



Epidemiology of Zoonotic Diseases in the United States: A Comprehensive Review

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Abstract

Zoonotic diseases or infections (Zoonoses) are ailments that are naturally transmitted from animals to humans (or vice versa). These diseases are transmitted either by the consumption of contaminated food and water, exposure to the pathogen during preparation, processing or by direct contact with infected animals or humans. Zoonotic diseases have a significant effect on public health worldwide, showing a higher incidence rate in developing countries due to lack of control strategies, as well as the lack of education in the communities. Studies have indicated that about 75% of emerging infectious disease in humans originates from animals. Many factors like agricultural practices, human and animal demography, social, cultural, religious and lifestyle habits have led to the emergence of zoonotic infections since the 1940s. Salmonella, Escherichia coli O157: H7 and Cryptosporidium are prevalent causes of disease outbreaks in the United States. The key factors that will prevent and control zoonotic diseases are based on recognition, investigation, and collaboration. Treatment is specific to the causative agent. In the last two decades, zoonotic diseases within the United States have increased in prevalence and have become a significant cause of infectious disease to humans; hence the need for continuous awareness.

Keywords

Zoonotic diseases, Prevention, Prevalence, Vector, United States, Epidemiology, Transmission, Public health, Disease outbreak

Introduction

Zoonotic diseases or Zoonoses are numbers of communicable diseases that are transmitted from animals to humans [1]. Table 1, table 2 and table 3 list the etiologic agents that cause Zoonotic diseases. These diseases are transmitted either by the consumption of contaminated food and water, exposure to the pathogen during preparation, processing or by direct contact with infected animals or humans [2,3]. Statistically, it is evident that the prevalence and incidence of zoonotic diseases is a major public health problem worldwide [2]. Estimates showed that zoonoses constitute 58% to 61% of all communicable diseases causing illness in humans worldwide [4,5],

and up to 75% of emerging human pathogens [4-6]. About 75% of the new diseases that have affected humans over the past decade have been associated with pathogens originating from animals or from products of animal origin [1]. Developing countries have a higher incidence and prevalence of zoonoses, and this is attributed to the lack of adequate control mechanism, inadequate infrastructure and lack of adequate information on their significance and distribution [2,3]. In the United States, the burden of zoonotic diseases is exacerbated by factors such as the method of control, environmental factors, behavioral factors, social factors, clinical manifestations, the socio-economic impact of such diseases and mode of transmission [2,3].

Some zoonotic diseases have expanded their range of host and increased in incidence; these types of zoonosis are called emerging zoonoses (e.g. Ebola, Severe Acute Respiratory Syndrome, Swine flu, Bird flu, and Hantavirus) [5]. According to a report, approximately 75% of recently emerging infectious diseases of humans is diseases of animal origin, therefore, indicating that the burden of zoonotic disease is an ongoing health concern [7]. Although the most common way to encounter organisms that cause zoonotic diseases (such as bacteria and viruses) is by direct contact, other ways include contact with feces, urine, and respiratory secretions of an infected animal and contact with materials from the animal's environment [8,9]. Another mode of transmission of a zoonotic disease could be through scratches or bite by a pet. This is not surprising as there is increased exposure of humans to pets as the number of pets in the United States is increasing. Furthermore, the introduction and exposure to exotic pets increases the burden of zoonotic diseases [8]. For instance, in the United States, there is an increasing trend of harboring prairie dogs as pets. These types of pets bring disease from the wild into human homes; in 2003, an outbreak of monkey-pox was linked to exposure and associations with individuals who recently purchased a prairie dog. It was later discovered that the dogs contacted the rare virus by exposure to the Gambian rat (another exotic species) [7-8].

Interestingly, human's adventurous nature has increased the burden of zoonotic diseases. Venturing into the wild increases the

Table 1: Zoonotic bacterial etiology in the United States.

Genus Species	Disease	Pathogen	Structure
Brucella <i>B melitensis</i> , <i>B abortus</i> , <i>B suis</i> , and <i>B canis</i>	Brucellosis [63].	Bacteria	Gram negative coccobacilli
Campylobacter spp <i>C. jejuni</i> , <i>C. fetus</i> , <i>C. hyointestinalis</i> , <i>C. upsaliensis</i> , <i>C. lari</i> (Javid&Ahmed 2016), <i>Ph</i> (England 2013)	Campylobacteriosis: Enteric Campylobacter infections produces inflammatory, and sometimes bloody diarrhea or dysentery syndrome [19].	Bacteria	Gram negative rods
Salmonella <i>S typhi</i> , <i>S paratyphi-A</i> , <i>S schottmuelleri</i> , <i>S choleraesuis</i> , <i>S typhimurium</i> , and <i>S enteritidis</i>	Salmonellosis <i>S typhi</i> , <i>S paratyphi-A</i> , and <i>S schottmuelleri</i> cause enteric fever. <i>S schottmuelleri</i> produces septicemia and focal infections. <i>S typhimurium</i> and <i>S enteritidis</i> produce gastroenteritis [63].	Bacteria	Gram negative, bacilli
Shigella <i>S dysenteriae</i> , <i>S sonnei</i> , <i>S boydii</i> , <i>S flexneri</i>	Shigellosis <i>S. dysenteriae</i> causes hemolytic –uremic syndrome, <i>S. Flexneri</i> causes dysentery diarrhea with a post complication of arthritis. <i>S sonnei</i> causes watery diarrhea [63].	Bacteria	Gram negative rods
<i>Leptospira interrogans</i>	Septospirosis Causing bacteremia [63].	Bacteria	Gram negative spirochete
<i>Borrelia recurrentis</i> (louse borne), <i>B hermsii</i> , <i>B turicatae</i> , <i>B miyamotoi</i> , <i>B parkeri</i> , <i>B hispanica</i> , <i>B crocidurae</i> (tick borne)	Relapsing fever bacteremia [63].	Bacteria	Gram negative spirochete
<i>Spirillum</i>	Rat bite fever [63].	Bacteria	Gram negative
<i>Francisella tularensis</i>	Tularemia with high fever, toxemia and acute septicemia [63].	Bacteria	Gram negative coccobacilli
<i>Pasteurella</i> <i>P multocida</i> , and <i>P haemolytica</i>	Life threatening pneumonia. Abscesses and edema with fibrosis. <i>P haemolytica</i> infects cattle and horses [63].	Bacteria	Gram negative coccobacilli
<i>Bacillus anthracis</i>	Anthrax [63].	Bacteria	Gram-positive rod-shaped

Table 2: Zoonotic viral etiology in the United States.

Genus Species	Disease	Pathogen	Structure
Lyssavirus (Rhabdoviridae) Lagos bat, Mokola virus, Duvenhage virus, European bat virus) Ephemerovirus, and Vesiculovirus	Rabies [63].	Virus	Bullet shaped single-stranded, negative sense, unsegmented, enveloped RNA virus
Filoviridae Ebola: (Ivory Coast, Sudan, Zaire, and Reston) and Marburg	Hemorrhagic fever [63].	Virus	Filamentous, negative sense, single stranded, enveloped RNA virus
Togaviridae Alphaviruses	Eastern equine encephalitis and western equine encephalitis [63].	Virus	Spherical, positive-sense, single stranded enveloped RNA virus
Arenaviruses 5 cause disease in human Lassa virus, Junin virus, Machupo virus, Guanarito virus, and lymphocytic choriomeningitis virus	Lassa virus, Junin virus, argentine pampas, Machupo virus, and Guanarito causes hemorrhagic fever in humans. Lymphocytic choriomeningitis virus cases neurologic, respiratory and GI infections [63].	Virus	Round, single stranded, enveloped RNA virus

Table 3: Zoonotic parasite etiology in the United States.

Genus Species	Disease	Pathogen	Structure
<i>Entamoeba Histolytica</i>	Amoebic Dysentery [63].	Parasite (Protozoa)	Trophozoite, ameboid, actively motile
<i>Giardia Lamblia</i>	Giardiasis [63].	Parasite (Protozoa)	Flagellate trophozoite
<i>Balantidium coli</i>	Balantidiasis [63].	Parasite (Protozoa)	Ciliated trophozoite
<i>Toxoplasma Gondii</i>	Mental retardation, encephalitis, vision impairment in infant [63].	Parasite (Protozoa)	Mature oocytes have eight infective sporozoites
Toxocara genus <i>T canis</i> , <i>T felis</i>	Visceral larva migrans and Ocular larva migrans [63].	Nematodes	Larvae are 400 µm × 20 µm long
<i>Ascaris lumbricoides</i>	Strongyloidiasis [63].	Nematodes	Females are up to 30 cm long
<i>Trichinella spiralis</i> [63]	Triad of myalgias, periorbital edema and eosinophilia [63].	Nematodes	Female is viviparous and 4 mm × 60 µm

chance of coming in contact with infected animals or insects [10]. Furthermore, the expansion of human population has led to land expansion and modern development in animal’s natural habitat [11]. This urbanization further increases the risk of being exposed to infected animals. Zoonotic diseases can cause human-to-human transmission while some are not transmitted between humans but cause an epidemic within human populations [2]. For instance, Rocky Mountain spotted fever is transmitted by a tick bite whereas West Nile virus, dengue,

malaria, and chikungunya can all be contracted through mosquito bites if one travels to an endemic area. Other infections such as *Salmonella* and *E. coli* can be contracted by handling or consuming infected food, for example, chicken and meat [10-12].

The rate of zoonotic disease incidence and prevalence has been on the rise since the 1940s, most likely due to increased traveling, urbanization, demographic changes, encroachment of land, agricultural practices, and human lifestyle [13]. Zoonotic diseases also

have an impact on socio economic status, for instance, an outbreak of bovine encephalopathy costs an estimate of \$6.3 billion annually; foodborne zoonotic disease costs about \$1.3 billion annually [13,14]. This narrative review, discusses the epidemiology of various zoonotic diseases, their causes, and treatment in the United States.

Methodology

A literature search for Zoonotic diseases / infection was carried out. Articles were retrieved by performing searches using online electronic databases (Pub Med, Medline plus, Mendeley, Google Scholar, Research Gate, Global Health and Scopus). The search ranged from the initial date for each database until 2016 and 70 results were identified. Articles were streamlined to zoonotic diseases, zoonotic vector and the burden of zoonotic infections in the United States. Titles and abstracts of these results were reviewed and selected for inclusion based on relevancy to the research question.

Prevalence

The most common intestinal parasitic infection in the United States is *Giardia intestinalis* [14]. Surveillance report on Giardiasis (2006-2008), by the CDC showed that total number of reported cases of Giardiasis increased 2.9% from 19,239 in 2006 to 19,704 in 2007, and decreased 3.3% to 19,140 in 2008 in the United States, with the exclusion of five states where the disease is not reportable (Indiana, Kentucky, Mississippi, North Carolina, and Texas) [15]. Higher incidence was reported in children less than 10-years-old and adults aged 35 to 44 years and cases were clustered geographically; typically, northern states reported higher incidences, which was likely due to increased exposure to recreational water contaminated by human sources [15]. In the United States, 22.5% of the population over 12 years of age has been infected with *Toxoplasma gondii* [16]. Estimated age-adjusted sero-prevalence rate of 10.8% in individuals aged 6 to 49 years for *T. gondii* was reported in the United States based on the 1999-2004 National Health and Nutrition Examination Survey (NHANES III) data; although a decrease from 14.1% to 9% was reported among US-born persons [17]. The Food Net Surveillance reviewed approximately 46 million people in the United States for foodborne illnesses. Majority of *Campylobacter* cases in the United States occur as isolated, sporadic events and not as part of recognized outbreaks. About 14 cases are diagnosed each year for each 100,000 persons in the population based on information from active surveillance by the CDC Foodborne Diseases Active Surveillance Network (FoodNet) [18]. An estimated 2 million cases of *Campylobacter* enteritis occur in the US annually, accounting for 5-7% of cases of gastroenteritis. *Campylobacter* organisms have a large animal reservoir, with up to 100% of poultry, including chickens, turkeys, and waterfowl having asymptomatic intestinal infections [19]. The California Department of Public Health (CDPH) received reports of 27,346 cases of confirmed and probable campylobacteriosis with estimated symptom onset dates from 2009 through 2012. Within the same surveillance period, 29 case-patients were reported to have died with the disease [20].

There was an increase of 3% in the prevalence of *Salmonella* in 2010 [21]. *Salmonella* causes an estimated 1.2 million U.S. illnesses annually, approximately 1 million of which are transmitted by food consumed in the United States [22]. Human tularemia incidence in the United States peaked in 1939 with 2,291 reported cases and since then has decreased to 100-200 cases annually [23]. Rocky Mountain spotted fever has been reported in the United States since 1920's. In 2000, there were less than two cases reported per million people compared to six cases reported per million people in 2010. There has also been an increase in incidence during the last decade of Rocky Mountain spotted fever. Males who are 40 years and above are most at risk [24]. Cases of babesiosis occur across the Eastern Seaboard of the United States and the U.S. West Coast, with foci of infection in Wisconsin and Minnesota. Three species are believed to be present in the United States: *B. microti*, in the East Coast, Wisconsin and Minnesota; *B. duncani* and *B. conradae*, in the West Coast; and the widely distributed *B. divergens*-like organisms. Seroprevalence rates of 1.4% and 1.1% were reported in Massachusetts and Connecticut,

respectively for *B. microti* from 2000 to 2007 in a blood donors serosurvey. From 1 January 2007 when the American Red Cross and Blood Systems Inc. began screening blood for *T. cruzi* to 28 June 2012, there were 1,668 confirmed seropositive donations. Rates for congenital transmission of Chagas diseases may be approximately 58 to 502 cases per year [25]. Two hundred and three cases of *Trichinella* were reported in Alaska, from 1974 to 1994. Out of the 34 outbreaks reported, 20 (59%) were caused by the consumption of bear meat, 13 (38%) were from walrus meat while one case (3%) was from the consumption of either walrus or seal meat [26]. Seventy cases of alveolar hydatid disease were diagnosed mainly from Northwestern Alaska and among Alaska Natives. Higher human rates were reported from western Alaska (especially Saint Lawrence Island) in 1990 with an annual incidence of diagnosis ranging from 7 to 98/100,000 [26].

Transmission

Transmission of zoonotic diseases can be as variable as the diseases themselves [21]. Although organisms are transmitted by their typical methodology, most can be acquired via non-typical routes and thus it becomes harder to protect oneself from the infections. The modes of transmission are many and pervasive to most activities humans must partake in to survive, whether it is through drinking contaminated water or using contaminated water to clean food [27]. Our interactions with animals are growing and thus, because of our ever-increasing presence in the world, the "zoonotic pool" of organisms that can cause humans harm is rapidly growing while their modes of transmission are expanding [27].

Waterborne

Water is a rapidly growing source of zoonotic disease spread in the world. Infection can spread through contaminated drinking water or water used for sanitation. The human dependence on water makes us more susceptible to contracting waterborne zoonotic diseases. Typhoid and paratyphoid fever are often acquired through consumption of water or food that has been contaminated by feces of an acutely infected person [28,29], or convalescent person or a chronic, asymptomatic carrier [28]. Helminthiasis, caused by trematodes, plays a large role in waterborne zoonotic diseases within endemic countries. Waterborne helminths cause diseases such as schistosomiasis, cercarial dermatitis, fascioliasis and fasciolopsiasis; these are some of the most prevalent waterborne zoonotic diseases [30].

Fecal-Oral

The fecal-oral mode of transmission can be acquired in different ways: person to person, from animals directly or indirectly from water or food that has been contaminated with animal faeces. Cryptosporidiosis is transmitted from the oocytes of the parasite *Cryptosporidium parvum* found in the fecal matter of cattle and pigs [31]. Additionally, it can also be transmitted from domesticated animals such as dogs and cats. Diseases such as bacillary dysentery can occur due to more than thirty serotypes of *Shigella* from both food and water supply contamination. Cysts of the organism *Giardia intestinalis* can transmit by spreading from one contaminated person to another [32]. Even within restaurants, the risk for *Giardia intestinalis* is substantial if proper food preparation methods are not used. Food handlers have often been responsible for infecting people in restaurants due to the fecal-oral mode of transmission [33]. Drinking water contaminated with *E. histolytica* where cysts can last for extended periods can cause the disease Amoebiasis. *S. enterica* can survive in fresh water for an average of 4 weeks [34] which can lead to typhoid outbreaks occurring from contamination of water supplies [35]. Hepatitis A and E are also very common viral infections around the world [36]. Hepatitis A is typically acquired by eating raw food or food infected by a handler infected with the virus, whereas, Hepatitis E is typically transmitted through drinking water contaminated by the fecal matter due to poor sanitation [37].

Food borne

Some zoonotic diseases are only transmitted by food, meaning that unsanitary conditions and improper cooking can cause

contamination. Foodborne disease is one of the most common causes of acute illness [38]. The most common bacteria that cause food poisoning are *Salmonella*, *Staphylococcus* and *Clostridia*. *Salmonella* generally infects food in its living state within reservoirs such as cattle, poultry or eggs. However, it can also be transmitted via unhygienic slaughterhouses or improper food preparation [39]. Fish poisoning can occur when fish or shellfish are not eaten in a timely manner and decomposition is allowed to occur producing toxins such as Ciguatera [40]. The organism *Campylobacter enteritis* is acquired by the consumption of undercooked chicken or by domesticated animals such as cats and dogs. In the majority of these cases the other specie *Campylobacter jejuni* is isolated and thus the cause of infection [41].

Vector borne

Another important disease transmission of zoonotic diseases is through a vector. Mosquito-borne diseases can be spread easily because of their abundance and their need to feed on blood; oftentimes, people do not realize that they have been bit until disease arises. Ticks, fleas and mites are all major contributors of zoonotic diseases through vector transmission. Some of the most prevalent diseases caused by vectors are Tularemia, Plague, Ehrlichia and West Nile virus [42]. Yellow fever, Dengue and Rift Valley are causes of viral hemorrhagic fevers that often occur as complications [43] such as malaise, rashes, bruising and bleeding. Onchocerciasis is a parasitic disease caused by the nematode worm *Onchocerca volvulus* that is transmitted by the *Simulium* fly vector, which takes up the parasite from an infected human and then transmits it to an uninfected human during feeding.

Outbreak of Zoonotic Diseases

Salmonella is a prevalent cause of disease outbreaks in the United States. It made headlines in 1998 [44], as a strain of *Salmonella* called *S. enterica* serovar typhimurium DT 104 infected many cattle and dairy products in the United States [44]. It was then transmitted to humans through the ingestion of these infected foods. *Salmonella* is a facultative intracellular organism that invades phagolysosomes of macrophages disabling their antibodies and complement immune responses [45]. This epidemic was resolved by the USDA food safety and inspection service, as it implemented regulations on poultry and meat processing industries. One of the regulations included the prohibition of selling any products with high amounts of *Salmonella* positive samples. By controlling the amount of positive *Salmonella* samples, the number of *Salmonella* infected products sold in stores was reduced [44]. Outbreak of *Escherichia coli* O157: H7 had also been documented by the CDC from poultry and beef products [46].

Cryptosporidium is another organism of outbreak in the United States. It was reported to have reached highest incidence in Wisconsin between the years of 1999 and 2002 [47]. A study aimed at controlling the outbreak was initiated, to figure out the mode of transmission of this disease. It concluded that *Cryptosporidium* in humans originated from a zoonotic transmission. It was detected in cattle in Michigan and in calves in Ontario, Canada, making the spread of this organism a non-localized epidemic. Furthermore, the transmission was more likely to be found in farm animals rather than wild animals. A PCR and RFLP analysis was later conducted, which led to the resolution that the dominant strain in Wisconsin was *Cryptosporidium parvum*. This study led to the prevention measure of restricting contact with cattle, as they were the original reservoir [47].

Zoonotics are a major cause of disease outbreaks. A study done by Chomel, Belotto and Meslin (2007) showed that 75% of infectious diseases were zoonotic. The research showed that this emergence was due to human activity, modification of natural habitat, and globalization of trade and change in agricultural practices [48]. They found that North American forests were a main reservoir of *Burrelia Burgferdi* and its vector *Ixodes* ticks with 3.2 million ruminants [48]. The reason for the outbreak in humans was the expansion of human settlements into pre-urban areas where ticks lived. In addition, wildlife trade was another contributing factor for the disease outbreak. Rabies was introduced to Mid-Atlantic States in the 1970s by relocating raccoons carrying rabies from Southern American states [48]. A

surveillance program was created to monitor the emergence of new diseases within animals to control it before an outbreak occurs. Other ways of prevention included, protection of animal biodiversity and educating tourists of the risks of getting in contact with wildlife [48].

During 2007-2012, 81 outbreaks associated with non-pasteurized milk were reported from 26 states in the United States. These outbreaks resulted in 979 illnesses and 73 hospitalizations. However, there was no death reported. Of the 78 outbreaks with a single etiologic agent, *Campylobacter* spp. was the most common pathogen, causing 62 (81%) outbreaks. The number of outbreaks of *Campylobacter* spp. infection within the period increased, from 22 during 2007-2009 to 40 during 2010-2012 [49].

From 1997-2006, *Giardia* was identified as a causal agent of six (3.7%) of 162 reported recreational water-associated gastroenteritis outbreaks and 15 (10.6%) of 141 reported drinking water-associated gastroenteritis outbreaks in the United States [15]. From 2009 through 2012, there were 10 reported outbreaks of foodborne campylobacteriosis in California involving 132 cases [20].

Prevention and Control of Zoonotic Infections

In the past couple of years, there has been a rise in outbreaks of zoonotic diseases. The goal is to prevent and control the spread of these diseases as it is virtually impossible to predict when and where the next outbreak will be; a plan needs to be developed in order to act fast at the first sign of an outbreak. The key factors that will prevent and control zoonotic diseases are based on recognition, investigation, and collaboration. Education, information, communication, and technology transfer will help in prevention and control as well [50].

To correctly prevent and control zoonotic diseases, first they have to be identified. The diseases are not usually identified when they have occurred in the animal reservoir; only after there is recognition of a health problem in the human population will there be identification of the disease, as can be seen with Q fever or chlamydiosis [50]. The best approach would be to investigate health problems in both animals and humans together; this creates a link that can be made between human and animal diseases [50].

There needs to be collaboration between medical and veterinary scientists as well as public health practitioners and laboratory scientists in order to investigate new and emerging zoonotic diseases. Fully equipped laboratories that contain subtyping technique tools are essential in helping to detect disease outbreaks and characterizing transmission routes [51]. By using a process called molecular subtyping, different strains can be differentiated based on their genotypes and phenotypes. This data is useful in drawing connections between the outbreak and the source of the disease, or the transmission routes of the pathogen [51]. In addition to the laboratory techniques, the work of epidemiologists, ecologists, and environmentalists is crucial in establishing patterns and preventing outbreaks. The goal is to identify risk factors and reservoirs; control measures cannot be undertaken until these factors are identified. For example, the Nipah virus outbreak in Malaysia was controlled once it was identified that exposure to a pig was the cause of the virus [50]. Furthermore, another approach to preventing the occurrence of zoonotic diseases is to conduct an inventory of pathogens that can be carried by wildlife species especially those that can invade the human habitat [50]. For example, it has been found that opossums (*Didelphis virginiana*) are heavily infected with cat fleas (*Ctenocephalides felis*) and is a major reservoir of *Rickettsia typhi*, *Rickettsia felis* and *Sarcocystis neurona*. Trained professionals in the field of zoonotic diseases should be educating physicians and/or veterinarians who may see the first human or animal case of zoonoses. In order to improve our abilities to control zoonotic infections, training in molecular epidemiology will allow us to understand the diversity of reservoirs and pathogens of zoonotic diseases [50].

In addition, communication of findings to the public in an accurate and timely fashion will further help to prevent and control the spread and/or emergence of zoonotic diseases. For example, the public knows about West Nile virus and its association with dead birds. Knowledge of the public about zoonotic diseases will make

Table 4: Zoonotic parasitic disease surveillance in the United States.

Disease	Surveillance
Babesiosis	In 2011, Centers for Disease Control and Prevention (CDC) notified 1,124 cases of babesiosis: 847 were classified as confirmed cases and 277 as probable cases [64]. The reported cases occurred most frequently in the spring and summer and in the Northeast and upper Midwest but cases were identified in other seasons and regions.
Cryptosporidiosis	The total number of reported cases has increased 16.9% from 7,556 for 2009 to 8,951 for 2010. The annual rate in USA was relatively stable during 1995-2004, which ranged from 0.4-1.3 per 100,000 individuals. The rates reported from CDC in 2005-2010 ranged from 2.3-2.9 per 100,000, which had peaked in 2007.
Cyclosporiasis	Cyclosporiasis has been reported in over 35 states, primarily in Texas, Iowa, and Nebraska. Investigations in Iowa and Nebraska have shown that restaurant associated cases in the two states were linked to a salad mix that contained iceberg lettuce, romaine lettuce, red cabbage, and carrots.
Giardiasis	During 2009-2010, the total number of reported cases increased from 19,403 in 2009 to 19,888 in 2010 [65]. During this period, 50 jurisdictions reported giardiasis cases, indicating large number of cases occurring in children aged 1-9 years. The number of cases has peaked annually during early summer through early fall.

Table 5: Zoonotic bacterial disease surveillance in the United States.

Disease	Surveillance
Anaplasmosis	Anaplasmosis is a tick-borne disease recognized in humans in mid-1990s. The number of cases has increased steadily over the years from 348 cases in 2000 to 1,006 cases in 2008. It has been most frequently reported from the upper Midwest and Northeast, including six other states (New York, Connecticut, Massachusetts, Rhode Island, Minnesota, and Wisconsin), which accounts for 88% of all reported cases.
Anthrax	Cutaneous anthrax has been the most common type reported in USA. Before the US bioterrorism attack, inhalation anthrax was last reported in 1976. Recently, cutaneous anthrax has occurred in 2000. Anthrax in livestock does occur infrequently in USA but occurs most commonly in agricultural regions including Africa, Asia, the Caribbean, Central and South America, southern and eastern Europe, and Middle East [66].
Botulism	Foodborne botulism has been accounted for 8%, infant botulism has been 76%, wound botulism has been 15% and botulism of unknown etiology has been reported less than 1%. As of 2012, foodborne intoxication was reported from five states in which toxin type A and B were the highest ones reported. Wound and infant botulism have mostly seen as occurring in California although Pennsylvania also has a high amount of infant botulism attack.
Brucellosis	Reports by CDC in 2010, indicates that Brucellosis has been highly reported in California and Texas. The current status shows that most of US is either at or approaching disease elimination. As of July 10, 2009, all 50 States were class free for the disease.
Ehrlichiosis	Ehrlichiosis was recognized in USA in the late 1980's but was not reported until 1999. <i>E. Chaffeensis</i> is the most common type that has increased from 200 cases in 2000 to 961 cases in 2008. It later went on to be decreased in 2010 and the annual case fatality rate has declined.
<i>Escherichia coli</i> (E.coli)	Shiga toxin E.coli (STEC) has been reported as being the largest cause of illness each year in USA. Approximately, 265,000 illnesses each year have been reported, with more than 3,600 hospitalizations and 30 deaths. An estimated 96,534 STEC O157 and 168,698 non-O157 infections occur each year. There have been many STEC outbreaks reported such as from brand A cookie dough and Maple Leaf foods, causing <i>E.coli</i> to be the most common foodborne disease.
Leptospirosis	As of January 2013, leptospirosis has been reinstated as a nationally notifiable disease.
Listeriosis	<i>Listeria monocytogenes</i> causes nearly 1,600 illnesses each year in US; more than 1,400 hospitalizations and 250 related deaths. This can even affect newborn infants if their mother ate contaminated food during pregnancy. The proportions of all cases reported continue to increase. There have been many multistate outbreak that are linked to commercially produced pre-packages such as Caramel Apples, Wholesome Soy Products, Oasis Brands and Roos Foods Dairy Products.
Lyme Disease	Lyme disease has been a national condition in US since 1991. Since 2009 and 2013, the cases that have been reported have increased from 144 cases to 682 cases [67]. Each year, CDC reports approximately 30,000 cases however; this does not reflect every case of Lyme disease. The CDC estimates that 300,000 people are diagnosed each year [68].

Table 6: Zoonotic viral disease surveillance in the United States.

Disease	Surveillance
Chickenpox (Shingles or Varicella)	Varicella used to be very common before the chickenpox vaccine became available in 1995. Severe complications and deaths has been seen to occur in individuals who were previously healthy. According to CDC, each year more than 3.5 million cases of varicella, 9 000 hospitalizations and 100 deaths are prevented by varicella vaccination.
Chikungunya	As of February 10, 2015, 25 cases have been reported; mostly from travelers returning from affected areas [59]. This virus has been associated to come from Puerto Rico and the US Virgin Islands.
Eastern equine encephalitis (EEE)	An average of 8 human cases of EEE is reported annually in USA. Most of them have been reported from Florida, Georgia, Massachusetts, and New Jersey. This occurs due to transmission of the virus around freshwater hardwood swamps in the Atlantic and Gulf Coast states and the Great Lakes region.
Ebola	As of October 14, 2014, CDC indicated that Ebola virus incident in New York from healthcare workers who traveled to West Africa. Since early 2014, there have been more than 6,000 reported deaths. On July 9, 2014, CDC activated its Emergency Operations Center for Ebola outbreak response to provide assistance to the public [69].
Enterovirus	Enterovirus has been reported to be most common in the summer and fall, however there is no predictable pattern. Coxsackievirus A16 is the most common cause of hand, foot and mouth disease in USA but in 2011-2012, cases of coxsackievirus A6 was common. Enterovirus D68 caused a nationwide outbreak in 2014 causing severe respiratory illness in the United States.
Hantavirus Pulmonary Syndrome (HPS)	HPS is a severe disease of the lungs that was first recognized in 1993 in the "Four Corners" area (where Utah, Colorado, Arizona, and New Mexico meet) of the Southwestern US. Most of the cases reported have been from California. Through December 31, 2013, 637 cases of HPS have been reported, of these 606 cases have occurred from 1993 and onward. More than 95% of reported cases have occurred in states west of Mississippi River.
Middle East Respiratory Syndrome (MERS-CoV)	MERS in US is a very low risk to the public. In May 2014, CDC confirmed two unlinked cases, one in Indiana and the other in Florida; both traveled to US from Saudi Arabia where they may have been infected. To date, active MERS-CoV has not been found in any contact in US MERS patient.
Norovirus	In US, each year norovirus causes 19-21 million cases of acute gastroenteritis, 56,000-71,000 hospitalizations and 570-800 deaths (mostly among young children and elderly). Primarily common outbreak settings are healthcare facilities, in restaurants, on cruise ships, and in schools.

them to be careful around certain species thus, further preventing the spread of the disease [50].

The spread of zoonotic infections is monitored in order to establish a pattern of progression of a disease caused by animal or insects. Organizations such as the Centers for Disease Control

and Prevention (CDC), World Health Organization (WHO) and other agencies conduct disease surveillance of zoonotic diseases. In addition, they observe and predict outbreaks that may lead to epidemics and pandemics. However, most importantly, they inform the public about the transmission and risk factors of zoonotic diseases (Table 4, Table 5 and Table 6).

Depending on the zoonotic disease, it is mandatory to report the incidence of the disease, whether it is in human or animal [52] to the regional and national government agency. Scotch, Rabinowitz and Brandt (2010) believe that there are deficiencies in the surveillance of zoonotic diseases even though the majority of emerging infectious diseases are zoonotic [43]. There should be better communication between veterinary and human medicine in order to track emerging zoonotic diseases at their early stage and prevent spread [45]. There are two types of surveillances: active and passive [52]. Active surveillance refers to the collection of case reports from veterinary health authorities. An example of active surveillance would be putting out surveys in order to determine the status of a disease or infection in a population at a given time [52]. An issue that arises with this type of surveillance is that it is cost-intensive. When finding the status of a rare disease, a large sample size is required due to the low prevalence of the disease [52]. One-way to make active surveillance more effective is to apply risk-based surveillance, which targets populations that are high-risk and so the probability of finding cases of the disease would be greatest [52]. Passive surveillance refers to reporting clinical cases to health authorities [52]. An issue that arises with passive surveillance is the bias that comes with reporting cases. Veterinarians believe that there is an increased risk in the livestock industry if certain information is made available to the public [53].

Another issue that arises is the difference in the missions between the health and the agricultural department [45]. The health department is concerned with how the diseases affect people while maintaining confidentiality. Whereas, the agricultural agencies are concerned with the effect of diseases on the livestock industry and how diseases affect livestock animals [53]. The differences in missions affect what diseases are reported. For example, in Utah, there are over 90 reportable diseases for animals made by the State Department of Agricultural and over 60 reportable diseases for humans made by the Utah Department of Health [53]. These two lists only have about 15-20 of the same diseases even though the majority of emerging infectious diseases are zoonotic [53]. Therefore, in order to improve on the surveillance of zoonotic diseases, there should be better communication between the health and agricultural agencies. This would allow emerging zoonotic disease to be detected as early as possible.

Zoonotic Infections as Agents of Bioterrorism

There are many agents that can be used in attacks of bioterrorism, however, but the most frequently used agents include: anthrax, botulism, tularemia, smallpox and viral hemorrhagic fever. These zoonotic agents are high priority agents and therefore can be considered a threat to national security because they can easily be disseminated or transmitted through person-to-person contact causing secondary and tertiary cases [54]. These agents cause high mortality, resulting in major public health impact. They may also cause public panic and social disruption and therefore, require special action for public health preparedness [55].

Yersinia pestis is a gram-negative, rod shaped coccobacillus usually infecting rodents and fleas. Humans become infected after being bitten by an infected flea. *Yersinia* comes in three forms: pneumonic, septicemic and bubonic plagues [56]. In humans, the disease usually occurs as bubonic plague, but in rare cases can also occur as pneumonic plague if it spreads to the lungs through the bloodstream. Plague is recognized as an agent of bioterrorism and has been one of the most devastating epidemic diseases known to humanity, secondary to smallpox [56].

There are many examples throughout history, in as early as 1000 BC, *Yersinia*, was used as bioterrorism agent causing epidemics [56]. One well-known example was during World War II when the Japanese got billions of infected flies and released them over northern Chinese cities causing numerous epidemics. The Centers for Disease Control and Prevention (CDC) have thus categorized plague as a Category A agent [56].

Tularemia is a natural occurring zoonotic disease that is

transmitted to humans through contact with infected animals. *Francisella tularensis* is very infectious and can be used as a weapon in a bioterrorist attack. The bacteria would likely be made airborne and would require some form of laboratory sophistication. Exposure to this infectious aerosol generally causes severe respiratory illness which is usually life threatening, if not treated [57]. *Francisella tularensis* is endemic in rural areas, mostly in the Midwestern United States. Over the last decade, annual incidence has been less than 200 cases nationwide. Based on research, there are no known bioterrorism events in the United States with the use of *Francisella tularensis*, however, outbreaks of any form of tularemia is investigated rapidly to rule out a bioterrorism attack [57].

Treatment of Zoonotic Diseases

Bacterial zoonosis

Brucellosis is commonly treated with tetracycline, trimethoprim-sulfamethoxazole, aminoglycosides, rifampicin, quinolones and chloramphenicol [58]. However, due to frequent relapses, the world health organization recommends the combination of doxycycline plus rifampin or doxycycline plus streptomycin [58]. The drug of choice for salmonellosis has been chloramphenicol, however due to side effects like aplastic anemia and the incidence of relapse found in chronic carriers, there has been a shift in research for the discovery of a more effective treatment [59]. The emergence of *S. typhi* resistant to chloramphenicol has added impetus to finding a better treatment [59]. After many trials it was discovered that trimethoprim-sulfamethoxazole is the most effective treatment for salmonellosis along with supportive therapy and oral rehydration [60]. The drugs of choice for shigellosis have been ampicillin and trimethoprim-sulfamethoxazole especially for *S. sonnei* found in day care facilities in the United States [60]. However, clinical trials have found that Nalidixic acid, a newer quinolone, and amdinocillin pivoxil are more effective, although more studies need to be conducted to ensure the safety of quinolones in children. Cephalosporins were also found to be highly active in vitro against most strains of *Shigella* [60]. Lyme disease associated with erythema migrans is treated with doxycycline, cefuroxime axetil and amoxicillin for a recommended 14-21 days. Doxycycline is contraindicated for pregnant and lactating women as well as children. Therefore, a better alternative for children would be Amoxicillin. Ceftriaxone is not the first choice of treatment for early stages of Lyme disease with erythema migrans; however, it is recommended if Lyme disease presents with neurological symptoms [61]. Although not as common but still seen in the United States is Tularemia, current treatment recommendations are aminoglycosides, such as streptomycin or gentamicin, and tetracyclines [62]. According to the CDC, doxycycline is the treatment of choice for Rocky Mountain spotted fever.

Viral zoonosis

It has been found that the most effective way to treat rabies is to remove the free virus from the tissue by cleansing and neutralizing it in addition to inducing a rabies virus specific immune response with passive antibodies and active immunization before the virus is able to replicate in the central nervous system [63]. According to the CDC, there are no specific antiviral treatments for West Nile Virus infections nor are there vaccines; they recommend over the counter supportive treatment for pain relief. Studies conducted during the St. Louis outbreak showed that patients who were treated with IFN-Alpha 2B and patients treated with supportive care had no mortality, however, 3 weeks later the patients who were not treated with IFN-alpha 2B were found to have a decline in neurological scores [64]. According to Mupapa, *et al.* at the time of the first Ebola outbreak in the democratic republic of Congo there was no effective treatment for the virus [65]. However, they found that patients who were transfused with blood, given infusion of electrolytes and glucose, antimalarial drugs as well as antibiotics were more likely to survive than those who were not. In the recent 2014 outbreak, two American survivors were treated with blood transfusions from people who previously had and survived the Ebola virus as well as a cocktail of antibiotics and

electrolyte infusions. The use of platelet transfusion in the early stage of the virus is highly recommended since platelets are responsible for producing soluble CD40 ligands [66]. As of now, there are still no definitive treatments for Ebola; however, it has been observed that in both the United States and other countries aggressive intravenous, oral rehydration, blood transfusion and electrolyte supplementation have had positive results. Arenavirus, another cause of hemorrhagic fever is effectively treated with ribavirin, which is a guanosine analogue, as well as supportive care that targets specific symptoms [67].

Parasitic zoonosis

Hookworm infections are treated with albendazole and mebendazole; they kill the adult worm by binding to the beta-tubulin and inhibit microtubule polymerization [68]. Levamisole and pyrantel pamoate are also used but not as first line drug of choice. The 2008 study by Keiser and Utzinger, “*Efficacy of Current Drugs Against Soil-Transmitted Helminth Infections: Systematic Review and Meta-analysis*”, examined the relative efficacies of different drug treatments. They found that the efficacy of single-dose treatments for Hookworm infections were as follows: 72% for albendazole, 15% for mebendazole, and 31% for pyrantel pamoate [69]. Nitazoxanide is a broad-spectrum antimicrobial agent that is the treatment of choice for protozoa, nematodes, cestodes, and trematodes [69]. A 3-day course treatment with Nitazoxanide has been effective for enteric protozoan and helminth infections caused by *G. intestinalis*, *E. histolytica*, *Blastocystis hominis*, *Balantidium coli*, *Isospora belli*, *Ascaris lumbricoides*, hookworms, *Trichuris trichiura*, *Taenia saginata*, and *Hymenolepis nana* [69]. Benznidazole and nifurtimox are the most efficacious treatment for Chagas disease, therefore, are first line treatments. Toxoplasmosis is treated with sulfonamides such as sulfadiazine, sulfamerazine, sulfamethazine and pyrimethamine [70]. Therapy for Leishmaniasis in the United States is limited, however, oral miltefosine was found to be the treatment of choice for cutaneous leishmaniasis, while the treatment of choice for visceral leishmaniasis is amphotericin B. Babesiosis is treated with a combination of either atovaquone and azithromycin or clindamycin and quinine, for 7 to 10 days [61].

Conclusion

The increasing proximity between humans and animals and the continuous expansion of humans into their natural habitat is greater now than ever before. Within the last two decades, zoonotic diseases within the United States have increased in prevalence and have become a significant cause of infectious disease to humans. Despite efforts in screening, prevention, control and the gathering and sharing of information learned through outbreak investigations and disease surveillance, zoonotic diseases have found a way to continue to affect the human population. This is perhaps due to the wide range of modes of transmission that zoonotic diseases can employ. The different modes of transmission of zoonotic diseases varying from food and waterborne to vector borne to airborne, have made the effective control of these diseases somewhat difficult. However, there have been many successful campaigns to limit the spread of zoonotic diseases and there is continuous effort to protect, educate and aid the population in the fight against these diseases.

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