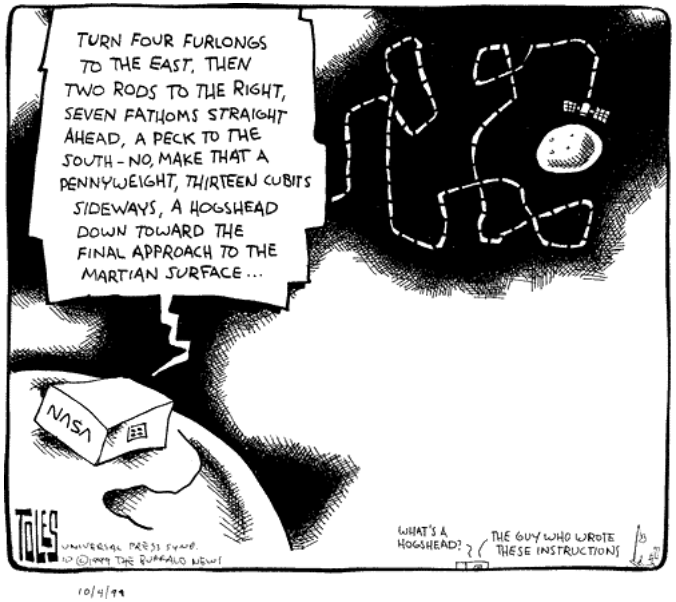
Salmonella risks pre-harvest and their importance for food safety

Karin Hoelzer, DVM, Ph.D.

March 14, 2016

Outline of today's presentation

1. **A brief history of The Pew Charitable Trusts**
   - **The Pew family**
   - **The Charitable Trusts**
   - **Pew's work in the agricultural space**
2. **The role of risk assessment**
   - **What it adds in this context**
3. ***Salmonella* risks pre-harvest**
   - **What we know about *Salmonella***
   - **Why we care about pre-harvest risks**
   - **What we can do about it**



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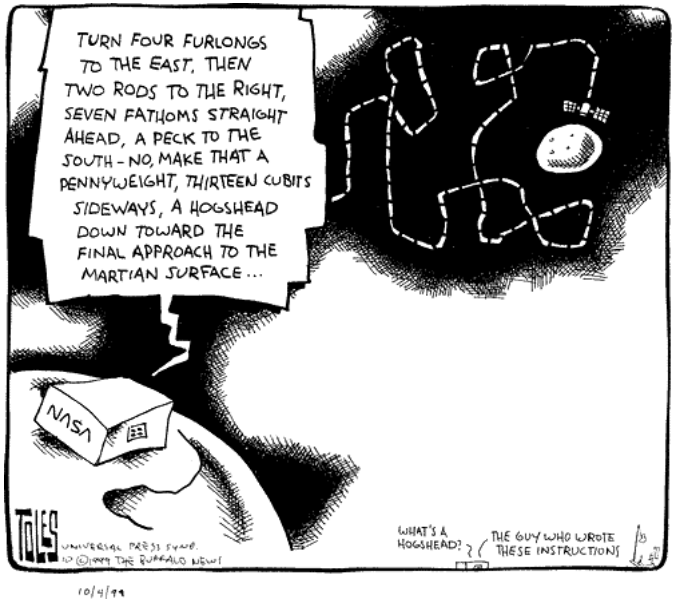

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Establishing The Pew Charitable Trusts

The Pew Charitable Trusts

- Based on 7 separate trusts established 1957 – 1979
- Established by four children of J.N. Pew Sr.
- Early Priorities:
  - Democracy
  - Religion
  - Health Care
  - Arts & Culture
  - Environment

Growth and Evolution of the Trusts

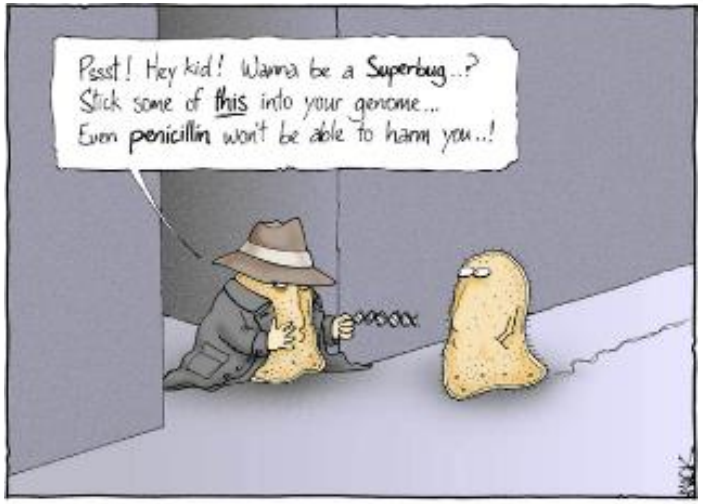
The Pew Charitable Trusts evolved over time

- **1985** Pew Scholars in the Biomedical Sciences
- **1986** First Federal Policy Project
- **1994** State Policy work begins
- **1995** Pew Research Center work begins
- **2002** The Pew Charitable Trusts becomes a public charity

Today's Priorities

- 5 Key priorities remain unaltered, plus:
  - State policy
  - Consumer protection
  - Public opinion and demographics

Pew's antibiotic resistance project



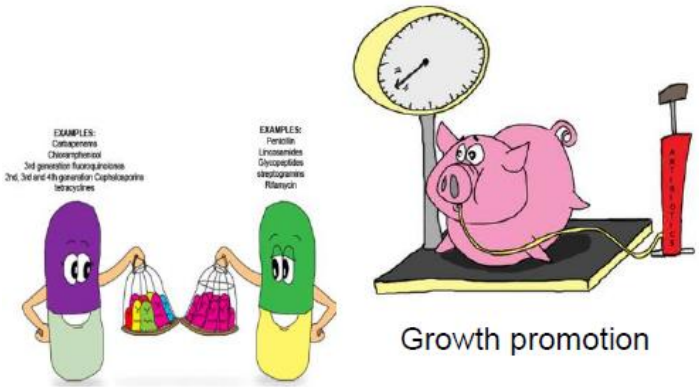
It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.

Source: http://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.0050112

Prudent antibiotic use & robust drug pipeline

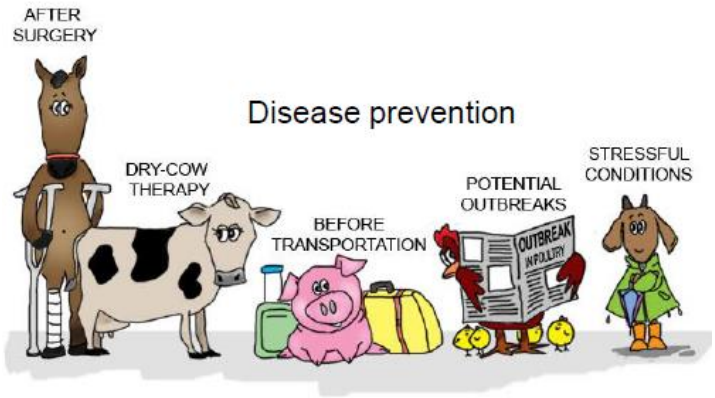
- **Prevent overuse in food animals**
  - Phase out antimicrobial growth promoters
  - Use antimicrobial drugs judiciously
  - Reduce the need for antibiotic treatments
    - ⇒ Certified Responsible Antibiotic Use (CRAU) standard
- **Prevent unnecessary antibiotic prescriptions**
  - Human stewardship programs
    - Inpatient settings
    - Outpatient settings
- **Spur the creation of new antibiotics**
  - Foster drug discovery & development
    - Remove regulatory, economic & scientific obstacles

Pew's antibiotics work in the animal sector



Judicious use

Growth promotion



Source: Michigan State University, AR learning site

Pew's goals to improve antibiotic stewardship

- **Improve on-farm data collection to answer**
  - How are antibiotics actually use in agriculture?
  - What is the impact of FDA's policy changes?
  - What are appropriate goals?
- **Spur development & uptake of alternatives**
  - Reduce the need to use antibiotics through
    - Improved management practices
    - Use of alternatives (e.g., vaccines, probiotics)
- **Increase market demand & supply**
  - Incentivize responsible use practices
    - Certified Responsible Antibiotic Use (CRAU) standard

History of Pew's Safe Food Project

Pew's Food Safety efforts date back to 2008

- **2008** Pew funds the **Produce Safety Project** at Georgetown University
  - Focus: develop science and risk based produce safety standards
- **2009** Pew's **Food Safety Campaign** receives board approval
  - Focus: modernize FDA's oversight over produce, processed foods & imports
- **2011** Pew's **Safe Food Project** is approved
  - Focus: FSMA implementation and research on meat & poultry safety

Pew's role in food safety

Guiding principles for improving food safety

- **Function as an honest broker**
  - Facilitate dialogue among all stakeholders
- **Convene stakeholder meetings to solve issues**
  - Example: Collaborative Food Safety Forum
    - Forum for regulatory agencies (federal & state), industry, and consumer groups
    - Discuss topics such as FSMA metrics
- **Join forces with other food safety advocates**
  - Example: Make our food safe campaign
    - Advocate for FSMA implementation
- **Build relationships through outreach**
- **Foster research to inform recommendations**

Pew research on meat and poultry safety

Examples of Pew (sponsored) research

- **Risks posed by meat and poultry consumption**
  - Foodborne outbreaks (report authored with CSPI)
  - Emerging microbial hazards (report expected: 2016)
  - Retail sampling & testing (reports authored by CR)
    - Beef, Chicken, Turkey, Shrimp
- **Current policies, laws and regulations**
  - USDA's HACCP (report authored by CFA)
  - Meat Inspections (report co-authored with CSPI)
  - *Salmonella* performance standards (report published 2014)
  - Culture-Independent Diagnostic Tests (report by CFI)
  - National Residue Program (report published 2016)
- **Recommendations for improvement**
  - Pre-harvest Interventions (report expected: 2016)
  - Meat and Poultry Dialogue

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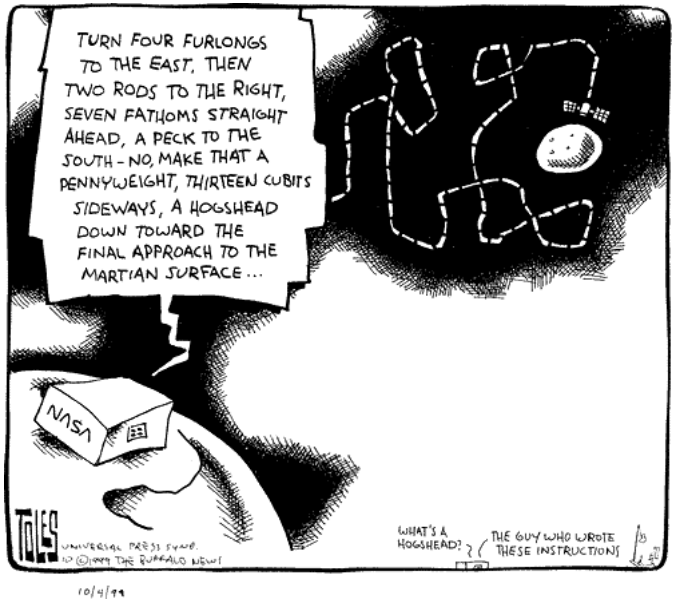

Source: Buffalo (NY) News, 10/04/1999

Salmonella : what risk assessments can add here

The value: risk-based approaches pre-harvest

- Identify and prioritize pathogen introduction routes
  - Example: EFSA risk assessment on *Salmonella* in pigs
  - Identify potential differences among operations & countries
- Predict impact of interventions on actual risk to consumer
- Quantify public health benefits associated with interventions
  - Examples: measure change in illness per annum or serving
- Systematically characterize strength of evidence & uncertainties
  - Examples: variable efficacy data
- Target interventions to the most appropriate step in food chain
- Sketch out different options that account for structural differences (e.g., industry segments, animal species)

Salmonella risks pre-harvest: risk assessment

The reality: risk-based approaches pre-harvest

- Fully quantitative microbial risk assessments farm –to-fork
  - Are very data intensive, and have to be tailored
  - Many data gaps and research needs exist
  - Various sources of uncertainty and variability
  - Not currently feasible for all major species and interventions

- Pew selected a qualitative risk assessment approach to answer
  - What are the key pathogens of concern?
  - What are the key routes of pathogen introduction and how do they vary by species, operation, pathogen, etc.?
  - What are the potential intervention steps pre-harvest
    - Include elite / breeding herds or flocks?
    - Focus on downstream steps before harvest only?
  - What data do we have to support efficacy? How good is it?
  - What are the risks of potential unintended consequences?
  - What are data gaps and potential sources of heterogeneity?

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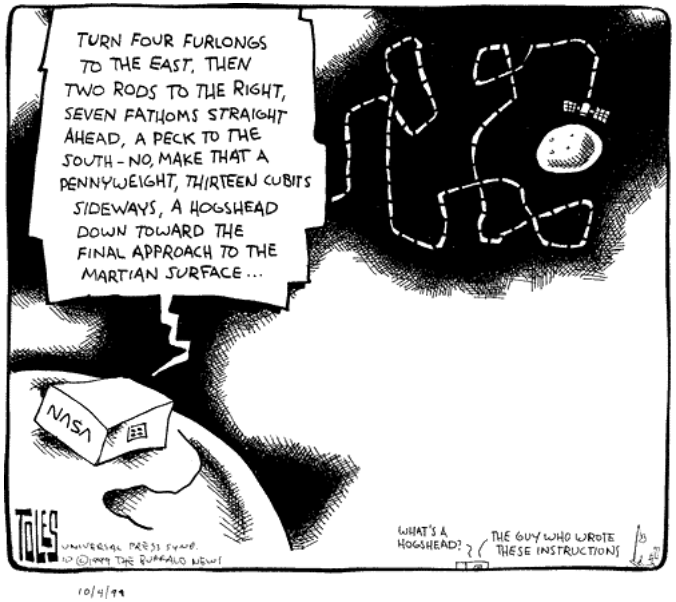

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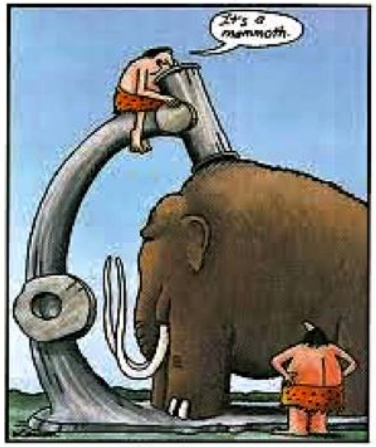
Introduction to *Salmonella* and salmonellosis

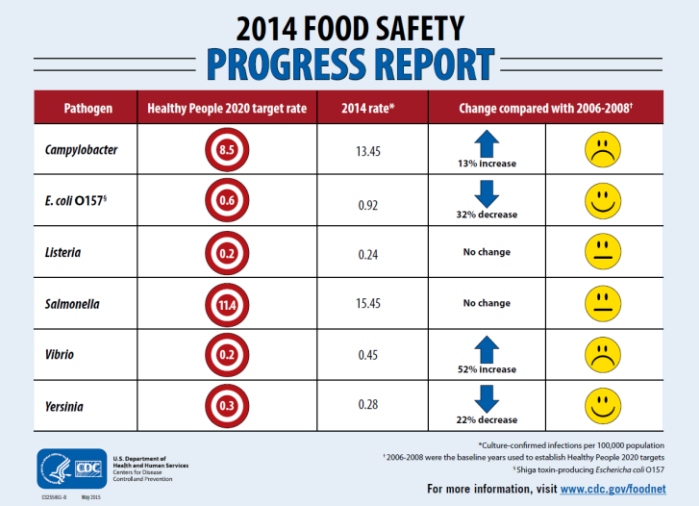


Early microscope

Salmonella (non-typhoidal) and salmonellosis

- **Microbiology**
  - *Enterobacteriaceae* family
  - Gram-negative, rod-shaped bacterium
  - Very stable in the environment
  - Two species (*Salmonella* enterica and bongori)
    - *Salmonella* enterica: six subspecies, > 2500 serotypes
  - Serotypes based on Kauffman-White classification
    - O antigen, H1 antigen, H2 antigen
- **Clinical manifestations**
  - Gastrointestinal illness
    - Diarrhea, abdominal cramps, fever, nausea, vomiting …
  - Invasive infections
    - Bacteremia, septicemia
    - Meningitis
    - Osteomyelitis, septic arthritis

Salmonella is not an easy pathogen to control



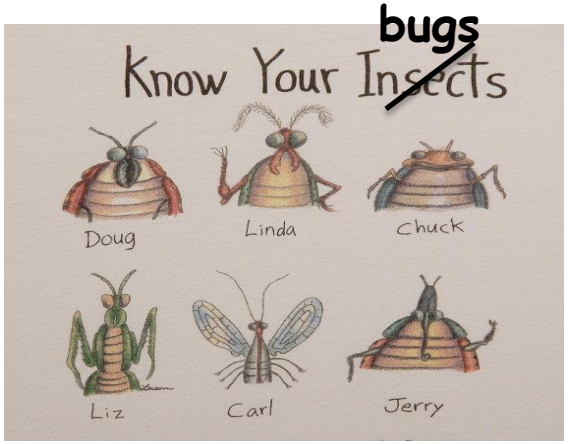
2014 FOOD SAFETY PROGRESS REPORT

Pathogen	Healthy People 2020 target rate	2014 rate*	Change compared with 2006-2008†	
Campylobacter	8.5	13.45	↑ 13% increase	☹
E. coli O157§	0.6	0.92	↓ 32% decrease	☺
Listeria	0.2	0.24	No change	😐
Salmonella	11.4	15.45	No change	😐
Vibrio	0.2	0.45	↑ 52% increase	☹
Yersinia	0.3	0.28	↓ 22% decrease	☺

*Culture-confirmed infections per 100,000 population
†2006-2008 were the baseline years used to establish Healthy People 2020 targets
§Shiga toxin-producing *Escherichia coli* O157

U.S. Department of Health and Human Services, Centers for Disease Control and Prevention

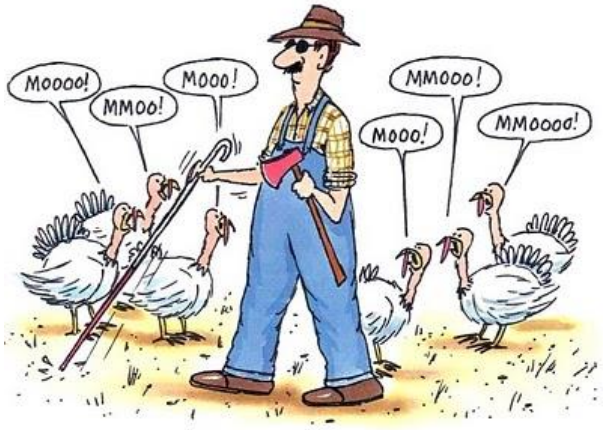
For more information, visit www.cdc.gov/foodnet



Not all *Salmonella* serotypes are created equal

- **Epidemiology**
  - *Salmonella* incidence has remained nearly unchanged
  - 1.2 million illnesses & 450 deaths in US per year
  - Primarily foodborne, some zoonotic, waterborne, other
  - Risk factors : age, season, medications, contact with pets
- **Not all serotypes are created equal**
  - Host range
    - Host specific (e.g., Gallinarum, Pullorum)
    - Host restricted (e.g., Dublin, Choleraesuis)
    - Generalist (e.g., Typhimurium)
  - Clinical outcome (e.g., Jones et al. 2008; JID 2008: 198)
    - Hospitalization rates
      - Ranged from < 15% to > 60%
    - Rates of invasive infection
      - Ranged from < 1% to > 60%

Salmonella infection in animals – contact is a risk



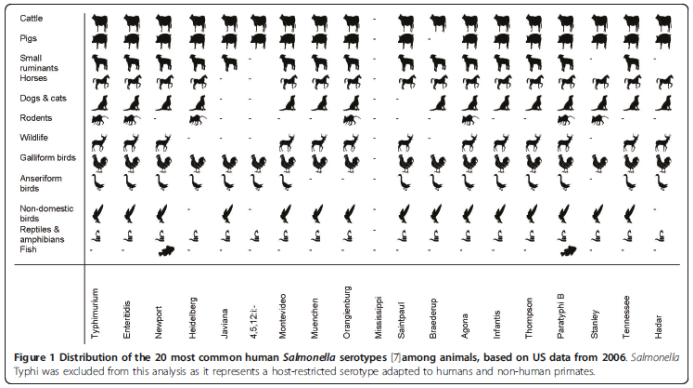


Figure 1 Distribution of the 20 most common human *Salmonella* serotypes [7]among animals, based on US data from 2006. *Salmonella* Typhi was excluded from this analysis as it represents a host-restricted serotype adapted to humans and non-human primates.

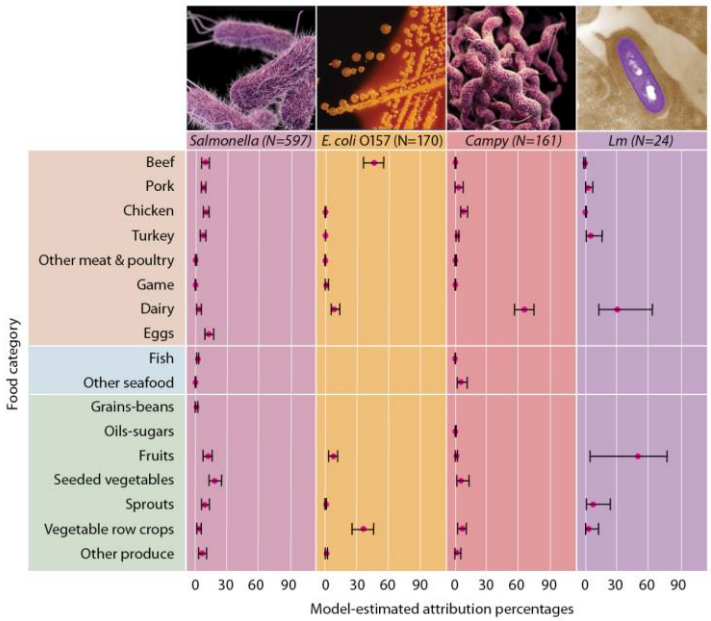
Source: Hoelzer et al. Vet Res 2011, 42:34

Salmonella is also an animal pathogen

- ***Salmonella* can infect a variety of animals**
  - Livestock and poultry
  - Pets (dogs, cats, horses, reptiles, fish, etc.)
  - Wildlife (wild birds, reptiles and amphibians, etc.)
- **Animals often show no clinical symptoms**
  - Young animals are at increased morbidity & mortality risk
  - Animals can show a varied number of symptoms
    - Diarrhea, fever, depression, anorexia, dehydration
    - Abortion, respiratory disease, abscesses, etc.
    - Shedding can be intermittent, stress-induced
- **Direct animal contact poses a potential risk**
  - Outbreaks have been linked to direct animal contact, e.g.
    - Farm visits, petting zoos or other public settings
    - Veterinary clinics and other occupational exposures

Salmonella infection in animals – consumption risk

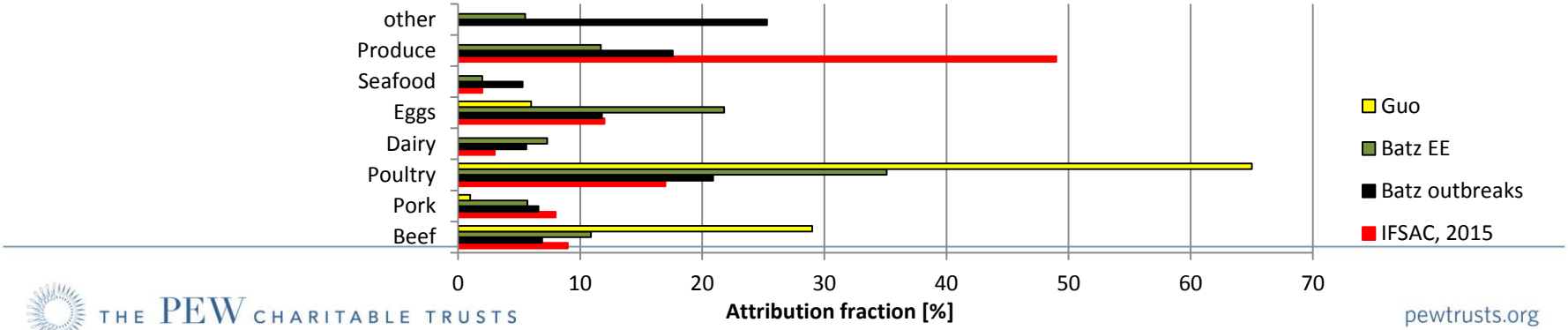
Figure 1. Model-estimated attribution percentages (and 90% credibility intervals) for *Salmonella*, *Escherichia coli* O157 (*E. coli* O157), *Campylobacter* (Campy), *Listeria monocytogenes* (Lm).



Salmonella is primarily a foodborne illness

- ***Salmonella* infections are primarily foodborne**
  - 6 – 20 % of illnesses attributable to animal contact
    - Hale et al. CID 2012:54 (Suppl. 5)
  - 94% of illnesses foodborne
    - Scallan et al. EID 17(1): 2011
- **A variety of foods are responsible**
  - Source attribution estimates vary somewhat by study
  - However, food of animal origin is clearly important
    - Beef, pork, poultry, dairy and eggs
  - Produce is also an important source of *Salmonella* infection

Source: IFSAC Project, 02/2015

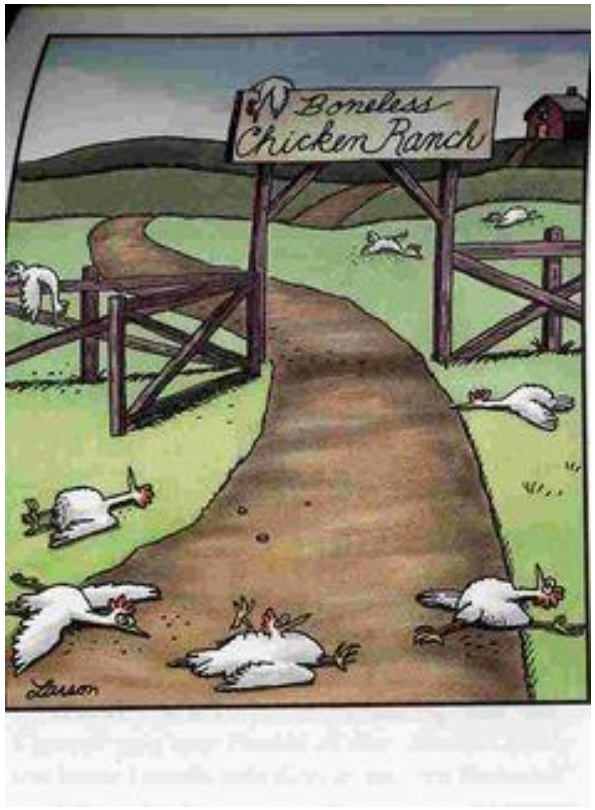


Salmonella risks pre-harvest : why it matters

The need for a comprehensive approach

- ***Salmonella* can be common pre-harvest**
  - Various livestock species can harbor *Salmonella*
    - Various surveys published
  - Contamination can be difficult to detect
    - Asymptomatic infections & intermittent shedding
- **Slaughter interventions can reduce the risk**
  - Interventions during and after harvest reduce contamination
  - However, a comprehensive approach is needed
- **Controlling pathogens pre-harvest**
  - Can reduce foodborne risks
  - Can reduce risk of run-offs from the farm
  - Can reduce direct infection risks
- **Successful programs in other countries**
  - Examples include Denmark, Sweden
  - Decrease frequency and level of microbial contamination

Salmonella risks pre-harvest : introduction routes



Salmonella can find many ways onto a farm

- ***Salmonella* is stable in the environment**
  - Can survive in the environment for long periods of time
  - Much more hardy than, for instance, *Campylobacter* spp.
  - Has a wide host range – vermin, wildlife, pets, etc.
- **A variety of introduction routes are important**
  - Contaminated feed, water, litter, farm personnel, equipment
  - Wildlife, vermin, replacement animals etc.
- **Successful *Salmonella* control programs**
  - Feasibility varies by species and external situation
  - Some success in other countries (e.g., Sweden, Denmark)
  - Focus on three aspects
    - *Salmonella*-free replacement animals (elite stocks)
    - Hygiene and management practices (e.g., all-in/all-out)
    - *Salmonella* control during animal rearing
      - control in feed, water, farm environment

Salmonella risks pre-harvest: study rationale

Farmer Brown froze in his tracks; the cows stared wide-eyed back at him. Somewhere, off in the distance, a dog barked.

Pew's work on pre-harvest food safety

- **Improve the safety of meat and poultry**
  - Review current pre-harvest interventions available to
    - Reduce microbial contamination on farms & feedlots
  - Pew is currently developing a report
    - What pre-harvest interventions currently exist for
      - Poultry
      - Cattle
      - Swine
    - How do they work and how effective are they?
    - What are current data gaps and research needs?
- **Methodological approach**
  - Systematic review
    - Focused on large field trials and systematic reviews
  - Narrative review
  - Expert elicitation workshops

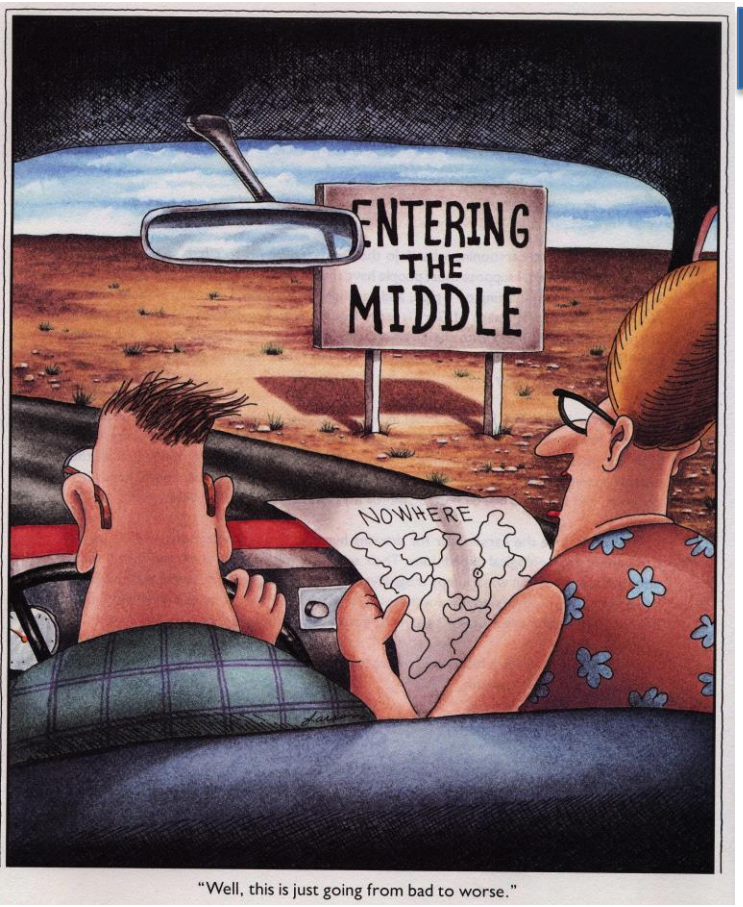
Salmonella risks pre-harvest: interventions

"It's going to be great! All natural ingredients."

Pre-harvest interventions available to date

- **Procommensal strategies**
  - Favor competition with non-pathogenic bacteria
    - Pre-and probiotics
- **Antipathogenic strategies**
  - Directly target the pathogen
    - Vaccines
    - Bacteriophages, bacteriocins and colicins
    - Antimicrobial drugs
    - Sodium chlorate
    - Essential oils
    - Heavy metals (e.g., zinc, copper)
- **Exposure-reduction strategies**
  - Minimize risk of pathogen introduction
    - Biosecurity, feed and water hygiene, housing

Salmonella risks pre-harvest: overall findings

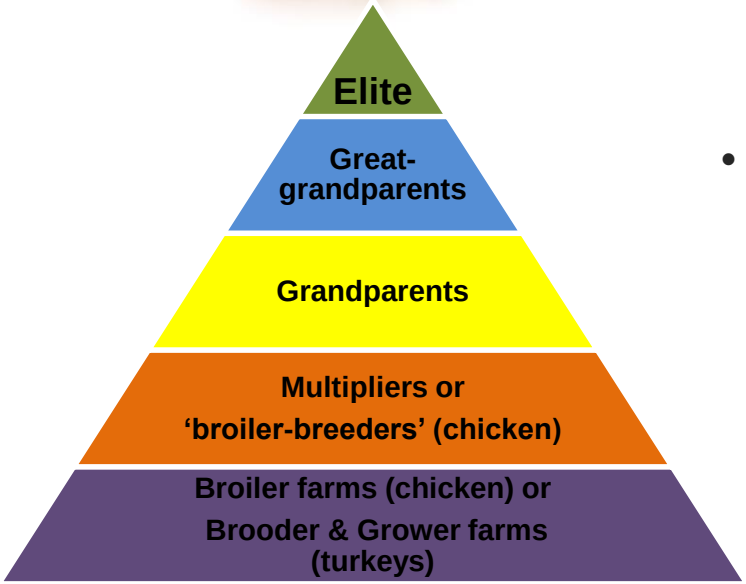


"Well, this is just going from bad to worse."

Pre-harvest interventions have to be tailored

- **Remember the biosecurity!**
  - The **only** intervention that works across settings
    - Pretty basic things – quarantine, vermin control, etc.
    - Limited quantitative data but widely seen as prerequisite
- **No one intervention is a magic bullet**
  - Interventions have to be tailored to the specific situation
    - Account for physiological and industry differences
    - Target interventions to where they are feasible
    - Every species is different!
  - A comprehensive approach is needed
    - Interventions have to be combined for effectiveness
    - Limited data on potential synergisms / antagonisms
- **There are many challenges to implementation**
  - Data gaps and variable efficacy
  - Regulatory and economic challenges

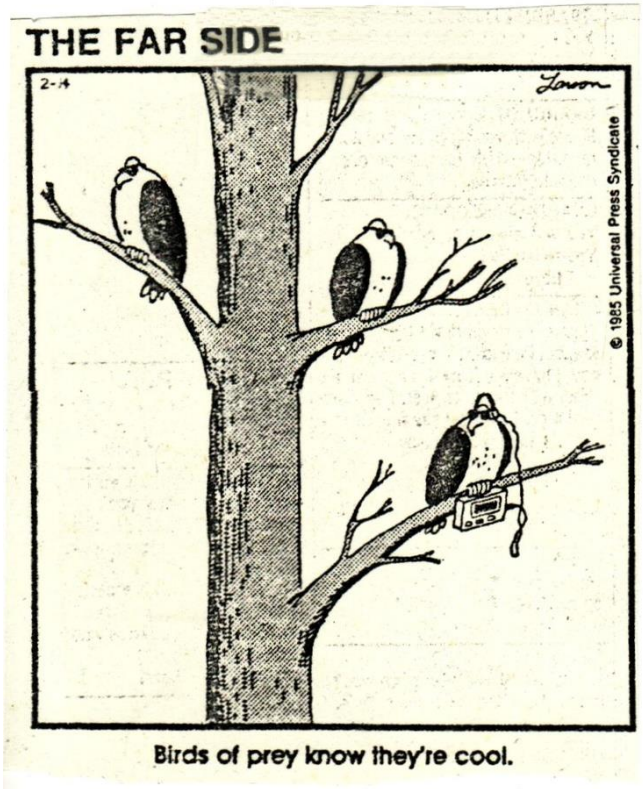
Salmonella risks pre-harvest: poultry results



Pre-harvest interventions: feasible for broilers

- **A number of factors favor interventions**
  - Industry structure: highly integrated and pyramid structure
    - Target interventions to include breeder flocks
  - Animal physiology:
    - Average age of chicken at slaughter: 38 days
    - One breeder lays 150 – 180 eggs per year
    - Bird house environment can be controlled
- **Promising interventions include**
  - Vaccination
    - Limited by vaccine availability and cross-protection
    - Promising for at least some common serotypes
    - Can be used in breeders and broilers (DIVA)
  - Pre- and probiotics incl. competitive exclusion products
    - Highly promising results, in particular if given in feed
  - Biosecurity and management (e.g., feed acidification)

Salmonella risks pre-harvest: poultry results II



Pre-harvest interventions: feasible for broilers

- **Interventions that may work – more data!**
  - Bacteriocins
    - Promising under limited experimental conditions
    - Questions about availability, feasibility and cost
  - Bacteriophages
    - Somewhat modest and possibly short-lived results
    - Phage cocktails of multiple strains may be promising
  - Sodium chlorate
    - Promising experimental studies (based on limited data)
    - Reduced crop colonization & gut concentrations
- **Interventions that are clearly not indicated**
  - Antimicrobial drugs
    - Risk of resistance emergence
    - Risk of gut microflora disruption & increased shedding
    - EFSA opinion strongly discourages use

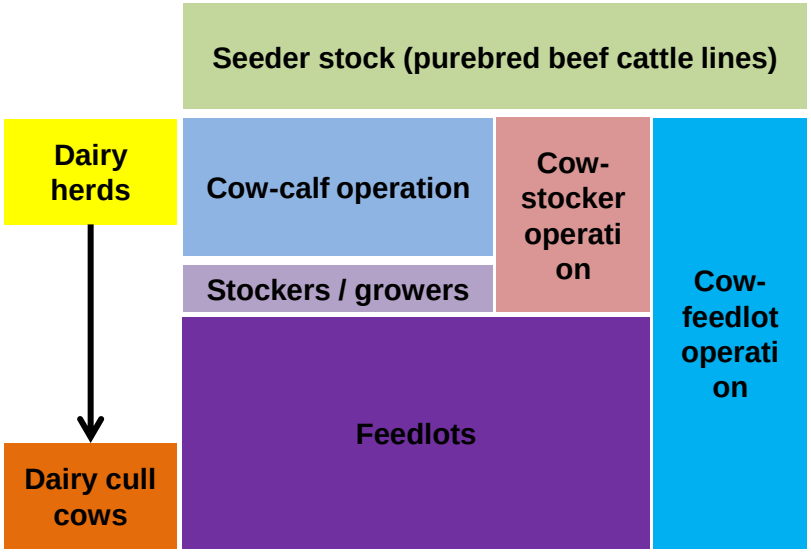
Salmonella risks pre-harvest: poultry results III

Returning from vacation, Roy and Barbara find their friends — in fact, all of Atlantis — just plain gone.

Pre-harvest interventions: feasible for poultry?

- **Key data gaps and research needs**
  - Data on efficacy in other species than chickens (turkeys!)
    - Most data collected in broilers, less for breeders
  - Field trials under real-world conditions needed
  - Effectiveness across *Salmonella* serotypes unclear
  - Synergisms and potential interferences across interventions
  - Mechanism of action not always clear
  - Potential non-scientific hurdles to implementation
    - Cost and cost-effectiveness
    - Regulatory challenges
    - Societal acceptance
    - Practical challenges (e.g., undefined probiotics)

Salmonella risks pre-harvest: cattle results



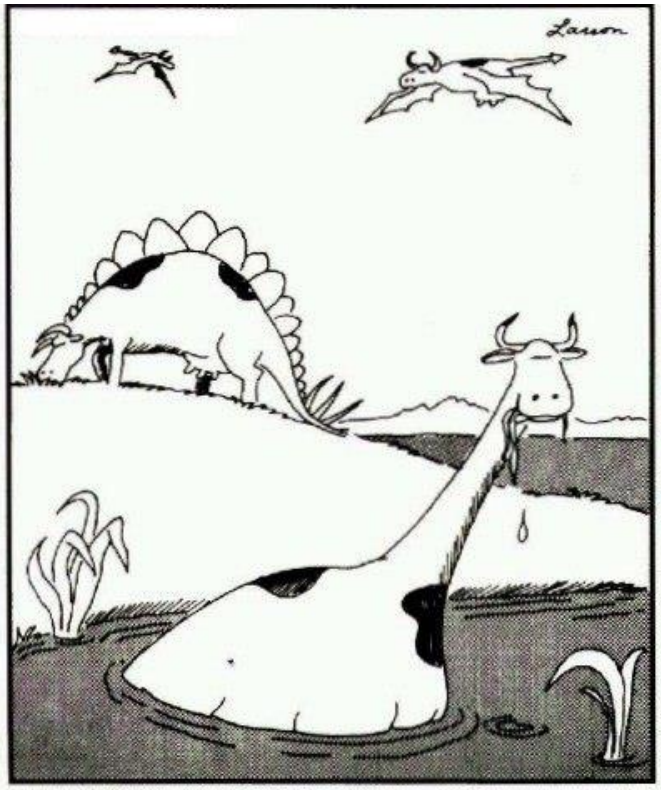
Cows are cows & how that complicates things

- **Cattle industry & physiology complicate things**
  - Industry structure: highly fragmented, no pyramid structure
    - Focusing on feedlot cattle may be most feasible
  - Animal physiology:
    - Average age at slaughter: 18 – 24 months
    - Difficult to control environment, particularly on pastures
    - Rumen limits applicability of certain interventions

Salmonella is not the same as STEC _E. coli_

- Vaccination
  - The most promising intervention for *E. coli* O157:H7
  - Results for *Salmonella* less clear
  - Some promising results but variable conclusions
- Don't forget about biosecurity!
  - Biosecurity, feed and water hygiene, wildlife control, etc.
  - Should be considered a prerequisite

Salmonella risks pre-harvest: cattle results II



Sixty-five million years ago, when cows ruled the earth

Pre-harvest interventions: any luck for cattle?

- **Interventions that may work – more data!**
  - Probiotics (direct-fed microbials & competitive exclusion)
    - More data available for STEC *E. coli* than *Salmonella*
  - Bacteriocins
    - Efficacy for *Salmonella* / in ruminating animals unclear
  - Bacteriophages
    - Topical application during slaughter most promising now
  - Sodium chlorate
    - More data on STEC *E. coli* than *Salmonella*
- **Interventions that clearly are not indicated**
  - Prebiotics
    - No current mechanism to survive rumen fermentation
  - Antimicrobial drugs
    - Most antibiotics actually failed to show significant effect
    - Neomycin may have effect on STEC *E. coli*

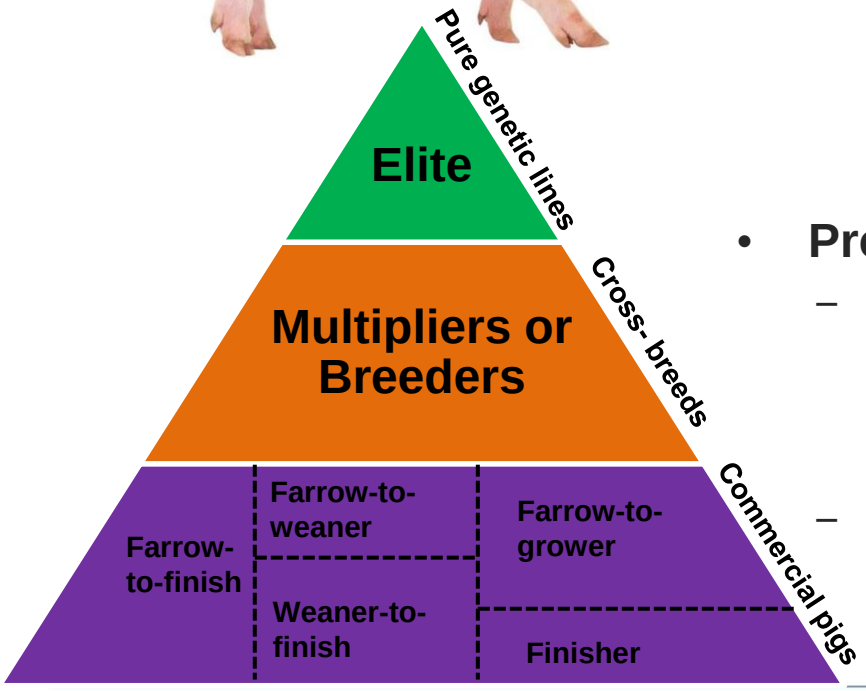
Salmonella risks pre-harvest: cattle results III

"Mmmmmm ... Interesting ... interesting. ... I'd say we taste a little like chicken."

Pre-harvest interventions: data gaps

- **Key data gaps and research needs**
  - Studies specific to *Salmonella* (far more for STEC *E. coli*)
  - Studies in adult animals
    - Most data collected in calves
  - Field trials under real-world conditions
    - Ideally on actual commercial feedlots
  - Systematic reviews and meta-analyses
    - Understand variability in results
  - Data on the synergisms or antagonisms across products
    - Most products probably not silver bullet
    - Need for a comprehensive approach
    - Need to combine approaches as feasible

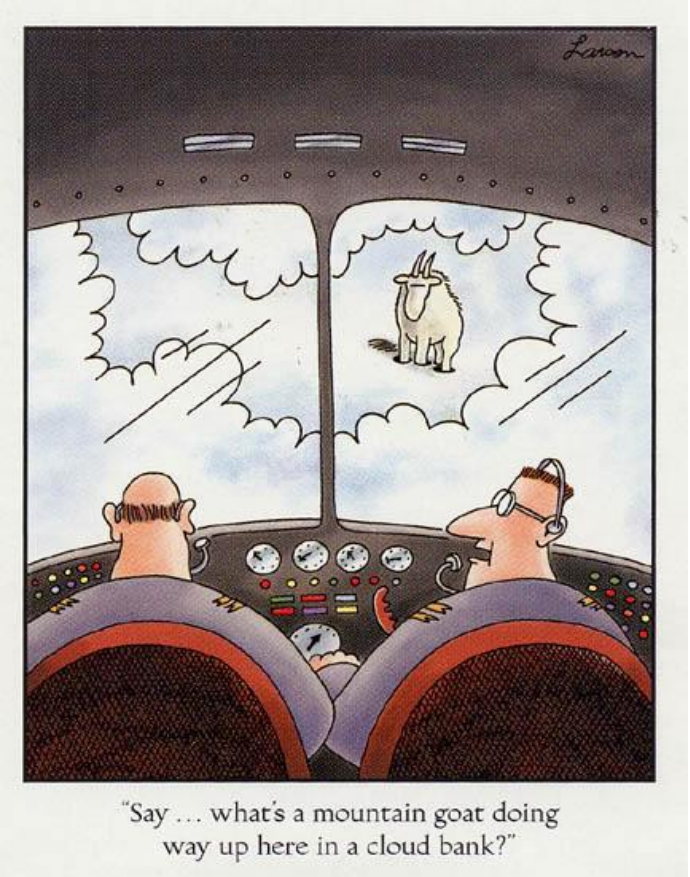
Salmonella risks pre-harvest: swine results



Pre-harvest interventions: jury still out on pigs

- **Some factors favor interventions**
  - Industry structure: increasingly integrated & pyramid
  - Animal physiology:
    - Average age of pigs at slaughter: 22 – 26 weeks
    - Reproduction per sow: 2 litters a 10 – 12 piglets / year
    - Include breeding herds in control programs
    - Environment can be controlled
- **Promising interventions include**
  - Vaccination
    - Systematic reviews show reduced *Salmonella* shedding
    - More effective against closely related serotypes
    - Both live and inactivated vaccines promising
  - Don't forget biosecurity!
    - Considered a pre-requisite
    - Poor biosecurity &*Salmonella*-positive status correlated

Salmonella risks pre-harvest: swine results II

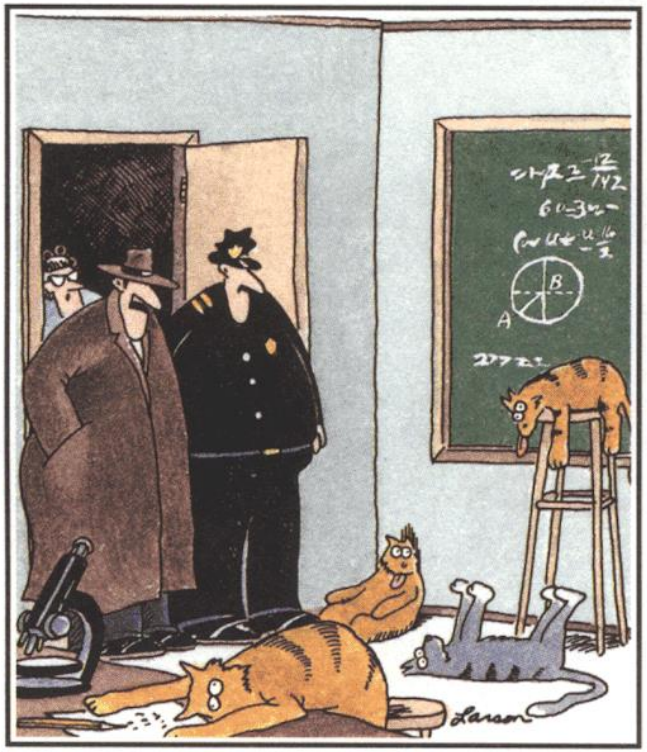


"Say … what's a mountain goat doing way up here in a cloud bank?"

Pre-harvest interventions: the jury is still out

- **Interventions that may work – more data!**
  - Pre- and probiotics
    - Studies have focused more on growth promotion effects
    - Some promising results but results have been variable
  - Bacteriocins
    - Some effectiveness for animal diseases
    - More data needed on pre-harvest food safety effects
  - Bacteriophages
    - Some promising results under experimental conditions
  - Sodium chlorate
    - Promising results for *Salmonella* as well as *E. coli*
- **Interventions that clearly are not indicated**
  - Antimicrobial drugs
    - Results are somewhat variable
    - Meta-analysis: limited efficacy, shedding can increase

Salmonella risks pre-harvest: swine results III

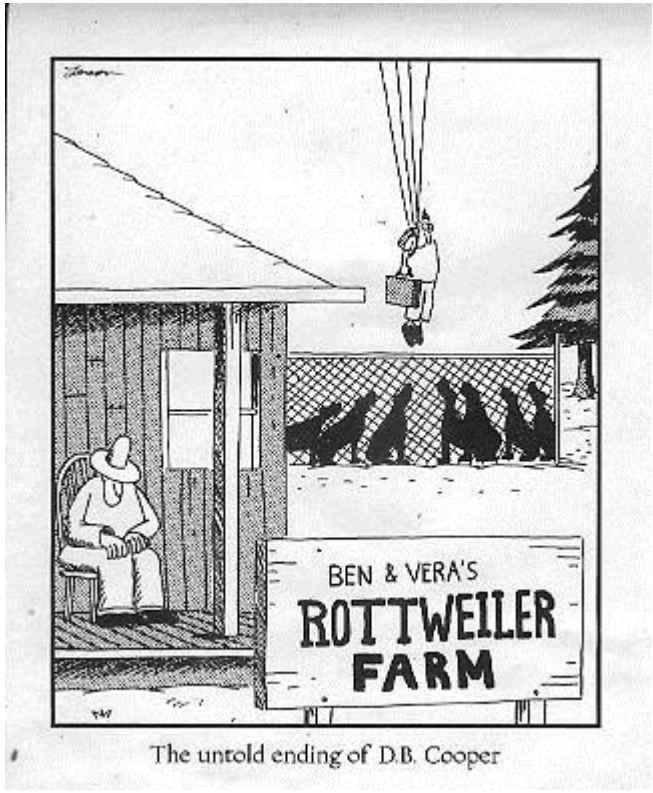


"Notice all the computations, theoretical scribblings, and lab equipment, Norm. ... Yes, curiosity killed these cats."

Pre-harvest interventions: data gaps

- **Key data gaps and research needs**
  - Sources of *Salmonella* infection in swine herds
    - Expert elicitation has identified several potential routes
    - 2006 EFSA opinion identified infected pigs as central
    - 2010 EFSA risk assessment: contribution varies by *Salmonella* status
  - Systematic reviews and meta-analyses
    - Few studies available for pre-harvest interventions
    - Heterogeneous and variable results
  - Large field trials under field conditions
    - Efficacy and cost-effectiveness

Salmonella risks pre-harvest: recommendations



The untold ending of D.B. Cooper

Key recommendations to regulatory agencies

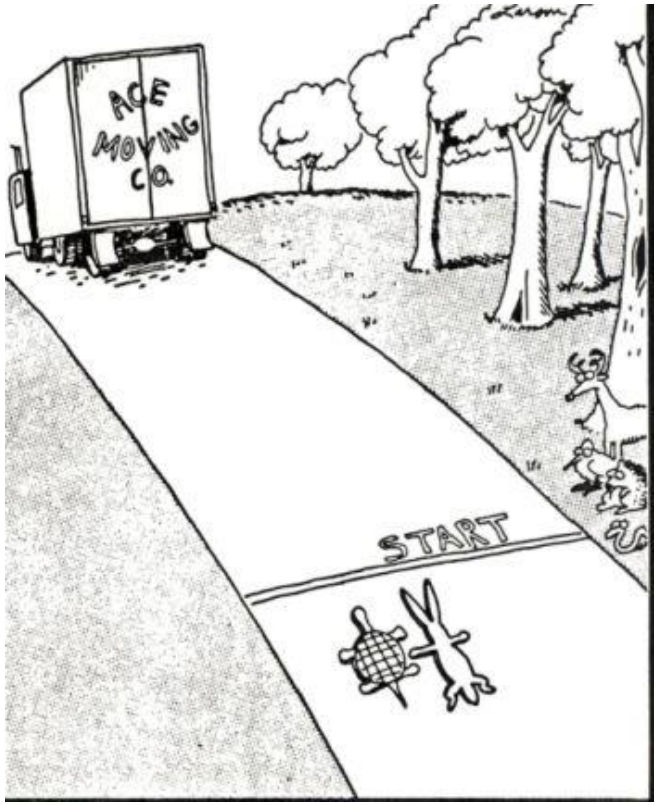
- Provide **incentives** for the implementation of pre-harvest food safety interventions, be they regulatory or economically motivated.
- Improve the **regulatory approval processes** in such a way that product safety, consistency, and efficacy can be guaranteed while making sure promising products can reach the market in a timely fashion.
- Consider the role of pre-harvest food safety in a **risk-based system**.
- Improve **collaboration and communication** among all stakeholders (farmers, meat producers, consumers, regulatory agencies, academic researchers, pharmaceutical industry) to increase the availability, and use of promising interventions.

Salmonella risks pre-harvest: recommendations II

Key recommendations to funding agencies

- **Fund large field trials** on commercial operations for interventions that may be promising but currently lack efficiency data, particularly for hard-to-address issues such as *Salmonella* in swine.
- Increase funding to study the **basic science, mechanism of action, and ancillary benefits** associated with poorly understood yet promising interventions such as pre- and probiotics.
- Consider incentives to **spur research and development** in the pre-harvest food safety area, by providing, for instance, grants and fostering private-public partnerships.

Salmonella risks pre-harvest: recommendations III



Key recommendations to industry

- Consider individual pre-harvest interventions as one part of an **animal health and management program**, in the context in which they will be used (e.g., animal species and age group, production system), along with potential synergisms or antagonisms between interventions. Evaluate whether ancillary benefits may be achieved, such as improvements in overall animal health that may reduce treatment costs and animal losses.

- Provide adequate biosecurity, feed and water safety, and basic animal health standards as a pre-requisite for the production of meat and poultry on farms and feedlots.

Questions or Comments?

For questions or comments please contact:

Karin Hoelzer, DVM, PhD
Officer, Health Programs
The Pew Charitable Trusts
901 E Street, NW, Washington, DC 20004
p: 202-540-6986 | *e:* khoelzer@pewtrusts.org |
www.pewtrusts.org

"Is the asparagus farm-raised or wild-caught?"

Source: New Yorker, 12/06/2004