The global burden of bacterial and viral zoonotic infections

L. Christou
Department of Internal Medicine, Medical School, University of Ioannina, Ioannina, Greece

Abstract

Bacterial and viral zoonotic infections comprise a practically endless, ever-expanding list of pathogens that have the potential to induce human disease of varying severity, with varying means of transmission to humans (including vector-borne and foodborne agents) and of varying epidemiology. Not all theoretically zoonotic pathogens are truly zoonotic in practice, the prime example being influenza viruses; avian H5N1 influenza remains strictly zoonotic, whereas novel H1N1 influenza displays an anthropocentric cycle that led to a pandemic, despite being of zoonotic origin. The burden of disease induced by zoonotic and viral pathogens is enormous: there are more than ten bacterial zoonoses, each of which affects hundreds of thousands patients annually, often leading to chronic infections and causing significant economic losses of a medical and livestock-related nature. Viral zoonotic agents are constantly emerging or re-emerging, and are associated with outbreaks of limited or expanded geographical spread: the typical trends of viral zoonotic infections, however, is to extend their ecological horizon, sometimes in an unexpected but successful manner, as in the case of West Nile virus, and in other instances less effectively, as was the case, fortunately, in the case of avian influenza. The majority of bacterial and viral zoonotic infections attract disproportionately low scientific and public health interest. Understanding their burden may allow for improved surveillance and prevention measures.

Keywords: Bacterial zoonoses, disease burden, influenza, review, viral zoonoses, zoonoses

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Corresponding author: L. Christou, Department of Internal Medicine, Medical School, University of Ioannina, Ioannina, Greece
E-mail: lchristu@cc.uoi.gr

Introduction

Zoonotic infections are defined as infections that can be transmitted between vertebrate animals and humans, with either human or the animal as the recipient, either through direct contact, or as foodborne infections, or via intermediate vectors such as ticks and mosquitoes [1]. Infections transmitted from animals to humans are of concern regarding clinical medicine, although diseases transmitted from humans to animals may raise concern about species conservation, as in the case of measles and influenza affecting primates (chimpanzees and mountain gorillas) through human contact [2].

Zoonoses affecting humans can originate in domestic animals or in wildlife; the latter are becoming an increasingly important reservoir for human disease, as recognized in susceptible human groups, including hunters, adventurous tourists camping in forests or cave explorers.

A detailed evaluation of all human pathogens a few years ago demonstrated that the majority of infectious species affecting humans are of a zoonotic nature [3]: of the 1415 species recorded as pathogenic for humans in 2001, 868 (a staggering 61%) could be characterized as zoonotic. Furthermore, the zoonotic nature of a pathogen has been unanimously considered to be an independent factor that increases its potential for emergence or re-emergence: Emergence refers to the appearance of a newly recognized or newly evolved pathogen or the appearance of a known pathogen in a geographical area where it has never been recognized before. Re-emergence similarly refers to known pathogens whose incidence in a given geographical area (ranging from a county to the world in the case of pandemics) is significantly increasing or whose ecology is newly altered, enhancing its potential to cause human disease (e.g. by using novel hosts, jumping from wild animals to domestic ones, exhibiting a wider vector range, and so on) [4]. As the vast majority of novel species pathogenic for humans recognized since 2001 are also of a zoonotic nature, including SARS coronavirus and novel H1N1 influenza virus (pandemic influenza of swine origin), one can presume that the spectrum of human infection attributed to animals is continuing to evolve...
and remains understudied with regard to its actual burden. The world of infectious diseases is currently dominated by multidrug-resistant pathogens such as methicillin-resistant Staphylococcus aureus, Pseudomonas aeruginosa (both technically zoonotic pathogens), or Acinetobacter species and novel pan-resistant strains; research and scientific publications are largely targeted towards such pathogens. The world of humanitarian relief and global public health campaigns is dominated by the big three, AIDS, tuberculosis, and malaria. Although the first is strictly a zoonotic infection, jumping species to humans from simians, and although the latter two are, at least in a minority of cases, depending on the species implicated, also zoonotic, it is not their zoonotic nature that has moved these infections to the centre of the Millenium Development Goals, for example [5]. Overshadowed by these scientific and public health targets, millions of people worldwide are susceptible to a wide array of bacterial, viral, parasitic and fungal zoonotic infections that cause millions of new annual cases, exhibit a considerable mortality toll, are often followed by debilitating chronic sequelae, and are directly correlated with a significant burden in terms of veterinary medicine, agriculture, livestock production, and regional and national economies. Zoonoses have been disproportionately neglected until recently, remaining the ‘other diseases’ of the Millenium Development Goals. Interest in the impact of certain of these neglected diseases, most of them zoonotic, has been slowly resurfacings [6] in terms of science and research funding, but many other zoonoses remain the true neglected ‘neglected diseases’.

It is surprising that, apart from the 2001 effort by Taylor et al. [3] cited above, there are scarce efforts to actually list the existing zoonotic diseases and evaluate their global effect in terms of actual disease and its socio-economic correlations, particularly as almost all recent outbreaks, pandemic threats, and the single 21st-century pandemic, have been of zoonotic origin.

The present review focuses specifically on outlining in detail the extensive range of zoonotic pathogens affecting humans, and describing their burden in terms of morbidity and mortality, and, where available information exists, the impact of these pathogens on socio-economic parameters, and their dynamics regarding emergence or re-emergence.

**Bacterial Zoonoses**

The clinically significant bacterial zoonotic pathogens are shown in Table 1, in alphabetical order. Numerous other bacteria can be classified as zoonotic: the reader can refer to the appendix of the review by Taylor et al. [3] for a listing of other bacteria. Bacteria that cause a minimal clinical burden of human disease, in terms of cases recorded or geographical extent, have not been included. It should be noted that a zoonotic potential exists for numerous other major pathogens, including Enterococcus sp. and P. aeruginosa, and also for less frequent ones, such as Morganella morganii. However, the vertebrate animal reservoirs of these pathogens, as well as their animal-related life cycles, are of minimal significance for the burden and evolution of human disease, at least at present; this is why such pathogens are not included in Table 1.

**Viral Zoonoses**

Table 2 shows viral zoonotic infections of clinical significance to humans: this is an ever-expanding list, in terms of both pathogens included and importance, as recent years have shown, with the emergence of novel pathogens of zoonotic origin such as SARS coronavirus and novel H1N1 influenza virus. However, the significance of the diseases caused by both of these viruses was related to their capacity for person-to-person transmission, and not their zoonotic nature, in contrast to, for example, the transmission of avian HSN1 influenza virus, for which animal contact is necessary. Neither of these new diseases would have emerged from the context of zoonotic infection and species jumping from animals to humans. In a historical context, the same could be said about human immune-deficiency virus. Person-to-person transmission is essential for dengue outbreaks and sustaining dengue virus in nature, with animals playing a minor role in this cycle; thus, dengue is not considered to be an essential zoonosis. In order for Table 2 to be more concise, viral pathogens that induce a minimal burden of human disease (in terms of cases recorded or geographical extent), e.g. eastern/western equine and St Louis encephalitis (roughly ten annual cases in the USA each), are not included. The same is true for viral pathogens that have been documented only occasionally in the past as pathogenic for humans.

As shown in Tables 1 and 2, a wide array of pathogens are emerging or re-emerging, and more agents are being introduced into non-endemic areas through the expansion of international travel, in terms of both human travel and global trade. As is also easily seen in Tables 1 and 2, millions of annual cases of human disease are directly attributable to bacterial and viral agents with direct zoonotic correlations. The need for an interdisciplinary approach that extends beyond medical and veterinary specialists cannot be stressed strongly enough. Understanding the enormous economic burden of these diseases might assist international and regional decision-makers in fully evaluating the huge effect of bacterial and viral zoonoses. The implementation of surveillance and prevention measures for these zoonotic infections might
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### TABLE 1. Clinically significant bacterial zoonoses

| Pathogen | Comments |
|----------|----------|
| Anaplasma phagocytophilum | Human granulocytic anaplasmosis has been increasing and expanding its incidence; recently recognized in Canada; an outbreak is reported from China [7]. Exceeding 1000 cases annually in the USA, as of 2008 [8]. |
| Bacillus anthracis | The, fortunately, only case of emergence caused by deliberate release |
| Bartonella sp. | There are 22 000 new annual cases of cat scratch disease reported annually in the USA [9]; Bartonellosis may be caused by Bartonella henselae, Bartonella quintana, and Bartonella cohnii. |
| Borrelia sp. | Borrelia burgdorferi, which is a zoonotic species, has been recognized in Europe—1300–1500 EU cases annually [15]; declining incidence in the USA that has stabilized below |
| Brucella sp. | There are more than 500 000 new cases annually [11], excluding chronic cases. Reported outbreaks in former Communist |
| Burkholderia mallei and Burkholderia pseudomallei | The former causes glanders, a typical but very rare zoonosis. Melioidosis annual incidence in southeast Thailand exceeds 12 cases/10^5 |
| Campylobacter sp. | The O157:H7 strain is consistently causing zoonotic foodborne and waterborne outbreaks [20]. Secondary effect through risk of |
| Chlamydia trachomatis | The number of human monocytotropic ehrlichiosis cases reported in the USA is continuously increasing, exceeding 900 in 2008 [8]. |
| Clostridium tetani | Human epidemiology has resulted in the re-emergence of Lyme disease in the USA: 28 921 confirmed cases were reported in 2008 [8]. |
| Coxiella burnetii | The number of human monocytotropic ehrlichiosis cases reported in the USA is continuously increasing, exceeding 900 in 2008 [8]. |
| Corynebacterium ulcerans | The O157:H7 strain is consistently causing zoonotic foodborne and waterborne outbreaks [20]. Secondary effect through risk of |
| Coxella burnetii | The tularaemia outbreak in Kosovo underlined the relationship of zoonoses with socio-economic and political factors [21]. Outbreaks |
| Ehrlichia chaffeensis and Ehrlichia ewingii | This disease is not typically zoonotic, even when foodborne |
| Escherichia coli | There are 20–200 cases of foodborne illnesses annually in the USA [8]. Micro-outbreaks are regularly reported, predominantly |
| Francisella tularensis | There are 20–200 cases of foodborne illnesses annually in the USA [8]. Micro-outbreaks are regularly reported, predominantly |
| Helicobacter pylori | This disease is not typically zoonotic, even when foodborne |
| Helicobacter sp. | The annual number of cases may exceed 500 000, the majority arising from India and Southeast Asia |
| Legionella pneumophila | The number of human monocytotropic ehrlichiosis cases reported in the USA is continuously increasing, exceeding 900 in 2008 [8]. |
| Mycobacterium avium | The annual number of cases may exceed 500 000, the majority arising from India and Southeast Asia |
| Mycobacterium bovis | The annual number of cases may exceed 500 000, the majority arising from India and Southeast Asia |
| Mycobacterium ulcerans | The annual number of cases may exceed 500 000, the majority arising from India and Southeast Asia |
| Mycoplasma pneumoniae | The annual number of cases may exceed 500 000, the majority arising from India and Southeast Asia |
| Pasteurella sp. | The annual number of cases may exceed 500 000, the majority arising from India and Southeast Asia |
| Pasteurella multocida | The annual number of cases may exceed 500 000, the majority arising from India and Southeast Asia |
| Pasteurella pseudotuberculosis | The annual number of cases may exceed 500 000, the majority arising from India and Southeast Asia |
| Salmonella enterica | There are 20–200 cases of foodborne illnesses annually in the USA [8]. Micro-outbreaks are regularly reported, predominantly |
| Salmonella typhimurium | There are 20–200 cases of foodborne illnesses annually in the USA [8]. Micro-outbreaks are regularly reported, predominantly |
| Salmonella typhi | There are 20–200 cases of foodborne illnesses annually in the USA [8]. Micro-outbreaks are regularly reported, predominantly |
| Shigella sp. | Shigellosis remains a major health issue worldwide, with tens of millions of cases and tens of thousands of deaths annually being |
| Streptococcus agalactiae | The number of human monocytotropic ehrlichiosis cases reported in the USA is continuously increasing, exceeding 900 in 2008 [8]. |
| Streptococcus bovis | The number of human monocytotropic ehrlichiosis cases reported in the USA is continuously increasing, exceeding 900 in 2008 [8]. |
| Streptococcus pneumoniae | The number of human monocytotropic ehrlichiosis cases reported in the USA is continuously increasing, exceeding 900 in 2008 [8]. |
| Vibrio cholerae | The number of human monocytotropic ehrlichiosis cases reported in the USA is continuously increasing, exceeding 900 in 2008 [8]. |
| Vibrio parahaemolyticus | The number of human monocytotropic ehrlichiosis cases reported in the USA is continuously increasing, exceeding 900 in 2008 [8]. |
| Vibrio vulnificus | The number of human monocytotropic ehrlichiosis cases reported in the USA is continuously increasing, exceeding 900 in 2008 [8]. |
| Yersinia enterocolitica | The number of human monocytotropic ehrlichiosis cases reported in the USA is continuously increasing, exceeding 900 in 2008 [8]. |
| Yersinia pestis | The number of human monocytotropic ehrlichiosis cases reported in the USA is continuously increasing, exceeding 900 in 2008 [8]. |
| Yersinia pseudotuberculosis | The number of human monocytotropic ehrlichiosis cases reported in the USA is continuously increasing, exceeding 900 in 2008 [8]. |
### TABLE 2. Clinically significant viral zoonoses

| Pathogen | Comments |
|----------|----------|
| Borna disease virus | Subject of continuing debate on its potential role in human neuropsychiatric disorders [35] |
| California serogroup viruses | California encephalitis, Jamestown Canyon, Keystone, La Crosse, Snowshoe hare and Trivittatus viruses—in total causing 60–80 cases annually in the USA [8] |
| Chikungunya virus | Primates serve as the reservoir in between human outbreaks, when human-to-human vector-mediated transmission occurs. Repeated outbreaks with hundreds of thousands of cases in recent years in the Indian Ocean and Africa, particularly Kenya, Reunion, and India [36]. The situation is similar for Mayaro virus, which has recently re-emerged in South America |
| Cowpox virus | Of historical significance, illustrating an adverse, beneficial effect of zoonoses. Orf is also a zoonosis |
| Crimean–Congo haemorrhagic fever virus | Emerging/re-emerging in eastern Europe, the Balkans, and Turkey, with evidence of a spread west, raising concerns for European epidemiology [37]. Still a significant issue in Central Asia and, partly, in sub-Saharan Africa; in the latter, the similar Dugbe virus may account for a few cases |
| Ebola virus | Zoonotic in true spirit, as wildlife serves as the virus reservoir between outbreaks and the trigger of outbreaks. Most recent outbreak in Democratic Republic of the Congo in 2008; Ebola Reston variant in Philippines with different behaviour regarding human infection |
| Hendra virus | Limited to Australia and with minimal numbers of cases and fatalities (four), but a novel emerging pathogen with significant environmental correlations. A similar natural history and epidemiology applies to Menangle virus. Also of importance only for Australia are Murray Valley encephalitis and Kunjin viruses, which rarely induce clinical disease |
| Hepatitis E virus | Zoonotic reservoir of the disease; may not be implicated directly in outbreaks. Isolated cases of direct transmission by ingestion of deer or wild-boar meat [39] |
| Influenza viruses | The principal zoonotic aspects of influenza are the role of animal hosts as substrates for the development of novel strains, and their role in the introduction of these strains into human pathology. Avian H5N1 influenza is a typical zoonotic infection, requiring close contact with infected animal hosts: at present, after the 2004 outbreak, novel cases with a high fatality ratio are reported randomly from Indonesia, Egypt, Vietnam, and China. The novel H1N1 influenza virus pandemic stopped being zoonotic after human-to-human transmission emerged as the cause of the pandemic. The single non-human host for each of influenza B virus and influenza C virus play a minimal role regarding human disease |
| Japanese encephalitis virus | Tens of thousands of annual cases reported in East and Southeast Asia. Slow expansion to Western Pacific may highlight risks and significant mortality in future years |
| Kysanur forest disease virus | There are 100–500 cases annually in India. Relative of the novel Akhthuma virus in Saudi Arabia |
| Lassa virus | Other Arenaviridae causing localized viral haemorrhagic fevers are Guanarito virus (Venezuela), Machupo virus (Bolivia), Sabia virus (Brazil), Junin virus (Argentina), and the recently emerging Lujo virus (southern Africa) |
| Lympohocytic choriomeningitis virus | Extensive seropositivity in studies indicates potential overestimation of morbidity. An emerging infection through pet mice |
| Marburg virus | The 2004–2005 Angola outbreak resulted in 329/374 fatalities. Two cases, one fatal, were imported into the USA and The Netherlands from Uganda in recent times |
| Monkeypox virus | Mostly notorious for the multistate outbreak in the USA in 2003, traced back to an imported primate from Africa |
| Nipah virus | Human-to-human transmission important for outbreaks; however, zoonotic origin (bats) and reservoir (pigs). Limited cases with major mortality ratio reported particularly from Bangladesh |
| Omkha haemorrhagic fever virus | Localized epidemiology; of interest is its recent switch to direct, non-vector-mediated, transmission from rodents to humans [40] |
| Oropouche virus | Re-emerging in Brazil in recent years [41]. Siblings are the main hosts; vector-borne, clinically similar to dengue |
| Rabies and lyssaviruses | Extremely rare in Europe, the few existing cases typically imported, extremely rare in the USA [8,15]. More than 20 000 deaths annually in India [42]. Major mortality foci are also China, Pakistan, Bangladesh, and Myanmar. Lyssaviruses include Duvenhage virus (Africa, bat-related cases), Moloka virus (Africa), and Australian and European bat lyssaviruses |
| Rift Valley fever virus | Ongoing (2010) outbreak in South Africa, recent outbreaks in Sudan, Kenya, Somalia, and Tanzania, with hundreds of cases and varying mortality ratio (23–45%). Outbreaks in Yemen and Saudi Arabia in 2000 with similar morbidity and mortality toll |
| Ross River virus | Present in Oceania—more than 5600 cases recorded in 2008 [43]. Potential for chronic symptom induction is under investigation. Barmah Forest virus causes similar disease; more than 2000 cases were reported in 2008 |
| SARS coronavirus | Zoonotic in origin, not in subsequent outbreak dynamics |
| Sindbis virus | Traditionally linked with Egypt, it was nevertheless demonstrated as an outbreak cause in Finland (Pogosta disease) [44] |
| Tick-borne encephalitis | More than 5000 cases reported in Europe in 2010 [45]. The majority from Russia, and central–northern Europe. Incidence on the rise, possibly owing to climate changes |
| Venezuelan equine encephalitis virus | Outbreaks in Venezuela and Colombia in the mid-1990s with tens of thousands of cases but minimal mortality (<0.2%) |
| West Nile virus (WNV) | The most characteristic example of a zoonotically sustained massive outbreak. WNV movement through North America in the last decade has resulted in sustained presence in the community. More than 80 000 cases were reported in the USA in 2008 [8]. Furthermore, the ongoing WNV outbreak in Greece, with 34/261 deaths [46], demonstrates the trend of the virus to move to Europe, following the previous outbreaks in Romania and Russia |
| Yellow fever virus | The WHO estimates that there are more than 200 000 annual cases worldwide, with 30 000 deaths—the ongoing vaccination campaign is one of the most ambitious global public health programmes. Both theylvatic and intermediate cycles of disease transmission are zoonotic in character |

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