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Emerging foodborne pathogens

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Abstract

The broad spectrum of foodborne infections has changed dramatically over time, as well-established pathogens have been controlled or eliminated, and new ones have emerged. The burden of foodborne disease remains substantial: one in four Americans is estimated to have a significant foodborne illness each year. The majority of these illnesses are not accounted for by known pathogens, so more must remain to be discovered. Among the known foodborne pathogens, those more recently identified predominate, suggesting that as more and more is learned about pathogens, they come under control. In addition to the emergence or recognition of new pathogens, other trends include global pandemics of some foodborne pathogens, the emergence of antimicrobial resistance, the identification of pathogens that are highly opportunistic, affecting only the most high-risk subpopulations, and the increasing identification of large and dispersed outbreaks. New pathogens can emerge because of changing ecology or changing technology that connects a potential pathogen with the food chain. They also can emerge de novo by transfer of mobile virulence factors, often through bacteriophage. Though this is rarely observed, it can be reconstructed. Better understanding of the ecology and dynamics of phage transmission among bacteria will help us to understand the appearance of new pathogens in the future. One may look for emerging foodborne pathogens among the silent zoonoses, and among the severe infections affecting the immunocompromised humans. We should expect the unexpected. In the past, separating human sewage and animal manure from human food and water supplies was critical to improving public health. Now, our health depends increasingly on the safety of the feed and water supplies for the animals themselves. The successes of the 20th century and the new challenges we face mean that public health vigilance, careful investigation of new problems, responsible attention to food safety from farm to table, and partnerships to bring about new foodborne disease control measures will be needed for the foreseeable future.

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How does newness come into the world?
How is it born?
Of what fusions, translations, conjoinings is it
made?

How does it survive, extreme and dangerous as it
is?

Salman Rushdie

A broad spectrum of microbial pathogens can
contaminate human food and water supplies, and
cause illness after they or their toxins are consumed.

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The spectrum of foodborne pathogens includes a variety of enteric bacteria, aerobes and anaerobes, viral pathogens, and parasites, as well as marine dinoflagellates, bacteria that produce biotoxins in fish and shellfish, and the self-inducing prions of the transmissible encephalopathies. Some pathogens, like the *Shigella* spp. or the Norwalk-like viruses, require the human host as part of their life cycle, while many others have primary reservoirs in other animals or in the environment; for these, the infected human is an unfortunate, but accidental victim. Some are professional foodborne pathogens, which are always transmitted through food, while others are capable of being transmitted via several different routes in addition to food. This broad spectrum causes an array of illnesses in the human host, most with a gastrointestinal component of vomiting or diarrhea. The invasive ones produce other clinical syndromes, and the foodborne toxins can affect almost any system in the body. Thus, to speak of “foodborne disease” is to speak of many pathogens and many diseases. Within this broad spectrum, my own experience has been chiefly with the bacterial pathogens, and so most of the examples that I will cite are from that realm. In particular, I am not expert in transmissible encephalopathies, and others can speak to that issue far better than me.

1. A shifting spectrum of pathogens

The pathogenic spectrum can change substantially over time. This happens for several reasons. Pathogens for which transmission is well understood may ultimately be controlled. Others may emerge through mutation, or may move into a new niche in the food chain. As a result, the frequency of specific infections can change substantially, reflecting a balance between the ecologies that support bacterial populations that contaminate food, and the cultural habits, and technologies that limit or prevent that contamination from occurring. For example, in the first decades of the 1900s, some of the principle infections that were recognized as foodborne included typhoid fever, tuberculosis, brucellosis, and septic sore throat, a zoonotic streptococcal infection (Rosenau, 1926). These conditions have largely disappeared from the industrialized world as foodborne diseases, as a result

of milk sanitation and pasteurization, disease control efforts in animals, better regulation of shellfish beds, and other measures (Tauxe and Esteban, in press). Trichinosis, which was once common, also virtually disappeared by the 1970s when the practice of feeding pigs uncooked garbage was ended (Schantz, 1983). When it does occur, it is almost exclusively among ethnic groups that eat raw pork or horse meat (Mead and Mintz, 1996; CDC, 1986). More recently, outbreaks of food poisoning caused by *Staphylococcus aureus* and by *Clostridium perfringens* have become uncommon in the United States, for reasons that remain to be clarified.

Although many foodborne infections have been controlled, the burden of foodborne disease remains substantial. For the United States, we have recently estimated this annual burden at 76 million cases of illness, 323,000 hospitalizations per year, and 5000 deaths (Mead et al., 1999). This means that 1 in 4 Americans gets a foodborne illness each year, and more than 1 in 1000 is hospitalized. This estimate was arrived at by estimating the proportion of the population that gets a significant gastrointestinal illness each year, and then estimating the proportion of gastrointestinal illness that is likely to be foodborne. We arrived at this latter estimate by taking the major known pathogens in the United States in the 1990s, and for each one estimating the total number of infections it causes, accounting for under diagnosis and under reporting, and estimating the fraction of those illnesses that is foodborne. We did this for 27 foodborne pathogens of importance in the United States, and summed up the proportion of all their illness that was foodborne—this fraction, 36%, was what we used as our best guess for the fraction of all the acute gastrointestinal illness that was related to foods. Thus, the estimate of foodborne illness is the total incidence of acute gastrointestinal illness, about 79 illness episodes per 100 persons per year, and the fraction of 36% estimated as foodborne, or 28 per 100 per year. This large burden means that there are still many foodborne infections to be controlled, despite the successes of the 20th century.

Curiously, when we added up all the illness attributed to the 27 principal foodborne pathogens, we were left with a substantial gap, even after accounting for under diagnosis and under reporting. These pathogens accounted for only 19% of the total estimated number

of cases attributable to foodborne infections and 36% of the deaths. The great majority of our estimate remains unaccounted for. This gap suggests that there are many more foodborne pathogens yet to be identified. Furthermore, if we examine the list of the 27 pathogens, we find that 13 of them have been identified as foodborne pathogens only within the last 25 years (see Table 1). Some, like *Escherichia coli* O157:H7, are likely to have evolved relatively recently, and may represent genuinely new pathogens. Others, such as the caliciviruses in the Norwalk-like virus group, and *Vibrio vulnificus*, have been identified as pathogens relatively recently, though they have probably been causing foodborne disease for centuries. Still, others like *Campylobacter jejuni*, *Listeria monocytogenes*,

and *Vibrio cholerae* have been known as pathogens for many decades, but were not known to be often foodborne—it is the importance of the foodborne route in their transmission that has been clarified more recently. These 13 pathogens, newly recognized, or newly recognized as foodborne, represent the emerging foodborne diseases. As a group, they are the majority of the foodborne pathogens and represent the majority of foodborne illnesses. These 13 pathogens account for the bulk of the burden caused by the principal known foodborne pathogens: 82% of the estimated 13.8 million cases and 61% of the 1800 deaths attributable to all known foodborne pathogens in the United States. The greatest single contributor to morbidity is the calicivirus group, which includes an ever growing number of viral types, with both human and animal reservoirs (Ando et al., 2000). Expanding diagnostic capacity for these new species may explain an important fraction of currently undiagnosed illness (de Wit et al., 2001). In contrast, five pathogens that were major causes of foodborne disease before 1900, *Brucella*, *Clostridium botulinum*, *Salmonella typhi*, *Trichinella*, and toxigenic *V. cholerae*, together account only for 0.01% of those cases and less than 1% of the deaths in 1997, and many of those were associated with foreign travel. This illustrates how, in the long run, after pathogens are identified and studied, often they eventually come under control.

Table 1

Principal foodborne infections, as estimated for 1997, ranked by estimated number of cases caused by foodborne transmission each year in the United States (Mead et al., 1999) (values over 1000 are rounded to the nearest 1000)

Norwalk-like viruses *	9,200,000
<i>Campylobacter</i> *	1,963,000
<i>Salmonella</i> (nontyphoid)	1,342,000
<i>Clostridium perfringens</i>	249,000
<i>Giardia lamblia</i>	200,000
Staphylococcus food poisoning	185,000
<i>Toxoplasma gondii</i>	112,000
<i>Escherichia coli</i> O157:H7 and other Shiga-toxin producing <i>E. coli</i> *	92,000
<i>Shigella</i>	90,000
<i>Yersinia enterocolitica</i> *	87,000
Enterotoxigenic <i>E. coli</i> *	56,000
Streptococci	51,000
Astrovirus *	39,000
Rotavirus *	39,000
<i>Cryptosporidium parvum</i> *	30,000
<i>Bacillus cereus</i>	27,000
Other <i>Escherichia coli</i>	23,000
<i>Cyclospora cayetanensis</i> *	14,000
<i>Vibrio</i> (noncholera) *	5000
Hepatitis A	4000
<i>Listeria monocytogenes</i> *	2000
<i>Brucella</i>	777
<i>Salmonella typhi</i> (typhoid fever)	659
Botulism	56
<i>Trichinella</i>	52
<i>Vibrio cholerae</i> , toxigenic *	49
<i>Vibrio vulnificus</i> *	47
Prions *	0

Those that have emerged in the last 30 years are indicated by an asterisk.

2. Other emerging trends

In addition to the recognition of new foodborne pathogens, other trends characterize the modern landscape of foodborne disease. First is the global dissemination of some foodborne pathogens in pandemic form. For example, in the 1980s, a few strains of *Salmonella* Enteritidis swept through the egg laying and broiler flocks of much of the world, making it the most common *Salmonella* serotype worldwide (Rodrigue et al., 1990). The precise means of dissemination has yet to be clarified, and it involved more than one strain, as defined by phage susceptibility or pulsed field gel electrophoresis genotyping. The peculiar property of these strains to seek the ovarian tissues of the hen, and to infect the eggs, usually without causing overt pathology in either hen or egg, suggests that this virulence capacity itself might be what was

disseminated. Australia and New Zealand remain unaffected by this global pandemic. Something similar has happened with highly resistant strains of *Salmonella* Typhimurium, defined by phage typing as type 104. These strains emerged in the 1990s in Europe and North America simultaneously, first in cattle and then in other animals (Tauxe, 1999). These DT104 complex strains have since appeared in many other parts of the world, though again, not in Australia or New Zealand. The fact that neither *S. Enteritidis* nor *S. Typhimurium* DT104 has appeared in Australia or New Zealand offers an important clue as to how such strains spread. Human carriers and wild birds which travel freely did not introduce these strains. If they spread through shipments of live animals and feedstuffs, the tight quarantine controls on such shipments in those two countries might have kept them out (Crump et al., 2001). The resistance genes are encoded on chromosomal integrons, and may themselves be the mobile pandemic element. A third example of a global pandemic is the appearance of *Yersinia enterocolitica* strains of serogroups O3 and O9 in Europe, Japan in the 1970s, and in North America by the end of the 1980s (Anon., 1976; Lee et al., 1990a,b). These strains appear to have a reservoir in pigs, where they cause little more than pharyngitis, but are transmitted to humans by consumption of or contact with raw pork or pork products (Lee et al., 1990a,b). The mechanism of spread of these strains among pig herds is unclear, but may be related to the exchange of breeding stocks. Finally, we have recently witnessed the spread of a new serotype of *V. parahaemolyticus*, O3:K6, from Southeast Asia, to Japan, to the United States. This sea-going organism causes illness when it appears in shellfish beds, and contaminates oysters and other seafoods that are eaten raw. This new serotype of *V. parahaemolyticus* emerged in Southeast Asia in the early 1990s, caused numerous seafood-associated outbreaks in Japan later in that decade, and caused large oyster-related outbreaks in the United States in 1997 and 1998 (Daniels et al., 2000). The largest epidemic in the United States occurred in Galveston, TX, where oysters are harvested adjacent to the sea lanes and empty oil tankers appear from the orient to load with oil and gasoline for Japan. The common practice of using harbor water as ballast in empty tankers means that huge volumes of water are transported from one harbor to the next, and may play a role in the spread of

vibrios and other harmful organisms around the world (CDC, 1993).

Increasing antimicrobial resistance is another general trend among the foodborne bacterial pathogens. For those with primary human reservoirs, such as *Shigella* spp. and *S. Typhi*, the agent of typhoid fever, the emergence of resistance is related to the use of antibiotic agents in human populations. However, for those pathogens with primary food animal reservoirs, the principal driver of increasing resistance is the use of antibiotics in agriculture. This use, for purposes of disease treatment and for growth promotion, contributes to the selection of resistant strains and to their subsequent spread. For example, the use of a fluoroquinolone in a chicken flock can convert or replace the prevalent *C. jejuni* strains from 100% susceptibility to 100% resistance within days (McDermott et al., 2001). The use of therapeutic third generation cephalosporins in cattle may be associated with the worrisome appearance of *Salmonella* strains that are resistant to ceftriaxone (Dunne et al., 2000). The longstanding use of the combination dalfopristin/quinupristin in chickens meant that when these agents were later approved for use in human medicine to treat infections with vancomycin-resistant *Enterococcus*, strains of *Enterococcus* spp. that were highly resistant to these agents were already common in poultry meat (McDonald et al., 2001). The appearance of linked resistance, such as the penta-resistance of DT104 strains of *S. Typhimurium*, is of particular concern, as the use of any member of the five agent classes may select for the presence of all five resistance genes. Thus, this strain will have a selective advantage where ampicillin-like agents, florfenicol, streptomycin, sulfonamides, or tetracyclines, are used. In the year 2000, the proportion of *Salmonella* spp. isolated from humans in the United States that were at least penta-resistant was 11%, and some of the penta-resistant strains have also acquired resistance to gentamicin and third generation cephalosporins (CDC, 2002). Among *Campylobacter* strains from humans, 14% are resistant to fluoroquinolones, and these infections have been linked to the consumption of poultry (CDC, 2002). This underlines the need for prudent use of agricultural antibiotics to prolong their usefulness in agriculture and to protect the public health. Agricultural uses are not the only source of resistance, even among nontyphoid strains of *Salmonella*. A persistent nosocomial outbreak of fluoroqui-

nolone resistant *Salmonella* Senftenberg began with the transfer of a paralyzed patient from a hospital in the Philippines to a long-term care facility in the United States; this strain is presumed to have a nosocomial niche in the developing world (Olsen et al., 2001).

A third important recent trend in foodborne diseases has been the recognition of foodborne pathogens that affect only specific high-risk subgroups of the population. One such opportunistic pathogen is *L. monocytogenes*, which causes severe illness in the elderly, the immunocompromised, and in the fetus, leading to septicemia, meningitis, and loss of the fetus; 25% of recognized infections result in death (Slutsker et al., 2000). These infections often have origin in unpasteurized dairy products, or with ready-to-eat meats that have become recontaminated at the factory. Preventing them requires making the high-risk populations aware of their special risk and encouraging them to avoid or heat such foods. In the future, irradiation or other treatments of ready-to-eat meats in their packages offers the potential of dramatically reducing the risk of listeriosis. Among healthy hosts, a high dose of ingested *Listeria* organisms leads only to febrile gastroenteritis, as was demonstrated in a milk-associated outbreak of illness among cattle fanciers, who consumed an estimated 10^9 organisms (Dalton et al., 1997). A second such opportunist is *V. vulnificus*, which can cause a devastating bacteremia and necrotising fasciitis in persons who have compromised liver function or iron overload. The fatality rate of these infections is 50%, while infections in healthy hosts are rare and rarely fatal. It is a public health challenge to try to reach the specific population of those with liver disease, and to try to craft messages that will be heeded (Tuttle et al., 1994). Irradiation and pressure treatment of oysters are control technologies that may see greater use in the future.

3. A new kind of outbreak

Finally, the broad distribution of foods from more centralized production and processing facilities has brought about a new type of highly dispersed foodborne outbreak. In the past, recognized foodborne outbreaks typically fit the textbook pattern of a sharp local increase in cases of a particular illness following

a local common exposure. The event was usually recognized by the victims themselves as an outbreak, and local health officials identified the etiology of the illness and its source. Disease control efforts would often be local in nature, including perhaps closure of a restaurant, destruction of a batch of food, or education of a food handler. In recent years, highly dispersed outbreaks are being recognized more frequently as microbial subtyping systems such as serotyping or pulsed field gel electrophoresis are used (Swaminathan et al., 2001). These dispersed outbreaks do not present as a sharp local increase in cases, but rather as a diffuse increase in the number of apparently sporadic cases in several jurisdictions. These outbreaks are caused by foods that may be contaminated at a low level before they are shipped from a central facility to many places. The increase in cases in any one place may not be sufficient to attract notice, so these outbreaks may only be detected because the bacterial strains are received and subtyped in public health laboratories, allowing strains from many jurisdictions to be compared, as happens with PulseNet in the United States and EnterNet in Europe. Investigation may identify a systematic problem in production or processing with implications for the entire industry. Identifying and investigating these industrial scale outbreaks drive the cycle of prevention faster.

In recent years, such “new scenario” outbreaks have been dramatic, and investigations of them have led to important advances in foodborne disease prevention. In 1997, shortly after the state health department of Colorado began testing their *E. coli* O157:H7 isolates in PulseNet, 16 cases of infection with the same unusual pattern were detected in Colorado and a neighboring state (CDC, 1997). These cases were linked to ground beef produced at a large factory. Because that plant had the routine practice of carrying over leftover beef from one production lot and working it into subsequent days production, thereby contaminating that lot, an astounding 25 million pounds of meat was recalled, and the carryover practice was strongly discouraged throughout the industry. In 1998, an increase in apparently sporadic cases of listeriosis occurred in several states, just as the PulseNet method for *L. monocytogenes* was ready for first implementation. Ultimately, 101 cases with the same pattern were identified in 22 states and were associated with eating cooked hot dogs from one production plant

(CDC, 1999). The company itself instituted a recall of the hot dog products. Investigation at that plant suggested that further measures were needed to control recontamination of hot dogs after processing. Such measures are now being considered by the entire industry. In 1999, a cluster of *Salmonella* Newport infections was detected by serotyping and PFGE subtyping within the serotype (Sivapalasingam et al., 2000). Ultimately, 78 infections with the same PFGE profile in 13 states were identified. Epidemiologic investigation linked these cases to consumption of fresh imported mangoes. The mangoes had been treated with a new hot water dip process to eliminate fruit fly infestation before export, a process that may have also introduced *Salmonella* organisms into the mangoes. As a result, the process is being modified, as it is introduced worldwide to replace methyl bromide treatments. In 2000, a cluster of *S. Enteritidis* infections with the same unusual PFGE pattern was detected in western states; 88 infections in eight states were ultimately associated with drinking unpasteurized orange juice that had been treated with an alternative to pasteurization (Rangel et al., 2000). Following this outbreak, the federal regulations for juice were revised to make contamination less likely to recur (FDA, 2001).

4. Predicting the future

We can learn something from the pathogens that have been recognized recently, as a guide to the future. Since 1977, new or newly characterized foodborne pathogens have been recognized at the rate of approximately one every 2 years. Many of these are zoonotic in origin with some common characteristics. These zoonoses tend to cause little apparent illness in their animal hosts, acting more like commensal organisms. They are established in the animal reservoirs with long-term carriage. They tend to cause infection at relatively low doses in humans, and to appear in food vehicles that are not subjected to cooking conditions that kill them. Many were first described in animals, so one place to look for new zoonotic public health threats would be in the index of a veterinary textbook of infectious diseases.

Another arena to search for foodborne pathogens is the unusual and exotic opportunistic pathogens that cause serious illness in the immunocompromised. This

is because routine culture methods can identify pathogens from blood or other sterile sites, while specific selective methods are required to isolate the same pathogen from feces or food. For example, *C. jejuni* was first recognized as a human pathogen when it was recognized as a rare cause of bacteremia in leukemic children, though it was observed that these cases were often preceded by diarrhea (King, 1962). It was only after selective methods were applied to feces that the high frequency of campylobacteriosis in pediatric diarrhea was appreciated. There are many other *Campylobacter* species, some of which cause bacteremia in the compromised host, and some of which are inhibited by the selective media used to isolate *C. jejuni* from feces. Search for these campylobacters using nonselective culture methods can identify a variety of them, though their status as pathogens remains to be clarified (Engberg et al., 2000). It is likely that some of these are enteric pathogens, particularly in immunocompromised patients in the developing world (Lastovica and Skirrow, 2000).

New pathogens can arise because of new ecologies and technologies that bring existing pathogens into our food supply in new and surprising ways. For example, in 1996, 1465 persons in 20 states, the District of Columbia, and two Canadian provinces fell ill with a distinctive combination of recurrent diarrhea and extreme fatigue, caused by a recently recognized parasitic pathogen, *Cyclospora caytanensis* (Herwaldt, 2000). These illnesses were linked to eating fresh raspberries imported in the spring from Guatemala, where this new crop had been recently introduced. It is still not clear how the berries became contaminated. Investigators in Guatemala found that the same organism caused a springtime wave of diarrhea in children of agricultural workers, and the children got it by drinking untreated water (Bern et al., 1999). After changes were made in procedures on the raspberry farms and in the living conditions among the workers there, raspberry imports resumed cautiously, and so far, there have been no further outbreaks. Fundamental observations remain unexplained, such as why raspberries harvested from the same farms in late summer were not associated with illness, or why blackberries harvested from the same farms at the same time as the implicated raspberries were likewise unaffected. The outbreak, which brought the previously little known *Cyclospora* organism to the forefront, is a graphic example of how new and

unexpected foodborne pathogens can suddenly appear. It shows the potential hazard of raising fresh perishable produce in the developing world, flying it to the developed world overnight, and eating it after nothing more than a quick rinse. This outbreak put the fresh produce industry on notice that they must address conditions of life in the rural developing world where they grow and harvest, as these are now directly connected to our dinner plates.

New pathogens can evolve when existing organisms acquire new virulence properties. Many enteric pathogens have virulence factors that are on mobile genetic elements, and appear to have acquired the critical pathogenic capacity as the result of horizontal evolution. For example, it has recently been shown that *V. cholerae* O1, the causative agent of cholera, harbors a filamentous phage that bears the cholera toxin genes (Waldor and Mekalanos, 1996). Cholera toxin is the fundamental virulence factor of *V. cholerae*. Horizontal transfer of cholera toxin at some time in the not too distant past would conveniently explain several puzzling features of the epidemiology of *V. cholerae* O1, an organism supremely adapted to the brackish marine invertebrate ecology, which causes no illness in any vertebrate other than humans (Levin and Tauxe, 1996).

More is known about *E. coli* O157:H7, though it is a more recently recognized pathogen. This organism was first identified in 1976, and first described as a human pathogen in 1982, although the serotyping methods that were used to characterize it were established half a century earlier. The most characteristic clinical syndrome it causes, hemolytic uremic syndrome, was described in the mid-1950s in rural Switzerland, although it could have been easily diagnosed by any skilled pathologist decades earlier (Gasser et al., 1955). For this organism, the key virulence factor is Shiga toxin, which is known to be carried by several different phages with relatively indiscriminant host ranges. Recent investigations have demonstrated that the phage is mobilized under specific conditions, the same conditions that increase production of toxin itself. One of the most powerful inducers of both toxin and phage production is the exposure of the organism to sublethal doses of certain antimicrobial agents (Zhang et al., 2000). Both the laboratory observations and the historical context suggest that this zoonotic pathogen could have

evolved in, and perhaps as a result of, the antibiotic era and consequent increase in antibiotic-associated phage transfers. Clearly, better understanding of the factors that lead to virulence mobility and stability, and of the ecology of the virulence bearing phages themselves, would help us to understand the emergence of these pathogens.

Other less well understood recent zoonotic foodborne epidemics, such as *S. Enteritidis* in eggs, or *S. typhimurium* DT104, or *Y. enterocolitica* serogroup O3 or O9, may also be the result of spread of an as yet undocumented mobile virulence factor. In the case of *Y. enterocolitica*, an association between the virulence plasmid and arsenic resistance has been described (Neyt et al., 1997). Plasmid-mediated arsenic resistance may have given some strains of *Y. enterocolitica* a survival advantage in old swine yards, where arsenical anti-spirochetal treatments were used in the past, and where arsenic may still persist. Perhaps a new virulence factor has been selected for by an old antimicrobial treatment.

As information grows concerning the ecology of these new foodborne zoonoses on the farm, the role played by transmission through feed and water on the farm also grows. *C. jejuni* can spread rapidly through a flock of chickens through their drinking water system. *S. Enteritidis* may well have a side reservoir in the rodent population, which re infect the young chickens by contaminating their feed as it rests in the feed troughs at night. *E. coli* O157:H7 may not persist in the bovines themselves so much as in their environment, as it persists in water troughs for long periods of time. The use of subtherapeutic antimicrobial agents in animal feeds may be lowering the resistance of many animals to *Salmonella* organisms via a reversal of the competitive exclusion effect. It is also likely that the new larger scale and higher density animal rearing practices have increased the transmission of some zoonoses among the animals. Intensive agriculture bears some resemblance to the human condition earlier in the industrial revolution. In the 19th century, human populations crowded into the cities were afflicted with a variety of new epidemic food and waterborne diseases, such as cholera, typhoid fever, and dysentery. These diseases were controlled by systematic efforts to collect and treat sewage and prevent it from contaminating the food and water supplies. More recent successes in the control of foodborne diseases have come

from limiting the contamination of the human food and water supply with animal manure. A major effort in the future will involve improving the safety of the animals own feed and water supply, protecting it from manure and other microbial contaminants.

The explosion of the bovine spongiform encephalopathy among the cattle herds of Great Britain offers an extraordinary example of a new class of pathogen, the infectious protein, or prion. The European epidemic of bovine spongiform encephalopathy was foodborne in cattle when they were fed brain tissue from cattle with the disease; it subsequently spread to people who presumably consumed beef. Control depends on elimination of cattle protein byproducts from cattle feed (Taylor and Woodgate, 1997; Will et al., 1997).

The current challenge of transmissible spongiform encephalopathies must raise the question of whether other unforeseen events may lurk around the corner. There are several broad directions in which we might shine the torch. First, it remains likely that some pathogens that are present in foods cause infections in humans by some other route than ingestion. The simplest example is that of the foodborne wound infections. For example, both the newly recognized human pathogen *Streptococcus iniae* and a new biotype of *V. vulnificus* called biotype 3 cause severe wound infections in persons who handled live tilapia fish, and who pricked themselves on a dorsal spine in the process (CDC, 1996; Bisharat et al., 1999). Ebola virus outbreaks may have begun when someone slaughtering a wild primate for food was infected with the virus. Can we speculate that some of the “typical” hand lesions of the food handler in a staphylococcal outbreak are actually wound infections that may come from staphylococci present on raw meat itself? Are there other infections transmitted through direct contact with food, or even by inhalation or other routes of exposure? Second, there are still many syndromes and chronic diseases without explanation, which may turn out to have an infectious or post-infectious etiology. In recent years, peptic ulcer disease and gastric cancer have been associated with *Helicobacter pylori* infection, and hemolytic uremic syndrome (the most common cause of acute renal failure in children) and Guillain Barre syndrome (the most common cause of acute flaccid paralysis in the developed world) are now known to

be post-infectious sequela of infection with *E. coli* O157:H7 and *C. jejuni*, respectively. Are there not other syndromes with similar relationships waiting to be explained? Third, the worlds of plant pathology and animal pathology rarely seem to intersect, though if we met more often together, we might find we shared some concerns. There is, for example, the extraordinary pathogen *Burkholderia cepacia*, a pseudomonad that causes severe illness in children already suffering from the genetic pulmonary disease cystic fibrosis. Similar strains of *B. cepacia* were first described as an opportunistic vegetable pathogen, as they attack onions that have been cut or bruised, and invade, turning them mushy (Coenye et al., 2001). Related strains cause seed-borne disease in rice, and have recently been identified as a cause of subclinical mastitis in sheep (Berriatua et al., 2001). Because it is easy to confuse with *Pseudomonas*, perhaps it is more common, and possibly more pathogenic, than would appear. Are there other pathogens which infect both plants and animals? Finally, there is a huge gap in our knowledge about the mega-kingdom of *Archaea*. Pathogens have been described from all other kingdoms, but none from *Archaea*. Given that these organisms were the first to evolve, it seems unlikely that there are not species of *Archaea* that have acquired pathogenic properties—it seems far more likely that we are simply unable to recognize them.

5. Conclusion

We should expect the unexpected (Swerdlow and Altekruze, 1998). New pathogens are likely to continue to be recognized, and established pathogens will appear in novel food vehicles. A population that is aging and subject to more immunocompromising conditions and treatments will be at higher risk. The continued globalization of food production and distribution and increasing international travel will combine with new tastes, cuisines, and food processing methods to provide more challenges. The recent bioterror attacks with anthrax increase the probability that someone will contaminate food as an instrument of mischief, crime or terror. We can meet these challenges with a flexible and responsive public health system and a commitment to the surveillance,

investigations, and research needed to find solutions. Collaborative international efforts will be critical to increase cooperation across international borders.

At the same time, responsibility for food safety is spreading from the final cook or consumer to the entire food chain. While consumer food safety education has an important role, more consumers are likely to demand safer food to begin with. The entire food industry will be increasingly involved in developing food safety plans and standards. Each link in the chain can impose them on their supplier. It is no longer simply the consumer's responsibility to handle food safely or cook it thoroughly. Indeed, in Europe, the consumer perspective now governs much of food safety, following the collapse of consumer confidence in traditional food safety systems in the wake of the bovine spongiform encephalopathy epidemic. The transformation in food safety in Europe is likely to affect the entire world.

New prevention technologies will be critical to food safety in the future. Composting or other treatments that reliably rid manure of pathogens should be defined and standardized. It may be possible to vaccinate animals against a number of zoonotic foodborne pathogens. Feeding nonpathogenic enteric organisms and complex feedstuffs to animals can prevent them from being colonized with harmful microbes via competitive exclusion and other mechanisms. Treatment with ionizing radiation can eliminate many pathogens from a variety of foods, and would substantially reduce the burden of bacterial foodborne illness; this is the next major food safety technology to adopt (Tauxe, 2001). Other pathogen elimination technologies may become commonly used in the future, such as high-pressure treatment, ultrasound, or high-intensity light. The successes of the 20th century and the new challenges we face mean that public health vigilance, careful investigation of new problems, responsible attention to food safety from farm to table, and partnerships to bring about new control measures will be needed for the foreseeable future.

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