



The Long-Term Health Outcomes of Selected Foodborne Pathogens

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Foodborne disease is a serious public health issue that, according to the Centers for Disease Control and Prevention (CDC), causes tens of millions of acute illnesses, hundreds of thousands of hospitalizations, and thousands of deaths each year in the United States. While the severity of acute foodborne disease varies greatly, depending on the pathogen and the vulnerability of the person infected, the impact of foodborne illness on children, as well as for the elderly and immune-suppressed (e.g., pregnant women, people undergoing chemotherapy, organ-transplant recipients, HIV/AIDS patients), is more likely to be serious and/or long-lasting.

Diarrhea and vomiting are common symptoms, and in most cases, last for only a few days. However, most foodborne pathogens can cause, in a small percentage of cases, serious acute and/or life-long complications, including: kidney failure; paralysis; seizures; hearing/visual impairments and mental retardation.

This report reviews much of what is currently known about the health outcomes for five foodborne pathogens.

Campylobacter infection, which is generally transmitted by food, afflicts millions of Americans annually and hospitalizes over ten thousand. *Campylobacter* is associated with Guillain-Barré syndrome (GBS), the most common cause of neuromuscular paralysis in the United States. GBS patients can become permanently disabled and paralyzed; many require hospital care,

and about a third of them require care at rehabilitation facilities, long-term care hospitals, and/or nursing homes. *Campylobacter* also can trigger arthritis, heart infections, and blood infections.

E. coli O157:H7 infection poses great risk for children, especially those in the younger age groups. Children have the highest incidence rate and are at the greatest risk for developing serious complications. *E. coli* O157:H7 can develop into hemolytic uremic syndrome (HUS), the leading cause of acute kidney failure in children in the United States. HUS can lead to death, or in some cases to long-term or permanent health problems, including end-stage kidney disease, neurological complications, and insulin-dependent diabetes.

Listeria monocytogenes infects thousands of Americans every year, nearly all of them from contaminated food, and has been associated with infections of the brain and spinal cord, resulting in serious neurological dysfunctions or death. Most reported cases occur in children under the age of 4, and about 1 in 5 people afflicted die as a result of the infection. In pregnant women, listeriosis can cause miscarriage, premature birth or stillbirth. Listeriosis survivors often are left with serious neurological dysfunctions, including seizures, paralysis, and impaired ability to see, hear, swallow, or speak. Severe cases often result in partial to total impairment and can require life-long residential care with no possibility of work.

Salmonella, as well as other foodborne bacteria, can trigger reactive arthritis (ReA) in certain individuals. ReA causes painful and swollen joints and can greatly affect an individual's ability to work and quality of life. In recent years, antibiotic-resistant strains of *Salmonella* have emerged and their incidence appears to be increasing, particularly in children. Nearly half of all reported *Salmonella* cases occur in children.

Toxoplasma gondii infection can result in cognitive or visual disabilities, with 80% of infected fetuses/infants manifesting impairment by age 17. Impairments from acute fetal or newborn infection by *T. gondii* can include mild to severe mental retardation, moderate visual impairment, crossed-eyes, and in some cases blindness in one or both eyes.

The long-term health burden of foodborne disease is not well understood and there are few guidelines for long-term medical care. Additional research is needed to improve our knowledge about these diseases so that we can better understand the impact that foodborne illness is having on different populations, particularly young children.

Scientific investigations, including epidemiological studies, will play a critical role in improving our knowledge about foodborne disease and its long-term health consequences. Very few follow-up studies have been conducted to examine the long-term health

outcomes associated with foodborne illness, and the studies that have been conducted have significant limitations, restricting the ability to generalize the results to all foodborne illnesses. As a result, it is difficult to accurately assess the connections between acute foodborne illness and the development of long-term health outcomes.

Systematic follow-up of foodborne illness cases will greatly enhance our ability to attribute long-term health problems to acute foodborne illnesses. Population-based studies, improved public health surveillance, and increased data sharing will improve our knowledge about the sources, trends, and health outcomes associated with foodborne disease, but sustaining these efforts will require dedicated funding. To lower the health, social, and economic burdens of foodborne illness, associated with both its acute impact and its long-term consequences, the United States must support applied foodborne illness research, and begin focusing on the long-term health outcomes associated with foodborne disease.

■ **FOODBORNE ILLNESS MUST BE
RECOGNIZED AS A SERIOUS PUBLIC HEALTH
ISSUE IF WE WANT TO MAKE MEANINGFUL
PROGRESS IN REDUCING SICKNESS,
INJURY AND DEATH ASSOCIATED WITH
FOODBORNE DISEASE.**

Introduction

According to the Centers for Disease Control and Prevention (CDC), foodborne disease is a serious public health issue that causes tens of millions of acute illnesses, hundreds of thousands of hospitalizations, and thousands of deaths each year in the United States (Mead et al. 1999). Foodborne disease is caused by pathogens transmitted in food and/or water (ICMSF 2006), but person-to-person and animal-to-person¹ transmission is also possible. Over 200 known foodborne pathogens (bacteria, viruses, fungi, and parasites)² may contaminate raw foods and are capable of causing disease (Jay 2000). Moreover, estimates of the economic impact of foodborne illness on the well-being of individuals are in the billions of dollars annually (Buzby and Roberts 1997; Roberts 2007).

The severity of acute foodborne disease varies greatly, depending on the pathogen and the vulnerability of the person infected. Diarrhea and vomiting are common

symptoms and, in most cases, last for only a few days. However, some pathogens—such as *Campylobacter*, *E. coli* O157:H7, *Listeria monocytogenes*, *Salmonella* and *Toxoplasma gondii*—have the ability to cause very serious acute illnesses, with parasites, bacteria or bacterial toxins invading the bloodstream. When this occurs, various organs may become compromised or fail, leading to serious health complications or premature death (Mead et al. 1999). For a subset of patients, other serious long-term health outcomes, such as kidney failure, paralysis, seizures, and neurological/cognitive impacts, can develop (Reese et al. 2004; Lindsay 1997; Table 1). Children, the elderly, pregnant women, and other individuals with compromised immune systems are at high risk for developing serious cases of foodborne illness. Children are of special concern: about half of the *reported* cases of foodborne illnesses occur in children under 15 years of age (CDC, FoodNet data, 2008), and children have more years of life ahead of them in which the impact of long-term health outcomes can be manifested.

TABLE 1:
HEALTH OUTCOMES DUE TO SELECTED FOODBORNE/WATERBORNE PATHOGENS

Bacterial, parasitic and viral pathogens	Health outcome
■ BACTERIA	
<i>Brucella</i>	<p>Epididymo-orchitis — inflammation of one or both of the testicles.</p> <p>Meningitis — inflammation/infection of the membranes covering the brain and spinal cord.</p> <p>Pericarditis — inflammation of the sac-like covering around the heart (pericardium).</p> <p>Spondylitis — inflammation of the joints between the spinal bones and the joints between the spine and the pelvis.</p>
<i>Campylobacter</i>	<p>Carditis — inflammation of the muscle tissue of the heart.</p> <p>Cholecystitis — inflammation of the gallbladder that can cause severe abdominal pain.</p> <p>Endocarditis — infection of the inside lining of the heart chambers and heart valves.</p> <p>Guillain-Barré syndrome — body's immune system attacks part of the peripheral nervous system.</p> <p>Meningitis — see <i>Brucella</i></p> <p>Pancreatitis — inflammation of the pancreas.</p> <p>Reactive arthritis (ReA) — a condition triggered by an infection that occurs in another part of the body. ReA can affect the joints, urethra and eyes. ReA is also known as Reiter's syndrome.</p> <p>Septicemia — presence of bacteria in the blood and is often associated with severe infection/disease.</p>

...continued

TABLE 1:
HEALTH OUTCOMES DUE TO SELECTED FOODBORNE/WATERBORNE PATHOGENS ...continued

Bacterial, parasitic and viral pathogens	Health outcome
■ BACTERIA	
<i>Escherichia coli</i> O157:H7	Hemolytic uremic syndrome (HUS)* — a disorder that usually occurs when infection in the digestive system produces toxic substances that destroy red blood cells. HUS can affect all body organs, resulting in: kidney failure; hypertension; neurological problems; diabetes; digestive problems; gallstones; irritable bowel syndrome; intestinal strictures, and pneumonitis (infection of the lung from food or vomit).
<i>Listeria monocytogenes</i>	Meningitis — see <i>Brucella</i> Neurological dysfunctions , such as life-long seizures, and/or an impaired ability to see, hear, swallow, or speak. Sepsis — a severe illness in which the bloodstream is overwhelmed with bacteria.
<i>Salmonella</i>	Aortitis — inflammation of the aorta. Cholecystitis — see <i>Campylobacter</i> Colitis — inflammation of the large intestine. Endocarditis — see <i>Campylobacter</i> Epididymo-orchitis — see <i>Brucella</i> Meningitis — see <i>Brucella</i> Myocarditis — inflammation of the heart muscle. Osteomyelitis — infection of bone or bone marrow. Pancreatitis — inflammation/infection of the pancreas. Reactive arthritis — see <i>Campylobacter</i> Septicemia — see <i>Campylobacter</i> Splenic abscesses — a high level of pus in the spleen caused by a bacterial infection. Septic arthritis (sickle-cell anemic persons) — inflammation of a joint caused by a bacterial infection; also known as infectious arthritis.
<i>Shigella</i>	Hemolytic-uremic syndrome — see <i>Escherichia coli</i> O157:H7 Reactive arthritis — see <i>Campylobacter</i> Splenic abscesses — see <i>Salmonella</i> Synovitis — inflammation of the synovial (joint) membrane.
<i>Vibrio parahaemolyticus</i>	Septicemia — see <i>Campylobacter</i>
<i>Yersinia</i>	Cholangitis — infection/inflammation of common bile duct. Liver and splenic abscesses — high level of pus in the spleen and/or liver. Lymphadenitis — infection/inflammation of the lymph nodes. Pneumonia — infection of the lungs. Pyomyositis — bacterial infection of skeletal muscle which results in abscesses. Reactive arthritis — see <i>Campylobacter</i> Septicemia — see <i>Campylobacter</i> Spondylitis — see <i>Brucella</i>

...continued

TABLE 1:
HEALTH OUTCOMES DUE TO SELECTED FOODBORNE/WATERBORNE PATHOGENS ...continued

Bacterial, parasitic and viral pathogens	Health outcome
■ PARASITES	
<i>Taenia</i>	Cysticercosis — illness caused by a parasite called <i>Taenia solium</i> (<i>T. solium</i>), a pork tapeworm that creates cysts and can affect the brain; spinal cord; muscles; eyes.
<i>Toxoplasma gondii</i>	Central nervous system diseases — any one of the diseases that involve the brain or spinal cord. Encephalitis — inflammation of the brain. Mental retardation. Pancarditis — inflammation of the entire heart. Polymyositis — type of inflammatory myopathy, which is characterized by muscle inflammation and weakness. Retinochoroiditis — inflammation of the retina and choroid. Visual impairment.
<i>Trichinella</i>	Myocarditis — see <i>Salmonella</i> Myositis — inflammation of skeletal muscles that can cause pain (myalgia) and weakness.
■ VIRUS	
<i>Hepatitis A</i>	Liver disease

* Besides HUS, the blood vessel consequences of *E. coli* gut infections are occasionally termed TTP (thrombotic thrombocytopenic purpura). However, HUS and TTP are completely different diseases and TTP should not be used in the post-*E. coli* context. (Tarr et al. 2005).

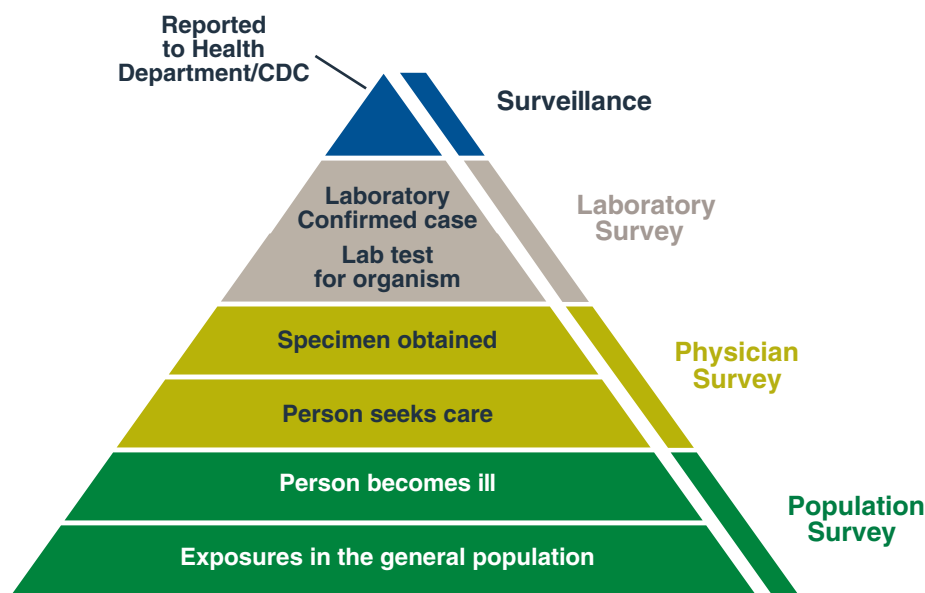
Source: Adapted from the Council for Agricultural Science and Technology (CAST), *Foodborne Pathogens: Risks and Consequences*, CAST, Ames, IA, 1994.

Although some of the health outcomes due to bacterial, parasitic and viral pathogens have been identified, the mechanisms, frequency and severity of the long-term health outcomes of foodborne disease are not well defined and certainly not well-quantified. Complications can vary greatly and sometimes occur even if there are no acute symptoms (Lindsay et al. 1997). In some cases, the chronic health problems may be associated with the person's immune response to the foodborne illness, not the foodborne pathogen itself. For example, reactive arthritis can be triggered by the person's immune response to *Salmonella* or *Campylobacter*, without any acute illness.

Further compounding the issue, the vast majority of foodborne illnesses are undiagnosed or misdiagnosed, resulting in a severe lack of information about foodborne

diseases. Patients frequently endure a few days of acute foodborne illness without seeking medical attention, increasing the likelihood that a disease gets missed entirely or inaccurately diagnosed. Of those who do seek medical attention, only a small percentage of patients are tested and even fewer cases are laboratory-confirmed. As a result, only a small fraction of foodborne illnesses are actually reported to state public health departments and the national surveillance systems at CDC. Under-reporting, coupled with multiple diagnostic challenges, make it difficult to identify foodborne illness outbreaks and/or the source(s) of the illnesses (Holtz, et al. 2009). In an effort to compensate for under-reporting, CDC conducts surveys of physicians and the general population about foodborne illness symptoms, but these efforts are inadequate for filling all of the gaps created by under-reporting.

FIGURE 1:
CDC's FoodNet Surveillance, Burden of Illness Pyramid



Source: CDC. National Center for Infectious Diseases.
http://www.cdc.gov/foodnet/surveillance_pages/burden_pyramid.htm

Currently, the best information on the impact, range, and frequency of human foodborne illness is generated from well-defined investigations of foodborne illness outbreaks,³ and from information obtained through federal surveillance programs, such as FoodNet (Foodborne Diseases Surveillance Active Network),⁴ PulseNet⁵ and OutbreakNet.⁶

While investigating outbreaks is extremely useful, outbreaks account for only a small fraction of all reported foodborne illnesses. The vast majority of cases reported to surveillance programs appear to be sporadic,⁷ making it even more challenging to identify the source of the illness. In addition, sporadic cases may have sources or causative factors that are different from outbreaks, which in turn, would limit the generalizability of studies based on outbreaks. Furthermore, there is no systematic follow-up of foodborne illness cases, making it extremely difficult to attribute long-term health problems to acute foodborne illness.

Currently, many of the associations between foodborne disease and long-term health outcomes have been derived from evidence obtained through investigating individual cases and through small-scale studies. Little is known about the relative frequency of the health outcomes associated with foodborne illness. As a result, the list of health outcomes and the severity and scope of those outcomes as presented in Table 1 is incomplete.

In recent years, there have been many acute foodborne illness outbreaks that have affected thousands of Americans. Many of these outbreaks involve common food products—such as ground beef, peppers, peanut butter, and cookie dough—and have renewed interest in foodborne illness prevention. To develop more effective prevention strategies, researchers need to investigate the sources, trends, and health burdens associated with foodborne disease. In fact, many researchers believe that the burden of the long-term health outcomes related to foodborne illness outweigh the burden of acute foodborne illness (Lindsay et al. 1997).

What follows is a review of the current knowledge about some of the long-term health outcomes of five foodborne pathogens. The paper also identifies some of the major gaps in the current food safety system and proposes areas for future research. *Salmonella* and *Listeria monocytogenes* (bacterial pathogens) and *T. gondii* (a parasitic pathogen) have the highest death rates for acute cases of foodborne disease (Mead et al. 1999). *Campylobacter* is one of the most common bacterial foodborne pathogens in the United States, and *E. coli* O157:H7, a Shiga toxin-producing *E. coli* (STEC), has a large impact on children less than 15 years of age (CDC, *MMWR* 2008). Taken together, these five foodborne pathogens place heavy health and economic burdens on Americans and can cause serious short- and long-term health impacts, both for individuals and society.

Campylobacter: Guillain-Barré Syndrome

MARTIN J. BLASER, M.D.

Each year in the United States, *Campylobacter* foodborne infections are estimated to cause 2 million acute human illnesses, associated with an estimated 10,539 hospitalizations and 124 deaths (Mead et al. 1999). In some cases, campylobacteriosis can be transmitted by farm animals and/or pets, but raw or undercooked poultry product remains the primary foodborne source of *Campylobacter* infections in the United States (Frenzen 2008). Symptoms of

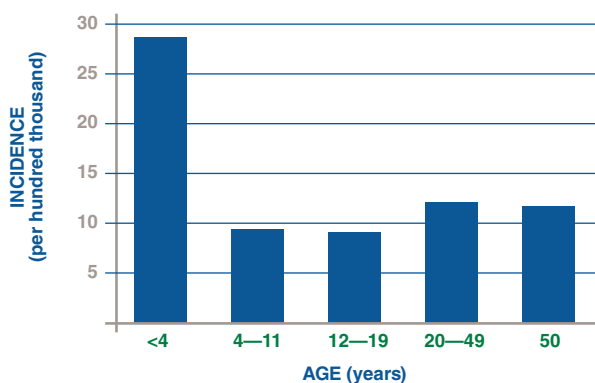
campylobacteriosis can vary from mild to severe and include watery/bloody diarrhea, abdominal cramps, fever, nausea and vomiting. Campylobacteriosis is associated with several long-term or severe complications, such as paralysis, arthritis, heart infections, and septicemia (Table 1). While children have the highest incidence of *Campylobacter* infection in the United States (Figure 2), the severity of the acute infection and the long-term health outcomes often increase with age.

One long-term health outcome that has been studied in detail is Guillain-Barré syndrome (GBS), an autoimmune reaction that can occur within several weeks of an acute infection. Campylobacteriosis is the most common trigger, and it is estimated to be responsible for up to 40% of the 5,500 GBS cases that occur annually in the United States. Currently, GBS is the most common cause of acquired paralysis in the United States, with an estimated 240 previously-employed persons becoming permanently disabled each year. Most young GBS patients (age 18-34) recover spontaneously, but approximately 12% are permanently disabled. GBS patients aged 35-64 years have a 22% permanent disability rate, and those 65 years and older have a 49% permanent disability rate. All GBS patients require care in a community hospital, while 34% also receive inpatient care at rehabilitation facilities, long-term care hospitals, and/or nursing homes. Approximately 100 GBS patients die each year (Frenzen 2008).

In 2004, the annual medical costs and productivity losses in the United States for *Campylobacter*-induced GBS cases was estimated to be \$700 million annually (Frenzen 2008). In 2002, a Dutch study also examined the severity of the long-term consequences of GBS (Robert et al. 2002). The Dutch researchers interviewed GBS patients 2.5 to 6.5 years after the onset of GBS and asked the participants about the impact that GBS had on their health, work potential and private lives:

- 31% reported moderate to serious physical effects;
- 38% of those who were employed prior to their illness had to change jobs;
- 44% altered their leisure activities;
- 37% did not function at home as well as before;
- 39% reported changes in family life.

FIGURE 2:
Incidence of *Campylobacter* Infections by Age, 2008



Source: Centers for Disease Control and Prevention (CDC). Preliminary FoodNet data on the incidence of infection with pathogens transmitted commonly through food—10 States, 2008. *MMWR*, 2009; 58 (13):333-7.

The research also found that GBS victims needed more emotional support and physical assistance, and were less able to contribute to daily household work. If the psychosocial impact of GBS had been included in Frenzen's estimates, the societal costs would be even higher.

While GBS is the most studied long-term health outcome of acute foodborne campylobacteriosis, other serious health outcomes, such as meningitis, septicemia, and reactive arthritis have been associated with campylobacteriosis (Table 1). Additional research is needed to improve our knowledge about the impact and long-term health outcomes of campylobacteriosis.

Escherichia coli O157:H7: Hemolytic uremic syndrome (HUS) and the long-term impacts of *E. coli* infections

DR. PHILLIP TARR, M.D.

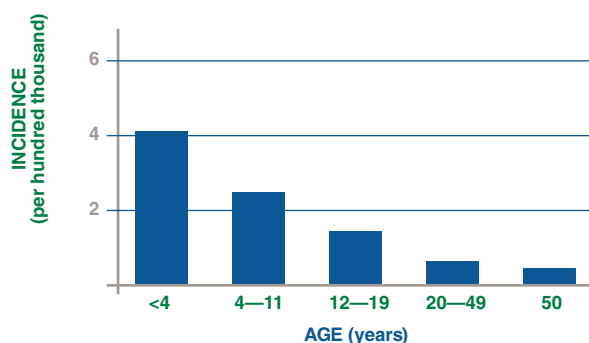
Escherichia coli O157:H7 and possibly other non-O157:H7 Shiga toxin-producing *E. coli* (STEC) are major causes of serious foodborne illnesses. Most *E. coli* O157:H7 infections are sporadic and might be contracted from sources where control of the pathogen could be difficult (Denno et al. 2009). Children have the highest incidence of *E. coli* O157:H7 infection in the United States (Figure 3) and are at highest risk for developing serious complications (Gould et al. 2009).

Most patients who seek medical attention during the acute stage of an *E. coli* O157:H7 infection experience extremely painful diarrhea, with visible bloody diarrhea occurring in about 80% of the laboratory-confirmed cases (Jelacic et al 2003; Chandler et al. 2002; Wong et al. 2000). About 15% of all *E. coli* O157:H7 patients will develop hemolytic uremic syndrome (HUS), a condition that consists of acute kidney failure, anemia, and decreased platelet counts. HUS generally runs its course within 15 days, but once it develops, a cascading series of events can lead to serious illness or premature death. A subset of HUS and *E. coli* O157:H7 patients develop temporary or permanent health outcomes (Chandler et al. 2002; Wong et al. 2000; Bell et al. 1997; Figure 4).

The severity of HUS varies considerably. It is likely that the long-term health outcomes associated with an HUS episode are related to the severity of the acute disease. Research indicates that early diagnosis and intervention might lessen the severity of HUS (Ake et al. 2005). Kidney failure is an important component of HUS. In its mildest form, children with HUS *who can pass urine* do not require dialysis and generally are hospitalized for about a week after diagnosis (Ake et al. 2005).

Impaired urine production during HUS and the development of long-term health consequences appear related. Children with HUS *whose urine output stops* have more severe disease progression and usually require dialysis. These children have longer hospitalizations and have more severe complications during the course of their illness (Ake et al 2005). Siegler et al. (1994) studied 61 patients for approximately a decade after experiencing an episode of childhood HUS. Failure to pass urine during the acute phase of HUS was the strongest predictor of persisting abnormalities at follow-up. All patients whose inability to pass urine lasted 8 days or more had some evidence of chronic kidney impairment. A continuing analysis of this population reinforces this association (Oakes et al. 2008). Garg et al. (2003) conducted a thorough assessment of long-term kidney injury in published literature from 18 countries over 50 years. In this study, the overall pooled incidence of death or end-stage kidney disease was about 12%, while the incidence

FIGURE 3:
Incidence of *E. coli* O157:H7 Infections by Age, 2008



Source: Centers for Disease Control and Prevention (CDC). Preliminary FoodNet data on the incidence of infection with pathogens transmitted commonly through food—10 States, 2008. *MMWR*, 2009; 58 (13):333-7.

for milder impairment was about 24%. However, a more recent analysis of the 2000 Walkerton Canada outbreak identified a lower frequency of severe chronic kidney impairment (Garg et al. 2008; Garg et al. 2009).

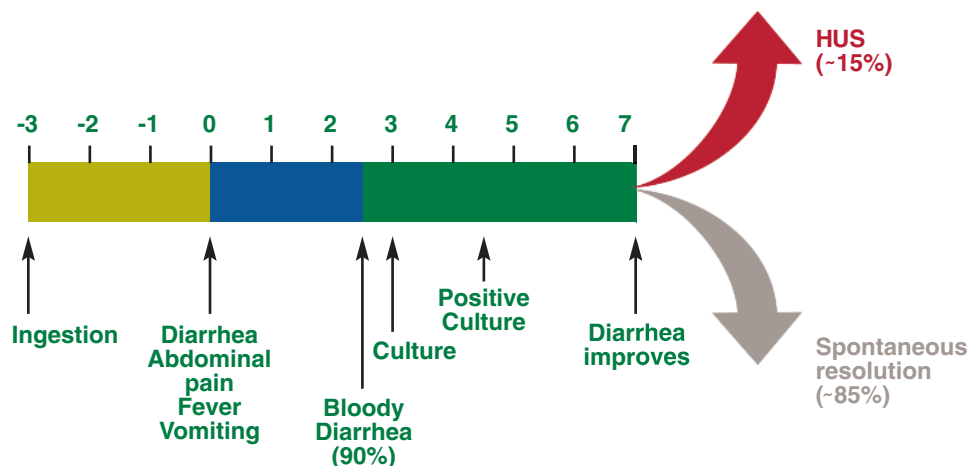
The acute stage of HUS occasionally includes neurological complications (Bale et al. 1980; Sheth et al. 1986). These early complications can be quite severe and include coma, seizures, and stroke (Sieglar et al. 1994). However, even severe neurological injury in the acute phase of HUS, such as coma, is not uniformly associated with poor outcomes (Steinborn et al. 2004; Kahn et al. 1982; Steele et al. 1986). In the 1993 Jack-in-the-Box *E. coli* O157:H7 outbreak, patients followed at Seattle Children's Hospital who sustained severe neurological complications of HUS during the acute stage had complete neurological recoveries within four years (Brandt et al. 1998), a resiliency noted previously (Steele et al. 1983). The most comprehensive analysis of the long-term neurological consequences of HUS studied 91 children an average of 4.1 years after their acute episode and identified no associated long-term neurological injury when compared to individuals hospitalized for other reasons (Schlieper et al. 1999).

Another serious complication during HUS is acute diabetes. In some patients, this condition can persist,

causing permanent, or at least prolonged, insulin dependence. Insulin dependent diabetes following a case of HUS is likely rare. However, due to incomplete patient follow-up, it is difficult to estimate the percentage of patients who experience long-term insulin dependence. Further compounding the issue, a subset of patients with glucose intolerance die during acute HUS (Suri et al. 2009), and the extent to which this condition contributed to the death is not known.

Gastrointestinal complications following HUS have not been studied systematically. In the 1993 Jack-in-the-Box outbreak patients studied at Seattle Children's Hospital, approximately 10% of the childhood survivors developed symptomatic gall stones (Brandt et al. 1998). A small percentage of *E. coli* O157:H7 patients with HUS develop an abnormal narrowing (stricture) in the small intestine and/or colon. Symptoms of these LTHOs, which include abdominal pain and/or vomiting, may take weeks or months to appear after HUS resolves (Whittington et al. 1979; Crabbe et al. 1990; Kirks 1982; Bax et al. 1981; Sebbag et al. 1999). Irritable bowel syndrome can follow some bacterial infections of the intestines and can be caused by many different pathogens (Rees et al. 2004). In a Canadian outbreak caused by *E. coli* O157:H7 and *Campylobacter*, infection-induced irritable bowel syndrome was documented (Marshall 2009).

FIGURE 4:
***E. coli* O157:H7 Progression and Outcome Diagram**



Source: Tarr, P.I., C.A. Gordon, and W.L. Chandler. Shiga-toxin-producing *Escherichia coli* and haemolytic uraemic syndrome. *Lancet*, 2005. 365(9464):1073-86.

Additional details about long term studies on HUS associated with *E. coli* O157:H7 are cited in Appendix A. However, it is important to note that all of these studies, including the ones discussed above, have significant methodological limitations⁸ and cannot be used to quantify risk for long-term injury following acute *E. coli* O157:H7 infection in individual cases. Even so, these studies do portray the spectrum of long-term consequences of HUS. Additional research would benefit physicians and families to make appropriate decisions regarding the care of patients, and most particularly children, who have had *E. coli* O157:H7 infections or HUS.

Listeria monocytogenes: Premature death and brain infections

BENNETT LORBER, M.D.

Listeriosis is a leading cause of foodborne illness death in the United States. It is estimated that more than 2,500 persons are infected with *Listeria monocytogenes* each year, resulting in approximately 500 reported deaths (Voetsch et al. 2007; Mead et al. 1999). Nearly all cases of listeriosis are caused by contaminated food. A large portion of the reported cases occur in children under the age of 4 (most often in infants/newborns) and adults over the age of 50 (Figure 5).

Common symptoms include fever, muscle aches, and sometimes gastrointestinal symptoms. If the infection spreads to the nervous system, headache, stiff neck, confusion, loss of balance or convulsions can occur. Foodborne listeriosis can lead to infections of the brain and/or spinal cord, resulting in death in about 20% of patients. Survivors often are left with serious neurological dysfunctions, including life-long seizures, paralysis, and impaired ability to see, hear, swallow, or speak. They are often unable to work and require medical attention or supportive care throughout the remainder of their lives. The elderly and immune compromised adults are at high risk for developing serious cases of listeriosis (Roberts and Pinner 1990).

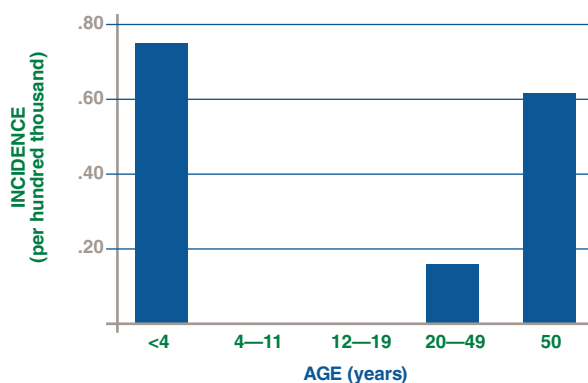
Pregnant women are also at high risk for getting listeriosis — about one-third of listeriosis cases occur

during pregnancy. Typically, the pregnant woman experiences mild, flu-like symptoms, but occasionally severe illness can result. However, due to the fetus's immature immune system, when the bacteria is transmitted from the mother through the placenta, listeriosis can turn deadly, causing miscarriage, premature birth or stillbirth (Roberts and Pinner 1990). Infection may also be spread to a newborn at the time of delivery through the birth canal, resulting in blood or brain infections during the early weeks of life. Newborn infants who survive acute listeriosis may have long-term health outcomes, such as permanent brain damage, mental retardation, or hearing loss (Schuchat et al. 1997).

Roberts and Pinner (1990) examined the impact of acute listeriosis on fetal/newborn infants. Of the 374 cases, there were 79 fetal/newborn deaths and 295 surviving newborns. For the infants who survived acute listeriosis, more than 80% (252) had a full recovery, but 43 survived with long-term health outcomes. For the 43 infants who survived with long-term health outcomes,

- 20% had a mild disability, frequently requiring some educational assistance;
- 60% had a moderate to severe disability requiring educational assistance, with severe cases requiring residential care and no possibility of work;
- 20% had total impairment requiring life-long residential care.

FIGURE 5:
Incidence of *Listeria monocytogenes* Infections by Age, 2008



Source: Centers for Disease Control and Prevention (CDC). Preliminary FoodNet data on the incidence of infection with pathogens transmitted commonly through food—10 States, 2008. *MMWR*, 2009; 58 (13):333-7.

A recent prospective study in the Netherlands examined outcomes for 30 hospitalized adult cases of listeriosis (Brouwer et al. 2006). Complications developed in a high percentage of patients, with 20% experiencing seizures, 33% experiencing cardio-respiratory failure and 40% having impaired consciousness. Of these 30 patients, five died; one became severely disabled; two were moderately disabled, and the remaining 22 patients were discharged with either a mild disability or no disability. Of the mildly disabled group, four had paralysis on one side of their body or had impaired vision, hearing, and/or difficulty with swallowing.

Foodborne listeriosis can be a serious disease, especially for the elderly, pregnant women, and infants/fetuses whose mothers transfer *L. monocytogenes* to them prior to or during birth. More research on the causes of miscarriages, premature birth and fetal/infant death may help develop a better understanding about the scope and impact of *L. monocytogenes* infections.

Salmonella and other foodborne pathogens: Reactive arthritis (ReA)

JAMES L. SMITH, PH.D.

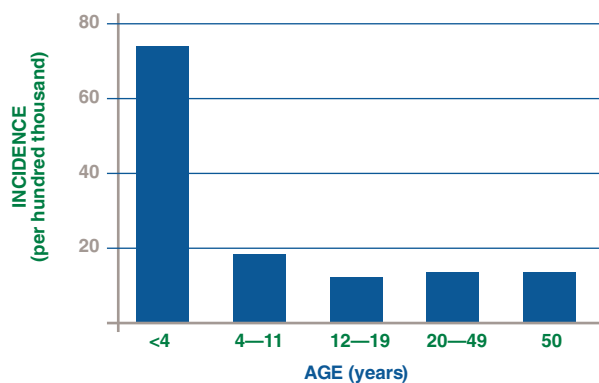
Salmonella is a leading cause of foodborne illness in the United States, causing an estimated 16,000 illnesses and 556 deaths each year (Mead et al. 1999). *Salmonella* serotypes are common to most, if not

all, food animals (CDC website, Salmonellosis), and *Salmonella* can cause many short- and long-term health outcomes (Table 1). In recent years, new multi-drug resistant strains of *Salmonella* have emerged and their incidence appears to be increasing (CDC, Summary of Notifiable Diseases, 2007). Children are at increased risk of infection with antibiotic-resistant strains and are at great risk of severe complications (Shea et al. 2004). More than one third of all reported cases of salmonellosis occur in children under the age of 10, and the incidence in children under 1 year of age is 10 times higher than in the general population (Figure 6).

Salmonella, as well as *Campylobacter*, *E. coli* O157:H7, *Shigella* and *Yersinia*, can trigger an arthritic condition known as reactive arthritis (ReA). ReA causes painful and swollen joints, generally of the lower limbs. However, ReA does not destroy cartilage in joints, as commonly occurs in rheumatoid arthritis. Both men and women have a similar incidence rate for ReA induced by foodborne pathogens (Kim et al. 2008). A population survey conducted in Minnesota and Oregon found that a number of individuals with laboratory-confirmed cases of foodborne illness reported possible ReA symptoms; however, the rate varied depending on the pathogen (Townes et al. 2008; Table 2).

Individuals with ReA usually recover within 2 to 6 months, although some develop additional long-term health outcomes. Raybourne et al. (2000) reviewed

FIGURE 6:
Incidence of *Salmonella* Infections by Age, 2008



Source: Centers for Disease Control and Prevention (CDC). Preliminary FoodNet data on the incidence of infection with pathogens transmitted commonly through food—10 States, 2008. *MMWR*, 2009; 58 (13):333-7.

TABLE 2:
Pathogens associated with self-reported ReA symptoms

Pathogen	Percent with Symptoms
<i>Salmonella</i>	15
<i>Yersinia</i>	14.3
<i>Campylobacter</i>	12.7
<i>Shigella</i>	9.7
<i>E. coli</i> O157:H7	8.9

Source: Townes, J.M., A.A. Deodhar, E.S. Laine et al. Reactive arthritis following culture-confirmed infections with bacterial enteric pathogens in Minnesota and Oregon: a population-based study. *Ann Rheum Dis*, 2008; 67:1689-96.

the sparse literature on ReA for all foodborne pathogens and developed the disease-outcome tree shown in Figure 7. On average, 8% of individuals with acute foodborne illness developed ReA, however, the percentages from individual studies ranged from 2.3% to 15%. According to Raybourne and colleagues, 40% of persons with ReA illness fully recovered and 60% of ReA cases developed progressive or recurrent arthritis, which were further categorized as having mild or intermittent joint pain (1.9% of the initial foodborne cases), severe or chronic joint pain (1.4% of the initial foodborne cases), and spinal complications, such as curvature of the spine (1.4% of the initial foodborne cases).

Treatments for ReA are aimed at decreasing pain and inflammation; minimizing disability; preventing relapses, and halting the progression to chronic disease. Non-steroidal anti-inflammatory drugs, such as ibuprofen or indomethacin, provide symptom relief and may facilitate physical therapy. Disease modifying drugs, such as sulfasalazine have been shown to be beneficial in patients with ReA lasting longer than 6 months (Hannu et al. 2006; Kim et al. 2008; Rihl et al. 2006).

ReA induced by foodborne illness can cause significant health outcomes that can greatly affect an individual's ability to work and quality of life.

Economic losses are incurred by these individuals and society due to the cost of treatment and the loss of salary and productivity. Obviously, the health and economic losses are greater for those more severely affected. Efforts to lower the incidence of foodborne illness will help reduce the number of cases of ReA, benefitting both individuals and society. Additional research is needed to better understand the role that foodborne pathogens play in causing ReA.

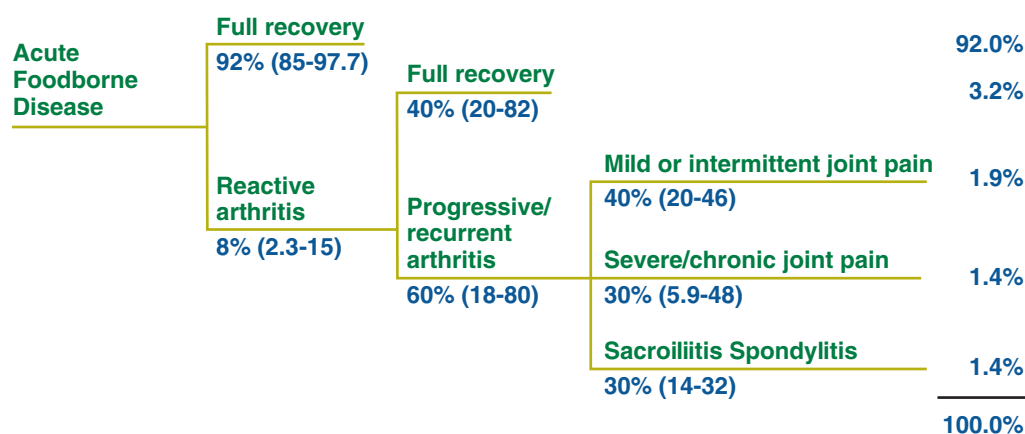
***Toxoplasma gondii*: Mental retardation and impacts on vision**

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Toxoplasma gondii is a protozoan parasite and is the third leading cause of foodborne deaths in the United States (Lopez et al. 2000). Modes of infection for *T. gondii* are ingestion of contaminated food, contact with cat feces or soil, or reactivation of a long-standing latent infection (CDC website, Toxoplasmosis). In the United States, more than 50% of all cases of toxoplasmosis are estimated to be of foodborne origin, resulting in an estimated 112,500 acute illnesses, 2,500 hospitalizations and 375 deaths annually (Mead et al. 1999). Unborn infants and immune-compromised individuals are at highest risk of developing serious complications from toxoplasmosis.

FIGURE 7:

Disease Outcome Tree of Arthropathies*



* Following Exposure to Bacterial Foodborne Pathogens.

Source: Raybourne, R.B., K.M. Williams, T. Roberts and the Arthritis Working Group. Food poisoning: economic considerations, p. 2672-82. In L. Trugo and P. Finglas (eds.), *Encyclopedia of Food Sciences and Nutrition*, Elsevier Science Ltd., London, UK, 2000.

T. gondii tissue cysts persist in chronically infected animals and are a constant source of infection (Dubey et al. 2005). Raw pork, goat and lamb products, as well as soil, are documented sources of human infection (CDC website, Toxoplasmosis). Taking preventive measures, such as following safe food practices (use safe food/water; clean; separate; cook; chill; report foodborne illness)⁹ or wearing gloves when gardening/cleaning cat litter boxes may help reduce exposure to this disease.

In congenital toxoplasmosis, a pregnant woman develops an active infection by eating contaminated food or by being in contact with cat feces or contaminated soil, such as through gardening. In rare cases, such as a pregnant woman with AIDS, a latent *T. gondii* infection can be reactivated. Frequently, the pregnant woman's symptoms may be mild — in fact, for many women, the symptoms will go unnoticed. However, once the acute infection begins, the *T. gondii* parasite may cross through the placenta and infect the fetus.

The probability of fetal infection and its consequences vary depending on the trimester of the pregnancy in which the mother was infected, or in which trimester the pregnant woman's latent *T. gondii* was reactivated.

During the first trimester, if the parasite crosses the placenta to the fetus, it can multiply rapidly in the placenta, as well as in fetus's developing lungs, brain, eyes, and heart. As a result, the fetus usually dies and miscarriage results. Some fetuses survive when infected during the second trimester, but the live infants may experience lesions in the retina (eye) or brain, or the fetus may develop encephalitis, hydrocephalus, or microencephaly. Fetuses infected in the third trimester usually survive, but may suffer residual infection in the brain and eyes (Commodaro et al. 2009; Frenkel and Jacobs 1958).

Within one or two weeks of the acute infection, the mother's body will develop an antibody and transfer

TABLE 3:
Impairments caused by congenital toxoplasmosis in human beings (reported in percentages)

Impairment	First Year	Additional in Second Year	Additional in 3 to 17 Years**	Total Affected
Death	2	0	0	2
Severe illness	11	0	0	11
Severe mental retardation	11	+ 2	+20	33
Moderate mental retardation	5	+ 3	+ 9	17
Slight mental retardation	5	+ 6	+12	23
Blindness (both eyes)	6	0	+ 2	8
Moderate visual impairment	16	+17	+20	53
Crossed-eyed	5	+ 2	+13	20
Deafness	2	0	0	2
Moderate hearing loss (1 ear)	0	0	+10	10
Percentage with impairment***, at specific ages	45%	64%	80%	80%

* Couyreur et al. 1984, ** Wilson et al. 1980, *** Percentages do not equal 100% because of multiple impairments in one person.

Source: Adapted from Roberts, T. and J.K. Frenkel. Estimating income losses and other preventable costs caused by congenital toxoplasmosis in people in the United States. *J Am Vet Med Assoc*, Jan 15, 1990. 196 (2): 249-56

it to the fetus. This maternal antibody may help control the dissemination of *T. gondii* in the blood stream, which is important since the fetus will not have its own cellular immunity until late in the third trimester. Estimates for the yearly number of newborns infected with *T. gondii* in the United States range between 400 to 4,000 cases (Jones et al. 2001). The range is so wide because toxoplasmosis in pregnant women is frequently not diagnosed and is grossly under-reported.

The long-term health outcomes of an acute fetal/newborn infection with *T. gondii* become apparent at various ages during childhood and adolescence. Roberts and Frenkel (1990) examined the literature to assess the probability of the different impacts of toxoplasmosis. During the first year, congenital toxoplasmosis resulted in death in 2% of the reported cases; severe illness in 11% of the reported cases; and severe retardation in 11% of the reported cases (Table 3).

During the developmental years of childhood and adolescence, the impacts of toxoplasmosis become more observable, with 80% of infected fetuses/newborns experiencing some level of impairment by age 17. The percentage of cases that develop severe, moderate, and mild retardation increases by age 17 to 33%, 17%, and 23% of infected cases, respectively (Table 3). In other words, nearly three-quarters of the newborns infected with *T. gondii* developed some level of brain impairment by the age of 17. Impacts on vision are also common, with 53% of cases experiencing moderate visual impairment, such as loss of depth perception when blindness occurs in one eye. Eight percent developed blindness in both eyes by age 17. Fortunately, such visual outcomes can be arrested, even in the later stages of disease, if chemotherapy is used as a treatment (McAuley et al. 1994).

In some cases, a subclinical, chronic *T. gondii* infection can activate to clinical disease. AIDS and other immune-suppressed patients — especially those who have had transplants, large doses of corticosteroids, toxic anti-cancer therapies, or anti-rheumatic chemotherapy with remicade — are particularly susceptible. Occasionally, *T. gondii* can cause serious illness in patients not

known to be immune-suppressed, such as patients who have cloudy vision, focal retinal destruction, and focal blind spots because of recurrent retinochoroiditis (Holland et al. 1999). Fortunately, these cases of toxoplasmosis are generally responsive to chemotherapy with sulfadiazine and pyrimethamine; however, the destroyed retina does not regenerate and blind spots can remain (Frenkel and Jacobs 1958). Individuals who have had delayed treatment may experience residual sight problems that hinder reading and driving.

The frequency and severity of the acute and long-term health outcomes for *T. gondii* that have been suggested here cannot be well quantified because of the lack of data on this disease. More studies are needed to clarify the congenital (pre-birth and newborn) and adult consequences of acute infection with toxoplasmosis.

Discussion

The 21st Century has a rapidly growing population and a food supply that is now global. Recent large, national outbreaks have raised doubts about the safety of the nation's food supply and undermined consumer confidence in the food they feed their families. In 2008, the Government Accountability Office (GAO 2008) issued a report to Congress adding the federal oversight of food safety as a high priority for the federal government because of the risks to the economy and to public health. In November 2008, the GAO identified reforming America's food safety oversight programs as one of the 13 "Urgent Issues" facing President Obama and the 111th Congress (GAO 2009). Most recently, in April 2009 — during another national outbreak of *Salmonella* from peanut products — CDC's preliminary 2008 data from its Foodborne Diseases Active Surveillance Network (FoodNet) showed that the incidence of *Campylobacter*, *Listeria*, *Salmonella*, *E. coli* O157:H7, *Shigella*, *Vibrio*, and *Yersinia* have not changed significantly in recent years (Figure 8). Clearly, foodborne illness is a serious public health challenge for both developing and industrialized nations (Helms et al. 2003).

Foodborne illness can result in significant short- and long-term health outcomes that can negatively affect

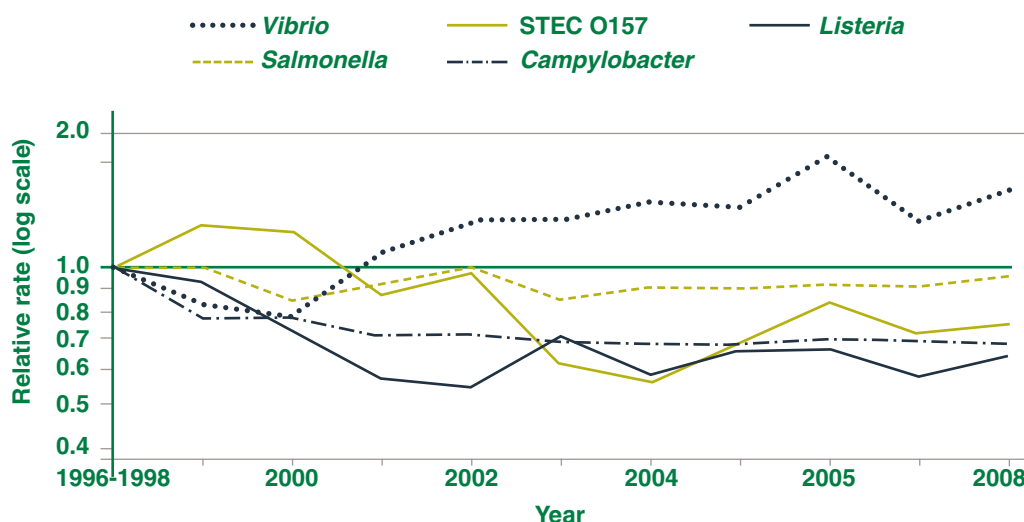
the public's health and the economy. *Campylobacter* infection has been associated with Guillain-Barré syndrome, the most common cause of neuromuscular paralysis in the United States (Buzby and Roberts 1997). *E. coli* O157:H7 infection can lead to HUS, the leading cause of acute kidney failure in children (Williams et al. 2002). *Toxoplasma gondii* can lead to significant visual and cognitive disabilities, with 80% of the fetuses/infants infected having observable impairments by age 17 (Roberts and Frenkel 1990). *Salmonella*, as well as *Campylobacter*, *E. coli* O157:H7, *Shigella* and *Yersinia*, can trigger ReA in certain individuals, leaving them with temporary or permanent arthritis (Rayborne et al. 2003, Townes et al. 2008). *Listeria monocytogenes* has been associated with infections of the brain and spinal cord, resulting in serious neurological dysfunctions or death. Further, in pregnant women, listeriosis can cause premature birth or stillbirth (Roberts and Pinner 1990). Finally, two of the pathogens highlighted in this report, *Salmonella* and *Campylobacter*, have been found to have excess mortality up to one year after acute infection (Helms et al. 2003).

Of particular concern are the vulnerable populations — especially children. According to a 2004 technical report issued by the American Academy of Pediatrics (AAP), the rate of acute *Campylobacter* infections in infants under one year of age is twice that of the general population, and almost 20% of all reported cases of campylobacteriosis occurs in children younger than 10 years of age (Shea et al. 2004). Likewise, *Salmonella* has a major impact on children, particularly infants and children less than 10 years of age. In addition, AAP is very concerned about the emergence of multi-drug resistant strains of these two pathogens and concluded in its 2004 report that “Children are at increased risk of acquiring many of these infections with resistant bacteria and are at great risk of severe complications if they become infected” (Shea et al. 2004). Further, a recent FoodNet study found that females and young children had increased risk of developing HUS following an *E. coli* O157:H7 infection (Gould et al. 2009).

The impact of foodborne disease, including the long-term health burden, on children and other vulnerable

FIGURE 8:

Relative rates of laboratory-confirmed infections with *Vibrio*, *Salmonella*, STEC* O157, *Campylobacter*, and *Listeria* compared with 1996-1998 rates, by year—Foodborne Diseases Active Surveillance Network, United States, 1996-2008.**



* Shiga toxin-producing *Escherichia coli*.

** The position of each line indicates the relative change in the incidence of that pathogen compared with 1996-1998. The actual incidences of these infections can differ. Data for 2008 are preliminary.

Source: Centers for Disease Control and Prevention (CDC). Preliminary FoodNet data on the incidence of infection with pathogens transmitted commonly through food—10 states, 2008. *MMWR* 2009. 58(13):333-37.

populations is not well understood. As a consequence, there are few guidelines for physicians about long-term medical care¹⁰ following acute foodborne illness. Additional research is needed to improve our understanding about the impact that foodborne illness is having on all segments of the population, especially the vulnerable populations.

Scientific investigations, in particular epidemiological studies,¹¹ will play a critical role in improving our knowledge about acute foodborne disease and its long-term health consequences. Epidemiologic data generated from public health surveillance, as well as cohort and case-control studies, can provide valuable information about the nature and magnitude of foodborne disease. Currently, multiple federal, state, and local agencies, as well as the food industry, are involved in the surveillance of foodborne pathogens and foodborne illness. Unfortunately, political and economic barriers have impeded data collection and sharing, resulting in stand-alone databases that cannot be easily linked. To date, very few long-term, follow-up studies have been conducted to examine the long-term health outcomes associated with foodborne disease, and the studies that have been conducted have significant limitations.¹² These studies can be biased toward negative events, thereby limiting the ability to generalize the results to all foodborne illnesses. As a result, it is difficult to accurately assess the overall health burden of foodborne illness, especially the connections between acute foodborne illness and the development of long-term health outcomes.

Mead et al. (1999) attempted to estimate the burden of acute foodborne disease using the limited data available at the time. Beginning in the late 1990s, CDC established FoodNet, PulseNet, and OutbreakNet to help improve public health surveillance of foodborne illness. These programs have led to better estimates regarding the burden of acute foodborne disease, but the programs are generally underfunded. For example, FoodNet's database is limited to active surveillance of seven bacterial and two parasitic foodborne pathogens and one syndrome (HUS). With additional funding, FoodNet could study more pathogens, and perhaps conduct a study on the long-term health outcomes associated with foodborne pathogenic diseases.

As noted above, many researchers believe that the burden of the long-term health outcomes outweighs the burden of acute foodborne illnesses (Lindsay et al. 1997). Yet, there is little epidemiologic data on the long-term health outcomes associated with foodborne disease. To date, the most comprehensive study of the long-term health outcomes associated with foodborne illness has been conducted by Dr. David Mossel, University of Utrecht, Netherlands. Mossel's data was used by the Council for Agricultural Science and Technology (CAST) in its 1994 report, *Foodborne Pathogens: Risks and Consequences*, and provides the backbone for Table 1 in this report.

In 2004, FoodNet conducted a pilot study in California to determine the frequency of self-reported complications of bacterial enteric infections from 1998-1999 (Rees et al. 2004). The study identified a range of symptoms that may be attributable to gastrointestinal infection, including persistent diarrhea, a variety of rheumatologic symptoms, irritable bowel syndrome, and hair loss. Rees et al. concluded that there was a possible association between bacterial enteric infections and a variety of chronic symptoms. The authors also recommended that long-term, population-based epidemiological studies should be initiated to further investigate associations between these infections and long-term human health outcomes, as well as the possible role that antibiotics play in the development and prevention of long-term health complications associated with foodborne diseases.

Conclusion

A new approach is needed to improve our knowledge about the prevalence and scope of foodborne illnesses, as well as the overall burden of foodborne disease. More research is needed to increase our knowledge about the frequency and severity of the long-term health outcomes of foodborne illness, which will, in turn, help identify food safety priorities so that limited resources can be applied appropriately to ensure the greatest public health benefit. State and federal public health agencies charged with the surveillance and oversight of food need stronger research capabilities. Systematic follow-up of foodborne illness cases will greatly enhance our ability to attribute long-term

health problems to acute food borne illnesses. Population-based studies, improved public health surveillance, and increased data sharing will improve our knowledge about the sources, trends, and health outcomes associated with foodborne disease, but sustaining these efforts will require dedicated funding.

To lower the health, social, and economic burdens of foodborne illness, associated with both its acute impact and its long-term consequences, the United States must support applied foodborne illness research, and begin focusing on the long-term health outcomes associated with foodborne disease.

Notes

¹ CDC website. Healthy Pets Healthy People. <http://www.cdc.gov/healthypets/>

² Individual foodborne pathogens and their diseases are described on CDC's website. General information can be found at: http://www.cdc.gov/ncidod/dbmd/diseaseinfo/files/foodborne_illness_FQA.pdf.

³ CDC website. OutbreakNet Team Overview. <http://www.cdc.gov/foodborneoutbreaks/>

⁴ FoodNet does active surveillance of foodborne pathogens and is a collaborative project of the CDC, the U.S. Department of Agriculture (USDA), and the Food and Drug Administration (FDA). There are ten FoodNet sites across the country and include 15% of the U.S. population. For more information: <http://www.cdc.gov/foodnet/>

⁵ PulseNet is a national network of state and local health departments and laboratories and federal agencies (CDC, USDA, FDA) and federal laboratories. CDC coordinates PulseNet and maintains large databases that contain molecular subtyping information.

⁶ OutbreakNet works with epidemiologists, public health departments, federal agencies (CDC, USDA, FDA) and PulseNet to investigate foodborne and waterborne outbreaks of disease. For more information: <http://cdc.gov/foodborneoutbreaks>

⁷ Sporadic cases are foodborne illnesses that are not linked to outbreaks.

⁸ Study limitations include: small number of participants in a study; length that participants were followed; discrepancy between the total number of reported cases and the actual number of cases; bias, which can result if the participants being studied are part of groups that regularly seek medical attention.

⁹ See Appendix B for information on CFI's Six Safe Food Practices.

¹⁰ Guidelines for the acute stage of foodborne disease can be found in several sources, such as CDC's *Diagnosis and Management of Foodborne Illnesses: A Primer for Physicians*. However, there is little on long-term health care management.

¹¹ Epidemiology investigates the occurrences and patterns of disease.

¹² See above, footnote 8.

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Appendix A. Review of Studies on *E. coli* O157:H7 with HUS and Long-Term Health Outcomes

REFERENCE, YEARS OF DISEASE OCCURRENCE, SITE OF STUDY	OUTBREAK?	AGE AT TIME OF HUS	CASE DEFINITION OF HUS SUPPLIED	FOLLOW-UP INTERVAL	NO. STUDIED/ NO. ELIGIBLE (%)	ABNORMALITIES SOUGHT	ABNORMALITIES IDENTIFIED	RISK FACTORS FOR ABNORMALITIES	COMMENTS
Oakes 1970-2003 Utah	No	0-17 y	No	8.75 y	159/357 (44.5%)	Proteinuria Low GFR Hypertension Low GFR and proteinuria Any long term complications	16% 32% 14% 8% 47%	Duration of anuria	10 days appears critical
Siegler Before 1983 Utah	No	*children*	No	9.6 y	61/106 (57.6%)	Proteinuria Low creatinine clearance Proteinuria & low creatinine clearance Proteinuria & low creatinine clearance & hypertension	11% 10% 13% 5%	Oliguria and anuria were associated with sequelae, but were not absolutely associated	10 days appears critical
Gagnadoux 1950-1978 Paris, France	No	*children*	No	18 y	29/96 (30%)	Hypertension Proteinuria Mildly reduced GFR Chronic renal failure End stage renal failure	24% 14% 3% 10% 14%	Anuria over 7 days was associated with more severe sequelae	Late (>5 years) recoveries and deteriorations noted

REFERENCE, YEARS OF DISEASE OCCURRENCE, SITE OF STUDY	OUTBREAK?	AGE AT TIME OF HUS	CASE DEFINITION OF HUS SUPPLIED	FOLLOW-UP INTERVAL	NO. STUDIED/ NO. ELIGIBLE (%)	ABNORMALITIES SOUGHT	ABNORMALITIES IDENTIFIED	RISK FACTORS FOR ABNORMALITIES	COMMENTS
Brandt 1993 Seattle, WA	Yes	1-12.5 y	Yes	27 mo (median)	29/35 (83%)	Proteinuria Hematuria	14% 14%	Duration of thrombocytopenia, and not anuria, had greatest association with sequelae	
Spizziri Buenos Aires, Argentina Years: 1968-1984	No	Mean 13.4 months, range: 3-48 months	No	10-19.8 years, mean 13 years	118/303	Proteinuria Proteinuria and abnormal creatinine clearance	18% 19%	No relation sequelae to characteristics of or events in acute illness	

Brandt, J.R., M.W. Joseph, L.S. Fouser, P.I. Tarr, I. Zeilkovic, R.A. McDonald, E.D. Avner, N.G. McAfee, and S.L. Watkins. Cholelithiasis following *Escherichia coli* O157:H7-associated hemolytic uremic syndrome. *Pediatr Nephrol*, 1998; 12(3): p. 222-5.

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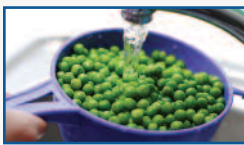
Appendix B. CFI's 6 Safe Food Practices

CFI promotes the World Health Organization's *Five Keys to Safer Food* and encourages the reporting of foodborne illness. Consumers can reduce — but not eliminate — the risk of foodborne illness by following CFI's 6 Safe Food Practices!



1 Use safe water and food.

Be aware of food associated with foodborne illness/food recalls. Read water reports and know the source of food. When in doubt, throw it out!



2 Clean.

Wash your hands often and disinfect surfaces that come in contact with raw food. Wash fruits and vegetables. Do **not** wash raw meat, poultry or fish.



3 Separate.

Keep raw foods — like meat, poultry, seafood, eggs — separated from foods that will be eaten uncooked, like produce or cheese. Use separate cutting boards and utensils.



4 Cook.

Cook foods to the correct temperature and time combination. Color is a poor indicator of doneness — the **only** way to be sure is to use a food thermometer!



5 Chill.

Refrigerate raw and perishable food within 2 hours, at or below 40°F; frozen food at or below 0°F. Use a refrigerator thermometer!



6 Report foodborne illness.

Seek medical attention if you are sickened, but especially if you have bloody diarrhea. Ask to be tested. Notify your public health department.



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