

A Review of Zoonotic Pathogens of Dromedary Camels

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Abstract: Dromedary, or one-humped, camels Camelus dromedarius are an almost exclusively domesticated species that are common in arid areas as both beasts of burden and production animals for meat and milk. Currently, there are approximately 30 million dromedary camels, with highest numbers in Africa and the Middle East. The hardiness of camels in arid regions has made humans more dependent on them, especially as a stable protein source. Camels also carry and may transmit disease-causing agents to humans and other animals. The ability for camels to act as a point source or vector for disease is a concern due to increasing human demands for meat, lack of biosafety and biosecurity protocols in many regions, and a growth in the interface with wildlife as camel herds become sympatric with non-domestic species. We conducted a literature review of camel-borne zoonotic diseases and found that the majority of publications (65%) focused on Middle East respiratory syndrome (MERS), brucellosis, Echinococcus granulosus, and Rift Valley fever. The high fatality from MERS outbreaks during 2012-2016 elicited an immediate response from the research community as demonstrated by a surge of MERS-related publications. However, we contend that other camel-borne diseases such as Yersinia pestis, Coxiella burnetii, and Crimean-Congo hemorrhagic fever are just as important to include in surveillance efforts. Camel populations, particularly in sub-Saharan Africa, are increasing exponentially in response to prolonged droughts, and thus, the risk of zoonoses increases as well. In this review, we provide an overview of the major zoonotic diseases present in dromedary camels, their risk to humans, and recommendations to minimize spillover events.

Keywords: Camel, Nomadic, One health, Pathogen, Spillover, Zoonoses

INTRODUCTION

Worldwide there are roughly 30 million dromedary camels, with highest numbers found in Africa and the Middle East (Figure 1). Due to increased consumption and contact with camel meat and milk, camels represent a significant point source for zoonotic disease transmission to humans. Pas-

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toralist camel production, in particular, is associated with a risk of disease spillover from wildlife into camel populations, and from camels to wildlife, as well as less opportunities for disease surveillance and control. By 2050 the human population is projected to grow by 2.5 billion, with nearly half of all population growth occurring in the African continent (Roser 2018). Along with the increase in human population in Africa and the Middle East, the camel population has also experienced steady growth as the de-

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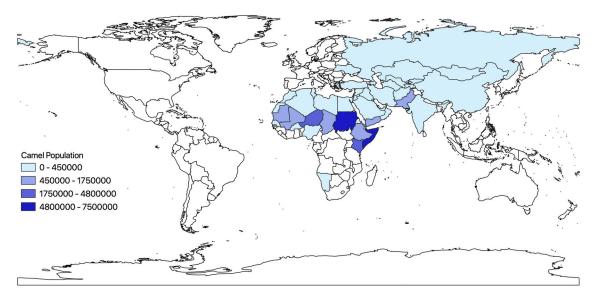


Figure 1. Map of domesticated dromedary camel population by country in 2016; data from Food and Agricultural Organization (Food and Agricultural Organization, 2016)

mand and production of camel meat and milk escalates (FAOSTAT 2016). More and more, nomadic herders are switching to an agricultural or urban setting to raise camels and this change in camel production brings potential risks of disease emergence and transmission. In addition, with the realities of climate change and the increase in drought conditions, camel hardiness has led to a shift in livestock choice in many regions of the world from cattle to camels, making camels even more abundant (Watson et al. 2016)

Limited resources, low levels of regulation, poor hygiene, high mobility of animals and herders, and lack of consistent veterinary care also act as drivers for disease spillover (Gossner et al. 2016; Megersa et al. 2011). Knowledge of camel-borne diseases, clinical signs, and pathways of transmission is thus important to mitigate human risks of camel-associated zoonoses. Many infectious diseases that have been an issue in Africa and the Middle East during the last decades, such as Middle East respiratory syndrome (MERS) and brucellosis, have an association with camel contact (Ahmed et al. 2010; Ferguson and Van Kerkhove 2014). Additionally, novel camel-borne diseases continue to be identified, as best exemplified by reports of a prion disease from Algerian abattoir camels published during the editing of this review paper (Babelhadj et al. 2018)

Significant research on seropositivity and detection of specific diseases of camels, those that have implications for human health, has been conducted; however, to the authors' knowledge no publication has summarized the current literature on these zoonotic diseases. Realizing the need for a thorough review of the literature to identify the risks that camels pose to human health was the impetus for this review. In this paper, we review publications of the most common confirmed and potential camel zoonoses of interest: bacterial, viral, and parasitic, and offer recommendations for surveillance and control of the diseases of highest priority.

METHODS

We utilized two search engines, Google Scholar and PubMed, to search for publications related to camel-borne disease and zoonotic spillover. We chose Google Scholar for breadth and volume of content, while PubMed was chosen from medical and public health-specific search engines for its specificity. Publications on Bactrian camels Camelus bactrianus were excluded because they are primarily wild but are used as beasts of burden and food in select countries and only account for 2 million out of 30 million total camels (IUCN 2008). To cast a wide net for possible diseases we did not search for specific zoonotic diseases and instead classified publications by disease after the initial literature search. All search terms included the words camel and human as well as one of six other words keywords: camel + human + zoonotic, illness, spillover, outbreak, transmission, or disease. For each set of search terms, we reviewed the first 100 results for relevancy or all results if < 100. Included publications were restricted to

those written in English, but there was no date limit, no other restrictions were set, and papers were sorted by relevance. From a total of 1054 papers, 619 were unique or non-duplicates and 304 of these were relevant (Figure 2). Five of these 304 papers reported on multiple diseases. Results that were excluded included papers that inconclusively related to transmission from camels n = 96, noncamelid animals n = 40, studies that focused on vaccines n = 25, camel-specific diseases n = 22, articles/seminars n = 15, and non-relevant topics n = 117. Examples of nonrelevance were papers that did not mention camels at all, papers that did not discuss transmission of disease, papers on human-to-human transmission, or papers that discussed laboratory testing and techniques related to these diseases. Food-borne bacterial diseases from pathogens such as Escherichia coli, Salmonella, and Campylobacter were consolidated into one category termed "food-borne" because they share transmission pathways, have similar symptoms, and were pre-grouped by several publications in this review. We also elected to present these pathogens in this fashion because there was a precedence set by said publications. Papers with positive serologic testing in camels, probable disease through an explained epidemiologic link between human disease and camel-borne pathogens, and isolation of similar strains in humans and camels fit criteria for inclusion. Relevant papers were sorted into bacterial, viral, and parasitic categories along with recorded

counts for each disease. Results were separated out in this manner to cover scope number of diseases as well as depth number of papers per disease. Figures were created in Quantum GIS 3.6 (QGIS Development Team 2019). We completed the literature search in February and March of 2018.

RESULTS

Through this literature review, we identified 304 papers published between 1970 and 2018 that described disease agents in camels with probable (see above definition) or confirmed transmission to humans. Thirty-seven camelborne diseases were identified, comprised of 12 bacterial diseases, 13 viral diseases, and 12 parasitic diseases (Table 1). The most frequently occurring diseases or diseasecausing agents in this study were MERS n = 118, *Echinococcus granulosus* n = 46, brucellosis n = 35, and Rift Valley fever n = 19. In this study, 42 countries were represented in the literature, with most papers originating from Saudi Arabia n = 36, Iran n = 27, Kenya n = 15, and Egypt n = 14 (Figure 3). There has been a dramatic increase in publications over the last eight years with a peak during 2012-2016, when research on MERS was undertaken in a number of laboratories following the first diagnosis of a human fatality reported in 2012 (Fig. 4) (Kupferschmidt 2014).

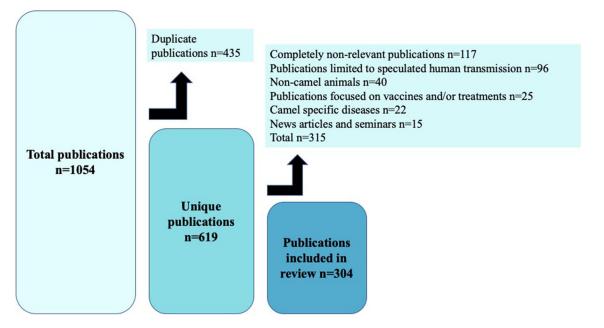


Figure 2. Methodology for inclusion and exclusion of publications of camel-borne zoonoses. Out of an initial 1054 eligible publications, 619 were unique and non-duplicate and 304 of those were included in the final selection of journal articles for further analysis

Table 1. Camel-borne diseases found in review by paper count

Disease/agent	Туре	Paper count	References	
Middle East respiratory syndrome	Virus	118	Adney et al. (2014), Ahmed (2017a, b), Al Hammadi et al. (2015), Al salihi and Alrodhan (2017), Al-Tawfiq and Memish (2014a, b), Al-Tawfiq et al. (2014), Ala- gaili et al. (2014), Aleanizy et al. (2017), Alexandersen et al. (2014), Alhakeem et al. (2016), Alhamlan et al. (2017), Ali et al. (2017), Alraddadi et al. (2016), Alsolamy et al. (2017), Assiri et al. (2016), Azhar et al. (2014, b), Balkhy et al. (2016), Banik et al. (2015), Buchholz et al. (2013), Chan et al. (2014, 2015), Chu et al. (2016), Banik et al. (2015), Buchholz et al. (2013), Chan et al. (2014, 2015), Chu et al. (2014, 2015), 2018), Corman et al. (2015), Devi et al. (2014), Drosten et al. (2015), Du and Han (2016), Dudas et al. (2018), Durai et al. (2015), Eckerle et al. (2015), Du and Han (2016), Dudas et al. (2014), Farag et al. (2015), Eckerle et al. (2017), Ferguson and Van Kerkhove (2014), Food and Agriculture Organization of the United Nations (2017), Funk et al. (2016), Gardner and MacIntyre (2014), Gossner et al. (2016), Gutiérrez et al. (2015), Haagmans et al. (2014, 2016), Han et al. (2016), Hemida et al. (2013, 2014, 2015, 2017), Holmes (2014), Hunter et al. (2016), Kayali and Peiris (2015), Khalafalla et al. (2015), Kupferschmidt (2015), Liljander et al. (2016), Mackay and Arden (2015, 2017), Majumder (2015), Memish et al. (2013, 2014a, b, 2015), Meyer et al. (2014, 2016), Miguel et al. (2016, 2017), Mohd et al. (2016), Muhairi et al. (2016), Müller et al. (2014, 2015), Ng et al. (2016), Nowotny and Kolodziejek (2014), Oladipo (2015), Olival and Epstein (2015), Cmrani et al. (2014a, b, 2015), Omrani and Shalhoub (2015), Park et al. (2015), Rabaan (2017), Raj et al. (2014a, b, 2014a, b, 2015, 2016), Reuss et al. (2014), Sabir et al. (2016), Salkeld et al. (2016), Saqib et al. (2017), Shapiro et al. (2016), Sharif-Yakan and Kanj (2014), Shehata et al. (2016), Su et al. (2016), Tai et al. (2017), Watson et al. (2014), Wernery et al. (2015, 2016), Widagdo et al. (2016), de Wit et al. (2016), de Wit and Munster (2013), World Health Org	
Hydatidosis (Echinococcus granulosus)	Parasite	46	 Abdel Aaty et al. (2012), Abushhewa et al. (2010), Ahmadi (2005), Alvarez Rojas et al. (2014), Azab et al. (2004), Bardonnet et al. (2002, 2003), Casulli et al. (2010), Dink et al. (2004), Eckert and Deplazes (2004), Eckert et al. (1989), Elmahdi et al. (2004) Hailemariam et al. (2012), Hajialilo et al. (2012), Fasihi Harandi et al. (2002), Hassanain et al. (2012), Hajialilo et al. (2012), Karimi et al. (2017), Kia et al. (2010), Kinkar et al. (2017), Latif et al. (2010), Macpherson and McManus (1982) Macpherson and Smyth (1985), Maillard et al. (2006), Mandal and Deb Mandal (2012), McManus (1981), McManus and Rishi (1989), Mirzaei et al. (2016), Mobedi et al. (1970), Mrad et al. (2005), Oksanen and Lavikainen (2015), Ome et al. 2010a, b, Sadjjadi (2006), Salem et al. (2011), Shahnazi et al. (2011), Shariatzadeh et al. (2015), Sharma et al. (2013b), Singh et al. (2014), Spotin et al. (2015, 2017), Tigre et al. (2016), Thompson (2008), Utuk et al. (2008), Wachiratet al. (1993), Youssef and Uga (2014), Zhang et al. (1998) 	

Table 1. continued

Disease/agent	Туре	Paper count	References	
Brucellosis	Bacteria	35	Abbas and Agab (2002), Ahmed et al. (2010), Al Dahouk et al. (2013), Bekele et al. (2013), Cooper (1992), Ducrotoy et al. (2015), El-Ansary et al. (2001), Fiori et al. (2000), Garcell et al. (2016), Gautret et al. (2013), Godfroid et al. (2005, 2013), Gumaa et al. (2014), Gwida et al. (2010, 2012), Kiel and Yousuf (1989), Megersa et al. (2011), Megersa et al. (2012), Memish and Balkhy (2004), Nimri (2003), Omer et al. 2010a, b, Osoro et al. (2015), Pappas (2010), Rhodes et al. (2016), Schelling et al. (2003), Schelling et al. (2004), Seleem et al. (2010), Shaalan et al. (2002), Shimol et al. (2012), Smits and Kadri (2005), Sprague et al. (2012), Teshome et al. (2003), Wernery (2014), Yahya (2015), Zewolda and Wereta (2012)	
Rift Valley fever	Virus	19	Abdo-Salem et al. (2006), Ahmed Kamal (2011), Bird et al. (2008), Britch et al. (2013), Chevalier et al. (2010), Chinikar et al. (2013), El Mamy et al. (2011, 2014), Faye et al. (2014), Gerdes (2004), Horton et al. (2014), Jäckel et al. (2013), Linthicum et al. (2016), Lutomiah et al. (2014), Merrill et al. (2015), Macharia et al. (2010), Paweska (2015), Swai and Sindato (2015), Weaver and Reisen (2010)	
Food-borne	Bacteria	15	Dehkordi et al. (2013), Fadlelmula et al. (2016), Ghoneim et al. (2017), Hajialilo et al. (2012), Horton et al. (2014), Jaros et al. (2008), Kaindi et al. (2012), Rahimi et al. (2010, 2012), Rahimi and Kheirabadi (2012), Raufu et al. (2015), Salehi et al. (2012), Shabana et al. (2013), Sung et al. (2008), Tadesse (2015), Tejedor-Junco et al. (2015)	
Plague (Yersinia pestis)	Bacteria	10	Aikimbajev et al. (2003), Arbaji et al. (2005), Bramanti et al. (2016), Cabanel et al. (2013), Christie et al. (1980), Drancourt et al. (2006), El-Bahnasawy et al. (2012), Leslie et al. (2011), Saeed et al. (2005), Stenseth et al. (2008)	
Camelpox	Virus	9	Balamurugan et al. (2013), Bera et al. (2010, 2011, 2015), Duraffour et al. (2011), Jezek et al. (1983), Khalafalla and Abdelazim (2017), Pearce-Duvet (2006), Shchelkunov (2013)	
Q fever (<i>Coxiella burnetii</i>)	Bacteria	7	Klemmer et al. (2018), Mohabbati Mobarez et al. (2017), Njeru et al. (2016), Pirouz et al. (2015), Schelling et al. (2003, 2004), Vanderburg et al. (2014)	
Linguatula serrata	Parasite	7	Bamorovat et al. (2014), Farjanikish and Shokrani (2016), Haddadzadeh et al. (2010), Oryan et al. (2011), Rezaei et al. (2012), Sadjjadi et al. (1998), Shakerian et al. (2008)	
Hepatitis E	Virus	5	Khuroo and Khuroo (2016), Lee et al. (2016), Pavio et al. (2015), Rasche et al. (2016), Spahr et al. (2018)	
Crimean–Congo hemorrhagic fever	Virus	4	Champour et al. (2016), Khan et al. (1997), Mertens et al. (2013), Walker et al. (2016)	
Tuberculosis	Bacteria	4	Cosivi et al. (1995), Garine-Wichatitsky et al. (2013), Gumi et al. (2012), Moda et al. (1996)	
Anthrax	Bacteria	3	Aikembayev et al. (2010), Musa et al. (1993), Woods et al. (2004)	
Trypanosoma evansi	Parasite	2	Bennoune et al. (2013), Haridy et al. (2011)	
Ecthyma	Virus	2	Bazargani et al. (2010), Moallin and Zessin (1988)	
Rotavirus	Virus	2	Ghosh et al. (2011), Jere et al. (2014)	
Helminth	Parasite	2	Anvari-Tafti et al. (2013), McCarthy and Moore (2000)	
Toxoplasmosis	Parasite	2	Alanazi (2013), Dehkordi et al. (2013)	
Alkhurma hemor- rhagic fever	Virus	1	Carletti (2010)	
Betacoronavirus UAE-HKU23	Virus	1	Woo et al. (2014)	
Dera Ghazi Khan virus	Virus	1	Walker et al. (2016)	
HCoV-229E	Virus	1	Corman et al. (2018)	

Disease/agent	Type	Paper count	References
Rabies	Virus	1	Bloch and Diallo (1995)
Torque teno virus	Virus	1	Al-Moslih et al. (2007)
Aeromonas spp.	Bacteria	1	Ghenghesh et al. (2001)
Bartonella	Bacteria	1	Rasis et al. (2014)
Glanders (Burkholderia mallei)	Bacteria	1	Scholz et al. (2014)
Johne's disease (paratuberculosis)	Bacteria	1	Ghosh et al. (2012)
Klebsiella pneumoniae	Bacteria	1	Sharma et al. (2013a)
Rickettsia aeschlimannii	Bacteria	1	Kleinerman et al. (2013)
Babesia bovis	Parasite	1	Ereqat et al. (2016)
Cryptosporidium	Parasite	1	Sazmand et al. (2012)
Fascioliasis	Parasite	1	Younan et al. (2016)
Leishmaniosis	Parasite	1	Ashford (2000)
Onchocerciasis	Parasite	1	El-Bahnasawy et al. (2015)
Sarcocystis	Parasite	1	Chhabra and Samantaray (2012)
Trichinellosis	Parasite	1	Bommer et al. (1980)

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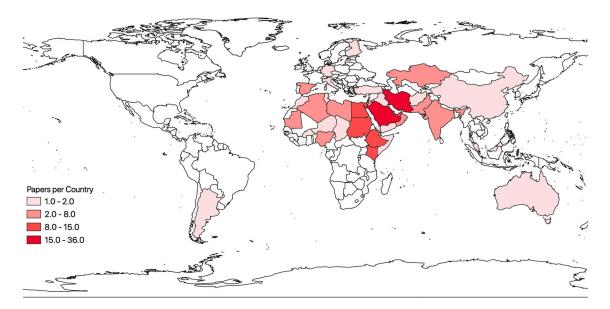


Figure 3. Number of publications by country of study, range n = 1 Finland, Argentina to n = 36 Saudi Arabia

Viral

The large majority of publications were related to MERS n = 118, a novel coronavirus. Genetic comparisons between camel and human isolated MERS are highly similar and camels continue to exhibit positive seropositivity for MERS in recent tests (Chu et al. 2018).

The review identified 19 papers on Rift Valley fever (RVF) transmission, most of which detailed how common seropositivity to RVF virus was in camel herds. Four of these papers emphasized that livestock like camels, cattle, and sheep served as important amplifiers for the virus, especially prior to outbreaks in Kenya and Mauritania (Bird et al. 2008; Britch et al. 2013; El Mamy et al. 2011, 2014).

Four of nine publications on Camelpox discussed human transmission, including a paper that reported the first laboratory-confirmed case of human Camelpox (Bera et al. 2011).

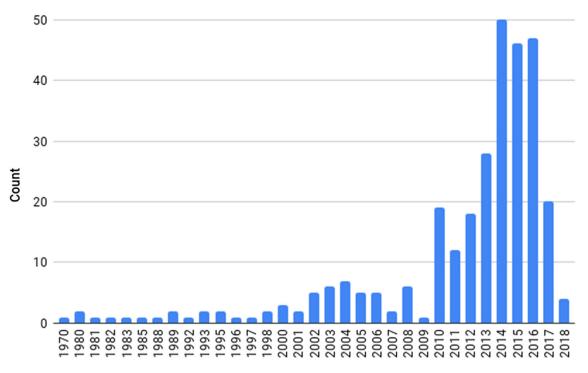


Fig. 4. Frequency of camel-borne disease publications between 1970 and 2018 identified in this review

There were five papers on hepatitis E, one of the five known human hepatitis virus strains, in which camel meat and milk were implicated as risk factors in humans through whole-genome sequencing, HEV IgM, or HEV RNA detection (Pavio et al. 2015 Khuroo and Khuroo 2016; Lee et al. 2016; Rasche et al. 2016; Spahr et al. 2018). In one of these reports, a liver transplant patient in the United Arab Emirates consumed camel meat and milk regularly and was chronically infected with hepatitis E (Lee et al. 2016).

While no publication documented clinical evidence of camel-human rabies transmission, one paper presented probable evidence of camel-to-human rabies transmission (Bloch and Diallo 1995).

A 2018 publication noted that HCoV-229E, a primarily non-lethal coronavirus responsible for a proportion of upper and lower respiratory tract infections, can be transmitted from camels to humans similar to MERS transmission, thus implicating dromedary camels as a possible reservoir of coronaviruses (Corman et al. 2018). Woo et al. (2014) identified a novel betacoronavirus UAE-HKU23 or dromedary camel coronavirus DcCOV in the United Arab Emirates that was detected in 52% of tested camel serum samples.

Other viruses that were found in camels include Alkhurma hemorrhagic fever (AHF) virus n = 1, Crimean– Congo hemorrhagic fever (CCHF) virus n = 4, rotavirus n = 2, camel contagious ecthyma n = 2, torque teno virus n = 1, and Dera Ghazi Khan virus n = 1 (Moallin and Zessin 1988; Khan et al. 1997; Al-Moslih et al. 2007; Bazargani et al. 2010; Carletti 2010; Ghosh et al. 2011; Horton et al. 2014; Jere et al. 2014; Champour et al. 2016; Walker et al. 2016).

Bacterial

A total of 35 papers discussed the risk of brucellosis as a public health threat from camels. Most of these 35 papers (18; 51%) were seroprevalence studies of brucellosis in camels, which reported a prevalence range of between 1.4 and 37.5% (Schelling et al. 2004; Omer et al. 2010a, b).

Bacterial diseases that are transmitted through food, water, or other types of fecal-oral transmission were grouped together as "food-borne." This group included *Salmonella*, *E. coli*, *Helicobacter*, *Staphylococcus*, *Enterococci*, *Campylobacter*, and *Leptospirosis*. These diarrheal bacteria were reported in 15 papers, four of which discussed testing for antimicrobial resistance in camels and camel products (Rahimi et al. 2010; Tadesse 2015; Tejedor-Junco et al. 2015; Fadlelmula et al. 2016).

Ten papers described camel transmission of plague, *Yersinia pestis.* In fact, three papers documented plague infection in patients who directly consumed raw camel meat (Christie et al. 1980; Arbaji et al. 2005; Cabanel et al. 2013).

Seven papers detailed high Q fever *Coxiella burnetii* seropositivity in camels (Schelling et al. 2003; Schelling et al. 2004; Vanderburg et al. 2014; Pirouz et al. 2015; Njeru et al. 2016; Mohabbati Mobarez et al. 2017; Klemmer et al. 2018). Seroprevalence levels of up to 73% were present in camels in Chad (Schelling et al. 2004). Humans that work in close contact with camels such as herders, farmers, and breeders are especially at risk of Q fever transmission, with one study finding a high odds ratio (OR = 9) for the association of being a camel breeder and Q fever seropositivity (Schelling et al. 2003).

The four papers on camel tuberculosis all discussed positive detection of *M. bovis*, indicating that camels are likely also a reservoir for human transmission (Cosivi et al. 1995; Moda et al. 1996; Gumi et al. 2012; Garine-Wichatitsky et al. 2013). Gumi et al. (2012) found isolated *M. tuberculosis* from camels and *M. bovis* from humans, which suggests cross-species transmission of both strains of bacteria.

One of three papers on anthrax conclusively extracted anthrax spores from infected camel meat, which led to illness in ten people (Musa et al. 1993).

Other bacterial diseases in the literature but occurring less frequently included *Rickettsia aeschlimannii* 1, *Klebsiella pneumoniae* 1, *Aeromonas spp.* 1, *Bartonella spp.* 1, *Burkholderia mallei* 1, and *M. avium subsp. paratuberculosis* 1 (Ghenghesh et al. 2001; Ghosh et al. 2012; Kleinerman et al. 2013; Sharma et al. 2013a, b; Rasis et al. 2014; Scholz et al. 2014).

Parasitic

The most common zoonotic parasite transmitted from camels to humans was *Echinococcus granulosus* n = 46. This parasite has a variety of hosts but is often found in livestock as intermediate hosts, including camels. A review by Alvarez Rojas et al. (2014) estimated that the camel strain of *E. granulosus* causes between 7 and 11% of all hydatid infections in humans. This attributable risk estimate likely varies by geographic location; a molecular survey by Omar et al. (2010a, b) found that 59% of camels in Sudan were infected with *E. granulosus*, and a subsequent Sudanese paper found that camels and cattle were the principal intermediate host, not sheep as previously believed (Elmahdi et al. 2004).

There were two papers on the parasite *Trypanosoma evansi*. Prevalence rates of up to 14% were found in camels in Algeria which is comparatively high to other countries and increases risk for human transmission (Bennoune et al. 2013). Human cases, confirmed with ELISA and stained blood films, of *T. evansi* have been reported in India and Egypt (Haridy et al. 2011).

Parasitic diseases are commonly passed from camels to humans through meat and milk consumption. One paper on a trichinellosis outbreak in Germany detailed how camel meat brought from Egypt was responsible for zoonotic transmission (Bommer et al. 1980), and in 2013, researchers detected Toxoplasma gondii in camel milk (Dehkordi et al. 2013). Other fecal- and meat-/milktransmitted parasites included Leishmania spp. n = 1, Babesia bovis n = 1, Cryptosporidium spp. n = 1, and Sarco*cystis* spp. n = 1 (Ashford 2000; Sazmand et al. 2012; Chhabra and Samantaray 2012; Ereqat et al. 2016). Four other parasite species found in this cohort were helminths Haemonchus tataricus, Trichostrongylus hamatus, and Trichuris infundibulus n = 2; Linguatula serrata n = 7; Onchocerca volvulus n = 1; and Fasciola hepatica or Fasciola gigantica n = 1 (Sadjjadi et al. 1998; McCarthy and Moore 2000; Shakerian et al. 2008; Haddadzadeh et al. 2010; Oryan et al. 2011; Rezaei et al. 2012; Anvari-Tafti et al. 2013; Bamorovat et al. 2014; Youssef and Uga 2014; El-Bahnasawy et al. 2015; Farjanikish and Shokrani 2016).

Discussion

As determined by publication count as well as known mortality rates, viruses in this review are of highest interest, followed by bacteria and parasites (Table 1). Camels are as ubiquitous as cattle or sheep in many parts of the world; yet, knowledge on potential health risks lags behind that of other livestock species. The combination of human-related climate change, population growth, decline in biodiversity, and land-use change are major drivers for the evolution and spread of zoonotic disease (Engering et al. 2013).

The emergence of MERS, with outbreaks between 2012 and 2016, was an outcome of these realities, and it is no surprise that MERS continues to receive high amounts of publicity and funding due to its high human fatality rates \sim 35% and pandemic potential (World Health Organization 2017). There are currently no widely used vaccines against MERS, but knowledge of its transmission is critical to better implement food safety and sanitation practices within the camel value chain. Rift Valley fever (RVF) was the second most common camel-borne zoonosis in this review and is not a significant source of mortality as less than 3% of patients develop lethal symptoms. However, it is a significant cause of morbidity especially in high-risk populations such as veterinarians, butchers, scientists, animal health workers, farmers, and herders (Ikegami and Makino 2011). The same goes for Camelpox, which is a minor health problem for camel farmers but incurs significant economic damages from the death of young camels, reduced milk yield, and lasting morbidity (Balamurugan et al. 2013). MERS, RVF, and Camelpox were some of the most commonly reported camel-borne zoonotic viruses in this literature review, but for preventive purposes awareness of the following viruses is important to promote. Crimean-Congo hemorrhagic fever is listed as a disease with epidemic potential due to its high mortality rate, growing prevalence in Asia and Europe, and lack of vaccines (Mertens et al. 2013). Alkhurma hemorrhagic fever (AHF) is also a disease of interest because of its hemorrhagic symptoms, recent emergence, and lack of detailed knowledge of its symptoms and transmission. Mortality rates for these viruses along with other hemorrhagic fevers are high because of difficulties in disease diagnosis (World Health Organization 2016). Alkhurma hemorrhagic fever, CCHF, and Dera Ghazi Khan are mosquito- and tick-borne diseases where camels act as reservoirs and amplifiers (Carletti 2010; Walker et al. 2016). Thus, vector surveillance and management around camels in addition to the aforementioned sanitation practices could be highly beneficial to control the spread of these diseases.

The bacterial disease of greatest concern is brucellosis, which is not only zoonotic but also causes severe economic losses for farmers and ranchers across the world in lost milk, reduced fertility, stillbirths, and abortions (Akakpo et al. 2010). Camel farmers should be cautious and aware when handling camels, and this exemplifies another area where increased attention to sanitation practices would be beneficial. Food-borne diseases are of high importance as evidenced by the rapid establishment of complex camel milk value chains in urban Kenya as well as the breadth of food-borne pathogens found in our review (Muloi et al. 2018). These locations exemplify the high-risk transmission interfaces that are formed due to a lack of proper protocol and oversight by government agencies in regard to food safety training and hygienic practices (Muloi et al. 2018). Camels contract plague from infected fleas and may infect humans through contact with infected bodily fluids or

consumption of infected meat (Leslie et al. 2011). However, vaccination in humans can be used to control the spread and occurrence of outbreaks. For example, vaccination rates have steadily increased in Kazakhstan since 2001 and the usage of vaccines in combination with antibiotics has greatly reduced case fatality across the country (Aikimbajev et al. 2003). The abundance of publications on brucellosis, plague, and food-borne bacterial illnesses reaffirms their presence in camels.

The earliest papers in this review came from the 1970s and almost exclusively discussed parasites like E. granulosus with occasional papers on viral and bacterial disease. This finding is consistent with a historical lack of widespread high-quality technology for viral and bacterial detection, as well as increased focus on viruses today as compared to 30-40 years ago. Parasitic diseases in this review were not significant sources of mortality. Cysts from E. granulosus occur on lung and liver tissue along with other internal organs and contribute to morbidity in humans through pressure effects and problematic locations of cysts (Mandal and Deb Mandal 2012). Vaccination of camels against E. granulosus is not widely practiced because sheep and dogs are considered to be more important hosts: This, in combination with unsanitary practices and high camel and sheep densities, creates higher risk for humans in these areas (Zhang and McManus 2006). No other publications on parasites showed that they were significant sources of human mortality, and there were low paper counts for most parasites, which could indicate their rarity in camels and largely non-lethal status.

Many studies demonstrated a high seroprevalence to a variety of zoonotic pathogens in camel populations along with current or past examples of camel-human transmission. However, few validated standardized tests exist for camels, making disease detection and confirmation difficult (Gwida et al. 2011). Seropositivity is an indication of antibodies and not antigens, so while this shows that a camel was exposed, it does not provide information on the infection status of the individual or the ability of the camel to transmit a pathogen. These papers may not have exact confirmation for each strain in each country or population, but high prevalence coupled with known instances of transmission provides a guideline for prospective risks. Additionally, because we did not analyze our results with statistical methods we were unable to assess the strength of association between pathogens and human risk. Another limitation of our review was the absence of certain pivotal papers; this may have been due to the use of Google Scholar as one of the two major search engines. A serosurvey of Q fever in Laikipia County, Kenya, that revealed high seroprevalence 18.6% in dromedaries was one such paper that fit our inclusion and search criteria keywords: camel, zoonotic, human, but did not appear in any searches (Browne et al. 2017). A common critique of Google Scholar is the limited ability to sort results, which thus provides evidence that it misses important literature in many case studies (Haddaway et al. 2015). Although we did use PubMed we still may have missed eligible publications because of relevance sorting and/or using only the first 100 results. Our study was limited to peer-reviewed material in English and excludes a thorough review of French, Turkish, Farsi, and Arabic literature which could have provided more information in target regions. The use of additional search engines or search terms may improve the scope of literature reviews, which we will make note of for the future.

Lastly, a limitation not necessary related to methodology but rather the epidemiology of diseases relates to missing diseases at the camel–other livestock/wildlife–human interface that we would not have captured in our review. Although we did not include them as part of this review there were papers found in our initial searches that described camel–livestock and camel–wildlife transmission. These shared pathogens may be zoonotic and include camels as part of the transmission cycle but are not necessarily identified as a camel-borne zoonosis. For example, other animals may be the original or primary source of many pathogens, such as the case of MERS in bats, with the camel being an intermediate host in the transmission from animal to human (Corman et al. 2014a, b).

Dromedary camels are a staple in the diets and lives of humans like their cattle and pig counterparts, but research on their zoonotic disease potential is lacking in comparison. When the map of camel population density is compared to the geographic site of published papers found in this review, we see that the two have high levels of intersection in Africa, Asia, and the Middle East (Figures 1 and 3). However, these maps also show that in many instances camel-borne zoonoses are not restricted to areas of high camel numbers and human infections can and do occur in countries with very low camel populations, and even in countries with no camels as a person may be exposed in one region and travel to another. Therefore, veterinarians, farmers, and others working in close contact with camels and camel products should be cognizant of these potential pathogens, not just in areas where camels are raised but also where camel products may be processed and transported. Additionally, physicians must be aware of where their patients have traveled. Knowledge of potential camelborne diseases is thus important for researchers and health workers to consider globally.

CONCLUSION

Camels are not common outside of hot and arid areas such as sub-Saharan Africa or the Middle East, but knowledge of their potential carrier status is important to researchers, zoo personnel, and travelers. The MERS and Ebola outbreaks in recent years have shown how rapidly pathogens can travel and erupt in novel human populations; population expansion and a lack of extensive healthcare systems make camel-endemic areas a potential hot spot for zoonotic spillover. Many of the zoonotic pathogens of camels are a current or possible future risk to human health and must be considered by medical professionals, especially in light of the increased use of camels as a growing protein source globally. As we collect epidemiologic data on the routes of transmission and sources of these infectious agents, we become better prepared to manage and mitigate their impact on humans. Camel milk and meat act as a point source for infection and should be managed with proper slaughter protocols, pasteurization, and improved overall sanitation practices. Dromedary camels also act as a significant source and amplifier for vector-borne disease; therefore, vaccination of camels, control of mosquitoes and ticks, insecticide application, and consistent screening will help control infection rates in camels and humans. In this literature review, we highlight a number of camel-borne zoonotic diseases. The number of pathogens and spillover events will most likely continue to grow as human and camel populations increase and increasingly intersect.

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COMPLIANCE WITH ETHICAL STANDARDS

CONFLICT OF INTEREST The authors declare that they have no conflict of interest.

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