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Jillian Leigh Fitzpatrick Date

Travel-related zoonotic diseases associated with human exposure to rodents: a review of GeoSentinel Surveillance Data, 1996 – 2011

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Bachelor of Science
Xavier University
2009

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Abstract

Travel-related zoonotic diseases associated with human exposure to rodents: a review of GeoSentinel Surveillance Data, 1996 – 2011

By Jillian Leigh Fitzpatrick

Current knowledge of the incidence and risk factors associated with rodent-borne zoonoses in travelers is limited. Travelers and physicians alike must be properly educated so that they are aware of the risks and the protective measures that should be taken. This study investigated rodent-borne zoonoses in travelers and associated risk factors using GeoSentinel, a multi-site global surveillance network established for the surveillance of travel-related morbidity. 18 rodent-borne zoonoses were chosen for analysis. This study analyzed only diseases that were either directly transmitted from rodents to humans (including contact with infected urine or droppings) or indirectly transmitted via an arthropod reservoir, where the rodent plays a major role in the life cycle of the disease. Over a 15 year span there were 962 reports of illness associated with one or more of these 18 rodent-borne zoonotic diseases. Ill travelers with rodent zoonoses were found to be significantly more likely to be male and traveling as tourists than those ill travelers with some other diagnosis. Adventure travel and risky behavior may increase the risk of contact with rodent zoonoses for both groups, as males were more likely to engage in adventure travel than females and tourists were also more likely to engage in risk taking behavior. Further, when compared to all other ill travelers, those with rodent zoonoses were 21 times more likely to have been exposed in South America, 12 times more likely to have been exposed in Sub-Saharan Africa, and 11 times more likely to have been exposed in Central America. Travelers to these areas should be aware of their increased risk of contracting a rodent-borne zoonosis and should take proper preventative measures. Analysis of the GeoSentinel database can provide epidemiologic information about rodent-borne zoonoses in travelers and ultimately decrease the disease burden in this population.

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Jillian L. Fitzpatrick

Contents

LIST OF TABLES

BACKGROUND

Since the end of the 20th century, emerging and re-emerging zoonotic diseases have garnered increased attention, both globally and in the United States. An estimated 75% of all emerging infectious diseases are of zoonotic origin (1). Of all human pathogens, 60% are zoonotic, and of these, 71% originate from wildlife (2). This emergence has brought with it a great need for an increase in surveillance, detection, and control of zoonotic diseases.

Escalating speed and ease of travel have expanded the global mobility of society, allowing almost any person or product to travel around the world in a single day. This increase in international trade and travel has been cited as one of the most important drivers of emerging infections in the 21st century (3). In 2010, an estimated 935 million travelers arrived internationally throughout the world, a number that has been steadily growing and represents a 6.6% increase over 2009 (4). Global travel of people and animals has resulted in outbreaks of zoonotic diseases such as monkeypox, avian influenza, and severe acute respiratory syndrome (SARS) (5-7). Therefore, monitoring travelers for infectious diseases, particularly infectious diseases of zoonotic origin, is now more crucial than ever.

Rodents are one of the most important groups of animal hosts of disease worldwide (8). If one considers all diseases associated with rodents, including both those spread directly by rodents and those that are spread by vectors but exist in rodent reservoirs, the number is impressive (9). There are more than 60 known bacterial, viral, or parasitic diseases spread by rodents worldwide (8). Rodent zoonoses are of great public health concern, both domestically and abroad, including both emerging diseases, such as Lassa Fever, and well known or historical diseases, such as Hantavirus and plague. Furthermore, widespread and rapid urbanization have encouraged an

explosion of rodent populations, as well as increased contact between humans and these rodent hosts (10).

Climate plays an important role in the distribution of rodent zoonoses. Climate influences habitat quality and the availability of food for rodent hosts (11). Furthermore, climate also influences vector abundance, which is important in the enzootic rodent-arthropod cycle for the transmission of indirect rodent zoonoses (12). Global climate change could lead to a change in the incidence and distribution of rodent species and arthropod vectors, and therefore pathogens linked to these species (13).

In addition to a large impact on human health, rodent zoonoses account for huge economic losses. Rodent diseases result in significant human morbidity and economic production losses each year. As an example, patients hospitalized in the UK after a rat bite incident had to stay on average 11.2 days (14). Furthermore, rodents can serve as reservoirs to many diseases of livestock, causing huge economic damages to the animal husbandry industry (8).

Current knowledge of the incidence, associated factors, and symptoms associated with rodent-borne zoonoses in travelers is limited. A greater understanding of rodent-borne zoonotic diseases in travelers is important to predict future disease prevalence and emerging rodent-borne diseases. In areas where rodents thrive and certain rodent zoonoses are endemic, travelers must be properly educated so that they are aware of the risks and the protective measures they must take. Analysis of the GeoSentinel database can provide epidemiologic information about rodent zoonoses in travelers to ultimately decrease the disease burden in this population. This analysis considers five directly transmitted rodent zoonoses and thirteen indirectly transmitted rodent zoonoses, where direct transmission represents those diseases that are transmitted from rodents to humans, including contact with infected rodents or their urine and droppings, and indirect transmission

represents those diseases that exist in rodent reservoirs but are transmitted to humans by vectors such as mosquitoes or ticks. These diseases are listed in detail below.

LITERATURE REVIEW

Directly Transmitted Rodent Zoonoses

Hantavirus

Hantaviruses are viral pathogens of small mammals, usually mice of the Family *Muridae*. The Hantavirus genus contains more than twenty one species, which are usually host specific (15). Hantavirus occurs worldwide, especially in temperate climates. Infection in humans is due to spillover from the rodent population and is not part of the natural ecology of the virus (16). Nonetheless, hantaviruses cause two serious illnesses in humans, Hemorrhagic Fever with Renal Syndrome (HFRS) and Hantavirus Pulmonary Syndrome (HPS). These illnesses are caused by the inhalation of live hantavirus through the lungs and can cause acute illness and death (17).

Hemorrhagic fever syndrome

There are many rodent-borne diseases that can cause Hemorrhagic Fever Syndrome, including Omsk hemorrhagic fever and South American hemorrhagic fevers. The transmission of four viral South American hemorrhagic fevers are associated with direct transmission from rodent reservoirs and thought to be spread in a mechanism similar to the spread of hantavirus. These four are Bolivian hemorrhagic fever (caused by Machupo virus), Argentinean hemorrhagic fever (caused by Junin virus), Venezuelan hemorrhagic fever (caused by Guanarito virus), and Sabia hemorrhagic fever (caused by Sabia virus). Omsk hemorrhagic fever, a viral pathogen that is endemic in Western Siberia, is caused by Omsk hemorrhagic fever virus and spread by direct contact from infected rodents (such as water voles or muskrats), or from the bite of an infected tick. The case fatality rate of Omsk hemorrhagic fever is 0.5-3%. Like Hantavirus, each virus type is host specific. All of these South American hemorrhagic fevers can cause acute illness and death from massive hemorrhage or shock (8).

Lassa fever

Lassa fever is a viral illness caused by a single stranded RNA virus in the family *Arenaviridae*. The disease was isolated in the multimammate rat (*Mastomys natalensis*) and is endemic in West Africa. In West Africa, there are about 100,000-300,000 cases per year, with 5000 deaths. Lassa fever is a significant cause of morbidity and mortality, with the case fatality rate as high as 15-20%. People at greatest risk for contracting Lassa fever are those living rural in areas of poor sanitation and crowded living conditions where *Mastomys* are usually encountered. Lassa fever virus can be transmitted by breathing air that is contaminated with rodent excrement, by direct contact with rodent excrement or urine, by eating food that has been contaminated by rodents, by bite wounds, or by close contact with persons with Lassa fever (8).

Leptospirosis

Rodents are carriers of bacteria of the genus *Leptospira* throughout the world. *L. arborea*, *L. copenhagi*, *L. icterohaemorrhagiae*, *L. bim*, and *L. ballum* are strains that are directly linked to rodents. Cases of Leptospirosis are underreported and probably range from 0.1-1 per 100,000 per year in temperate climates to 10 per 100,000 per year in humid, tropical climates. During outbreaks, 100 or more per 100,000 may be infected. The case fatality rate ranges from 11% to as high as 20%. Leptospirosis has a major impact on developing countries in Asia. Most cases occur in poor, rural communities. *Leptospira* can be transmitted through consumption of food or water that has been contaminated by rodents or through the contact of skin or mucous membranes with soil or water that is contaminated by rodent urine (8). An increased risk of contracting leptospirosis has been shown to be associated with participating in recreational water sports in endemic areas (18).

Tularemia

Human infection of tularemia is primarily caused by two subspecies of the bacteria *Francisella tularensis*, subsp. *tularensis* (type A), and subsp. *holarctica* (type B). Type A is only found in North America. Its main reservoirs are cottontail rabbits and ticks. Type B is endemic throughout the Northern Hemisphere, with a mainly water-borne cycle involving aquatic rodents such as muskrats and beavers. Several thousand cases a year of this disease have been estimated. Case fatality rate ranges widely depending on subtype, but can be as high as 25%. Tularemia is acquired through contact with an infected animal carcass, consumption of food or water that has been contaminated by rodents, by breathing contaminated aerosols, or by the bite of an infected mammal, tick, deerfly, or other insect (8).

Indirectly Transmitted Rodent Zoonoses

Babesiosis

Babesiosis is caused by protozoan parasites of the *Babesia* genus. These parasites are transmitted to humans by the bite of an infected tick. Rodents are reservoirs of the infection, especially for infection with *B. microti*. This species causes human disease and is spread throughout North America, Europe, Asia, and Japan. Babesiosis is an uncommon disease. Depending on the strain, it can cause an asymptomatic infection or a mild non-specific illness. Especially in the young, old, or immunocompromised, severe disease and death can result from infection (8).

Leishmaniasis

Leishmaniasis, caused by the protozoa *Leishmania*, is important as an emerging infection in travelers. The disease is transmitted by hematophagus sandflies of the *Phlebotomus* genus (Old World leishmaniasis) or of the *Lutzomyia* genus (New World leishmaniasis) (19). Rodents have been shown to form a reservoir for the protozoa (8). Leishmaniasis is divided into three clinical

syndromes- visceral, cutaneous, and mucocutaneous. Leishmaniasis affects 12 million people in 88 countries worldwide, primarily in rural areas and underserved urban areas. Visceral leishmaniasis is endemic in 60 countries, while cutaneous leishmaniasis is endemic in more than 70. There are 500,000 cases of visceral leishmaniasis each year and 1-1.5 million cases of cutaneous leishmaniasis. Mucocutaneous leishmaniasis develops in a small portion of those with cutaneous leishmaniasis, and may be life-threatening(19).

Lyme disease

Lyme disease is caused by bacteria of the family *Borrelia*. This bacterium is maintained through an enzootic rodent-tick cycle. Humans acquire the disease from the bite of an infected tick. Lyme disease is characterized by cutaneous symptoms, such as a rash. If unnoticed, however, Lyme disease can affect the nervous system, heart, eyes, and joints. Lyme disease occurs in North America, Europe, and Asia (8).

Q fever

The infectious agent that causes Q fever is the bacterium *Coxiella burnetii*. Q fever is acquired through contact with contaminated animal products and inhalation of contaminated dust. Ticks can transmit the bacterium from animal to animal but not to humans. The main reservoirs for Q fever are cattle, sheep, and goats. Rodents are also suspected as a reservoir. *Coxiella* bacteria are present throughout the world. If untreated, Q fever is usually deadly. Q fever also causes reproductive problems in livestock, resulting in great economic losses for farmers around the world (8).

Flea-borne spotted fever

The bacteria *Rickettsia felis* is the infectious agent associated with this flea-borne spotted fever. The cat flea *Ctenocephalides felis felis* is currently the only biologically confirmed vector of *R.*

felis. The cat flea commonly lives on cats and dogs in temperate and tropical climates, but can also live on opossums, rodents, and raccoons. Human infection is rare; however, within the last 20 years, there have been a growing number of reports implicating *R. felis* as a human pathogen. There have been more than 70 documented cases worldwide. Symptoms include headache, fever, fatigue, and possible central nervous system involvement (20).

Tick-borne spotted fevers

Rocky Mountain spotted fever (RMSF) is the most frequently reported tick-borne spotted fever in the United States. It also occurs in Mexico and Central and South America. RMSF is caused by the bacterium *Rickettsia rickettsii*. Humans contract the disease by the bite of an infected ixodid tick. Rodents serve as a reservoir for the infectious agent. Symptoms of RMSP include fever, headache, pain, and a rash (8). Flinders Island spotted fever (FISF) is another tick-borne spotted fever. It is caused by *Rickettsia honei*, which was described as a new species in 1998 and identified as the causative agent of FISF. Flinders Island spotted fever occurs primarily in the spring and summer in Australia and Thailand (21).

Murine typhus

Murine typhus is caused by the bacterium *Rickettsia typhi*. *R. typhi* exists in an enzootic cycle with the Oriental rat flea, *Xenopsylla cheopis*, and the rat (*Rattus rattus* and closely allied species). Humans acquire the disease from an infected flea. Murine typhus is extremely widespread, occurring in most areas where the rat flea and the commensal rat are found (22). Symptoms of murine typhus include fever, nausea, and head and body aches, rash, and gastrointestinal symptoms. The mortality rate of murine typhus is between 1 and 4% (8).

Sylvatic epidemic typhus

Slyvatic epidemic typhus is caused by the bacterium *Rickettsia prowazekii*. Rodents host infected lice and fleas. *R. prowazekii* is then transmitted to humans from these infected ectoparasites. Epidemic typhus can also be transmitted between humans via the body louse in some areas of the world. The pathogen is maintained in the southern flying squirrel. The flying squirrel is thought to be able to transmit the disease directly to humans, although this mechanism is not fully understood (8).

Scrub typhus

Scrub typhus is caused by infection with the bacterium *Rickettsia (Orientia) tsutsugamushi*. Rodents host infected trombiculid mites, also known as chiggers, which can then transmit the disease to humans. Scrub typhus is found in Southern and Eastern Asia and Australia. In endemic areas, cases of scrub typhus can reach upwards of one million per year. The symptoms of scrub typhus include fever, headache, muscle pain, cough, and gastrointestinal symptoms. Rice farmers have been found to be particularly vulnerable to contracting the disease. If untreated, mortality rates can reach up to 40% (8).

Rickettsialpox

Rickettsialpox is caused by infection with the bacterium *Rickettsia akari*. This disease is widespread and occurs primarily in urban areas. The disease is most commonly transmitted to humans by an infected house mouse mite, which lives on the house mouse. There has been evidence that *R. akari* can adapt to other rodent hosts. Human infections have been reported in the United States, South Africa, Turkey, Croatia, Bosnia, Herzegovina, and Ukraine. Symptoms of rickettsialpox include fever, chills, and headache. No fatalities have been reported (8).

Toxoplasmosis

Toxoplasmosis, caused by the protozoan parasite *Toxoplasma gondii*, has a complex life cycle. Cats acquire the infection from prey, such as rodents, who are intermediate hosts. Infected cats shed oocysts in their feces. Livestock who take up these oocysts can form cysts in their organs. If they are slaughtered and their meat prepared improperly, the parasite can be transferred to humans. If a pregnant woman is infected either by eating contaminated meat or coming into contact with infected cat feces, the parasite can invade the tissues of the fetus and cause serious birth defects (8).

Tungiasis

Tungiasis is caused by the female sand flea *Tunga penetrans*. Tungiasis occurs predominantly in Latin America, the Caribbean, and sub-Saharan Africa, where it can cause significant morbidity. In some countries, the prevalence of tungiasis can be as high as 55%. Along with dogs, cats, and pigs, rodents are important hosts of tungiasis (23).

Bubonic plague

Plague is caused by the bacterium *Yersinia pestis*. It is transmitted to humans via the bite of an infected oriental rat flea (*Xenopsylla cheopis*) which lives on rodent hosts. Today, there are an estimated 1000-3000 cases of bubonic plague per year, mostly in North and South America, Africa, and Asia. Symptoms of bubonic plague include chills, a rise in temperature, aches, restlessness, and rapid pulse. This is followed by anxiety, delirium, and sometimes coma. Most patients have an enlarged, tender, hard lymph node (8).

Rodent Zoonoses in Travelers

Existing literature regarding rodent zoonoses in travelers focuses mainly on case reports of a limited number of diseases. For example, within a 2 month period there were three reported cases of murine typhus in travelers returning to France from Indonesia (24). Ten cases of Q fever in returned travelers were seen in a French hospital within four years (25). There was one case of imported Lassa Fever from West Africa to the United States in the year 2000. Although there have only been 20 cases of imported Lassa Fever reported to date worldwide, there is reason to believe that this number may increase with increasing international travel (26)

A growing interest in adventure travel is an important consideration when evaluating rodent zoonoses in travelers. Adventure travel is defined as travel outside one's normal environment for more than 24 hours but less than one year and involving interaction with nature, interaction with culture, and physical activity (27). With a growth rate of 10% per year, adventure travel is the largest growing segment of the leisure travel industry (28). With this increase comes an increase in the likelihood of contact with unusual pathogens, including many rodent zoonoses (29). Adventure travelers are more likely to come into contact with lakes, rivers, and insect vectors, increasing their chances of contracting a rodent zoonosis.

Participation in adventure travel is related to gender and age. Adventure travelers are more likely to be men than women. Those aged 18-34 are more likely to have taken an adventure travel trip than those aged 35-54 or those over 55. Therefore, it follows that rodent zoonoses may be more likely to be associated with male gender and a young age (28).

Leptospirosis is one example of a rodent borne disease that is commonly associated with the recreational water activities that are common in adventure travel. Leptospirosis is spread by

contact with water or soil that is contaminated with infected animal urine. Therefore, increased exposure to this contaminated water or soil due to adventure travel increases a travelers' risk of contracting the disease (30). A study conducted among Eco-Challenge adventure athletes in Malaysia found that increased adventure travel was associated with an increased risk of leptospirosis (29). Leptospirosis has also been found in adventure travelers who participated in caving and white water rafting (31, 32).

This analysis aims to provide a comprehensive assessment of direct and indirect rodent zoonoses in travelers over a 15-year period. Many imported microbial agents are not endemic to the United States and therefore present detection challenges to health care providers (26). Rodent zoonoses are often not suspected in febrile illness in travelers, leading to misdiagnosis and underreporting (25). Once the relative frequency of rodent zoonoses reported in travelers over time is established and characteristics of illness associated with rodent borne diseases are described, this information can be made available to travel medicine professionals and travelers alike, serving to ultimately decrease the individual health burden of these diseases.

METHODS

Hypotheses:

There are no significant differences in potential risk factors (gender, age, travel reason, trip duration, pre-travel physician encounter, risk of travel, clinical setting, and time to present) in those travelers who were diagnosed with one or more rodent zoonoses when compared to those ill travelers who were not.

There are no significant differences in the symptoms of travelers with rodent zoonoses when compared to travelers without.

There are no significant differences in country of exposure between those travelers diagnosed with a rodent zoonosis when compared to ill travelers without a rodent zoonosis diagnosis.

Primary Objective:

Determine if there is a significant difference in the country of exposure, gender, age, reason for travel, travel duration, pre-travel encounter status, risk level of travel, patient type, clinical setting, and time from travel to clinic visit between ill travelers with a rodent zoonosis and ill travelers without.

Secondary Objectives:

Determine the frequencies of presenting symptoms of travelers with rodent zoonoses and compare with the frequencies of presenting symptoms of other ill travelers without rodent zoonoses.

Compare regions of exposure between those travelers with rodent zoonoses and other ill travelers.

Dataset:

This manuscript examines data collected through GeoSentinel, a global surveillance network established by the International Society of Travel Medicine (ISTM) and the Centers for Disease Control and Prevention (CDC) in 1996 for the surveillance of travel-related morbidity. The 49 GeoSentinel travel clinic sites, located on 6 continents, collect clinician-based, anonymous data on all ill travelers seen either during or post-travel at these clinics. The database contains over 150,000 patient records. Emory IRB determination was requested and exemption was received.

Rodent Zoonosis Classification:

The analysis will include persons seen either during or post-travel. A case of rodent zoonosis will be defined as a patient record that has a travel-related, confirmed or probable final diagnosis of one or more of the rodent zoonoses listed in Appendix 1. For many diagnoses, classification as confirmed or probable is determined by a uniform case definition in GeoSentinel. For diagnoses that do not yet have a case definition in GeoSentinel, classification of confirmed or probable is based on the judgment of the site physician. All GeoSentinel diagnosis codes were thoroughly examined to produce a complete list of these diagnoses, which were then categorized by direct or indirect transmission to humans by rodents. The five diagnoses in the direct transmission category (Appendix 1) represent those diseases in the GeoSentinel database that are directly transmitted from rodents to humans, including contact with infected rodents or their urine and droppings. The 18 diagnoses categorized under indirect transmission (Appendix 1) are diseases that exist in rodent reservoirs that serve to maintain the cycle of these microbes and are transmitted to humans by vectors such as mosquitoes or ticks. To be classified as a rodent zoonosis, rodents must play a major role in the life cycle of the disease. All records from 1996 to March 2011 are included in this analysis, except those associated with immigration.

Variable Descriptions:

Demographic, travel, and clinical information was captured from each record, including country of exposure, season of travel, reason for travel, travel duration, risk level of travel, clinical setting, age, and sex. Information about symptoms was also reported. There can be more than one symptom per patient. Finally, country of exposure was reported, which can be used to determine the geographic origin of a disease. If a single patient visited multiple countries, the clinician determined country of exposure.

Comparison Groups:

Cases of direct and indirect rodent zoonoses, as described above, are compared with three separate control groups in order to identify factors and syndromes uniquely associated with rodent zoonoses. The first comparison group included records from final, confirmed, or probable, travel-related, nonimmigrant reports of zoonotic or vector-borne diseases (based on codes shown in Appendix 1); this group excluded the zoonotic or vector-borne diseases that were rodent-borne. The second comparison group included records of final, confirmed, or probable, travel-related, nonimmigrant reports of infectious diseases; this group also excluded rodent-borne diseases, but included zoonotic and vector-borne diseases. The final comparison group included all illness reports with a final diagnosis of confirmed or probable, travel-related, non-immigrations with any disease code, excluding rodent-borne diseases. In this way, the comparison groups will broaden sequentially, comparing those with rodent-borne zoonoses to those with all other zoonotic diseases, those with all other infectious diseases, and finally to all other illness reports in the GeoSentinel database.

Analysis Plan (Specific Aims):

After the rodent zoonoses group and relevant comparison groups were compiled, data were analyzed as follows:

-chi-squared tests for association to compare travelers with rodent zoonoses with other ill travelers with respect to country of exposure, season of travel, reason for travel, risk level qualifier, patient type, clinical setting, and sex

- ANOVA difference of means tests to compare travelers with rodent zoonoses to other ill travelers with respect to travel duration and age

- chi-squared tests for association to compare frequencies of presenting syndromes of travelers with rodent zoonoses with syndromes of other ill travelers

- multivariate logistic regression to identify risk factors and syndromes that may be associated with rodent zoonoses among travelers compared to other illnesses. Variables that were significant ($p<0.05$) in bivariate analysis were included in the multivariate model of risk factors. Variables that were close to significant ($0.05<p<0.25$) in bivariate analysis were tested for inclusion in the multivariate model. Variables associated with outcomes in previous studies were also tested for inclusion in the final model.

- chi-squared tests for association to compare regions of exposure between those travelers with rodent zoonoses and other ill travelers

Sample Size and Power Calculations

Population sizes are as follows:

959 records with a rodent zoonosis diagnosis code that also meet all inclusion criteria

17467 records with a zoonotic or vector-borne diagnosis code that also meet all inclusion criteria

35582 records with an infectious disease diagnosis code that also meet all inclusion criteria

87667 records with any diagnosis code that also meet all inclusion criteria

For each comparison group, given an alpha of 5% and the explanatory variable of interest, the multivariate analysis is powered at more than 99%. That is, the number of rodent zoonosis cases

and controls far exceed the number required for sufficient study power.

RESULTS

As shown in Table 1, there were 962 diagnoses of direct and indirect rodent zoonoses among 959 travelers in the GeoSentinel database from January 1996-March 2011. There were 18 total rodent zoonoses that comprised the 962 diagnoses. Three of these were directly transmitted by rodents (leptospirosis, hantavirus, and Lassa fever), while the remaining fifteen were indirectly transmitted by rodents (cutaneous, mucocutaneous, and visceral leishmaniasis, tick borne spotted fever, murine typhus, tungiasis, toxoplasmosis, Q fever, scrub typhus, arthritic and chronic Lyme disease, unknown rickettsial disease, babesiosis, rickettsialpox, and flea borne spotted fever). The 5 most common of these rodent zoonoses reported in the GeoSentinel database were cutaneous leishmaniasis (33.99%), Tick-borne spotted fevers (23.60%), Murine typhus (9.67%), Tungiasis (8.73%), and Leptospirosis (7.48%). There were five rodent zoonoses included in the GeoSentinel database as possible diagnoses that were not reported in any travelers within the study time frame (acute hemorrhagic fever syndrome, tularemia, epidemic typhus, rickettsia-other, and bubonic plague).

Of those travelers with rodent zoonoses, the majority were seen after travel (88.2% as compared in 11.8% seen during travel), as seen in Table 2a. In both the bivariate and multivariate analyses, (Tables 3 and 4), those ill travelers with rodent zoonoses were shown to be significantly less likely to be seen during travel (as compared to seen after travel) than ill travelers without a rodent zoonosis. These findings were consistent throughout all comparison groups.

Of travelers with rodent zoonoses, 65% of those travelers were male, seen in Table 2a. A bivariate analysis of gender found that those travelers with a rodent zoonosis were significantly more likely to be male than those without a rodent zoonosis, as seen in Table 3. Moreover, as seen in Table 4, when controlling for age, travel reason, trip duration, pre-travel encounter, risk

level of travel, patient type, clinical setting, time to present, and region of exposure, it was found that ill travelers with rodent zoonoses were up to 1.5 times more likely to be male than those ill travelers with some other diagnosis. These findings were consistent throughout all three comparison groups.

Table 2b shows the distribution of travel reasons for those with rodent zoonoses in the GeoSentinel database. 63.9% were traveling as tourists, 19.3% for business, 8.8% as missionaries, 3.2% for reasons relating to the military, 2.8% visiting friends or relatives, and 2.0% as students. A bivariate analysis showed that ill travelers with rodent zoonoses were significantly more likely to be traveling for reasons related to tourism than all other travelers (Table 3). Controlling for all other factors gave similar results. It was found that those ill travelers with rodent zoonoses were approximately 2 times more likely to be tourists than ill travelers without a rodent zoonosis (Table 4). The results were also consistent throughout all comparison groups.

Table 5 includes a breakdown of several variables of interest (sex, reason for travel, and clinical setting) by specific disease diagnosis. It should be noted that all members of the military who had a rodent zoonosis had either cutaneous or visceral leishmaniasis.

On average, it took a patient with a rodent zoonosis 41.5 days from travel to a clinic visit, as compared to 33.8 days for all other travelers, excluding those with rodent zoonoses, 28.9 days for those travelers with an infectious disease, and 34.5 days for those with a zoonotic or vector-borne disease (Table 2b). When using a multivariate model, shown in Table 4, and controlling for the factors mentioned above, there was anywhere from a 0.3-0.5% increase in the odds of having a rodent zoonosis for every one day increase in time to present to a clinic, depending on the control group used.

While controlling for all other factors in a multivariate model, several predictors were found not significant consistently throughout all three comparison groups. These non-significant predictors included age, trip duration, and whether or not the traveler had a pre-travel visit to a physician. These results can be seen in Table 4.

Detailed in Table 6, of those travelers in the GeoSentinel database diagnosed with a rodent-borne disease, 41.5% presented with a fever. 17.73% experienced fatigue, 16.27% had musculoskeletal symptoms, and 13.97% experienced gastrointestinal symptoms. All other symptoms were reported at relatively low rates, including cardiac, genitourinary, head, ears, eyes nose, and throat (HEENT), neurologic, lymphatic, and respiratory symptoms. No patients with rodent zoonoses reported symptoms of the skin or psychological symptoms.

Consistent with the bivariate results seen in Table 7, a multivariate analysis of reported symptoms, shown in Table 8, found that those travelers with rodent zoonoses were consistently shown to be significantly more likely to present with symptoms of the lymphatic system than travelers in any of the three comparison groups. Those with rodent zoonoses were 2.8 times more likely to experience these lymphatic symptoms than all other ill travelers, 3.3 times more likely than travelers with infectious diseases and over 10 times more likely to experience these symptoms than those travelers with zoonotic or vector-borne disease. When sub-analyses were done as shown in Table 9, those with rickettsial rodent zoonoses only were 2.4 times more likely to experience these lymphatic symptoms than all other ill travelers, 3.0 times more likely than travelers with infectious diseases and 9.6 times more likely to experience these symptoms than those travelers with zoonotic or vector-borne disease. Those with cutaneous leishmaniasis were only 0.84 times more likely to experience these lymphatic symptoms than all other ill travelers,

1.1 times more likely than travelers with infectious diseases and 3.2 times more likely to experience these symptoms than those travelers with zoonotic or vector-borne disease.

Additionally, when compared to all other travelers, those with rodent diseases were found more likely to experience fever. They were less likely to experience cardiac, gastrointestinal, genitourinary, HEENT, and respiratory symptoms. When compared to travelers with an infectious disease diagnosis, those with rodent zoonoses were found more likely to have musculoskeletal symptoms and less likely to experience gastrointestinal, genitourinary, HEENT, and respiratory symptoms. Finally, when compared to those travelers with zoonotic or vector-borne diseases only, those with rodent borne diseases were found more likely to experience HEENT, musculoskeletal, and respiratory symptoms and less likely to experience gastrointestinal symptoms.

Listed on the GeoSentinel diagnosis questionnaire were 14 possible regions of exposure: Antarctica, Australia/New Zealand, the Caribbean, Central America, Eastern Europe, the Middle East, North Africa, North America, North East Asia, Oceania, South America, South Central Asia, South East Asia, Sub-Saharan Africa, and Western Europe (Table 10). Among the 962 diagnoses of rodent zoonoses in the study population, almost 30% were thought to be contracted in Sub-Saharan Africa. 21.58% of travelers with rodent zoonoses listed their region of exposure as South America, while 15.33% were thought to be exposed in South East Asia and 8.55% in Central America.

A bivariate regional analysis was performed using Eastern Europe as a referent group and is shown in Table 11. Further, a multivariate regional analysis, controlling for all other relevant factors and using Eastern Europe as a referent group was carried out and shown in Table 12. It was found that, when compared to all other ill travelers, those with rodent zoonoses were 21

times more likely to have been exposed in South America, 12 times more likely to have been exposed in Sub-Saharan Africa, and 11 times more likely to have been exposed in Central America. Travelers with rodent zoonoses were also significantly more likely to have been exposed in the Middle East, North America, and Western Europe. Results were consistent when those travelers with rodent zoonoses were compared to ill travelers with an infectious disease diagnosis and ill travelers with a zoonotic or vector borne disease diagnosis.

DISCUSSION

As expected, those ill travelers with rodent zoonoses were significantly more likely to be male than those ill travelers with other diagnoses. It has been shown that males are more likely to engage in risk taking behavior than females (33). Furthermore, males are more likely than females to engage in adventure travel, which puts them at an increased risk of being exposed to the pathogens that cause rodent borne diseases (28).

It was also found that ill travelers with rodent zoonoses were significantly more likely to be traveling for tourism than ill travelers without a rodent zoonosis. It has been shown that tourists are more likely to engage in risk taking behavior than the same people would be when not on vacation. Tourists perceive risks as less perilous in the context of tourist travel than in the context of everyday life (34). This increase in risk taking behavior puts these tourists at an increased possibility of exposure to rodents, vectors, and the diseases they carry.

Military personnel may have living conditions that maximize contact with the environment, which puts them at increased risk for rodent or vector contact. All military personnel who had a rodent zoonosis were diagnosed with either cutaneous or visceral leishmaniasis. Cutaneous leishmaniasis has been identified as a significant risk for military personnel, particularly those deployed to Afghanistan, Iraq, and Kuwait. Measures that should be implemented to decrease the risk of cutaneous leishmaniasis among the military include improving living conditions, raising awareness of endemic leishmaniasis, and emphasizing the importance of vector control measures such as bed nets and insect repellent (35).

As stated, ill travelers with rodent zoonoses were significantly less likely to be seen during travel (as compared to seen after travel) than ill travelers without a rodent zoonosis. As many rodent

borne diseases are severe, it was hypothesized that travelers with rodent zoonoses were more likely to be seen during travel. However, these results may be explained by the fact that over 30% of the 962 rodent disease diagnoses were of cutaneous leishmaniasis (CL). CL has a long incubation period that can extend from a few weeks to a few years. Furthermore, the initial symptoms of CL are mild and usually begin with one or more painless ulcers (8). These reasons may account for the fact that those with rodent zoonoses were more likely to be seen for treatment after travel. Moreover, as most cases of rodent zoonoses in travelers were seen in those who were tourists, travelers may choose to see a physician after travel so as not to interrupt their trip if the symptoms are mild enough to ignore.

It was found that a pretravel encounter with a physician did not decrease the likelihood of contracting a rodent zoonosis while traveling. This suggests that pretravel visits may not be focused on dispersing information regarding preventative measures with respect to rodent zoonoses. Pretravel visits provide an excellent opportunity for physicians to introduce these concepts to travelers who otherwise may not be accessible. Physicians should review in detail a travelers' itinerary, noting the country of origin, length of visit, season of travel, and planned activities as well as the travelers' current health (36). Using this information, physicians should engage in preventative counseling, advising travelers visiting countries where rodent diseases are endemic to avoid rodents and possible vectors, as well as any rodent droppings or urine. Travelers should also be advised to limit participation in water sports to avoid contact with contaminated rodent urine or feces in water. Travelers should avoid situations in which exposure to rodents may be more likely, such as sleeping on the ground or in rodent infested dwellings.

With regards to symptoms associated with rodent zoonoses, an initial analysis showed that those with rodent zoonoses were over 10 times more likely to experience symptoms of the lymphatic system than those travelers with zoonotic or vector-borne disease. However, when examining

symptoms using only those travelers with rodent zoonoses of a rickettsial origin, very similar trends and OR estimates were found. This suggests that the rickettsial rodent zoonoses in this analysis are driving these lymphatic symptom findings. Therefore, it would be inaccurate to conclude that rodent zoonoses as a whole are associated with symptoms of the lymphatic system.

As mentioned, those with rodent zoonoses were much more likely to have been exposed in South America, Sub-Saharan Africa, and Central America than those travelers with some other illness. Therefore, travelers to these areas should be aware of their increased risk of contracting a rodent-borne zoonosis and take proper preventative measures.

Strengths and Limitations:

There are many strengths of the GeoSentinel database and of this study. Diagnoses were either clinically or laboratory confirmed-they were not self-reported. This decreases the likelihood of reporting bias. Furthermore, symptoms were reported by clinicians rather than by the patients themselves which further decreases the likelihood of misreporting. The three well-defined comparison groups that were used in this study add strength to the research. Consistency in results throughout the three groups adds strength and support to the study's significant findings. Finally, the large number of individuals and substantial power in this study adds robustness to the findings.

The GeoSentinel dataset does have a few limitations. In some instances, the GeoSentinel dataset does not provide a sufficient level of detail in order to accurately assess the intricacies of risk travel. For example, the dataset does not include information about a travelers' lodging, sleeping arrangements, or participation in water sports or other adventure activities during travel.

Future Directions:

As GeoSentinel was not designed to provide the level of detail necessary to assess specific risk travel behavior, one may consider future studies in order to ascertain this additional information. One may consider sending a follow-up questionnaire to those from the GeoSentinel database who were diagnosed with a rodent zoonosis that includes more detailed questions regarding their risk behaviors while traveling.

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TABLES

Table 1. Frequency of Directly and Indirectly Transmitted Rodent Zoonoses in GeoSentinel, March 1996-2011

Directly Transmitted Rodent Zoonoses	n	%
Leptospira	72	7.48
Hantavirus	3	0.31
Lassa Fever	1	0.10
Hemorrhagic Fever Syndrome, Acute	0	0.00
Tularemia	0	0.00
Indirectly Transmitted Rodent Zoonoses	**n**	**%**
Leishmania, Cutaneous	327	33.99
Rickettsia, Tick-Borne Spotted Fever	227	23.60
Rickettsia, Typhi	93	9.67
Tungiasis	84	8.73
Toxoplasma Gondii	38	3.95
Q Fever	22	2.29
Rickettsia (Now Orientia) Tsutsugamushi	19	1.98
Leishmania, Mucocutaneous	18	1.87
Lyme Disease, Arthritis	18	1.87
Leishmania, Visceral	13	1.35
Lyme Disease, Chronic	12	1.25
Rickettsia, Species Unknown	11	1.14
Babesiosis	2	0.21
Rickettsia, Akari	1	0.10
Rickettsia, Felis	1	0.10
Rickettsia, Prowazeki	0	0.00
Rickettsia, Other	0	0.00
Yersinia Pestis, Bubonic	0	0.00
Total*	962	

*The dataset includes 959 people with one or more rodent zoonosis diagnoses. 3 of these people had 2 rodent zoonosis diagnoses, making 962 diagnoses total.

Table 2a. Characteristics of Travelers with Rodent Zoonoses Compared to Travelers without Rodent Zoonoses in GeoSentinel, March 1996-2011

	No. (%) of ill travelers with RZ (n=962*)	**No. (%) of all other ill travelers (n=87666*)**	**No. (%) travelers with infectious disease diagnosis (n=35582*)**	**No. (%) of ill travelers with Z/V disease (n=17467*)**
Sex				
Male	626 (65.3)	43157 (49.4)	18,707 (52.8)	9,606 (55.4)
Female	332 (34.7)	44147 (50.6)	16,708 (47.2)	7,748 (44.7)
P value		<0.0001	<0.0001	<0.0001
Age, years				
Mean (years)	36.7	35.4	34.1	34.4
<18	49 (5.2)	7,868 (9.0)	3,329 (9.4)	1,073 (6.2)
18-25	238 (25.0)	16,118 (18.4)	7,406 (20.9)	3,980 (22.9)
26-44	371 (39.0)	39,714 (45.4)	16,194 (45.6)	8,359 (48.0)
45-64	230 (24.2)	19,887 (22.7)	7,192 (20.3)	3,394 (19.5)
>64	64 (6.7)	3,848 (22.7)	1,369 (3.9)	600 (3.5)
P value		0.0085	<.0001	<.0001
Trip Duration				
Mean (days)	106.0	96.4	92.1	112.5
≤ 2 weeks	218 (28.7)	25,407 (34.9)	9,886 (33.9)	4,252 (29.6)
> 2 weeks	542 (71.3)	47,497 (65.2)	19,316 (66.2)	10,116 (70.4)
P value		0.6186	0.4718	0.7352
Pretravel Encounter				
Patient did Report	442 (46.1)	42,690 (48.7)	16,610 (46.7)	8,013 (45.9)
Patient did not Report	517 (53.9)	44,976 (51.3)	18,972 (53.3)	9,454 (54.1)
P value		0.1082	0.7172	0.8967
Patient Type				
Inpatient	229 (24.1)	9,054 (10.4)	6,352 (18.0)	3,949 (22.9)
Outpatient	723 (76.0)	77,843 (89.6)	28,898 (82.0)	13,290 (77.1)
P value		<0.0001	<0.0001	0.4126
Clinical Setting				
Seen During Travel	113 (11.8)	34,970 (39.9)	12,554 (35.3)	3,556 (20.4)
Seen After Travel	846 (88.2)	52,690 (60.1)	23,023 (64.7)	13,909 (79.6)
P value		<0.0001	<0.0001	<0.0001

* Categories may not add up to total due to missing data.

Table 2b. Characteristics of Travelers with Rodent Zoonoses Compared to Travelers without Rodent Zoonoses in GeoSentinel, March 1996-2011

	No. (%) of ill travelers with RZ (n=962*)	**No. (%) of all other ill travelers (n=87666*)**	**No. (%) travelers with infectious disease diagnosis (n=35582*)**	**No. (%) of ill travelers with Z/V disease (n=17467*)**
Time from Travel to Clinic Visit				
Mean (days)	41.5	33.8	28.9	34.5
<14 days	357 (47.0)	42,139 (57.7)	17,514 (59.9)	8,041 (55.9)
14-30 days	122 (16.1)	9,735 (13.3)	4,085 (14.0)	2,347 (16.3)
>30 days	281 (36.0)	21,102 (28.9)	7,637 (26.1)	3,996 (27.8)
P value		<0.0041	<0.0001	0.0343
Reason for Travel				
Business	185 (19.3)	25339 (29.0)	9,873 (27.8)	3,927 (22.5)
Missionary	84 (8.8)	11265 (12.9)	3,789 (10.7)	2,158 (12.4)
Student	19 (2.0)	2392 (2.7)	1,081 (3.0)	446 (2.6)
Tourism	612 (63.9)	45598 (52.1)	19,062 (53.7)	9,865 (56.6)
Visiting Friends/Relatives	27 (2.8)	2575 (2.9)	1,503 (4.2)	910 (5.2)
Military	31 (3.2)	351 (0.4)	199 (0.6)	131 (0.8)
P value		<0.0001	<0.0001	<0.0001
Risk Level of Travel				
Organized Travel	192 (20.0)	15,211 (17.4)	6,055 (17.0)	2,956 (16.9)
Risk Travel	327 (34.1)	25,906 (29.6)	10,494 (29.5)	5,649 (32.3)
Expatriate	131 (13.7)	20,262 (23.1)	7,549 (21.2)	2,991 (17.1)
Unknown	309 (32.2)	26,287 (30.0)	11,484 (32.3)	5,871 (33.6)
P value		<0.0001	0.0044	0.3131

* Categories may not add up to total due to missing data.

Table 3. Bivariate Analyses of Characteristics Associated with Travelers with Rodent Zoonoses Compared to Travelers without Rodent Zoonoses in GeoSentinel, March 1996-2011

	No. of ill travelers with RZ vs. All Travelers			**No. of ill travelers with RZ vs. Travelers with Infectious Disease**			**No. of ill travelers with RZ vs. Travelers with Z/V Disease**		
	Unadjusted OR	95% CI		Unadjusted OR	95% CI		Unadjusted OR	95% CI	
Characteristic									
Male	1.929	1.687	2.205	1.684	1.472	1.927	1.521	1.327	1.743
Age (continuous)*	0.996	0.989	1.002	1.004	0.997	1.011	1.006	0.999	1.013
Trip Duration (continuous)*	1.000	1.000	1.000	1.000	1.000	1.000	1.000	0.999	1.000
Had Pretravel Encounter	1.110	0.977	1.261	1.024	0.900	1.165	0.991	0.870	1.129
Patient Treated as Inpatient	2.723	2.343	3.165	1.441	1.239	1.676	1.066	0.915	1.242
Patient Seen During Travel	0.201	0.165	0.245	0.245	0.201	0.298	0.522	0.428	0.638
Time to Present (continuous)*	1.005	1.004	1.007	1.005	1.003	1.006	1.005	1.004	1.007
Reason for Travel									
Business	0.696	0.464	1.045	1.043	0.694	1.568	1.588	1.054	2.393
Missionary	0.711	0.460	1.099	1.234	0.797	1.912	1.312	0.845	2.038
Student	0.758	0.420	1.366	0.978	0.541	1.769	1.436	0.790	2.610
Tourism	1.280	0.869	1.886	1.790	1.213	2.641	2.093	1.415	3.096
Visiting Friends/Relatives**	.	.	.	.	.	.	.	.	.
Military	8.423	4.968	14.279	8.674	5.072	14.836	7.976	4.613	13.790
Risk Level of Travel									
Organized Travel	1.074	0.896	1.287	1.178	0.982	1.415	1.234	1.025	1.486
Risk Travel	1.074	0.918	1.256	1.158	0.989	1.356	1.100	0.937	1.290
Expatriate	0.550	0.448	0.675	0.645	0.525	0.793	0.832	0.675	1.026
Unknown**	.	.	.	.	.	.	.	.	.

*Unadjusted OR and CI for Age, Trip Duration, and Time to Present were specified using cubic and quadratic terms due to a non-linear relationship and evaluated at the mean of the Age, Trip Duration, and Time to Present variables.

**'Visiting Friends and Relatives' and 'Unknown' are referent groups.

Table 4. Multivariate Analyses of Characteristics Associated with Travelers with Rodent Zoonoses Compared to Travelers without Rodent Zoonoses in GeoSentinel, March 1996-2011

	No. of ill travelers with RZ vs. All Travelers			**No. of ill travelers with RZ vs. Travelers with Infectious Disease**			**No. of ill travelers with RZ vs. Travelers with Z/V Disease**		
	Adjusted OR	95% CI		Adjusted OR	95% CI		Adjusted OR	95% CI	
Characteristic									
Male	1.506	1.291	1.757	1.339	1.145	1.567	1.295	1.104	1.519
Age (continuous)*	1.003	0.995	1.011	1.006	0.998	1.014	1.008	0.999	1.016
Trip Duration (continuous)*	1.000	1.000	1.000	1.000	1.000	1.000	1.000	0.999	1.000
Had Pretravel Encounter	0.997	0.851	1.167	0.961	0.819	1.129	0.910	0.772	1.073
Patient Treated as Inpatient	1.524	1.233	1.883	0.932	0.752	1.153	0.957	0.768	1.191
Patient Seen During Travel	0.157	0.099	0.248	0.245	0.154	0.388	0.510	0.324	0.805
Time to Present (continuous)*	1.003	1.002	1.005	1.005	1.003	1.007	1.004	1.002	1.005
Reason for Travel									
Business	0.833	0.536	1.455	1.127	0.682	1.863	3.788	2.027	7.079
Missionary	0.861	0.528	1.405	1.274	0.776	2.093	1.395	0.846	2.300
Student	1.122	0.576	2.185	1.407	0.717	2.759	1.631	0.825	3.225
Tourism	1.693	1.093	2.623	2.111	1.359	2.279	2.343	1.505	3.647
Visiting Friends/Relatives**	.	.	.	.	.	.	.	.	.
Military	4.837	2.645	8.845	4.421	2.384	8.200	3.788	2.027	7.079
Risk Level of Travel									
Organized Travel	1.051	0.845	1.307	1.131	0.905	1.412	1.309	1.042	1.644
Risk Travel	1.163	0.964	1.402	1.223	1.012	1.479	1.275	1.051	1.547
Expatriate	0.968	0.634	1.479	0.950	0.618	1.459	0.993	0.647	1.524
Unknown**	.	.	.	.	.	.	.	.	.

*Adjusted OR and CI for Age, Trip Duration, and Time to Present were specified using cubic and quadratic terms due to a non-linear relationship and evaluated at the mean of the Age, Trip Duration, and Time to Present variables.

**'Visiting Friends and Relatives' and 'Unknown' are referent groups.

Table 5. Relative Contribution of Each Rodent Zoonosis to Risk Factors of Interest in GeoSentinel, March 1996-2011

	No. (%) Sex	No. (%) Reason for Travel						No. (%) Clinical Setting
	Male	Business	Missionary	Student	Tourism	VFR	Military	Seen During Travel
Leptospira(n=72)	56 (77.8)	16 (22.5)	4 (5.6)	0 (0.0)	49 (69.0)	2 (2.8)	0 (0.0)	9 (12.5)
Hantavirus (n=3)	3 (100.0)	0 (0.0)	1 (33.3)	0 (0.0)	2 (66.7)	0 (0.0)	0 (0.0)	0 (0.0)
Lassa Fever (n=1)	0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Leishmania, Cutaneous (n=327)	220 (67.3)	23 (7.0)	35 (10.7)	11 (3.4)	214 (65.4)	14 (4.3)	30 (9.2)	7 (2.1)
Rickettsia, TBSF (n=227)	131 (57.7)	27 (11.9)	10 (4.4)	3 (1.3)	187 (82.4)	0 (0.0)	0 (0.0)	2 (0.8)
Rickettsia, Typhi (n=93)	81 (87.1)	78 (83.9)	2 (2.2)	1 (1.1)	9 (9.7)	3 (3.2)	0 (0.0)	78 (83.9)
Tungiasis (n=84)	43 (51.2)	10 (11.9)	19 (22.6)	4 (4.8)	49 (58.3)	2 (2.4)	0 (0.0)	0 (0.0)
Toxoplasma Gondii (n=38)	21 (56.8)	5 (13.2)	5 (13.2)	0 (0.0)	25 (65.8)	3 (7.9)	0 (0.0)	1 (2.6)
Q Fever (n=22)	11 (50.0)	3 (13.6)	2 (9.1)	0 (0.0)	16 (72.7)	1 (4.6)	0 (0.0)	2 (9.1)
Rickettsia Tsutsugamushi (n=19)	16 (84.2)	14 (73.7)	0 (0.0)	0 (0.0)	4 (21.1)	1 (5.3)	0 (0.0)	12 (63.2)
Leishmania, Mucocutaneous (n=18)	14 (77.8)	0 (0.0)	2 (11.1)	0 (0.0)	16 (88.9)	0 (0.0)	0 (0.0)	1 (5.6)
Lyme Disease, Arthritis (n=18)	6 (33.3)	5 (27.8)	1 (5.6)	0 (0.0)	12 (66.7)	0 (0.0)	0 (0.0)	1 (5.6)
Leishmania, Visceral (n=13)	11 (84.6)	0 (0.0)	0 (0.0)	0 (0.0)	11 (84.6)	1 (7.7)	1 (7.7)	0 (0.0)
Lyme Disease, Chronic (n=12)	6 (50.0)	3 (25.0)	2 (16.7)	0 (0.0)	7 (58.3)	0 (0.0)	0 (0.0)	0 (0.0)
Rickettsia, Species Unknown (n=11)	8 (72.7)	1 (9.1)	0 (0.0)	0 (0.0)	9 (81.8)	1 (9.1)	0 (0.0)	0 (0.0)
Babesiosis (n=2)	1 (50.0)	1 (50.0)	0 (0.0)	0 (0.0)	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rickettsia, Akari (n=1)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rickettsia, Felis (n=1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)

Table 6. Symptoms of Travelers with Rodent Zoonoses Compared to Travelers without Rodent Zoonoses in GeoSentinel, March 1996-2011

	No. (%) of ill travelers with RZ (n=962)	**No. (%) of all other ill travelers (n=87666)**	**No. (%) travelers with infectious disease diagnosis (n=35582)**	**No. (%) of ill travelers with Z/V disease (n=17467)**
Symptom				
Cardiac	6 (0.6)	1,396 (1.6)	308 (0.9)	129 (0.7)
P value		0.017	0.4269	0.6898
Fatigue	170 (17.7)	13,129 (15.0)	6,645 (18.7)	3,075 (17.6)
P value		0.0177	0.4569	0.9230
Fever	398 (41.5)	20,754 (23.7)	14,015 (39.4)	6,967 (39.9)
P value		<0.0001	0.1863	0.3202
Gastrointestinal	134 (14.0)	30,492 (34.8)	14,138 (39.7)	8,451 (48.4)
P value		<0.0001	<0.0001	<0.0001
Genitourinary	9 (0.9)	3,902 (4.5)	1,691 (4.8)	299 (1.7)
P value		<0.0001	<0.0001	0.069
HEENT*	84 (8.8)	10,414 (11.9)	5,170 (14.5)	744 (4.3)
P value		0.0029	<0.0001	<0.0001
Lymphatic	24 (2.5)	557 (0.6)	201 (0.6)	42 (0.2)
P value		<0.0001	<0.0001	<0.0001
Musculoskeletal	156 (16.3)	9,966 (11.4)	4,068 (11.4)	2,754 (15.8)
P value		<0.0001	<0.0001	0.6793
Neurologic	49 (5.1)	3,798 (4.3)	1,207 (3.4)	601 (3.4)
P value		0.2401	0.004	0.0064
Psychologic	0 (0.0)	1,905 (2.2)	223 (0.6)	78 (0.5)
P value		<0.0001	0.0139	0.0381
Respiratory	48 (5.0)	9,580 (10.9)	4,398 (12.4)	548 (3.1)
P value		<0.0001	<0.0001	0.0015

*Head, Ears, Eyes, Nose, and Throat

Table 7. Bivariate Analyses of Symptoms in Travelers with Rodent Zoonoses Compared to Travelers without Rodent Zoonoses in GeoSentinel, March 1996-2011

	No. of ill travelers with RZ vs. All Travelers			**No. of ill travelers with RZ vs. Travelers with Infectious Disease**			**No. of ill travelers with RZ vs. Travelers with Z/V Disease**		
	Unadjusted OR	95% CI		Unadjusted OR	95% CI		Unadjusted OR	95% CI	
Symptom									
Cardiac	0.389	0.174	0.870	0.721	0.321	1.622	0.846	0.372	1.924
Fatigue	1.223	1.035	1.445	0.938	0.793	1.120	1.008	0.851	1.120
Fever	2.287	2.001	2.603	1.092	0.959	1.244	1.069	0.937	1.220
Gastrointestinal	0.305	0.254	0.366	0.246	0.205	0.296	0.173	0.144	0.209
Genitourinary	0.203	0.105	0.392	0.190	0.098	0.367	0.544	0.279	1.059
HEENT*	0.712	0.569	0.892	0.564	0.451	0.708	2.158	1.705	2.731
Lymphatic	4.014	2.654	6.071	4.518	2.944	6.934	10.649	6.422	17.660
Musculoskeletal	1.515	1.274	1.800	1.505	1.264	1.792	1.038	0.870	1.238
Neurologic	1.189	0.890	1.588	1.534	1.144	2.056	1.511	1.121	1.037
Respiratory	0.430	0.321	0.575	0.374	0.279	0.500	1.627	1.202	2.201

*Head, Ears, Eyes, Nose, and Throat

Table 8. Multivariate Analyses of Symptoms in Travelers with Rodent Zoonoses Compared to Travelers without Rodent Zoonoses in GeoSentinel, March 1996-2011

	No. of ill travelers with RZ vs. All Travelers			**No. of ill travelers with RZ vs. Travelers with Infectious Disease**			**No. of ill travelers with RZ vs. Travelers with Z/V Disease**		
	Adjusted OR	95% CI		Adjusted OR	95% CI		Adjusted OR	95% CI	
Symptom									
Cardiac	0.417	0.186	0.934	1.004	0.441	2.282	0.758	0.324	1.774
Fatigue	1.123	0.942	1.338	1.014	0.849	1.211	0.911	0.754	1.100
Fever	2.283	1.994	2.613	0.910	0.793	1.045	0.906	0.783	1.047
Gastrointestinal	0.259	0.215	0.311	0.203	0.169	0.244	0.172	0.143	0.207
Genitourinary	0.178	0.092	0.344	0.143	0.074	0.277	0.549	0.280	1.075
HEENT*	0.555	0.442	0.697	0.472	0.375	0.593	2.237	1.732	2.889
Lymphatic	2.786	1.835	4.230	3.338	2.158	5.163	10.301	6.043	17.561
Musculoskeletal	1.179	0.990	1.403	1.645	1.369	1.976	1.262	1.043	1.528
Neurologic	0.989	0.739	1.323	1.277	0.946	1.722	1.324	0.971	1.804
Respiratory	0.315	0.235	0.422	0.312	0.233	0.419	1.539	1.124	2.108

*Head, Ears, Eyes, Nose, and Throat

Table 9. All Rodent Zoonoses Compared to Cutaneous Leishmaniasis and Rickettsial Diagnoses Only in GeoSentinel, March 1996-2011

	No. of Ill Travelers with RZ vs. All Travelers	**No. of Ill Travelers with RZ vs. Travelers with Infectious Disease**	**No. of Ill Travelers with RZ vs. Travelers with Z/V Disease**
	Adjusted OR	Adjusted OR	Adjusted OR
All Rodent Zoonoses	2.786	3.338	10.301
Cutaneous Leishmaniasis Only	0.843	1.063	3.159
Rickettsial Diseases Only	2.429	2.983	9.575

Table 10. Region of Exposure of Travelers with Rodent Zoonoses Compared to Travelers without Rodent Zoonoses in GeoSentinel, March 1996-2011

	No. (%) of ill travelers with RZ (n=962)	**No. (%) of all other ill travelers (n=87666)**	**No. (%) travelers with infectious disease diagnosis (n=35582)**	**No. (%) of ill travelers with Z/V disease (n=17467)**
Region				
Antarctica	0 (0.0)	3 (0.0)	2 (0.01)	2 (0.01)
P value				
Australia/New Zealand	4 (0.4)	391 (0.5)	121 (0.3)	37 (0.2)
P value		0.8937	0.6868	0.189
Carribean	11 (1.2)	3,118 (3.6)	1,243 (3.5)	652 (3.7)
P value		<.0001	<.0001	<.0001
Central America	82 (8.6)	4,035 (4.6)	1,514 (4.3)	771 (4.4)
P value		<.0001	<.0001	<.0001
Eastern Europe	4 (0.4)	561 (0.6)	246 (0.7)	103 (0.6)
P value		0.3885	0.3093	0.4934
Middle East	23 (2.4)	1,095 (1.3)	385 (1.1)	195 (1.1)
P value		0.0015	0.0001	0.0004
North Africa	35 (3.7)	2,285 (2.6)	762 (2.1)	434 (2.5)
P value		0.0442	0.0016	0.0257
North America	16 (1.7)	1,004 (1.2)	326 (0.9)	65 (0.4)
P value		0.1309	0.017	<.0001
North East Asia	10 (1.0)	6,880 (7.9)	2,137 (6.0)	302 (1.7)
P value		<.0001	<.0001	0.1088
Oceania	4 (0.4)	649 (0.7)	320 (0.9)	225 (1.3)
P value		0.2444	0.116	0.0178
South America	207 (21.6)	5,151 (5.9)	1,913 (5.4)	1,246 (7.1)
P value		<.0001	<.0001	<.0001
South Central Asia	44 (4.6)	22,551 (25.7)	8,489 (23.9)	3,287 (18.8)
P value		<.0001	<.0001	<.0001
South East Asia	147 (15.3)	13,557 (15.5)	7,254 (20.4)	4,491 (25.7)
P value		0.9078	0.0001	<.0001
Sub-Saharan Africa	286 (29.8)	13,922 (15.9)	6,343 (17.8)	4,152 (23.8)
P value		<.0001	<.0001	<.0001
Western Europe	50 (5.2)	2,354 (2.7)	915 (2.6)	287 (1.6)
P value		<.0001	<.0001	<.0001

Table 11. Region of Exposure Bivariate Analysis of Travelers with Rodent Zoonoses Compared to Travelers without Rodent Zoonoses in GeoSentinel, March 1996-2011

	No. of ill travelers with RZ vs. All Travelers			**No. of ill travelers with RZ vs. Travelers with Infectious Disease**			**No. of ill travelers with RZ vs. Travelers with Z/V Disease**		
	Unadjusted OR	95% CI		Unadjusted OR	95% CI		Unadjusted OR	95% CI	
Region									
Australia/New Zealand	1.424	0.354	5.727	2.000	0.492	8.132	2.641	0.629	11.081
Carribean	0.495	0.157	1.559	0.544	0.172	1.723	0.434	0.136	1.390
Central America	2.850	1.041	7.806	3.331	1.210	9.169	2.739	0.983	7.629
Eastern Europe*	.	.	.	.	.	.	.	.	.
Middle East	2.946	1.014	8.560	3.674	1.255	10.752	3.037	1.023	9.018
North Africa	2.148	0.760	6.069	2.825	0.994	8.027	2.077	0.722	5.973
North America	2.235	0.744	6.718	3.018	0.997	9.141	6.339	2.030	19.796
North East Asia	0.204	0.064	0.652	0.288	0.090	0.924	0.853	0.262	2.777
Oceania	0.864	0.215	3.472	0.769	0.190	3.104	0.458	0.112	1.866
South America	5.636	2.087	15.217	6.655	2.452	18.058	4.278	1.559	11.741
South Central Asia	0.274	0.098	0.764	0.319	0.114	0.894	0.345	0.122	0.977
South East Asia	1.521	0.561	4.121	1.246	0.458	3.392	0.843	0.306	2.319
Sub-Saharan Africa	2.881	1.070	7.757	2.773	1.025	7.500	1.774	0.649	4.850
Western Europe	2.979	1.071	8.283	3.361	1.202	9.396	4.486	1.581	12.730

*Eastern Europe is used as the referent group.

Table 12. Region of Exposure Multivariate Analysis of Travelers with Rodent Zoonoses Compared to Travelers without Rodent Zoonoses in GeoSentinel, March 1996-2011

	No. of ill travelers with RZ vs. All Travelers			**No. of ill travelers with RZ vs. Travelers with Infectious Disease**			**No. of ill travelers with RZ vs. Travelers with Z/V Disease**		
	Adjusted OR	95% CI		Adjusted OR	95% CI		Adjusted OR	95% CI	
Region									
Australia/New Zealand	4.414	0.455	42.803	6.345	0.648	63.143	8.840	0.882	88.605
Carribean	1.426	0.177	11.468	1.337	1.166	10.775	1.250	0.154	10.141
Central America	11.270	1.557	81.596	10.871	1.498	78.902	10.104	1.383	73.795
Eastern Europe*	.	.	.	.	.	.	.	.	.
Middle East	8.102	1.064	61.715	8.504	1.111	65.072	8.067	1.045	62.282
North Africa	6.722	0.909	49.700	7.459	1.006	55.306	8.827	0.914	51.010
North America	8.628	1.126	66.092	12.063	1.566	92.890	25.676	3.261	202.171
North East Asia	2.542	0.315	20.530	2.322	0.287	18.801	3.821	0.469	31.126
Oceania	2.658	0.274	25.750	2.090	0.215	20.319	1.528	0.156	14.976
South America	21.121	2.940	151.714	19.764	2.744	142.355	15.034	2.074	108.964
South Central Asia	1.957	0.265	14.432	1.589	0.215	11.750	1.335	0.180	9.918
South East Asia	3.039	0.418	22.103	2.284	0.313	16.638	1.759	0.240	12.896
Sub-Saharan Africa	12.250	1.708	87.837	10.202	1.420	73.300	8.075	1.117	58.402
Western Europe	7.422	1.007	54.702	7.505	1.015	55.462	11.987	1.607	89.431

*Eastern Europe is used as the referent group.

APPENDIX 1

Direct and Indirect Rodent Zoonoses and Codes

	Dx Code	Diagnosis
Direct	**613**	HANTAVIRUS
	568	HEMORRAGIC FEVER SYNDROME, ACUTE
	565	LASSA FEVER
	335	LEPTOSPIRA
	696	TULAREMIA
Indirect	**725**	BABESIOSIS
	171	LEISHMANIA, CUTANEOUS
	221	LEISHMANIA, MUCOCUTANEOUS
	172	LEISHMANIA, VISCERAL
	616	LYME DISEASE, ARTHRITIS
	617	LYME DISEASE, CHRONIC
	189	Q FEVER
	631	RICKETTSIA, AKARI
	733	RICKETTSIA, FELIS
	630	RICKETTSIA, PROWAZEKI
	732	RICKETTSIA, TICK BORNE SPOTTED FEVER
	302	RICKETTSIA (NOW ORIENTIA), TSUTSUGAMUSHI
	734	RICKETTSIA, TYPHI
	306	RICKETTSIA, OTHER
	303	RICKETTSIA, SPECIES UNKNOWN
	206	TOXOPLASMA GONDII
	212	TUNGIASIS
	564	YERSINIA PESTIS, BUBONIC

Zoonotic and Vector Borne Diseases and Codes

Dx Code	Diagnosis
106	AMEBAS, OTHER
728	ANGIOSTRONGYLIASIS
583	ANISAKIS
560	ANTHRAX, CUTANEOUS
584	ANTHRAX, PULMONARY
586	ASCARIS, EXTRAINTESTINAL
107	ASCARIS, INTESTINAL
730	BARMAH FOREST VIRUS

587	BARTONELLA, BACILLIFORMIS
588	BARTONELLA, HENSELAE
593	CAT SCRATCH DISEASE
112	BLASTOCYSTIS
114	BRUCELLOSIS, ACUTE
592	BRUCELLOSIS, CHRONIC
115	CAMPYLOBACTER
675	CHAGAS DISEASE, ACUTE
117	CHAGAS DISEASE, CHRONIC
757	CHIKUNGUNYA VIRUS INFECTION
577	CHILOMASTIX MESNILI
118	CLONORCHIS
122	CRYPTOSPORIDIUM
123	CUTANEOUS LARVA MIGRANS
600	CYSTICERCOSIS (MUSCULAR, CUTANEOUS)
127	DENGUE (DHF, DSS)
128	DENGUE, UNCOMPLICATED
602	DIARRHEA, ACUTE PARASITIC
134	DIENTAMEBIASIS (D. FRAGILIS)
103	E. HISTOLYTICA, AMEBOMA
270	E. HISTOLYTICA, DIARRHEA
104	E. HISTOLYTICA, DYSENTERY
105	E. HISTOLYTICA, EXTRAINTESTINAL
762	E. HISTOLYTICA/DISPAR, ACCOMPANYING DIARRHEA
102	E. HISTOLYTICA/DISPAR, ASYMPTOMATIC
567	EBOLA VIRUS
606	ECHINOCOCCOSIS, HEPATIC
605	ECHINOCOCCOSIS, HEPATIC and NON-HEPATIC
607	ECHINOCOCCOSIS, NON-HEPATIC
137	EHRLICHIA
609	ENCEPHALITIS, JAPANESE
731	ENCEPHALITIS, MURRAY VALLEY
610	ENCEPHALITIS, TICK BORNE
139	ENTEROBIAISIS (PINWORM)
174	ERYTHEMA CHRONICUM MIGRANS
324	FASCIOLA
153	FILARIA, BANCROFTI
154	FILARIA, LOA LOA
152	FILARIA, ONCHOCERCIASIS
155	FILARIA, OTHER
325	FILARIA, SPECIES UNKNOWN

157	GIARDIA
534	GNATHOSTOMA
714	HELMINTH, INTESTINAL (NOT DIARRHEA)
559	HETEROPHYES HETEROPHYES INFECTION
614	HISTOPLASMOSIS
166	HOOKWORM (A. DUODENALE, N. AMERICANA)
736	INFLUENZA, AVIAN
168	ISOSPORA
618	MALARIA, DRUG RESISTANT, CHLOROQUINE RES- P.f.
619	MALARIA, DRUG RESISTANT, CHLOROQUINE RES- P.v.
620	MALARIA, DRUG RESISTANT, PRIMAQUINE RES- P.v.
563	MALARIA, DRUG RESISTANT, QUININE RES- P.f.
697	MALARIA, MALARONE RESISTANT
735	MALARIA, MEFLOQUINE RESISTANT
175	MALARIA, P. FALCIPARUM
769	MALARIA, P. KNOWLESI
176	MALARIA, P. MALARIAE
177	MALARIA, P. OVALE
178	MALARIA, P. VIVAX
336	MALARIA, SEVERE AND COMPLICATED, CEREBRAL
628	MALARIA, SEVERE AND COMPLICATED, NONCEREBRAL
179	MALARIA, SPECIES UNKNOWN
182	MYIASIS
125	NEUROCYSTICERCOSIS
715	PROTOZOA, INTESTINAL (NOT DIARRHEA), UNSPECIFIED
349	RABIES
190	RABIES, POST EXPOSURE PROPHYLAXIS
116	RASH, CERCARIAL
195	RASH, SWIMMERS ITCH
643	RIFT VALLEY FEVER
575	ROSS RIVER VIRUS
192	SALMONELLA, OTHER
632	SALMONELLA, PARATYPHI
193	SALMONELLA, TYPHI
351	SCHISTOSOMIASIS, HUMAN SPECIES UNKNOWN

196	SCHISTOSOMIASIS, S. HEMATOBIUM
197	SCHISTOSOMIASIS, S. JAPONICUM
198	SCHISTOSOMIASIS, S. MANSONI
729	SEVERE ACUTE RESPIRATORY SYNDROME (SARS)
638	SPOROTRICHOSIS
636	STRONGYLOIDES, HYPERINFECTION SYNDROME
203	STRONGYLOIDES, SIMPLE INTESTINAL
672	TAPEWORM, D. LATUM
204	TAPEWORM, H. NANA
655	TAPEWORM, T. SAGINATA
304	TAPEWORM, T. SOLIUM
300	TAPEWORM, UNSPECIFIED
207	TRICHINELLA
208	TRICHURIS TRICHIURA (WHIPWORM)
671	TRYPANOSOMIASIS, AFRICAN (T. GAMBIENSE)
363	TRYPANOSOMIASIS, AFRICAN (T. RHODESIENSE)
624	VIBRIO, NONCHOLERA
205	VISCERAL LARVA MIGRANS
713	WEST NILE VIRUS
566	YELLOW FEVER
220	YERSINIA SPECIES, NON-PESTIS
582	YERSINIA PESTIS, PNEUMONIC

Infectious Diseases and Codes

Dx Code	**Diagnosis**
101	AIDS
106	AMEBAS, OTHER
728	ANGIOSTRONGYLIASIS
583	ANISAKIS
560	ANTHRAX, CUTANEOUS
584	ANTHRAX, PULMONARY
585	ANTIBIOTIC RESISTANT BACTERIA
586	ASCARIS, EXTRAINTESTINAL
107	ASCARIS, INTESTINAL
108	BACTEREMIA
730	BARMAH FOREST VIRUS
587	BARTONELLA, BACILLIFORMIS
588	BARTONELLA, HENSELAE
593	CAT SCRATCH DISEASE

112	BLASTOCYSTIS
590	BLASTOMYCOSIS
591	BOTULISM
114	BRUCELLOSIS, ACUTE
592	BRUCELLOSIS, CHRONIC
275	C. DIFFICILE ASSOCIATED DISEASE
115	CAMPYLOBACTER
235	CELLULITIS
388	CERVICITIS
675	CHAGAS DISEASE, ACUTE
117	CHAGAS DISEASE, CHRONIC
595	CHANCROID
757	CHIKUNGUNYA VIRUS INFECTION
577	CHILOMASTIX MESNILI
359	CHLAMYDIA TRACHOMATIS (OCULAR)
596	CHLAMYDIA, LYMPHOGRANULOMA VENEREUM
535	CHOLERA
118	CLONORCHIS
597	COCCIDIODOMYCOSIS
391	CONJUNCTIVITIS
598	CRYPTOCOCCOSIS
122	CRYPTOSPORIDIUM
123	CUTANEOUS LARVA MIGRANS
600	CYSTICERCOSIS (MUSCULAR, CUTANEOUS)
127	DENGUE (DHF, DSS)
128	DENGUE, UNCOMPLICATED
314	DIARRHEA, ACUTE BACTERIAL
602	DIARRHEA, ACUTE PARASITIC
603	DIARRHEA, ACUTE VIRAL
134	DIENTAMEBIASIS (D. FRAGILIS)
604	DIPHTHERIA
374	DYSENTERY, ACUTE UNSPECIFIED
103	E. HISTOLYTICA, AMEBOMA
270	E. HISTOLYTICA, DIARRHEA
104	E. HISTOLYTICA, DYSENTERY
105	E. HISTOLYTICA, EXTRAINTESTINAL
762	E. HISTOLYTICA/DISPAR, ACCOMPANYING DIARRHEA
102	E. HISTOLYTICA/DISPAR, ASYMPTOMATIC
567	EBOLA VIRUS
606	ECHINOCOCCOSIS, HEPATIC

605	ECHINOCOCCOSIS, HEPATIC and NON-HEPATIC
607	ECHINOCOCCOSIS, NON-HEPATIC
137	EHRLICHIA
138	ENCEPHALITIS, ACUTE
608	ENCEPHALITIS, CHRONIC
609	ENCEPHALITIS, JAPANESE
731	ENCEPHALITIS, MURRAY VALLEY
610	ENCEPHALITIS, TICK BORNE
139	ENTEROBIAISIS (PINWORM)
768	ENTEROVIRUS 71 (EV-71)
408	EPIDIDYMITIS
242	EPSTEIN-BARR VIRUS
142	ERYSIPELAS
174	ERYTHEMA CHRONICUM MIGRANS
324	FASCIOLA
153	FILARIA, BANCROFTI
154	FILARIA, LOA LOA
152	FILARIA, ONCHOCERCIASIS
155	FILARIA, OTHER
325	FILARIA, SPECIES UNKNOWN
181	FUNGAL INFECTION
746	FUNGAL INFECTION, SUBCUTANEOUS
326	GASTRITIS, H.PYLORI (+)
157	GIARDIA
534	GNATHOSTOMA
612	GONORRHEA
740	HAND-FOOT-AND-MOUTH SYNDROME
714	HELMINTH, INTESTINAL (NOT DIARRHEA)
159	HEPATITIS A, ACUTE
677	HEPATITIS B CARRIER, ASYMPTOMATIC
160	HEPATITIS B, ACUTE
328	HEPATITIS B, CHRONIC
329	HEPATITIS C, ACUTE
161	HEPATITIS C, CHRONIC
330	HEPATITIS DELTA
162	HEPATITIS E
163	HEPATITIS, ACUTE UNSPECIFIED
538	HEPATITIS, CHRONIC UNSPECIFIED
442	HERPES SIMPLEX E
290	HERPES ZOSTER, SHINGLES
559	HETEROPHYES HETEROPHYES INFECTION

614	HISTOPLASMOSIS
164	HIV - ASYMPTOMATIC
331	HIV, ACUTE INFECTION (FEBRILE)
763	HIV, ASYMPTOMATIC, NEWLY DIAGNOSED
166	HOOKWORM (A. DUODENALE, N. AMERICANA)
753	HTLV-1/HTLV-2
332	INFLUENZA A
333	INFLUENZA B
736	INFLUENZA, AVIAN
168	ISOSPORA
615	LEGIONNAIRES' DISEASE
173	LEPROSY
618	MALARIA, DRUG RESISTANT, CHLOROQUINE RES- P.f.
619	MALARIA, DRUG RESISTANT, CHLOROQUINE RES- P.v.
620	MALARIA, DRUG RESISTANT, PRIMAQUINE RES- P.v.
563	MALARIA, DRUG RESISTANT, QUININE RES- P.f.
697	MALARIA, MALARONE RESISTANT
735	MALARIA, MEFLOQUINE RESISTANT
175	MALARIA, P. FALCIPARUM
769	MALARIA, P. KNOWLESI
176	MALARIA, P. MALARIAE
177	MALARIA, P. OVALE
178	MALARIA, P. VIVAX
336	MALARIA, SEVERE AND COMPLICATED, CEREBRAL
628	MALARIA, SEVERE AND COMPLICATED, NONCEREBRAL
179	MALARIA, SPECIES UNKNOWN
224	MASTITIS
507	MEASLES
726	MELIOIDOSIS
460	MENINGITIS, BACTERIAL OTHER
653	MENINGITIS, EOSINOPHILIC
652	MENINGITIS, FREE LIVING AMOEBA
654	MENINGITIS, FUNGAL
651	MENINGITIS, H.
461	MENINGITIS, MENINGOCOCCAL
650	MENINGITIS, PNEUMOCOCCAL
462	MENINGITIS, VIRAL

459	MENINGOCOCCAL SEPSIS (NON-MENINGEAL)
467	MOLLUSCUM CONTAGIOSUM
180	MONONUCLEOSIS, UNSPECIFIED
468	MUMPS
766	MYCOBACTERIUM TUBERCULOSIS, (MDR OR XDR)
223	MYCOBACTERIUM TUBERCULOSIS, ATYPICAL (CUTANEOUS)
626	MYCOBACTERIUM TUBERCULOSIS, CNS TUBERCULOMA
625	MYCOBACTERIUM TUBERCULOSIS, DISSEMINATED/MILIARY
211	MYCOBACTERIUM TUBERCULOSIS, EXTRAPULMONARY
676	MYCOBACTERIUM TUBERCULOSIS, MENINGITIS
209	MYCOBACTERIUM TUBERCULOSIS, PULMONARY
230	MYCOBACTERIUM, ATYPICAL, IN THE LUNG
182	MYIASIS
125	NEUROCYSTICERCOSIS
637	PARACOCCIDIOIDOMYCOSIS
486	PARONYCHIA
569	PARVOVIRUS
342	PEPTIC ULCER DISEASE, H.PYLORI (+)
642	PERTUSSIS
492	PHARYNGITIS, STREPTOCOCCAL
496	PNEUMONIA / ARDS
187	PNEUMONIA, ATYPICAL (DIFFUSE)
188	PNEUMONIA, BACTERIAL (LOBAR)
639	PNEUMONIA, FUNGAL
715	PROTOZOA, INTESTINAL (NOT DIARRHEA), UNSPECIFIED
254	PYOMYOSITIS
349	RABIES
190	RABIES, POST EXPOSURE PROPHYLAXIS
116	RASH, CERCARIAL
415	RASH, FUNGAL
195	RASH, SWIMMERS ITCH
191	RESPIRATORY TRACT INF (UPPER)
643	RIFT VALLEY FEVER
549	ROSEOLA
575	ROSS RIVER VIRUS

550	RUBELLA
192	SALMONELLA, OTHER
632	SALMONELLA, PARATYPHI
193	SALMONELLA, TYPHI
351	SCHISTOSOMIASIS, HUMAN SPECIES UNKNOWN
196	SCHISTOSOMIASIS, S. HEMATOBIUM
197	SCHISTOSOMIASIS, S. JAPONICUM
198	SCHISTOSOMIASIS, S. MANSONI
699	SEPSIS
729	SEVERE ACUTE RESPIRATORY SYNDROME (SARS)
513	SEXUALLY TRANSMITTED DISEASE
635	SHIGELLA, S. BOYDII
633	SHIGELLA, S. DYSENTERIAE
634	SHIGELLA, S. FLEXNERI
200	SHIGELLA, S. SONNEI
695	SMALLPOX (VARIOLA MAJOR)
748	SOFT TISSUE INFECTIONS, MRSA
747	SOFT TISSUE INFECTIONS, STAPHYLOCOCCAL
638	SPOROTRICHOSIS
742	STREPTOCOCCAL TOXIN DISEASE, SCARLET FEVER
636	STRONGYLOIDES, HYPERINFECTION SYNDROME
203	STRONGYLOIDES, SIMPLE INTESTINAL
356	SYPHILIS
672	TAPEWORM, D. LATUM
204	TAPEWORM, H. NANA
655	TAPEWORM, T. SAGINATA
304	TAPEWORM, T. SOLIUM
300	TAPEWORM, UNSPECIFIED
358	TONSILLITIS
207	TRICHINELLA
360	TRICHOMONAS INTESTINALIS
361	TRICHOMONAS VAGINALIS
208	TRICHURIS TRICHIURA (WHIPWORM)
671	TRYPANOSOMIASIS, AFRICAN (T. GAMBIENSE)
363	TRYPANOSOMIASIS, AFRICAN (T. RHODESIENSE)
210	TUBERCULOSIS, POSITIVE PPD OR POSITIVE QUANTIFERON OR POSITIVE T-SPOT (NOT

	ACTIVE DISEASE)
756	TYPHOID FEVER, UNSPECIFIED
648	URETHRITIS, GONOCOCCAL
215	URINARY TRACT INF, ACUTE
526	VARICELLA (CHICKEN POX)
624	VIBRIO, NONCHOLERA
219	VIRAL SYNDROME (NO RASH)
623	VIRAL SYNDROME WITH RASH
205	VISCERAL LARVA MIGRANS
647	WARTS, GENITAL
767	WARTS, NON-GENITAL
713	WEST NILE VIRUS
719	YAWS
566	YELLOW FEVER
220	YERSINIA SPECIES, NON-PESTIS
582	YERSINIA PESTIS, PNEUMONIC