Andreas Sing *Editor*

Zoonoses - Infections Affecting Humans and Animals

Focus on Public Health Aspects

Springer

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Preface

Zoonoses are infectious diseases caused by microorganisms passing from animals to humans and vice versa. In the last few decades most emerging and re-emerging diseases were in fact either of zoonotic origin or zoonotic potential.

The term "zoonosis" was coined by the German physician Rudolf Virchow, mainly known as father of scientific pathology, but also as an important political figure in nineteenth century Germany. Although rooted in a classical faculty-based university system, he and his Canadian disciple William Osler, also a physician by training, very early recognized the need for interdisciplinary collaboration between human and veterinary medicine and also—probably even more importantly—the public health, social and political aspects of zoonotic diseases. While the scientific basis for both of them was pathology, the rise of microbiology as a medical discipline allowed to put the focus on microorganisms as the obvious and easiest walkable bridge between human and animal infectious diseases. This is even more true since the advent of especially DNA-based typing techniques for analyzing microorganisms isolated from different species thus allowing to study their real zoonotic potential.

By incorporating life and social science subdisciplines (e.g. immunology or epidemiology) a systemic paradigm was introduced in medical science thus preparing the ground for inter- and transdisciplinary approaches both in human and veterinary medicine. A striking example for the consequences of this paradigm shift on a population level are the concepts of New Public Health.

Not at last driven by the need for global public health efforts to combat both real or anticipated releases from Pandora's box in an interconnected and globalized world the One Health concept rapidly gained momentum in the last decade after the establishment of the 2004 "Manhattan Principles".

This book is based on the One Health concept with a focus on the public health impacts of zoonoses, both medically and societally. Important aspects in understanding zoonoses are not restricted to more classical issues, e.g. their epidemiology in both humans and animals or disease symptoms in the respective two-legged, four- or more-legged, feathered or unfeathered species, but have to take into account molecularly based epidemiological data and systemic, e.g. ecological approaches.

To give an impression of the wide range of zoonotic research issues, the authors of this book were chosen from a variety of academic and professional backgrounds, from the fields of human and veterinary medicine, from universities and public health institutions, and from all continents. The underlying ideas was not to get an encyclopedic review on all known zoonotic disease entities, but to have a forum for identifying or discussing urgent issues of zoonoses under a public health perspective. Accordingly, the main target groups are the respective scientific communities, medical and veterinary practitioners, their students, public health and veterinary public health practitioners as well as decision makers in the field of public health and veterinary public health.

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Part I
Zoonoses in Food-Chain Animals with Public Health Relevance

Chapter 1
Important Public Health Zoonoses Through Cattle

Mo D. Salman and Katie Steneroden

Abstract Cattle production is a vital component of the global food chain. Animal protein, through meat or milk, is an essential dietary requirement for the majority of people across the world. Increased cattle production will attempt to meet the need for more protein with both positive and negative impacts, including the spread of diseases from livestock to people directly or indirectly through products such as milk, meat, hide or manure. The following zoonotic diseases of cattle are included in this chapter due to their potential severity in humans or cattle population and/or their wide distribution or recent emergence: anthrax, bovine spongiform encephalopathy (BSE), bovine cysticercosis, bovine tuberculosis, brucellosis, cryptosporidium, *Escherichia coli* O157:H7, leptospirosis, methicillin resistant *Staphylococcus aureus* (MRSA), Q fever, Rift Valley Fever, and *Salmonella.*

Cattle production is a vital component of the global food chain. Animal protein, through meat or milk, is an essential dietary requirement for the majority of people across the world. The need for animal protein is increasing. An estimated 50 % increase in demand is expected by the year 2030 (Delgado et al. 1999; Jones and Thornton 2009). Increased cattle production will attempt to meet the need for more protein with both positive and negative impacts, including the spread of diseases from livestock to people directly or indirectly through products such as milk, meat, hide or manure.

Threats from old and new pathogens continue to emerge, with contribution from changes in the environment, agriculture and food production systems, food processing, and the demography and connectivity of our world. At one extreme is low-intensity cattle farming, the type traditionally practiced in developing countries and rural households. The impact of disease outbreaks on the lives and livelihoods of these poor farmers is significant (Jones and Thornton 2009). In contrast, intensive farming systems in developed countries may contribute to the large scale spread of pathogens during disease outbreaks. Zoonotic diseases can have a great impact on national and international trade in addition to contribution to human illness. We are faced with a changing landscape of infectious disease that affects both humans and

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animals. This change poses significant threats to the health and food security of the global citizenry (Atkins and Robinson 2013).

The majority of human pathogens now described are linked to animals. An average of three new infections are reported approximately every 2 years with a new pathogen published every week (Gideon Informatics 2013). Nevertheless, good progress continues to be made in the control of several important livestock pathogens and mechanisms are now in place to bring together the critical scientific expertise and political will to succeed.

The following zoonotic diseases of cattle are included in this chapter due to their potential severity in humans or cattle population and/or their wide distribution or recent emergence: anthrax, bovine spongiform encephalopathy (BSE), bovine cysticercosis, bovine tuberculosis, brucellosis, cryptosporidium, *Escherichia coli* O157:H7, leptospirosis, methicillin resistant *Staphylococcus aureus* (MRSA), Q fever, Rift Valley Fever, and *Salmonella*.

Considerable challenges are presented by zoonotic pathogens to the health and wellbeing of cattle and humans. For some critically important diseases, the first line of defense will be the implementation of scientific approaches to diagnosis and control. What the future will bring with regard to zoonotic diseases is difficult to predict. A future where human and animal health practitioners work together to discover, control and prevent zoonotic diseases will surely bring surprising and meaningful results.

1.1 Anthrax

Bacillus anthracis, the causative agent of anthrax has a worldwide distribution in both animal and human populations. In developing countries anthrax is a significant problem in livestock and wildlife and among occupationally exposed individuals including veterinarians, agricultural workers and butchers (WHO 2013a). In developed countries anthrax is no longer an important disease of livestock due to appropriate control measures including prophylactic vaccination. While anthrax does occur sporadically in developed countries, its main significance lies in its potential use as an agent of bioterrorism.

Bacillus anthracis is a Gram-positive bacterium that forms spores when exposed to oxygen, which are highly resistant and long lasting in the environment. Human cases of anthrax are associated with infection in livestock or exposure to contaminated products such as carcasses, hides or wool. Animal cases of anthrax are associated with spore-contaminated pastures. The incidence of anthrax varies with the soil type, climate, animal husbandry, industrial hygiene, and disease reporting status of the country. Globally, anthrax is underreported in both humans and animal populations due to under-diagnosis and lack of internal and international reporting.

Infection can enter the body by ingestion, inhalation, or direct contact. It is generally considered that animals are infected by ingestion of contaminated food or

water. In humans, infection mainly occurs by direct contact through a break in the skin. Biting flies and other insects have the ability to transmit the disease mechanically.

In cattle, anthrax usually manifests as peracute or acute disease. The peracute form is most common at the beginning of an outbreak and animals are found dead without premonitory signs. After death, discharge of blood from the nostrils, mouth, anus and vulva are common. The acute form runs a course of about 48 h with severe depression, lethargy, abortion and fever. Necropsy findings include absence of rigor mortis and gross enlargement of the spleen with natural orifices exuding dark, tarry unclotted blood. If anthrax is suspected, the carcass should not be opened, as exposure to oxygen will cause spores to form, which may infect individuals and contaminate the environment.

In humans the three main forms of disease are cutaneous, gastrointestinal and inhalation anthrax. Cutaneous anthrax is most common and accounts for the vast majority of cases. The gastrointestinal form occurs from ingesting contaminated meat. Inhalation anthrax occurs through inhalation of the spores and is the most severe form (Decker 2003).

There are different assays for screening and diagnosis of anthrax in cattle. A stained smear of peripheral blood is usually considered as the primary screening test to determine the presence of the bacilli in the blood. Confirmation is by blood culture to identify the bacterial colonies. Fluorescent antibody techniques may also be used to confirm the infection. Animal passage assay may be necessary, if antibiotic therapy is used (Dragon et al. 1999).

Two types of vaccines are currently used in cattle. The most commonly known vaccine is the living attenuated strain of *B. anthracis* that results in long-term immunity (26 months), but there is risk of causing the disease. The second vaccine is the cell-free filtrate of a culture of *B. anthracis*—incapable of causing anthrax, but it has only a short-term immunity (3–6 months) (WHO 2013a).

Treatment in animals and humans is mainly through the application of antibiotics. In animals, penicillin, streptomycin, and oxytetracycline are used. Anti-anthrax serum may be used in animals during the early stages of disease, but severely ill animals are unlikely to recover. Human treatment is by penicillin and other antibiotics (Dragon et al. 1999; CDC 2003).

Control measures are wide range and include the use of vaccination, appropriate carcass disposal methods and decontamination, quarantine, and movement restrictions on milk and meat.

1.2 Bovine Spongiform Encephalopathy (BSE)

Bovine Spongiform Encephalopathy (BSE), also known as “mad cow disease,” is a degenerative neurological disease of cattle. BSE is caused by misfolded proteins (prions) in the host cell that build up in the central nervous system (CNS)

and eventually kill nerve cells. The nature of the transmissible agent is not well understood. The most accepted theory so far is that the agent is a modified form of a normal protein known as prion protein. For reasons that are not yet understood, the normal prion protein changes into a pathogenic (harmful) form that then damages the central nervous system.

BSE is one of several rare neurological diseases called Transmissible Spongiform Encephalopathy (TSE). The other TSE diseases include scrapie, which affects sheep and goats; transmissible mink encephalopathy; feline spongiform encephalopathy; and chronic wasting disease of deer and elk. There are six TSE diseases that affect humans: kuru, classical Creutzfeldt-Jakob disease (CJD), variant Creutzfeldt-Jakob disease (vCJD), Gerstmann-Sträussler-Scheinker syndrome, fatal familial insomnia, and sporadic fatal insomnia.

Variant Creutzfeldt-Jakob disease (vCJD) is a rare human TSE that research from the United Kingdom has associated with consumption of products contaminated with CNS tissue from BSE-infected cattle. There have been about 200 cases of vCJD in the world (most of these in the United Kingdom). Human TSE's also include sporadic Creutzfeldt-Jakob disease (sCJD or CJD), which is not related to BSE. About 85 % of CJD cases are sporadic with an annual incidence of about one case per 1 million people worldwide. The new variant or variant form (vCJD) affects younger people (average age at onset is 26 years), and has different clinical features from CJD.

There is strong epidemiologic and laboratory evidence suggesting that vCJD and BSE are caused by the same infectious agent. All cases of confirmed vCJD have occurred in people who have lived in geographic areas with BSE cases; the majority occurred in the United Kingdom, which has had the largest number of cases of BSE in cattle. The specific foods, if any that may be associated with the transmission of this agent from cattle to humans are unknown. However, milk and milk products are unlikely to pose any risk for human exposure to the BSE agent.

Research indicates that the first probable infections of BSE in cows occurred during the 1970's with the first two cases of BSE being identified in 1986. BSE may have originated from feeding cattle meat-and-bone meal (MBM) that contained BSE-infected products from a spontaneously occurring case of BSE or scrapie-infected sheep products. There is strong evidence and general agreement that the outbreak was then amplified and spread throughout the United Kingdom cattle industry by feeding rendered, prion-infected, bovine meat-and-bone meal to young calves.

There is increasing evidence that there are different strains of BSE: the typical BSE strain responsible for the outbreak in the United Kingdom and two atypical strains (H and L strains). The typical BSE strain is responsible for most of the BSE cases in the world. In cattle naturally infected with BSE, the BSE agent has been found in brain tissue, in the spinal cord, and in the retina of the eye. Additional experimental studies suggest that the BSE agent may also be present in the small intestine, tonsil, bone marrow, and dorsal root ganglia (lying along the vertebral column).

In response to the BSE epidemic, several countries instituted a series of measures to minimize the risk of disease transmission among both animals and humans.

These included a ban on feeding ruminant protein to ruminants and removal of some "high risk" materials (such as brain, spinal cord and intestines) from cattle at slaughter. Following institution of these measures, the number of BSE cases has been decreased significantly (USDA-APHIS 2006, 2007).

To prevent BSE from entering the country, several countries prohibited the importation of live ruminants from countries where BSE is known to exist in native cattle. Some countries eliminated the importation of live ruminants and most ruminant products, including meat, meat-and-bone meal, offal, glands, etc. from all of Europe. The majority of these countries also prohibited the use of most mammalian protein in the manufacture of animal feeds given to ruminants. Testing for BSE under national surveillance program among slaughtered cattle was implemented in several developed countries. Due to these safeguard measures the risk of transmitting BSE agent to humans was becoming negligible (Salman et al. 2012).

1.3 Bovine Cysticercosis—Taeniasis

Although bovine cysticercosis does not in itself represent an exceptionally serious human health risk, it is a signal of much more serious food safety and public health concerns. A finding of bovine cysticercosis is a signal that the animal feed system is contaminated and that cows are consuming human feces. Aside from *Taenia saginata*, other contaminants that pose threats to bovine and human health would also be expected to be present in human feces. These contaminants include, but are not limited to drug resistant bacteria, such as *E. coli* and *Salmonella*, *Taenia solium* (the pork tapeworm), drug residues, pain killers, hormones, other prescription drugs, illicit drugs, heavy metals, solvents and other toxicants.

Taenia saginata (T. saginata) is a cestode tapeworm that causes bovine cysticercosis in cattle and taeniasis in humans. *T. saginata* is found worldwide and human disease is highly endemic in Latin America, Africa, Asia and some Mediterranean countries (Spickler 2003). Bovine cysticercosis occurs in areas where poor sanitation, poor food inspection and close contact between humans and livestock are common (Acha and Szyfres 2003).

T. saginata infection cycles between humans (primary host) and cattle (reservoir host). Humans infected with the tapeworm pass the eggs in their feces. Cattle become infected by ingesting materials contaminated with tapeworm eggs. Larvae form cysticerci in the animal's muscle tissue, humans ingest cysticerci in raw or under-cooked beef, and the cycle continues. Tapeworms cannot be passed from person to person or spread between cattle. Clinical signs of cysticercosis in cattle and humans are mild to non-existent (Acha and Szyfres 2003). The most visible sign of tapeworm infection in humans is the active passing of tapeworm segments through the anus and in the feces.

Diagnosis of bovine cysticercosis is largely done during visual inspection of the carcass at slaughter. Serological tests including ELISA have been used in epidemiological studies for individual and herd diagnosis (WHO 2005). Taeniasis in humans

is diagnosed by finding eggs or cestode segments on the human body or in the feces with peri-anal adhesive tape tests. Feces microscopy, ELISA and molecular tests such as PCR may also be utilized (WHO 2005).

Infection in humans can be prevented by proper meat inspection and handling of meat at slaughter. When disease is found in cattle the meat may be condemned or temperature treated by freezing or heating to kill the parasite. Preventing and treating disease in people will prevent disease in cattle. Tapeworm eggs can survive in the environment for many months depending on humidity and temperature. Infected people can shed hundreds of thousands of eggs each day, so it is important for people to seek treatment to break the cycle.

1.4 Bovine Tuberculosis

Bovine Tuberculosis (BTB) is a zoonotic and economically important disease of livestock. The disease was described over 2000 years ago and is responsible for devastating illness and death in both humans and animals. Bovine tuberculosis has been largely controlled in developing countries through government control programs and milk pasteurization. In developing nations where surveillance and control measures are lacking or inadequate, humans continue to become infected with BTB through animal contact and ingestion of unpasteurized dairy products. Few developing countries have BTB control programs and immune system compromising disease conditions such as HIV allow for co-infection and increased morbidity and mortality (Miller and Sweeney 2013).

Most warm-blooded vertebrates, including humans, are susceptible to the disease causing agents. Although the principle reservoir of *Mycobacterium bovis* (*M. bovis*) is cattle, this organism has a wide host range with the capacity to produce progressive disease. Ungulates differ somewhat in resistance to *M. bovis*, but have similar immune responses and pathological conditions. They all exhibit the classical lesions of tuberculosis.

The infection is caused by the bacterial genus *Mycobacterium*. Mycobacteria are acid-fast, aerobic, non-spore-forming, non-motile, gram-positive rods containing high lipid content. Some of the lipids possess virulent and immunologic properties. The possible pathogenic role and the effect on the immune response of components of the complex mycobacterial cell wall are the subject of much attention and controversy (Behr 2013).

Bovine tuberculosis occurs throughout the world. The prevalence of *M. bovis* in cattle is low in developed countries due to successful eradication programs. Other countries have experienced increases in the rate of infection due to relaxation in surveillance activities.

Risk factors for cattle include overcrowding, introduction of tuberculous animals, soil type, wild life contact in specific geographical regions (UK, Ireland: Badger, New Zealand: Possum), purpose of the cattle: dairy vs. beef; and type of management and husbandry—specifically in the type of disposal of the manure.

The most common mode of transmission of BTB is the aerogenous route. Infection can occur by ingestion and other less likely modes such as milk-borne, congenital, or sexually transmitted. Bacteria are excreted in exhaled air, sputum, feces, urine, milk, and discharges from uterus, vagina, and draining peripheral lymph nodes. Cattle can develop bovine tuberculosis through exposure to other *M. bovis* infected species such as humans, deer, and elk (Bovine TB Advisory Group 2009).

Clinical signs of disease in cattle are variable depending on the location and extent of the lesions. Even with advanced disease, visible signs are frequently absent. If superficial lymph nodes are involved, they may be visibly enlarged and can rupture and drain through the skin. Enlarged internal nodes can cause signs of obstruction. With pulmonary involvement, a chronic cough can develop due to bronchopneumonia. In advanced lung disease, dyspnea occurs with increased respiratory rate and depth. Tuberculosis mastitis causes a marked induration and hypertrophy of the udder. General findings include anorexia, dyspnea, weight loss, weakness, and low-grade fluctuating fever. Often the main sign of tuberculosis is emaciation, despite adequate nutrition and care.

A definitive diagnosis for mycobacterial infection can be made by bacterial isolation and identification, which can be difficult and time consuming. For example, in *M. bovis* cultures visible growth arises following 3–8 weeks of incubation. Conventional mycobacteriological identification procedures on culture media rely on differences in culture growth times, colony morphology, cellular morphology, antimicrobial sensitivity, and various biochemical test reactions. More recent techniques such as radiometric procedures can expedite mycobacterial detection times, whereas gas-liquid chromatography, and DNA robes can accelerate mycobacterial identification from cultures. Research on the use of the DNA probes, specifically polymerase chain reaction (PCR), is currently in progress to be used for molecular epidemiology of the disease in livestock species.

The tuberculin skin test is an in vivo diagnostic test used to evaluate the cell-mediated immune response to mycobacteria exposure. The test is unable to differentiate between disease and immunity. To determine whether or not an animal is infected with *M. bovis*, tuberculin made from either the human or bovine bacilli (the mammalian tuberculins) is injected intradermally into the animal. Reactivity to tuberculin made from either of these bacilli is similar and is normally the greatest in animals sensitized specifically to these bacilli. The inflammatory response to the injection peaks from 24 to 72 h following tuberculin injection and can linger for several weeks before diminishing. Failure of animals with observable evidence of tuberculosis to show a palpable skin response to tuberculin at the time of test reading has been defined as anergy. Anergy is indicative of deficient T lymphocyte function.

Vaccines against *M. bovis* stimulate cell-mediated immunity. BCG (Bacillus of Calmette–Guerin, the modified *M. bovis* vaccine strain named after its two developers) is an attenuated strain of *M. bovis* used in human vaccination. BCG has also been utilized extensively to vaccinate cattle in numerous countries for many years. Protection produced by BCG vaccination of cattle is poor and causes tuberculin

sensitivity in the animals, interfering with control and eradication programs based on tuberculin skin testing. By 1968, none of the national control programs for bovine tuberculosis included vaccination.

Treatment of tuberculosis in animals in general is discouraged due to possible public health hazards in retaining tuberculous animals. However, throughout the years, numerous procedures have been tried without success to treat tuberculous cattle, including injection of live or dead bacilli, specific diets, fresh air, change of climatic conditions, x-ray therapy, serotherapy, pneumothorax, and pneumoperitoneum. Chemotherapeutic drugs, including isoniazid, have been used in cattle and were found to only suppress the bacilli during the duration of drug therapy, with shedding of the organism possible after treatment.

Control measures include test and slaughter, active detection of the lesioned cattle in slaughterhouses followed by trace back systems and control of the disease in wildlife populations.

1.5 Brucellosis

Brucellosis is a zoonotic disease of major social and economic importance in most countries of the world. It is caused by several species of *Brucella* bacteria and effects several livestock species—mainly cattle, sheep, and goats. The economic importance of the disease in cattle is due to a loss of production, primarily decreased milk production, abortion, and infertility. Brucellosis is found worldwide, however in some geographical areas it is limited to a specific *Brucella* species and host species. Several countries have succeeded in the eradication of the disease from specific host species; other countries are engaged in eradication programs. The growing phenomenon of international migration and tourism renew our concern with the prevalence and persistence of human brucellosis.

The *Brucella* spp. have a wide host range, however, they are not readily transmitted from preferential to dissimilar hosts. Non-preferential hosts may harbor the bacteria, but it is considered an incidental infection. This incidental infection is usually localized and/or shows different clinical and pathological manifestations from those observed in the specific host. The host preferences of this bacterial agent are: *Brucella abortus* in cattle, *Brucella melitensis* in sheep and goats, *Brucella suis* in swine and *Brucella ovis* in sheep (Moreno et al. 2002).

The bacteria is an intracellular organism which is an important factor in its survival in the host and may explain both the transitory titers occurring in some hosts following isolated episodes of bacteremia and the disappearance of titers in hosts with latent infection. The bacteria can survive on grass for variable periods depending on environmental conditions. In temperate climates, infectivity may persist for 100 days in winter and 30 days in summer. The organism is susceptible to heat, sunlight, and standard disinfectants, but freezing is conducive to almost indefinite survival (Blasco and Molina-Flores 2011).

Risk factors associated with infection and the diseases in cattle population include: (1) Contact with infected materials—aborted fetus, placenta, semen, secretion, etc.; (2) Direct contact with infected animals—including wildlife species; (3) High population density, particularly in dairy farming systems; (4) Breeding management and husbandry such as contaminated maternity pens, unregulated breeding time; and (5) Poor hygiene/husbandry—particularly during calving seasons.

The infection in humans is nonspecific and manifests as fluctuating fever, pain in joints, sweating, and weakness. Transmission to humans occurs through contact with contaminated materials from infected animals particularly as an occupational hazard; consumption of infected milk and dairy products; non-intentional injection of live animal vaccine; and inhalation of large amounts of bacteria contaminated aerosols. Human infection with brucellosis is most serious when it results from exposure to *B. melitensis*, which is usually linked to exposure to infected goats and sheep (Corbel 2006).

The disease in animals is transmitted through ingestion of contaminated materials; penetration of intact skin and conjunctiva; and contamination of the udder during milking. Intra-herd spread occurs by both vertical and horizontal transmission. Congenital infection due to *in utero* infection does occur, but its importance has not been defined. Horizontal transmission can occur both directly and indirectly. Flies, dogs, rats, ticks, infected boots, fodder, and other inanimate objects are possible ways for indirect transmission. Preventive measures in cattle population are mainly related to early detection of infected cattle with removal of serologically positive animals (test and culling) and the application of vaccine.

No reliable vaccine is available for human use. Humans are usually treated prophylactically with antibiotics if exposure is suspected. Preventive measures for human infection include precaution in handling contaminated materials from infected animals and precautions during the use of the vaccine in animals and avoiding consumption of unpasteurized milk or dairy products.

1.5.1 Cryptosporidium parvum

Cryptosporidium parvum is a coccidian protozoan that is an important cause of diarrhea in cattle and humans worldwide. It has emerged since the 1970's as a major cause calf-hood diarrhea. It is one of the top four agents responsible for moderate to severe gastrointestinal illness in children in developing countries and can be a fatal complication of AIDS (Kotloff et al. 2013) (Mosier and Oberst 2000). Cryptosporidiosis is one of the most common causes of waterborne disease among humans in the United States (CDC 2013a).

C. *parvum* resides in the small intestine of the host where it forms oocysts, which are shed in great numbers in the feces. Transmission occurs through ingestion of food and water contaminated with fecal matter from an infected animals or humans, direct contact with infected feces or ingestion of contaminated water. Large outbreaks have been associated with drinking water, food, swimming pools and lakes.

Community-wide outbreaks of cryptosporidiosis have been linked to drinking municipal water or recreational water contaminated with *Cryptosporidium*. One large-scale outbreak occurred in Wisconsin, USA in 1993 when more than 400,000 people became ill from a malfunctioning municipal water filtration system. The total cost of outbreak-associated illness was US$ 92 million. (Corso et al. 2003) The source of the *Cryptosporidium* oocysts in this outbreak, whether from cattle, slaughterhouse run off or from human sewage, remains speculative (Mac Kenzie et al. 1994).

In healthy humans, infection is usually asymptomatic and self-limiting. In immunodeficient people disease can be severe with profuse watery diarrhea and substantial fluid loss (Acha and Szyfres 2003). Most animals can become infected with *Cryptosporidium* spp., but clinical signs of diarrhea, tenesmus, anorexia and weight loss are most commonly observed in calves less than one month old.

Cryptosporidiosis is diagnosed by examining fecal samples using acid-fast staining, direct fluorescent antibody and/or enzyme immunoassays (CDC 2013a). The oocysts are not shed continuously and repeated sampling may be necessary. Cryptosporidiosis can also be diagnosed in stained biopsy/necropsy specimens or fresh intestinal scrapings. Molecular methods, which can detect *Cryptosporidium* species, are increasingly being used in diagnostic laboratories.

There is no specific treatment available for Cryptosporidiosis; supportive therapy is usually effective. Prevention efforts focus on hand washing, especially after handling or being around animals and before eating or handling food.

1.5.2 E. coli O157:H7

Escherichia coli is in the family *Enterobacteriaceae* and is a normal component of the flora in the large intestine of humans and warm-blooded animals. *E. coli* O157:H7 is a specific pathogenic subset of *E. coli* found worldwide, that produces watery diarrhea, hemorrhagic colitis and rarely, hemolytic-uremia syndrome (HUS) in children.

Cattle are a reservoir hosts, harbor the bacteria asymptomatically and are an important source of infection for humans. Prevalence estimates vary, and it appears that while a large percentage of cattle herds may have infected animals, the actual number of individual infected animals at any one time is relatively low (USDA 2003). The costs associated with attempts to control prevalence in cattle, contaminated food recall, and human healthcare costs make the economic and social burden *E. coli* O157:H7 high (Callaway 2010).

Transmission of *E. coli* O157:H7 occurs through consumption of contaminated food or water, direct contact with infected animals, their feces or contaminated soil. Primary sources of *E. coli* O157:H7 outbreaks are raw or undercooked ground meat products, raw milk and fecal contamination of vegetables. Person-to-person spread can occur during outbreaks (Spickler 2009). Visiting farms and other venues where the general public might come into direct contact with farm animals, particularly

calves, has been identified as an important risk factor for *E. coli* O157:H7 infection (WHO 2011a). A low dose of bacteria is sufficient for infection.

E. coli O157:H7 occurs asymptomatically in cattle and is shed intermittently. In humans, illness can range from mild diarrhea to severe hemorrhagic colitis. In most cases the illness is self-limiting. Hemolytic uremic syndrome, a particularly severe complication, can occur in a small percentage of cases leading to renal failure and death in children and elderly. Selective and differential culture media have been developed to diagnose *E. coli* O157:H7 in human and bovine fecal samples.

Measures to prevent and control *E. coli* O157:H7 in cattle include management changes (biosecurity, housing, transport and stress reduction), water and feed management, including additives and probiotics; bacteriophages and vaccines (Callaway 2010). Pre-harvest strategies are important, but do not eliminate the need for good sanitation in processing plants and households. Good hygienic slaughtering practices reduce contamination of carcasses. Education on hygienic handling of foods is essential for farm workers, abattoir and food production workers to reduce contamination. Household preventive measures are similar to those recommended for other foodborne diseases (WHO 2011a).

1.6 Leptospirosis

Leptospirosis is a zoonotic disease of worldwide importance. Also a neglected tropical disease, leptospirosis largely affects vulnerable rural and semi-urban populations. Global annual incidence of endemic human leptospirosis is grossly underestimated due to lack of awareness, under diagnosis, misdiagnosis and difficulty with diagnostic testing. Efforts to determine the burden of disease are ongoing (WHO 2011b). Leptospirosis is endemic in countries with humid subtropical and tropical climates, epidemics occur often as a result of flooding. Individuals at greatest risk include farmers, ranchers, slaughterhouse workers, trappers, loggers, veterinarians, sewer workers, rice field workers and military personnel.

Leptospirosis is caused by a variety of species of *Leptospira*, a spirochete with more than 250 pathogenic serovars that are adapted to different wild or domestic reservoir hosts. The classification system for *Leptospira* changed in 1989, leading to some confusion, as pathogenic and non-pathogenic serovars are now included in the same species. Serovars vary by geographic region (Spickler 2005). Host adaptation is not a static situation as serovars are adapting to new hosts, vaccine pressures are altering serovars in different species and climate change may be altering hosts and serovars (Hartskeerl et al. 2011). These facts lead to difficulties in prediction, prevention and use of vaccines. Reservoir hosts include wild mammals (rats and rodents are the most common) as well as domestic cattle, pigs, pigs and sheep and dogs. Reservoir hosts experience asymptomatic, mild or chronic disease and can shed for months to years.

Leptospires reside in the kidneys of infected reservoir hosts and are shed in urine into the environment where they can reside for long periods of time depending on