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Emerging microbiological food safety issues related to meat

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Abstract

Avian influenza viruses and antibiotic-resistant pathogens have become topics of current public health interest. This paper will focus on the significance of these pathogens to the meat industry as well as other emerging microbiological food safety topics likely to impact the meat industry. These include surveillance of foodborne pathogens, microbial source tracking, risk assessment, and human populations at increased risk of infection by foodborne microbes. These emerging issues will likely lead to even greater challenges to producing microbiologically safe meat products than the industry has ever experienced. However, accompanying such challenges will be innovative solutions that provide even greater public health protection to meat-containing foods.

Keywords: Avian flu; Antibiotic resistance; Surveillance; Microbial source tracking; Food attribution; Sensitive populations

1. Introduction

''Emerging'' is a relative term that is dependent on an individual's perspective of time. For the purposes of this paper, the emerging microbiological food safety issues to be addressed will be those subject areas that have grown to increasingly dominate food safety discussions during the past decade and consequently have had and will likely continue to have a major influence on food safety management practices. The first issues addressed in this paper, avian flu and antibiotic resistance are principally issues affecting the meat industry, whereas the concept of food attribution covering microbial source tracking, surveillance, risk assessment, and sensitive populations at increased risk of foodborne microbial infections, is a global issue that affects the entire food industry.

2. Avian flu

The most dominant issue currently affecting the poultry industry is avian flu with the highly-pathogenic avian influenza (HPAI) viruses contributing to a number of recent outbreaks in the poultry sector. While most avian influenza strains are of low pathogenicity and are considered benign in their natural habitats, HPAI-viruses can cause severe disease in poultry and occasionally humans with death in poultry occurring within 2–3 days of infection. Grouped on the basis of the antigenic relationships of the haemoglutinin (HA) and neuraminidase (NA) surface glycoproteins, there are at present 16 H subtypes and 9 N subtypes of avian influenza virus, with the most threatening being the HPAI H5N1 strain. It was originally thought that avian viruses (influenza A) could not directly infect humans because the human viruses (influenzas B and C) bound to epithelial cells in the human respiratory tract through a α-2,6 linkage between sialic acid and galactose, whereas the avian viruses bound to α-2,3 linkages found in duck epithelium. Consequently, to explain the influenza pandemics occurring in 1918, 1957, and 1968, the pig mixing vessel was proposed where reassortment of the virulent genes in avian and human viruses could occur in swine which has both types of receptors (Ito et al., 1998). In contrast to reassortment, however, the recent spread of avian influenza is attributed to the Z genotype of H5N1 viruses that is believed to have arisen from a process referred to

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as antigenic drift in which mutations in the RNA polymerase (PB2), insertions in the HA gene, and deletions in the NA and non-structural (NS) genes have occurred (Chen et al., 2005; Liu et al., 2005). Concomitant with these genetic changes, the ability of the influenza viruses to adapt to different animals has been evident (Hulse-Post et al., 2005; Sturm-Ramirez et al., 2005). For example, in addition to infecting the respiratory tract of ducks, these viruses also infect their intestinal tracts with a higher viral load at the trachea than the cloaca. Shedding of viruses by ducks also occurs over a longer period of time (up to 17 days) in contrast to the 2–5 days that occurred previously. More importantly, increased virulence to mammals has been shown to accompany these genetic changes (Maines et al., 2005).

As of February 27, 2006, 174 human cases in Cambodia, China, Indonesia, Iraq, Thailand, Turkey, and Vietnam had been reported to the World Health Organization (WHO) of which 93 were fatal (WHO, 2006a). Humans acquire avian influenza viruses primarily through direct contact of the mucous membranes with infectious secretions and excreta from infected birds or contaminated poultry products (Perdue & Swayne, 2005). Examples of these pathways include:

- Inhalation of dust generated from feces or respiratory secretions of infected poultry in the poultry farm environment.
- Inhalation of fine water droplets produced during slaughter and processing, especially at wet markets.
- Hand-to-mucous membrane (oral or nasal mucous membranes or the conjunctiva) transfer of feces or respiratory secretions of infected poultry from shoes, clothing, or environmental sources.
- Mucous membrane or inhalational exposure via mouth suction of clogged nasal passages of fighting cocks.
- Mucous membrane exposure through consumption of raw undercooked blood, organs, or meat.

The main portal of entry appears to be the upper respiratory tract and conjunctival mucosa (Wong & Yuen, 2006). Most patients have been healthy young children or adults with clinical symptoms that include an initially high fever and lower respiratory tract symptoms (i.e. cough, difficulty in breathing, chest pain, and wheezing). Upper respiratory tract symptoms (i.e. sneezing and nasal congestion) are present only occasionally. Watery diarrhea without blood or inflammatory changes is more common than in influenza caused by human viruses and may precede respiratory manifestations by up to 1 week. Death occurs on average 9–10 days after the onset of illness (range 6–30 days) and most patients die from progressive respiratory failure (WHO, 2005a).

Enormous press coverage has raised fears of the potential for avian viruses to become pandemic strains whereby human-to-human transmission would occur unabated. To date, three observed features of the H5N1 strain appear to be responsible for some restriction on its widespread transmission (Perdue & Swayne, 2005). First, not all H5N1s are infecting people but appear to be restricted to the Z genotype. Second, it is estimated that there have been millions of exposures, but relatively few infections implying that there is a dose–response restriction or a host restriction. Third, clusters indicate that very close contact is required to infect other humans, and thus far this has occurred only with blood relatives. While these features moderate its potential for a pandemic, recent studies suggest that transmission may be more common than anticipated and involve low-level infections (Thorson, Petzold, Chuc, & Ekdahl, 2006). For example, Puzelli et al. (2005) demonstrated through a multiplicity of serological tests following the outbreak in Europe of the HPAI virus strain, H7N7, that many exposed poultry workers who did not become ill were seropositive for this strain. Moreover, intensified surveillance of patients in northern Vietnam using the reverse-transcriptase-polymerase-chain reaction (RT-PCR) assay has led to the detection of mild cases, more infections in older adults, and an increased number and duration of clusters in families (WHO, 2005b).

Notwithstanding the public health implications, the poultry industry has been directly impacted by H5N1 virus outbreaks. To date, more than 140 million domesticated birds have been killed by the virus or culled to stem its spread (Webster, Peiris, Chen, & Guan, 2006). Costs associated with measures designed to impede or monitor the presence of the virus are significant. For example, economic losses associated with the H7N7 influenza outbreak in the Netherlands were estimated at 270 million Euro (Thomas et al., 2005). Moreover, national surveillance programs for the European Union in 2006 to conduct 60,000 tests in wild birds and 300,000 in domestic birds will require nearly 1.97 million Euro (MeatNews, 2006) while the World Bank estimates that between US $1.2 billion and US $1.5 billion will be needed over the next 3 years to upgrade both local surveillance and laboratory capabilities in developing countries (Normille, 2006). In countries where poultry is exported, restrictions in international trade have compounded the problem and affected employment. Fears about potential zoonotic spread have also reduced demand for poultry products in the countries affected (Rushton, Viscarra, Guerne Bleich, & McLeod, 2005).

To stem avian influenza outbreaks, several management practices have been implemented by the European Union (Hafez, 2005). Once the presence of avian influenza has been officially confirmed in a quarantined flock, all poultry in the flock should be killed without delay and all poultry killed or which have died from the infection should be destroyed in a manner that minimizes the risk of spreading the disease such as composting or incineration (Canada MAFF, 2004). Substances or waste, such as eggs, animal feed, litter, or manures, that are liable to be contaminated should also be destroyed or treated appropriately. Subsequently, all buildings used for housing poultry, their surroundings, the

vehicles used for transport and all equipment likely to be contaminated should be cleaned and disinfected. Fortunately, several disinfectants (phenolic disinfectants, a quaternary ammonium compound, Virkon – a blend of peroxygen compounds, and sodium hypochlorite) have proved effective in inactivating avian influenza viruses at recommended concentrations (Suarez et al., 2003). Reintroduction of poultry to the holding area may occur 21 days after completion of the disinfection. Such precautions are warranted in light of the identification of contaminated fomites as potential vehicles for transfer between farms (Thomas et al., 2005) and the survival of HPAI viruses in manure, water, soil, and contaminated equipment for at least 35 days (Ausvetplan, 2004).

The second management strategy to forestall the spread of avian influenza in affected areas is quarantine of non-infected poultry (WHO, 2004a). In recent months, evidence has mounted that at least some migratory waterfowl are directly spreading the H5N1 virus to parts of Central Asia and Europe (Chen et al., 2005; Liu et al., 2005; Wong & Yuen, 2006). Since culling migratory birds is not acceptable to any international authority, increased biosecurity is warranted. An alternative measure or one that may be used in addition to quarantine is vaccination. By increasing the resistance of birds to infection and decreasing the amount of virus shed in the environment, vaccination has proven to be an effective control measure (van der Goot, Koch, de Jong, & van Boven, 2005). Unfortunately, both good and bad agricultural vaccines have been advocated for use (Webster et al., 2006). Bad agricultural vaccines prevent disease signs but do not prevent shedding of transmissible levels of virus. The resurgence of H5N1 in Indonesian poultry and pigs (Cyranoski, 2005) and the detection of H5N1 in apparently healthy birds in live poultry markets in China (Chen et al., 2005) suggest that the vaccines used in these areas were of suboptimal quality or that coinfection masked disease. Improper application of vaccines could also be responsible for resurgence in infections. Generally, the immunity induced by vaccination is of short duration and it is necessary to inject the vaccine into each bird several times during one rearing period (Hafez, 2005). Since vaccination has been primarily with killed whole virus-adjuvanted vaccines, another limitation of vaccination is an inability to differentiate infected from vaccinated animals. This limitation has complicated surveillance efforts and often resulted in trade restrictions for those countries employing vaccination (Suarez, 2005).

Experimentally, low-pathogenicity avian influenza (LPAI) viruses cause localized viral infections in respiratory and gastrointestinal (GI) tracts of chickens but do not infect tissue (Swayne & Beck, 2005). HPAI viruses will also cause respiratory and GI tract infections; however, systemic spread occurs with high titers being detected in blood, bone marrow, and breast and thigh meat (Swayne & Beck, 2005). HPAI virus may also be found inside and on the surface of eggs laid by infected birds in the early phase of the disease (WHO, 2005c). For these reasons, the World Organization for Animal Health (OIE) recommends that poultry products not be traded from HPAI infected countries unless they are treated to inactivate the virus (Office International des Epizooties, 2003). Such precautions are justified based on studies in which feeding H5N1 virus-infected breast meat to other chickens resulted in virus infection and death (Swayne & Beck, 2005). Consequently, thermal inactivation is recommended for infected eggs and poultry meat with levels of inactivation dependent on virus concentration and virus strain (Swayne, 2006; Swayne & Beck, 2004). Based on D_t values (Table 1), HPAI virus was inactivated in liquid egg products using industry standard pasteurization protocols (e.g. whole egg, 60 °C, 210 s; liquid egg white, 55.6 °C, 372 s; 10% salted yolk, 63.3 °C, 210 s); however, HPAI virus was not inactivated completely in dried egg whites when using the low-temperature industry pasteurization protocol (54.4 °C, 7–10 days) (Swayne & Beck, 2004). HPAI viruses are inactivated in poultry meat by heating to an internal temperature of 70 °C for a minimum of 1 s (Swayne, 2006). Proper usage of vaccines, however, can prevent HPAI virus from infecting muscle tissue (Swayne & Beck, 2005). Importantly, HPAI-contaminated poultry that is properly handled and cooked is safe to eat.

Table 1
D_t values (time to reduce virus titre by 90%) for four egg products infected with HPAI H5N2 (Swayne & Beck, 2004)

Egg product	Temperature (°C)	D_t
Whole egg	60	27.2 s
Whole egg blends	60	27.2 s
Liquid egg white	56.7	331 s
10% salted yolk	62.2	<20 s
Dried egg white	54.4	3.1 days

3. Antibiotic resistance

Another issue that has plagued the animal husbandry industry is the use of antibiotics for animals and their potential to generate antibiotic-resistant pathogenic bacteria that can transfer to humans. Despite the lack of consensus on this issue, regulatory policies are continuing to be invoked that ban the use of antibiotics in animals. For example, the US Food and Drug Administration withdrew on September 12, 2005 its approval for use of fluoroquinolones in treating poultry. This decision marked the first time in 35 years that an approval for use of an animal drug was withdrawn due to its public health impact and concerns with antimicrobial resistance affecting humans.

There are several public health issues associated with the development and persistence of antibiotic-resistant foodborne pathogens. In the first case, treatment failure or a delay in treatment of an infection may occur if treatment includes antibiotics to which the pathogen has acquired resistance. In these circumstances, there are reduced therapeutic options for those patients infected by antibiotic-resistant pathogens. Another manifestation that often occurs with antibiotic-resistant pathogens is an increased severity of symptoms in

Table 2
Increased severity of illness in patients with antibiotic-resistant zoonotic pathogen infections compared to antibiotic-sensitive pathogen infections

Pathogen	Test population	Health consequence	Reference
Ciprofloxacin-resistant *Campylobacter*	740 persons identified in FoodNet site	Increased duration of diarrhea	Nelson et al. (2004)
Fluoroquinolone-resistant *Campylobacter*	36 patients	14 days compared to 9 days for duration of diarrhea	Engberg et al. (2004)
Campylobacter	Denmark – 3471 infections		Helms et al. (2005)
Quinolone-resistant		6× increased risk of adverse event within 30 days of receipt of clinical specimens	
Erythromycin-resistant		5× increased risk of adverse event within 90 days of receipt of clinical specimens	
MDR *Salmonella Typhimurium*	2047 patients in Danish Civil Registry system (1995–1997)		Helms et al. (2002)
Quinolone-resistant		10× greater mortality than general population for patients with gastrointestinal illness	
R-type ACSSuT + Nx (quinolone) resistant		13.1× greater mortality than general population for patients with gastrointestinal illness	
MDR *Salmonella Typhimurium* R-type AK/CSSuT	440 cases in Canada (12/99–11/00)	2.3× greater hospitalization	Martin et al. (2004)
MDR *Salmonella Typhimurium* DT104	Atlanta, Georgia health care system (1995–1999)		Fisk et al. (2005)
	50 cases – general population	83% vs. 50% occurrence of bacteremia	
	32 cases – HIV population	95% vs. 66% occurrence of bacteremia	
Non-Typhi *Salmonella* Resistant to ⩾1 clinically important antibiotic	*Salmonella* infections reported to U.S. National Antimicrobial Resistance Monitoring System (NARMS) and FoodNet, 1996–2001	1.6× increased occurrence of sepsis 3.1× increased occurrence of hospitalization	Varma et al. (2005)

the infection (Table 2). In such cases, increased severity may be associated with co-selection of virulence traits (e.g. toxin-encoding genes) when antibiotic resistance genes are selected. For example, multiple-antibiotic resistance (MDR) in *Salmonella Typhimurium* DT104 is conferred by an antibiotic resistance gene cluster carried by a chromosomal genomic island, SGI1. Besides the antibiotic resistance genes, other genes are also present on the cluster that encode for proteins of unknown function that may contribute to the virulence of this pathogen (Boyd et al., 2001).

Antibiotic resistance in bacteria is an inevitable side effect to the use of antibiotics and is attributed to the adaptability of bacteria to their environment. Resistance may be caused by a large number of induced mechanisms that include decreased antibiotic accumulation through changes in the pathogen's membrane permeability, physical modification or destruction of the antibiotics, alteration of the enzyme target of antibiotic action, or active efflux of antibiotics. Acquisition of antibiotic resistance occurs either through point mutations (intrinsic) or through horizontal transfer of mobile elements (plasmids, transposons, and bacteriophages). These mobile elements can collect and recombine numerous resistance gene cassettes in almost any combination. Consequently, treatment with one antimicrobial agent can enrich the population for bacteria resistant not only to that specific agent, but also to all antimicrobial agents whose resistance genes are genetically linked to the agent used (i.e. present as a cluster of genes on the same mobile element).

Several antibiotic-resistant pathogens that have been associated with animals used for food and are of public health concern include ciprofloxacin-resistant *Campylobacter*, extended-spectrum cephalosporin-resistant *Salmonella* and *Escherichia coli*, multi-drug resistant (MDR) *Salmonella Typhimurium* DT104 (R-Type ACSSuT), and MDR *Salmonella* Newport (R-Type MDR-AmpC). Normally, *Campylobacter* infections are self-limiting and therefore treatment with antibiotics is generally not required. Nevertheless, there are occasions where antibiotic therapy may be necessary and under those conditions patient recovery could be complicated by antimicrobial resistance. In the case of *E. coli* O157:H7, on the other hand, antibiotic resistance is not considered a public health concern because antibiotics are not typically used in treatment of *E. coli* O157:H7 infection so as to avoid exacerbation of the illness (such as renal failure) from antibiotic-induced increase in Shiga toxin levels.

To provide some perspective on the magnitude to which antibiotic-resistant pathogens contribute to foodborne illness, case rate data for several pathogens and time periods are provided in Table 3. In general, antibiotic-resistant pathogens comprise less than half the number of total cases. Of these, the proportion of cases of antibiotic-resistant *Salmonella* spp. and *Salmonella Typhimurium* have decreased, whereas the proportion of cases of antibiotic-resistant *Salmonella* Newport and *Campylobacter* spp. have increased. The relative distribution of antibiotic-resistant strains within clinical isolates is shown in Tables 4–6 along with

Table 3
Changes in the incidence of foodborne illness and corresponding changes in prevalence of antibiotic-resistant foodborne pathogens in the US (IFT Expert Panel, 2006)

Pathogen	Antibiotic-sensitive and antibiotic-resistant			Antibiotic-resistant only			
	Case rate (per 100,000)		Relative change (%)	Case rate (per 100,000)		Relative change (%)	Antibiotic test conditions
	1996–1998	2004		1996	2002		
Salmonella spp.	15.9	14.7	↓ 8	4.9	2.4	↓ 51	2 or more antibiotics
Salmonella Typhimurium	4.9	2.9	↓ 41	1.7	0.6	↓ 65	ACSSuT
Salmonella Newport	1.2	1.7	↑ 41	0.1	0.4	↑ 300	2 or more antibiotics
Campylobacter spp.	18.7	12.9	↓ 31%	2.4	2.6	↑ 8%	Ciprofloxacin

the relative distribution of antibiotic-resistant strains in meat products. Based on these data, antibiotic-resistant pathogens are more dominant in meat than in human specimens, suggesting that meat may serve as a significant source of these pathogens in human illnesses. Case–control studies also point to exposure to food-producing animals or animal food products as a risk factor in acquiring antibiotic-resistant infections. For example in MDR *Salmonella Typhimurium* DT104 infections, analysis of 1996–1997 FoodNet data identified consumption of eggs prepared outside the home during the 5 days preceding the illness as a risk factor (Glynn et al., 2004). In a case–control study of Canadian sporadic cases of diarrheal illness caused by *Salmonella Typhimurium* DT104 between 1999 and 2000, living on a livestock farm was identified as a risk factor (Doré et al., 2004). Similarly, exposure to a dairy farm was identified as a risk factor for acquiring MDR *Salmonella* Newport infections resistant to cephalosporins (Gupta et al., 2003).

Table 4
Trends in percentage of antibiotic-resistant *Salmonella Typhimurium* isolated from human cases, animals and animal products, and retail meats in the United States (NARMS-CDC, 2002; NARMS-FDA, 2002; NARMS-USDA, 2003)

Antibiotic(s)	Humans		Animals and products			Retail meat
	1996	2002	1997	1999	2003	2002
None of 14 agents	36	60				
ACSSuT	34	21		35	25	
Ciprofloxacin	0	0	0	0	0	0
Ceftiofur	4	4	2		27	20
Ampicillin	50	34	61	63	56	18
Tetracycline	49	32	64	64	46	46
Trimethoprim-sulfa	4	2	4	9	5	0

Table 5
Trends in percentage of antibiotic-resistant *Salmonella* Newport isolated from human cases, animals and animal products, and retail meats in the United States (NARMS-CDC, 2002; NARMS-FDA, 2002; NARMS-USDA, 2003)

Antibiotic(s)	Humans		Animals and products			Retail meat
	1996	2002	2000	2002	2003	2002
None of 14 agents	82	73				
MDR-Amp C	0	22				
Ciprofloxacin	0	0	0	0	0	0
Ceftiofur	4	22	75	78	74	62
Ampicillin	6	24	76	80	74	62
Tetracycline	8	25	78	83	77	62
Trimethoprim-sulfa	4	4	19		2	0

Table 6
Trends in percentage of antibiotic-resistant *Campylobacter* isolated from human cases, animals and animal products, and retail meats in the United States (NARMS-CDC, 2002; NARMS-FDA, 2002; NARMS-USDA, 2003)

Antibiotic(s)	Humans		Animals and products			Retail meat
	1996	2002	1998	2002	2003	2002
None of 5 or 6 agents	48	49				60
Tetracycline	47	40	60	46	49	
Ciprofloxacin	13	20	13	18	17	14
Erythromycin	1	2	10	7	9	6

The presence of antibiotic-resistant bacterial populations in food animals is consistent with the large quantities of antimicrobial agents used in this sector. For example, the European Federation of Animal Health estimated that the amount of antimicrobial agents used in 1999 for non-human medicine in the EU was 35% of the total usage (Shryock, 2003). Supplementing animal feed with antibiotics is estimated to constitute more than half the total amount of antimicrobials used worldwide (Wegener, Aarestrup, Bogø Jensen, Hammerum, & Bager, 1999). The primary use of antimicrobials in food animal production is to treat infectious diseases that are occurring in animals. In addition, antimicrobials may also be applied prophylatically to prevent infectious diseases for which vaccines are not available or effective. Prophylatic treatments are beneficial given the high stocking densities used in the production of food animals. In their absence, severe economic losses and unacceptable animal suffering, together with the risk of widespread epidemics, could occur. The most disputed application of antimicrobials in food animals, however, has been their use as growth promoters or performance enhancers. Possible mechanisms by which antibiotics promote growth include improved digestive efficiency due to a shift in the microbial ecology of the gut, controlling growth of anaerobes, stimulating

the immune system, or responding to a subclinical, undiagnosed infection (Gaskins, Collier, & Anderson, 2002).

Evidence linking veterinary usage of antimicrobials with antibiotic-resistant bacterial populations is strongest for fluoroquinolone-resistant *Campylobacter*. In this case, introduction of enrofloxacin in the poultry industry coincided with the increase in human cases involving fluoroquinolone-resistant *Campylobacter* (Aarestrup et al., 1998; Endtz et al., 1991; Nachamkin, Ung, & Li, 2002). Not to be discounted, however, is that application of the fluoroquinolone used for humans, ciprofloxacin, also increased during this period. Experimental studies have provided unequivocable evidence that fluoroquinolone treatment of *Campylobacter*-colonized broiler flocks induces fluoroquinolone resistance (Humphrey et al., 2005; Jacobs-Reitsma, Kan, & Bolder, 1994). In a recent study, five United Kindgom commercial broiler chicken flocks were treated in their drinking water for a clinically relevant infection by a 5-day application of either difloxacin or enrofloxacin fluoroquinolones (10 mg/kg body wt/bird). Before treatment, the prevalence of ciprofloxacin-resistant *Campylobacter* in feces was 16.7%, whereas during treatment it was 83%, and 1–4 weeks after treatment it was 88%, 80%, 40%, and 52%, respectively (Humphrey et al., 2005). Decreases in the presence of fluoroquinolone-resistant *C. jejuni* in chicken meat, on the other hand, has been attributed to the recently reduced application of fluoroquinolones to poultry (Andersen et al., 2006).

With the exception of ciprofloxacin resistance, there is a paucity of scientific evidence to document the association of antimicrobial agents used in veterinary medicine with increases in antimicrobial-resistant pathogens (Phillips et al., 2004). For example, it has been suggested that the increased prevalence of extended-spectrum cephalosporin-resistant strains is in part related to the use in food animals of ceftiofur, which is an extended-spectrum cephalosporin approved for use in veterinary medicine (White et al., 2001); however, scientific evidence is lacking. Antimicrobial agents used for intensive calf rearing in the 1970–1980s have also been speculated to contribute to the emergence of multiple-antibiotic resistant *Salmonella Typhimurium* DT104 strains. Genes included in the antibiotic resistance gene cluster of *Salmonella Typhimurium* DT104 confer resistance to four of the five antimicrobials used during that time to treat veal calves, therefore co-selection of the entire cluster could have arisen from the use of any one of those drugs (Velge, Cloeckaert, & Barrow, 2005). While there is no definitive evidence for this scenario, several reviews have been published presenting contrasting views regarding the role of veterinary usage of antimicrobials in the emergence of antibiotic-resistant foodborne pathogens. In support of a causal relationship are reviews by Angulo, Nargund, and Chiller (2004) and Mølbak (2004), whereas reviews by Phillips et al. (2004) and Wassenaar (2005) advocate that veterinary usage of antimicrobial agents are inaccurately incriminated as being a major contributor to antibiotic-resistant pathogens in humans. Debate on this topic will continue but should consider the additional routes which lead to resistant bacterial populations, that antimicrobial usage in animals is required for animal health and well-being, and that not every antimicrobial-resistant pathogen has human health consequences. On this latter point, clearly not all infections caused by resistant pathogens fail to respond to treatment. For example, in a study of 23 diarrhea cases in Thailand, nearly all were infected with ciprofloxacin-resistant *Campylobacter*, yet 58% of patients receiving ciprofloxaxin treatment were cured. This response implies that treatment with ciprofloxacin could still be effective in many cases (Sanders et al., 2002). Another consideration is that acquisition of drug resistance could entail a biological cost to the pathogen resulting in reduced fitness and competitiveness in the absence of antibiotic selection pressure. For example, most data on *E. coli* suggest that increased antibiotic resistance results in decreased fitness (Wassenaar, 2005). Alternatively, for some foodborne pathogens such as fluoroquinolone-resistant *C. jejuni*, resistance can be neutral or even beneficial in terms of fitness (Luo et al., 2005). When coinoculated into chickens, fluoroquinolone-resistant *Campylobacter* isolates either outcompeted or were outcompeted by most of the fluoroquinolone-susceptible strains, with the outcome being dependent on the genetic background of the recipient strain. These variable results highlight the complex nature of antibiotic resistance and the large data gaps that exist in making informed scientific decisions on use of antimicrobials in animals used for food.

4. Food attribution

The capacity to attribute cases of foodborne disease to the food vehicle or other source responsible for the illnesses is known as food attribution. Several of the major tools used for food attribution studies include microbial source tracking and surveillance that in turn are used in risk assessment studies. Limitations to these approaches have been discussed by the Food Attribution Working Group (Batz et al., 2005) and include the lack of a common food categorization scheme, underreporting of sporadic illnesses, and undercollection of stool specimens from ill patients to identify the pathogen and facilitate traceback to the contaminated food. Despite these limitations, significant advancements have been made with food attribution tools and are vital components to the prioritization of hazards and interventions in food systems.

4.1. Microbial source tracking

The concept of tracing pathogens to their origin using microbiological, genotypic, and phenotypic methods has been termed microbial source tracking (MST). MST methods are increasingly being used to identify sources of contamination ranging from animal facilities to food attribution studies. For example, there have been many food- and water-borne disease outbreaks in which contaminated manure was the original source of the pathogens (Table 7). With any of these events, MST methods would enable

traceback of pathogens to their source of contamination whether that source is human or animal waste. As an example of the potential benefit to source tracking, MST tests on water samples taken from various sites at Sedona Creek, Arizona revealed that leaking septic tanks were not the main source of high coliform bacteria counts. Rather, the main culprits were animals, with raccoons contributing 30–35% of the coliform bacteria and other animals, including skunks, coyotes, elks, horses, and even llamas contributing another 50%. Humans were responsible for only 16% of the bacteria (AWRN, 2003).

A major underlying assumption behind MST methodologies is that certain subgroups of bacteria become adapted to a particular host or environment, such as the intestinal tract, for various reasons, including differences in pH, availability of nutrients, and receptor specificity. The initial approach used to differentiate bacteria adapted to different hosts was to enumerate specific groups of indicator species, including sorbitol-fermenting *Bifidobacterium*, *Rhodococcus coprophilus*, F + RNA coliphage serotypes, phages of *Bacteroides fragilis*, and host-specific viruses (Long & Plummer, 2004; Fong, Griffin, & Lipp, 2005). A second approach was to utilize genotypic methods. Presumably, once microorganisms become adapted to a particular environment and establish residency, the progeny produced by subsequent replications will be genetically identical. Therefore, over time, a group of microorganisms within a particular host or environment should possess a similar or indistinguishable genetic fingerprint, which will differ from those microbes adapted to a different host or environment. The same type of rationale is used for microbial source tracking methodologies that address phenotypic differences within different lineages of bacteria except in this case the focus is on traits that may have been acquired from exposure to different host species or environments (Scott, Rose, Jenkins, Farrah, & Lukasik, 2002).

A number of MST genotypic methods have been investigated and include pulsed-field gel electrophoresis (PFGE), repetitive element PCR, ribotyping, and host-specific molecular markers (Scott et al., 2002). With these procedures, success often depends on the size of the reference fingerprint database that is being used for comparison, the choice of methods used for image analysis and pattern recognition, and the statistical methods used for comparison of environmental isolates with the reference collection (Lu, Lapen, Scott, Dang, & Topp, 2005). In the case of many phenotypic MST methods (biochemical tests, phage susceptibility, outer membrane protein profiles, antibody reactivity, fimbriation, and bacteriocin production and susceptibility), they are fraught with serious disadvantages including unstable phenotypes, low sensitivity at the intraspecies level, and limited specificity (Scott et al., 2002). Other phenotypic MST methods that are more promising include antibiotic resistance screening and fatty acid profiling of bacterial communities. Antibiotic resistance methods are based on the underlying principle that the bacterial flora present in the gut of various types of animals are subjected to different types, concentrations, and frequencies of antibiotics (Wiggins et al., 2003). Consequently, selective pressure within a specific group of animals selects for flora that possess specific "fingerprints" of antibiotic resistance; however, reference databases tend to be geographically specific. Fatty acid profiling methodology, on the other hand, is based on the assumption that the fatty acid profiles in the bacterial flora of animals are host specific due primarily to the variations in dietary habits and unique environments that the hosts provide (Haznedaroğlu, Zitomer, Hughes-Strange, & Duran, 2005). Again, large libraries of isolates from known hosts are required. Both the creation of national databases and further study of factors contributing to variable fingerprints will prove valuable to improving the utility of MST methods in the food industry.

4.2. Surveillance of foodborne pathogens

To minimize food safety risk to consumers particularly with respect to the global food supply, surveillance of foodborne disease is becoming an increasingly high priority in the public health and food safety agenda in many countries. A variety of surveillance systems exist but the most common form encountered throughout the world is epidemiologic surveillance wherein the incidence of specific illnesses is monitored. Depending on the public health system, mandated reporting of illnesses may be involved or the occurrences of illnesses may be passively collected through physician notification. In general terms, foodborne disease surveillance is essential for: (1) estimating the burden of foodborne disease, and monitoring trends; (2) identifying priorities and setting policy in the control and prevention of foodborne diseases; (3) detecting, controlling, and pre-

Table 7
Examples of human outbreaks with manure as a suspected source between 1989 and 2000 (Smith & Perdek, 2004)

Pathogen	Location	Year	Suspected source	Impact
Cryptosporidium parvum	Carrollton, GA, USA	1989	Manure runoff	13,000 cases
	Swindon and Oxfordshire, UK	1989	Runoff from farm fields	>516 cases
	Bradford, UK	1994	Storm runoff from farm fields	125 cases
Escherichia coli O157:H7	Cabool, MO, USA	1990	Water line breaks in farm community	243 cases, 4 deaths
	Maine and others, USA	1993	Animal manure spread in apple orchard	Several illnesses
Escherichia coli O157:H7 and *Campylobacter* spp.	Washington County, NY, USA	1999	Runoff at fairgrounds	116 cases, 2 deaths
	Walkerton, ON, Canada	2000	Runoff from farm fields entering town's water supply	2300 cases, 6 deaths

venting foodborne disease outbreaks; (4) identifying emerging food safety issues; and (5) evaluating foodborne disease prevention and control strategies (WHO, 2001). Some examples of epidemiologic surveillance systems are listed in Table 8. In addition to the programs addressing human illnesses, epidemiologic surveillance of diseases in animal populations is also important as such data is used for both implementation and evaluation of disease control programs as well as for international trade. In regards to this latter point, for a country to place restrictions on international trade, it must be able to provide scientific evidence of its status of freedom from the animal disease or diseases of concern. Irregardless, globalization of the food supply has necessitated development and expansion of active surveillance programs for both animal and human diseases. Consequently, at the 53rd World Health Assembly, WHO adopted a resolution to recognize food safety as an essential public health function and called for the development of a global strategy for reduction of the burden of foodborne disease (WHO, 2000). In resolution WHA 53.15, member states were encouraged to implement national, and when appropriate, regional mechanisms for foodborne diseases surveillance. In light of this resolution, a survey was conducted in 2002 to assess the need for and the feasibility of a European network on *Listeria* infections in humans (de Valk et al., 2005). The conclusion from that survey was that

Table 8
Selected examples of national and international surveillance systems in public health and food safety programs and their roles

Type of surveillance Surveillance system	Description
Epidemiological surveillance	
FoodNet	A collaborative project of the US Centers for Disease Control and Prevention, the United States Department of Agriculture, the US Food and Drug Administration, and 10 sites within the United States. More than 650 clinical laboratories in the FoodNet sites are contacted regularly to collect information on laboratory-confirmed cases of diarrheal illness. Pathogens m onitored include *Salmonella*, *Shigella*, *Campylobacter*, *Escherichia coli* O157, *Listeria monocytogenes*, *Yersinia enterocolitica*, *Vibrio*, *Cryptosporidium*, and *Cyclospora*.
Enter-net	Conducts surveillance for enteric infections (*Salmonella* and VTEC O157) within Europe. Over 25 European countries are participating together with Canada, Japan, South Africa, Australia and New Zealand.
National Animal Health Reporting System	US-based system designed to provide data from chief state animal health officials on the presence of confirmed Office International des Epizooties (OIE) LIST A and B clinical diseases in specific commercial livestock, poultry, and aquaculture species in the United States. It is intended to be one part of a comprehensive and integrated animal-health surveillance system.
Laboratory surveillance	
PulseNet	A national network of public health and food regulatory agency laboratories coordinated by the US Centers for Disease Control and Prevention. The network consists of state health departments, local health departments, and federal agencies. Participants perform standardized molecular subtyping of foodborne disease-causing bacteria by pulsed-field gel electrophoresis (PFGE). DNA "fingerprints" are submitted electronically to a dynamic database. Databases are on-demand to participants and allows for rapid comparison of PFGE patterns.
WHO Global Salm-Surv	Global network of laboratories and individuals from 141 countries involved in surveillance, isolation, serotype identification, and antimicrobial resistance testing of *Salmonella*, *E. coli*, and *Campylobacter*.
National Antimicrobial Resistance Monitoring System (NARMS)	A system based in the US that monitors changes in susceptibilities to 17 antimicrobial drugs of zoonotic enteric pathogens from human and animal clinical specimens, from healthy farm animals, from carcasses of food-producing animals at slaughter, and from isolates from samples of retail foods. The system includes a veterinary arm, a human arm, and a retail food-monitoring arm.
eLEXNET	A secure, integrated, web-based data exchange system for food safety inspection data, and a repository for analytical methods. It is hosted by the US Food and Drug Administration and enables multiple agencies to assess risks and analyze trends from stored data. As of January, 2005, there were 113 laboratories representing 50 states and the District of Columbia.
Global Environmental Monitoring System (GEMS)	Began as a joint project between FAO, the United Nations Environment Programme, and WHO in 1976. GEMS' purpose is to compile data on food contamination and human exposure from different countries for global synthesis, evaluation, and presentation.
Animal surveillance	
ANIMO	Computerized tracking system used in the European Union to monitor movements of animals within the EU. When animals are slaughtered, the abattoir notes the animal data in its records and has a system of traceability enabling it to link carcass to animal. The carcasses are stamped to identify the abattoir of origin. Meat for the market has an accompanying document stating the establishment of origin and the establishment of destination. This system is repeated at each subsequent level of product processing.
Australia's National Livestock Identification Scheme (NLIS)	Uses electronic ear tags or rumen boluses to individually identify and trace cattle. By this method, individual animal movements can be recorded on a central database and tracked from property of birth to slaughter.
Collaboration in Animal Health and Food Safety Epidemiology (CAHFSE)	Currently, blood and fecal samples are being collected quarterly from swine on sentinel farms in five states in the US. On-farm and in-plant trends in the prevalence of *Salmonella*, *Campylobacter*, generic *E. coli*, and *Enterococcus* spp. are being monitored and isolates are being characterized as to their genetic relatedness and their susceptibility to antibiotics. Findings are being related to on-farm management practices, including patterns of antibiotic use in market swine.

a common database would be feasible and would facilitate detection of widespread outbreaks involving many countries. Similarly, WHO (2001) has advocated that linking existing foodborne disease networks in a "network-of-networks" should enable rapid dissemination of information on urgent matters, such as outbreak alerts, as well as facilitate exchange of information on technical and methodological matters between networks (2001). In conjunction with the development of these new surveillance systems and the improvement of current surveillance systems, efforts are also underway to develop uniform case definitions and standardize diagnostic and typing methods (COST, 2000; de Valk et al., 2005). Submission of data through electronic communication has facilitated extensive sharing between countries and will be instrumental in the further development of regional and international collaborative efforts toward advancing public health protection.

Another type of surveillance system found in public health and food safety programs is laboratory-based. Currently, these systems are in a stage of active growth with some of the most recognized systems being those listed in Table 8. Integration of food monitoring data is a daunting task; however, by virtue of information technology, large volumes of data can readily be managed and stored to allow timely and thorough analysis on institutional, regional, national, and global levels (Sahm, Thornsberry, & Karlowsky, 2003). As was the case for disease surveillance programs, one of the major impediments is standardization of methods used to collect and manage data. Recognizing this problem, the US President's Council on Food Safety (2001) listed as one of its objectives and action items the development of national standards and the identification of state and local standards and regulations that should be applied within national standards. Canada has also recognized this necessity and drafted a series of national codes for integrating their food safety systems (CSCFSC, 2004). Another impediment toward integrated laboratory surveillance systems has been availability of resources for developing countries. For example, developing countries may lack complete antisera kits necessary to identify certain serotypes of specific pathogens. Hence, industrialized countries are more likely to contribute data to the surveillance system and therefore bias the results (Galanis et al., 2006).

Additional surveillance tools that have been adopted recently to assist in monitoring the safety of the entire food chain from farm to table include identification and tracking systems for livestock (Table 8). The European Union in 1999 was the first to require individual animal identification to support hormonal growth-promotant-free certification. In addition, Canada, Japan, Uruguay, and Brazil all have government- and industry-supported individual animal tracing systems in place. In the United States, several major supermarket chains are requesting full traceability, hence the US is engaged in the implementation of a voluntary National Animal Identification System (USDA, 2006). Implementation of these and other surveillance systems will play vital roles for enhancing public health protection of food imports and exports.

4.3. Microbial risk assessment

Understanding foodborne pathogen contamination, growth, and survival in foods and infectious dose is essential to assessing the impact foodborne pathogens have on public health. Hence, a systematic science-based approach is needed to assemble and analyze such data to improve the quality of public health decisions. One such approach is microbial risk assessment (MRA) and consists of describing a system that assesses the risk of a microbial hazard reaching a host and causing harm. Four major steps comprise MRA: hazard identification, hazard characterization, exposure assessment, and risk characterization (Lammerding & Paoli, 1997), and details of how to conduct a MRA are described elsewhere (Buchanan et al., 1998; Buchanan, Smith, & Long, 2000; Lammerding & Fazil, 2000). While MRAs are useful for food attribution purposes when used in conjunction with outbreak data or case–control studies (Batz et al., 2005), their greatest value lies in the potential for the user to develop targeted and effective risk management strategies based on MRA analyses. MRAs are very resource intensive, hence they should be reserved for issues where the science is complex or there are substantial differences of opinion concerning the interpretation of scientific data among the various interested parties (Buchanan & Dennis, 2002). When applied under these circumstances, MRAs provide scientific validity to the linkages between processes affecting pathogen contamination of foods and the probability and severity of illnesses resulting from consumption of that food. MRAs can be quite varied in their focus such as differing in the extent of the food chain continuum addressed or the number of pathogen–food combinations evaluated. As examples of this diversity, several risk assessments conducted recently on meat and poultry products are profiled in Table 9.

MRAs are inherently predictive and estimate the impact of interventions using a number of assumptions built into the model. To illustrate this application, the effect of a "test and divert" program was assessed in the MRA conducted by WHO for *Salmonella* spp. in eggs and broiler chickens. Testing three times per year for four years reduced the risk of human illness from shell eggs by more than 90% (i.e. >1 $\log_{10}$), whereas testing once a year for 4 years reduced the risk by over 70% (WHO, 2002b). Similarly, "what if" scenarios considered in the FDA *L. monocytogenes* risk assessment suggested several broad control strategies to reduce the risk of foodborne listeriosis including reformulation of products to reduce their ability to support the growth of *L. monocytogenes* or encouraging consumers to keep refrigerator temperatures at or below 10 °C and reducing refrigerated storage times (U.S. FDA, 2003).

A group of experts convened by the International Life Sciences Institute-Risk Science Institute used *L. monocytogenes* MRAs as the basis for developing a strategy to achieve con-

Table 9
Selected examples of risk assessments of significance to the poultry and meat industry (USDA, 2001, 2003, 2005a, 2005b, 2005c; US FDA, 2002; WHO, 2002a, 2002b, 2004b)

Organization	Year	Pathogen	Target foods(s)	Key findings
USDA FSIS	2001	*E. coli* O157:H7	Ground beef	• *E. coli* O157:H7 prevalence is significantly higher in feedlot cattle than in breeding cattle • Prevalence and levels of contamination found in combo bins and boxes is greater during the high-prevalence season with an average of 8% and 43% of combo bins produced from breeding and feedlot cattle, respectively, containing one or more *E. coli* O157:H7 organisms • While only a fraction of carcasses are contaminated, thousands of pounds of trim meat are combined in the grinding process, therefore, the proportion of grinder loads that contain one or more *E. coli* O157:H7 organisms is expected to be high • The median probability of illness for the general US population due to *E. coli* O157:H7 from a serving of ground beef is estimated to be 1 illness in every 1 million servings. For children aged 0 to 5, the risk is 2.5 illnesses in every 1 million consumed ground beef servings
WHO	2002	*Campylobacter* spp.	Broiler chickens	• A linear relationship between flock prevalence and probability of illness was found, i.e. a twofold reduction in flock prevalence would result in a corresponding twofold reduction in the probability of illness • Both external contamination and colonization need to be reduced concurrently to achieve a substantial impact on risk
WHO	2002	*Salmonella* spp.	Eggs and broiler chickens	• Reducing flock prevalence results in a directly proportional reduction in human health risk • Risk of human illness per serving appears to be insensitive to the number of *Salmonella Enteritidis* in contaminated eggs across the range considered at the time of lay
USDA FSIS	2003	*Listeria monocytogenes*	Deli meats	• The likelihood of finding RTE product lots positive for *L. monocytogenes* greatly increases when the food contact surface is found positive for *Listeria* species • Frequency of contamination of food contact surfaces with *Listeria* species appears to encompass a wide timeframe, and the duration of a contamination event lasts approximately a week • The proposed minimal frequency of testing and sanitation of food contact surfaces (66 FR 12589, 2/21/01) results in a small reduction in the levels of *L. monocytogenes* on deli meats at retail. Increased frequency of food contact surface testing and sanitation leads to a proportionally lower risk of listeriosis • Combinations of interventions appear to be much more effective than any single intervention in mitigating the potential contamination of RTE products with *L. monocytogenes* and reducing the subsequent risk of illness or death
US FDA	2002	*Listeria monocytogenes*	Ready-to-eat foods	• Reinforces past epidemiological conclusions that foodborne listeriosis is a moderately rare although severe disease • Certain foods are more likely to be vehicles of *L. monocytogenes* • The dose of *L. monocytogenes* necessary to cause listeriosis depends greatly upon the immune status of the individual • Identifies five critical factors that affect consumer exposure to *L. monocytogenes* at the time of food consumption: (1) amount and frequency of consumption of a ready-to-eat food; (2) frequency and levels of *L. monocytogenes* in a ready-to-eat food; (3) potential of the food to support growth of *L. monocytogenes* during refrigerated storage; (4) refrigerated storage temperature; and (5) duration of refrigerated storage before consumption
WHO	2004	*Listeria monocytogenes*	Ready-to-eat foods	• Nearly all cases of listeriosis result from the consumption of high numbers of the pathogen • Old age and pregnancy increase susceptibility and thus the risk of acquiring listeriosis. Likewise, diseases and medical interventions that severely compromise the immune system greatly increase the risks • Contamination with high numbers of *L. monocytogenes* at manufacturing and retail is rare, and foods such as ice cream and fermented meat products that do not permit growth during storage have relatively low risk per serving. Control measures that prevent the occurrence of high levels of contamination at consumption would be expected to have the greatest impact on reducing the rates of listeriosis in foods that permit growth during storage
USDA FSIS	2005	*Clostridium perfringens*	Ready-to-eat and partially cooked meat and poultry products	• Estimated that approximately 79,000 illnesses/year in the US occur from 1-$\log_{10}$ cfu/g growth of *C. perfringens* in RTE and partially cooked meat and poultry products • A change in growth during stabilization from 1-$\log_{10}$ to 2-$\log_{10}$ or 3-$\log_{10}$ cfu/g results in a median 1.23 or 1.59-fold increase, respectively, in annual diarrheal illness • Improper cold storage of RTE and partially cooked meat and poultry products at retail and the home accounts for approximately 90% of the predicted *C. perfringens* foodborne illness. Improper hot-holding of RTE and partially cooked meat and poultry products accounts for approximately 8% of the predicted illnesses at 1-$\log_{10}$ growth during stabilization • Temperature stabilization at processing plants accounts for 0.05% and 0.4% of predicted illnesses at 1-$\log_{10}$ and 2-$\log_{10}$ cfu/g allowable growth, respectively. Therefore, relatively few predicted illnesses are associated with temperature stabilization at processing plants

(*continued on next page*)

Table 9 (*continued*)

Organization	Year	Pathogen	Target foods(s)	Key findings
				• Non-proteolytic *Clostridium botulinum* grows at temperatures below the minimum temperature for *C. perfringens* growth. Any measures taken to reduce or prevent growth *of C. perfringens* will not necessarily have the same effects on growth of non-proteolytic *C. botulinum*
USDA FSIS	2005	*Salmonella* spp.	Ready-to-eat meat and poultry products	• Risk estimates for salmonellosis were generated for RTE meat and poultry products processed under different lethality scenarios for *Salmonella* spp. • Cooked chicken (nuggets, tenders, and non-deli) is by far the greatest contributor to the estimated number of cases of salmonellosis occurring annually
USDA FSIS	2005	*Salmonella Enteritidis* *Salmonella* spp.	Shell eggs Egg products	• Pasteurization conditions used were predicted to be effective for reducing illnesses from *S. Enteritidis* in shell eggs • Recommended storage time and temperature were predicted to be effective for reducing illnesses from *S. Enteritidis* in shell eggs • Pasteurization conditions currently used were predicted to be effective for reducing illnesses from *Salmonella* spp. in egg products

tinuous improvement in reductions in foodborne listeriosis (ILSI, 2005). The expert panel determined that the greatest impact on reducing foodborne listeriosis would be achieved by focusing on high-risk foods which are characterized by the following properties: (1) have the potential for contamination with *L. monocytogenes*; (2) support the growth of *L. monocytogenes* to high numbers; (3) are ready to eat; (4) require refrigeration; and (5) are stored for an extended period of time. The most effective strategies identified to control *L. monocytogenes* in high-risk foods included: (1) good manufacturing practices, sanitation standard operating procedures, and hazard analysis critical control point programs to minimize environmental *L. monocytogenes* contamination and prevent cross-contamination; (2) an intensive environmental sampling program and an effective corrective action plan; (3) time and temperature controls throughout entire distribution and storage period; (4) reformulating foods to prevent or retard the growth of *L. monocytogenes*; and (5) using postpackaging treatments to destroy *L. monocytogenes* on products. While these examples highlight the usefulness of MRAs, WHO has acknowledged that converting the output of risk assessments into effective risk management strategies has not met expectations (WHO, 2006b). In particular, limited experience of its use in countries has hindered the comprehension of how it could be used at the international or Codex level. It is envisioned that use of country-specific data will result in risk assessments that are more relevant and useful than those which do not use country-specific data (ILSI, 2006). Despite these limitations, MRA will continue to play a major role in food safety management activities of the meat and poultry industry. In conjunction with these activities, revisions of models will be needed as new information (changes in scientific approaches or data) becomes available. For example, Powell, Schlosser, and Ebel (2004) have suggested inclusion of microbial community dynamics into risk assessment models and Chen et al. (2006) have advocated that future risk assessments of *L. monocytogenes* include both exposure cell numbers and subtype prevalence. It is likely that MRAs will play an even greater role in regulatory activities for the meat and poultry industry as they are used to provide a basis for establishing food safety objectives that link public health objectives with performance objectives and performance criteria (Walls & Buchanan, 2005).

4.4. Sensitive populations at increased risk of foodbornemicrobial infections

In developing risk assessments and food safety objectives, increased emphasis in the future will likely be placed on dose–response relationships among highly sensitive populations (Gerba, Rose, & Haas, 1996). In particular, major demographic changes in the world's population is projected to occur during the coming 50 years as the world's elderly population ($\geqslant$65 years old) grows in both absolute and relative terms. In 2050, there will be three times as many elderly than in 2002 but more importantly they will com-

prise 17% of the global population (U.S. Census Bureau, 2004). This segment of the population is at increased risk to pathogenic agents due to weakened immune systems, a decreased protection by vaccines, prolonged stays in hospitals, permanent catheterization, malabsorption of nutrients, problems associated with the use of drugs, including drug interactions, and renal insufficiency (Ohlsen & Hacker, 2005). With regard to foodborne pathogens, uropathogenicity of *Salmonella* has doubled from 2% between 1980 and 1984 to 4% between 1995 and 1999, with elderly women exhibiting the greatest increase (Sivapalasingam, Hoekstra, McQuiston, Fields, & Tauxe, 2004). Age-related differences have also been found in the blood invasiveness of *Salmonella enterica* serotypes. Normally, a self-limiting and benign disease, invasion beyond the gastrointestinal tract occurs in approximately 5% of patients with salmonellosis. With children <2 years of age, blood invasiveness was highest for serotype Virchow and lowest for serotype Hadar, whereas in persons ⩾60 years, it was highest for serotype Enteritidis and lowest for serotype Infantis (Weinberger et al., 2004). The physiological and biochemical explanations for differences in serotype and strain invasiveness remain to be elucidated; however, explication of the genomic relationship will likely be forthcoming thereby resulting in the incorporation of genomic information into quantitative microbial risk assessments (Chen et al., 2006).

Another population group that requires special consideration in microbial risk assessments is the immunocompromised. Increased susceptibility to infection by this population group can take different forms. There may be a greater likelihood of infection if exposed, a greater likelihood of illness if infected, more severe or complicated disease if ill, a greater likelihood of death, and increased potential for illness with a non-pathogen or opportunistic pathogen (Neill, 2005). Furthermore, within this population group, there are different immunodeficient states, one group being primary or congenital and the second group being secondary or acquired (i.e. pregnancy, chronic disease, malignancy, or medication induced). Conditions of the immunocompromised that predispose them to foodborne zoonotic infections include age, decreased gastric acidity, inflammatory bowel disease, malignancy, immunosuppressive medications, chronic medical conditions, and HIV/AIDS (Trevejo, Barr, & Robinson, 2005). For example, a case–control study revealed an association between dietary tea ingestion and *Bacillus cereus* bacteremia among children with cancer (El Saleeby, Howard, Hayden, & McCullers, 2004). Predisposition to salmonellosis occurs in individuals with chronic atrophic gastritis, use of antacids and H-2 blockers, or alteration of endogenous bowel flora induced with antimicrobial therapy or surgery (Blaser & Newman, 1982; Hohmann, 2001). Increases in the immunocompromised population have occurred worldwide due to the HIV/AIDS epidemic, life-prolonging treatment of immunodeficiency diseases, and the use of chemotherapeutic agents and immunosuppressive drugs in cancer and transplantation patients (Davy, 2002). It is estimated that 3.6% of the US population is categorically immunodeficient and when pregnant women and the elderly are included, the proportion with some degree of immunodeficiency is about 20% (Gerba et al., 1996; Smith, 1997). Given the magnitude of this emerging issue, much of the food industry will likely have to make adjustments to its food safety programs.

5. Summary

The issues that have been covered in this paper are not all encompassing but represent many that are likely to significantly impact the meat and poultry industry in the coming decades. Other microbiological issues that will likely continue to be concerns for the meat industry for the near future include bovine spongiform encephalopathy (BSE), Johne's disease (*Mycobacterium avium* subsp. *paratuberculosis*), toxoplasmosis, and Shigatoxigenic *E. coli*, *L. monocytogenes*, *Salmonella* spp., and *Campylobacter* spp. With the development of new and more sophisticated tools for studying foodborne pathogens and sensitive hosts, including genomics, proteomics, and metabolomics, major advances will be made during the next decade in understanding more precisely the origin of foodborne disease agents, discriminating more virulent strains from less harmful microbes, identifying highly vulnerable populations, and tracing outbreak-associated pathogens to their source. These major advances for public health will provide even greater challenges for the meat and poultry industry in producing microbiologically safe products. The good news is that accompanying such challenges will be innovative solutions such as identifying the most impactful control strategies for ranking microbiological hazards through microbial risk assessments, developing creative antimicrobial treatments, providing practical and effective on-farm and in-plant interventions, and enabling rapid identification of microbial contamination to allow rapid response.

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