Reverse Zoonotic Disease Transmission (Zooanthroponosis): A Systematic Review of Seldom-Documented Human Biological Threats to Animals

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Abstract

Background: Research regarding zoonotic diseases often focuses on infectious diseases animals have given to humans. However, an increasing number of reports indicate that humans are transmitting pathogens to animals. Recent examples include methicillin-resistant Staphylococcus aureus, influenza A virus, Cryptosporidium parvum, and Ascaris lumbricoides. The aim of this review was to provide an overview of published literature regarding reverse zoonoses and highlight the need for future work in this area.

Methods: An initial broad literature review yielded 4763 titles, of which 4704 were excluded as not meeting inclusion criteria. After careful screening, 56 articles (from 56 countries over three decades) with documented human-to-animal disease transmission were included in this report.

Findings: In these publications, 21 (38%) pathogens studied were bacterial, 16 (29%) were viral, 12 (21%) were parasitic, and 7 (13%) were fungal, other, or involved multiple pathogens. Effected animals included wildlife (n = 28, 50%), livestock (n = 24, 43%), companion animals (n = 13, 23%), and various other animals or animals not explicitly mentioned (n = 2, 4%). Published reports of reverse zoonoses transmission occurred in every continent except Antarctica therefore indicating a worldwide disease threat.

Interpretation: As we see a global increase in industrial animal production, the rapid movement of humans and animals, and the habitats of humans and wild animals intertwining with great complexity, the future promises more opportunities for humans to cause reverse zoonoses. Scientific research must be conducted in this area to provide a richer understanding of emerging and reemerging disease threats. As a result, multidisciplinary approaches such as One Health will be needed to mitigate these problems.

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Introduction

With today’s rapid transport systems, modern public health problems are growing increasingly complex. A pathogen that emerges today in one country can easily be transported unnoticed in people, animals, plants, or food products to distant parts of the world in less than 24 hours [1]. This high level of mobility makes tracking and designing interventions against emerging pathogens exceedingly difficult, requiring close international and interdisciplinary collaborations. Fundamental to these efforts is an understanding of the ecology of emerging diseases. Published works often cite the large proportion of human emerging pathogens that originate in animals [2,3,4,5]. However, scientific reports seldom mention human contributions to the variety of emerging diseases that impact animals. The focus of this review is to examine and summarize the scientific literature regarding such zoonoses transmission. A comprehensive table of the results is included in this document.

Methods

For the purpose of this review several terms require definitions. Despite the fact that the term “zoonosis” usually refers to a disease that is transmitted from animals to humans (also called “anthropozoonosis”) [6], in this paper, “zoonosis” was defined as any disease that is transmitted from animals to humans, or vice versa [6]. There are two related terms (“zooanthroponosis” and “reverse zoonosis”) that refer to any pathogen normally reservoired in humans that can be transmitted to other vertebrates [6]. Acknowledging that the terms “reverse zoonosis” or “zooanthroponosis” are seldom used, and that the term “zoonosis” can have several meanings, search methods were designed to
include all of these terms in an effort to capture the widest possible subset of publications with documented human-to-animal transmission.

**Literature search**

In June 2012, we searched PubMed in addition to several databases within Web of Knowledge and ProQuest to find articles documenting reverse zoonoses transmission. Search terms included: reverse zoonosis, bidirectional zoonosis, anthroponosis, zooanthroponosis, and human-to-animal disease transmission. Articles were limited to clinical and observational type studies and were restricted to English only. Review articles were not included as they did not demonstrate a specific account of transmission. Letters to editors or similar correspondence were also excluded. Only publications with documented human-to-animal transmission were included. No time period was stipulated.

Four search strings were used for the PubMed database: (bidirectional OR reverse) AND (zoonosis OR “disease transmission”), OR anthroponosis OR “human-to-animal”, OR (bidirectional OR reverse OR “human-to-animal”) AND (zoonosis OR “disease transmission”), OR anthroponosis, OR “reverse zoonoses” OR “bidirectional zoonoses” OR “reverse zoonosis” OR “bidirectional zoonosis” OR “reverse zoonotic” OR “bidirectional zoonotic” OR anthroponosis OR “human-to-animal” AND disease* AND transmission*, and (bidirectional OR reverse OR “human-to-animal”) AND (zoonoses[majr] OR “Disease Transmission, Infectious”[majr] OR zoonosis[tiab] OR zoonoses[tiab] OR zoonotic[tiab]) OR Anthropozoonosis*[tiab] OR Zooanthroponosis*[tiab]. In the ProQuest and Web of Knowledge databases, we only used one string: (bidirectional OR reverse) AND (zoonosis OR zoonoses OR zoonotic) OR anthroponosis OR Zooanthroponosis OR anthroponosis OR “human-to-animal” OR “human to animal”). The lack of additional search strings for the latter databases was due to less comprehensive search capabilities. Duplicate articles were removed.

**Literature analyses**

Titles and abstracts were reviewed and articles were retained when there was evidence of disease transmission from humans to animals. During full text review, some citations proved straightforward in distinguishing transmission from humans to animals (e.g., via direct contact), while others were selected based on strong author suggestion or research implications toward reverse zoonotic transmission. In an effort to highlight trends in an otherwise diverse set of articles, citations were grouped by pathogen type and year of publication. To further clarify relationships, we also pictorially displayed the study locations and animal types discussed in the various articles.

**Results**

This comprehensive literature review yielded 4763 titles, 2507 of which were excluded as duplicates (Figure 1). During the review of abstracts, 2091 studies were excluded due to a lack of evidence of human-to-animal disease transmission. After consideration of the 165 eligible for full text review, 109 studies were excluded.
Table 1. Descriptors of reports included in review with documented human-to-animal transmission.

| Publications       | Study Location       | Specimen Source     | Pathogen Name                                      | Animal(s) Infected |
|--------------------|----------------------|---------------------|----------------------------------------------------|--------------------|
| **Bacteria**       |                      |                     |                                                    |                    |
| Cosivi et al (1995) [7] | Morocco             | Assorted            | *Mycobacterium tuberculosis, Mycobacterium bovis*1 | Wildlife           |
| Seguin et al (1999) [8] | United States      | Veterinary hospital | *Methicillin-resistant Staphylococcus aureus* (MRSA)1,2 | Livestock          |
| Donnelly et al (2000) [9] | United States    | 4H project livestock | *Streptococcus pneumonia*1                        | Livestock          |
| Nizeyi et al (2001) [10] | Uganda             | National park       | *Campylobacter spp., Salmonella spp., Shigella sonnei, Shigella boydii, Shigella flexneri*1,3 | Wildlife           |
| Michel et al (2003) [11] | South Africa       | Zoo                 | *M. tuberculosis*1,3                               | Wildlife           |
| Hackendahl et al (2004) [12]; also United States see Erwin et al (2004) [13] | Veterinary hospital |                     | *M. tuberculosis*1,4                               | Companion          |
| Prasad et al (2005) [14] | India              | Veterinary hospital | *M. tuberculosis*5                                 | Livestock          |
| Weese et al (2006) [15] | United States      | Household; Veterinary hospital | MRSA1                                       | Companion          |
| Morris et al (2006) [16] | United States      | Household; Veterinary hospital | MRSA1                                       | Companion          |
| Kwon et al (2006) [17] | Korea               | Slaughterhouse      | MRSA1,3                                           | Companion; Livestock |
| Rwego et al (2008) [18] | Uganda             | National park       | Escherichia coli1,3                                | Livestock; Wildlife |
| Hsieh et al (2008) [19] | Taiwan             | Livestock farm      | Oxacillin-resistant *Staphylococcus aureus* (ORSA) | Livestock          |
| Berg et al (2009) [20] | Ethiopia            | Slaughterhouse      | *M. tuberculosis*3                                 | Livestock          |
| Heller et al (2010) [21] | United Kingdom     | Household; Veterinary hospital | MRSA1,2                                       | Companion          |
| Kottler et al (2010) [22] | United States      | Household; Veterinary hospital | MRSA1                                       | Companion          |
| Ewers et al (2010) [23] | Germany, Italy, Netherlands, France, Spain, Denmark, Austria & Luxembourg | Veterinary hospital | Escherichia coli                                | Companion; Livestock |
| Every et al (2011) [24] | Australia           | University zoology department | *Helicobacter pylori*1                             | Wildlife           |
| Lin et al (2011) [25] | United States       | Veterinary hospital | MRSA1                                              | Companion; Livestock |
| Rubin et al (2011) [26] | Canada              | Veterinary hospital; Human hospital | MRSA1                                       | Companion          |
| Price et al (2012) [27] | Austria, Belgium, Canada, Switzerland, China, Germany, Denmark, Spain, Finland, France, French Guiana, Hungary, Italy, the Netherlands, Peru, Poland, Portugal, Slovenia, and United States | Animal meat for sale | MRSA1                                              | Livestock          |
| **Virus**          |                      |                     |                                                    |                    |
| Meng et al (1998) [28] | United States       | Veterinary laboratory; Human sample | Hepatitis E1                                      | Wildlife           |
| Willy et al (1999) [29] | United States       | Veterinary laboratory | Measles1,4                                         | Wildlife           |
| Kaur et al (2008) [30] | Tanzania            | National park       | Human metapneumovirus (hMPV)1,4                   | Wildlife           |
| Feagins et al (2008) [31] | United States       | Commercially sold laboratory animals |                                               |                    |
| Song et al (2010) [32] | South Korea         | Livestock farm      | Influenza A (2009 pandemic H1N1)1                  | Livestock          |
| Swenson et al (2010) [33] | United States       | Household; Veterinary hospital | Influenza A (2009 pandemic H1N1)1,4              | Companion          |
| Tischer et al (2010) [34] | Various; Unspecified |                      | Unknown (previous reports cited) Human herpesvirus 1, human herpesvirus 41,3,4 | Companion; Wildlife |
| Abe et al (2010) [35] | Japan                | Wildlife            | Rotavirus1,3                                       | Wildlife           |
| Berhane et al (2010) [36] | Canada, Chile       | Livestock farm      | Influenza A (2009 pandemic H1N1)1,4,5            | Livestock          |
| Poon et al (2010) [37] | Hong Kong            | Slaughterhouse      | Influenza A (2009 pandemic H1N1)                   | Livestock          |
| Furse et al (2011) [38] | Canada              | Veterinary laboratory | Influenza A (2009 pandemic H1N1)                  | Livestock          |
| Holyoake et al (2011) [39] | Australia           | Livestock farm      | Influenza A (2009 pandemic H1N1)4                 | Livestock          |
Table 1. Cont.

| Publications                  | Study Location                                                                 | Specimen Source                      | Pathogen Name                                      | Animal(s) Infected                      |
|-------------------------------|-------------------------------------------------------------------------------|--------------------------------------|----------------------------------------------------|----------------------------------------|
| Scotch et al (2011) [40]       | Mexico, United States, Canada, Australia, United Kingdom, France, Iceland, Argentina, Chile, Singapore, Norway, China, Italy, Thailand, South Korea, Indonesia, Germany, Japan, Russia, Finland, and Iceland | Unknown (previous reports cited)      | Influenza A (2009 pandemic H1N1)                   | Companion; Livestock; Wildlife          |
| Trevennec et al (2011) [41]    | Vietnam                                                                       | Livestock farm; Slaughterhouse       | Influenza A (2009 pandemic H1N1)                   | Livestock                              |
| Wevers et al (2011) [42]       | Cameroon, Democratic Republic of the Wildlife; Zoo Congo, Gabon, Côte d'Ivoire, Republic of Congo, Rwanda, Tanzania, Uganda, Germany (initial samples in Asia and South America) | Unknown                              | Human adenovirus A-F                          | Wildlife                               |
| Crossley et al (2012) [43]     | United States                                                                  | Private zoo                          | Influenza A (2009 pandemic H1N1)                   | Wildlife                               |
| Parasite                      |                                                                                |                                      |                                                    |                                        |
| Sleeman et al (2000) [44]      | Rwanda                                                                         | National park                        | Chlamastix mesnili, Endolimax nana, Strongyloides fuelleborni, Trichuris trichiura | Wildlife                               |
| Graczyk et al (2001) [45]      | Uganda                                                                         | National park                        | Cryptosporidium parvum                            | Wildlife                               |
| Graczyk et al (2002) [46]      | Uganda                                                                         | National park                        | Encephalitozoon intestinalis                        | Wildlife                               |
| Graczyk et al (2002) [47]      | Uganda                                                                         | National park                        | Giardia duodenalis                                | Wildlife                               |
| Guk et al (2004) [48]          | Korea                                                                          | Laboratory                           | C. parvum                                        | Livestock; Wildlife                    |
| Noël et al (2005) [49]         | Singapore, Pakistan, Japan, Thailand, United States, France, Czech Republic    | N/A                                  | Blastocystis spp                                  | Livestock; Wildlife                    |
| Coklin et al (2007) [50]       | Canada                                                                         | Livestock farm                       | G. duodenalis, C. parvum                          | Livestock                              |
| Adejinmi et al (2008) [51]     | Nigeria                                                                        | Zoo                                  | Ascaris lumbricoides, T. trichiura                | Wildlife                               |
| Teichroeb et al (2009) [52]    | Ghana                                                                          | Wildlife                             | Isospora spp., Giardia duodenalis                | Wildlife                               |
| Ash et al (2010) [53]          | Zambia; Namibia; Australia                                                    | Wildlife; Zoo                        | G. duodenalis                                      | Wildlife                               |
| Johnston et al (2010) [54]     | Uganda                                                                         | National park                        | G. duodenalis                                      | Livestock; Wildlife                    |
| Dixon et al (2011) [55]        | Canada                                                                         | Livestock farm                       | G. duodenalis, C. parvum                          | Livestock                              |
| Fungus                        |                                                                                |                                      |                                                    |                                        |
| Jacobs et al (1988) [56]       | Unspecified                                                                    | Assorted                             | Microsporum spp., Trichophyton spp.               | Assorted                               |
| Pal et al (1997) [57]          | India                                                                          | Household                            | Trichophyton rubrum                               | Wildlife                               |
| Wrobel (2008) [58]             | United States                                                                  | Veterinary hospital                  | Candida albicans                                   | Companion; Livestock; Wildlife         |
| Sharma et al (2009) [59]       | India                                                                          | Household; Veterinary hospital       | Microsporum gypseum                                | Wildlife                               |
| Other                         |                                                                                |                                      |                                                    |                                        |
| Epstein et al (2009) [60]      | Assorted                                                                        | Wildlife; Livestock farm; Zoo; Laboratory | Herpes simplex 1, influenza A, parasite spp, Measles, MRSA, M. tuberculosis | Assorted                               |
| Guyader et al (2000) [61]      | France                                                                          | Shellfish-growing waters             | Astrovirus, enterovirus, hepatitis A, Norwalk-like (norovirus), rotavirus | Wildlife                               |
| Muehlenbein et al (2010) [62]  | Malaysia                                                                        | Wildlife                             | Assorted illnesses                                 | Wildlife                               |

Other assorted pathogen types:
- virus; parasite/bacteria, virus/bacteria, assorted.
- Modes of transmission as indicated by authors:
direct contact, fomite, oral, aerosol, inoculation, other.

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based on full texts being written in a language other than English, absence of human-to-animal disease transmission, or full texts being unavailable. After all exclusions, 56 articles were considered for this review (Table 1).

Included reports were based in 56 different countries. Although the reports spanned three decades, there seems to be an increasing number of studies published in recent years (Figure 2). Twenty eight percent of the studies were conducted in the United States

Figure 2. Timeline and frequency of reverse zoonoses publications included in this review shown by pathogen type.
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Figure 3. Proportion of reverse zoonoses scientific reports included in review as illustrated by study location. Note: Many reports identified several countries therefore each country in this figure does not necessarily represent a single corresponding publication.
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Within the study results, 21 publications discussed human-to-animal transmission of bacterial pathogens (38%); 16 studies discussed viral pathogens (29%); 12 studies discussed human parasites (21%); and seven studies discussed transmission of fungi, other pathogens, or diseases of multiple etiologies (13%). Bacterial pathogen reports were centered in North America and Europe. Viral studies were well-distributed globally. Parasitic disease reports were conducted chiefly in Africa. Fungal studies were conducted almost exclusively in India (Figure 4).

As early as 1988, zoonoses research focusing on fungal pathogens was being conducted. Initial studies implied human transmission of *Microsporum* (n = 2) and *Trichophyton* (n = 2) to various animal species, with a later article centered on *Candida albicans* (n = 1) (Figure 2). These publications were set in India (n = 2) and the United States (n = 1).

Since 1988, research with implications of reverse zoonoses has been largely focused on infections of bacterial origin, beginning in 1995. The majority of articles in this review focused on methicillin-resistant *Staphylococcus aureus* (MRSA) (n = 9) and *Mycobacterium tuberculosis* (n = 5). Reports regarding these bacteria were primarily conducted in the United States (n = 8) among livestock (n = 10) or companion animals (n = 9).

Viruses were the second most common pathogen associated with human-to-animal transmission. Reverse zoonoses reports regarding viral pathogens began in 1998 and have since been focused primarily on influenza with great interest surrounding the 2009 H1N1 pandemic (n = 9). These studies were conducted largely in the United States (n = 6) in livestock (n = 8) and wildlife (n = 8).
Studies suggestive of transmission of human parasites to animals were first published in 2000. The most commonly reported parasitic agents to be transmitted from humans to animals were *Giardia duodenalis* (n = 6) and *Cryptosporidium parvum* (n = 4). Parasitic research has been carried out most frequently in Uganda (n = 4) and Canada (n = 2). The authors investigated human parasitic infections chiefly in wildlife (n = 10) and livestock (n = 5).

Human-to-animal transmission is plausible for a large number of diseases because the pathogens concerned are known to infect multiple species [3]. For instance, 77.3% of the pathogens infecting livestock are considered “multiple species pathogens [3].” However, this review only found 24 reports which considered reverse zoonoses disease transmission as a potential threat to livestock, underscoring a need for further research in this area [3]. Similarly, in companion animals this review found even fewer studies (n = 13) that implied reverse zoonoses as a possible cause of infection, despite the fact that 90% of known pathogens for domestic carnivores are recognized as “multiple species pathogens [3].” The majority of publications in this reverse zoonoses review involved studies documenting human-to-wildlife transmission (n = 28). Unfortunately, they too were severely lacking in comparison to the research need. Each type of animal- livestock, companion, or wildlife, represents a unique set of risk factors for reverse zoonoses through their specific routes of human contact.

**Discussion**

Human and animal relationships are likely to continue to intensify worldwide over the next several decades due in part to animal husbandry practices, the growth of the companion animal market, climate change and ecosystem disruption, anthropogenic development of habitats, and global travel and commerce [2]. As the human-animal connection escalates, so does the threat for pathogen spread [1,63]. This review notes a number of factors that influence the risk of disease transmission from humans to animals.

For instance, human population growth and expansion encourages different species to interact in ways and at rates previously not encountered, and to do so in novel geographical areas [4]. The term “pathogen pollution” refers to the process of bringing a foreign disease into a new locality due to human involvement [64]. In the case of the endangered African painted dog, wild dogs have been infected with human strains of *Giardia duodenalis*, leading researchers to believe that pathogen pollution occurred through open defecation in and around national parks by tourists and local residents [53]. Anthropogenic changes in the ecosystem increase the amount of shared habitats between humans and animals thus exposing both to new pathogens. Researchers discovered the human strain of pandemic *Escherichia coli* strain 025:H4-ST131 CTX-M-15 in many different species of animals indicating inter-species transmission from humans to pets and livestock [23]. This particular human strain found to be infecting animals was documented across Europe.

In addition to habitat change, growth, and/or destruction, there is the ever-increasing global movement of products and travelers that extends to both humans and animals. During the pandemic of 2009 H1N1 influenza, the novel virus was able to travel across the globe and from humans to swine in less than two months [32]. One driving force behind the movement of animals and animal products is the worldwide shipment of meat. This phenomenon is a relatively new event as developing countries adjust their diets to include more meat- and dairy-based products [4]. While food and animal safety guidelines attempt to keep up with the speed of global trade, international efforts appear to be outpaced by product demand. For example, it has been estimated that five tons of illegal bushmeat pass through Paris’ main Roissy-Charles de Gaulle airport each week in personal luggage [65]. However, overt
retail systems of animal and animal products can also contribute to the danger of zoonoses and reverse zoonoses transmission. Many animals are sold in markets which allow humans and a myriad of animal species to interact in conditions that are known to trigger emerging diseases [66]. Specifically, this is true for live animal markets and warehouses for exotic pets [4].

The pet industry is an enormous global business that now expands from domestic to exotic animals. A 2011–2012 national pet owners survey found that in the United States alone, 72.9 million homes or 62% of the population have a pet [67]. Of these pets, the majority of animals are dogs (78.2 million) or cats (86.4 million), but a large number of pets are birds (16.2 million), reptiles (13 million), or small animals (16 million) [67]. As pet ownership seems to be increasing worldwide and more exotic pets are being introduced to private homes, the potential for disease transmission between humans and animals will continue to increase. Veterinarians must more fervently protect animals under their care from human disease threats [66]. Adapting a One Health strategy for emerging disease surveillance and reporting will benefit both humans and animals and produce a more collaborative response plan.

Veterinarians, animal health workers, and public health professionals are not the only ones who should recognize the threat of reverse zoonoses. Increased awareness must also be communicated to the general public. Worldwide, there are 1,300 zoos and aquariums that sustain more than 700 million visitors each year [69]. The potential for pathogen spread to animals can come from a visitor with an illness, contamination of a shared environment or food, and the spread of disease through relocation of animals for captivity or educational purposes. In Tanzania, a fatal outbreak of human metapneumovirus in wild chimpanzees is believed to be the result of researchers and visitors viewing the animals in a national park that was once the great apes’ territory [30]. Public education and awareness should be augmented to include the potential health threats inflicted on a susceptible animal by an unhealthy human.

This report has limitations. As demonstrated in this review paper, the trend for reporting pathogen spread of human-to-animal transmission to animal disease manifestation is often unknown in these reports and not well documented in this review. Also the report did not examine articles that did not document human-to-animal transmission. We acknowledge that many additional works that have recorded the existence of human pathogens in animals were not evaluated. However, this review was designed to summarize only the publications that document reverse zoonotic transmission.

Many common and dangerous pathogens have not, to the authors’ knowledge, been researched as reverse zoonoses threats to animals representing a significant gap in the scientific literature. Future investigations of reverse zoonoses should take into account both transmission routes and disease prevalence. Prospective research should also include a wider variety of etiological agents and animal species. Scientific literature must document the presence and transmission of human diseases in animals such that the wealth of literature on this subject will become defined and accessible across multiple disciplines. A wider knowledge and understanding of reverse zoonoses should be sought for a successful One Health response. We recommend that future research be conducted on how human disease can, and does, affect the animals around us.

Supporting Information

File S1 PLOS PRISMA 2009 checklist. (DOC)

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Author Contributions

Analyzed the data: AM AB GG. Wrote the paper: AM AB GG.

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