Zoonoses in the Arabian Peninsula

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ABSTRACT

The human population is rising and will soon reach 9 billion people. In parallel, the demand for animal protein is increasing and with it is the threat of zoonotic diseases. We must therefore be on our guard. The close association of people with animals promotes the opportunity for zoonotic infections and real danger may arise when animals are imported with no health background. Therefore, it is essential to implement strict import controls, and establish efficient quarantine facilities. Many viral, bacterial, and zoonotic diseases have been diagnosed on the Arabian Peninsula, either by isolating the pathogens or through serological surveys. Most of them are briefly discussed in this paper.

Saudi Med J 2014; Vol. 35 (12): 1455-1462

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Zoonotic diseases are recognized as a major global threat to human health and sustainable development. The health of humans, the health of animals (both domestic and wild), and the environment are all interconnected; therefore, need a “One Health” approach. There was a period between 1960 and 1970 when it was widely expected that the antibiotic and vaccine era would reduce or eliminate infectious diseases, but as we know now, new microbes pursue every possible chance to escape from barriers that are erected to contain them and we must be forever on our guards. Influenza, severe acute respiratory syndrome (SARS), and Middle East respiratory syndrome (MERS) have shown us that the fear that new plagues are in the making is not unjustified. In most parts of the world; however, we are not well prepared because we have not enough water, not enough food, not sufficient shelter, and no peace. Drug resistant superbugs have spread to 40 countries and in India alone more than 600 million people defecate in the open.

Zoonoses are defined by the World Health Organization (WHO) as: “diseases and infections which are naturally transmitted between vertebrate animals and man.” The control of these diseases is a global challenge and requires joint veterinary and medical efforts. The close contact of people with their animals in vast areas of the Arabian Peninsula promotes the opportunity for zoonotic infections as recently experienced with the MERS coronavirus (CoV) outbreaks in the Middle East. Certain occupational groups may be at greater risk such as farmers, pastoralists, hunters, veterinarians, and wildlife workers, but zoonoses are not only a rural problem anymore. They undoubtedly have also spread into urban areas. Last but not least, mass gatherings like the annual Hajj pilgrimage to Saudi Arabia also poses a real zoonotic risk especially to people who come into close animal contact; for example, when a great number of animals of unknown origin are sacrificed. This review article highlights the most important viral, bacterial, and parasitic zoonotic diseases and briefly mentions the occurrence of some of these on the Arabian Peninsula.

Viral diseases. Table 1 shows 11 of the most important zoonotic viral diseases of which 8 were diagnosed on the
Arabian Peninsula over the last years either in dead or diseased animals or through antibody detection. Rabies has been diagnosed on the Arabian Peninsula in dogs, cats, sheep, goats, foxes, dromedaries, and in a horse. The first cases were reported in 1992/1993. In 1992/1993 the disease entered the United Arab Emirates (UAE) via Al-Ain from Oman and infected first 12 dromedaries, 5 sheep, 4 goats, and 3 foxes in the Al-Ain area. Four months later, it reached Abu Dhabi and Dubai where rabies killed 17 more dromedaries and one sheep. In total, 44 animals and 4 species were affected. The disease reemerged in 2013/2014 and infected 6 feral cats, 2 red foxes, and one horse, which was bitten by a rabid fox. Al-Dubaib reported rabies in dromedaries in Saudi Arabia in 2007. A rabies incidence of 0.2% was reported by 48 camel herdsmen looking after more than 4,000 animals. The disease was transmitted in 70% of cases by bites from feral dogs and 17% of the cases by rabid foxes. Camels were mainly bitten in the front and hind legs when defending their neonates. It is believed that rabies is transmitted by the red fox in the UAE and Oman and mainly by wild dogs (feral) in Saudi Arabia and Yemen. It can only be presumed that these animals species are the vectors of rabies on the Arabian Peninsula, as there are very few available reports. Rabies viruses isolated from camels in the UAE were indistinguishable from the Lyssavirus serotypes. A phylogenetic tree from Omani and UAE rabies strains was established, and this showed that rabies viruses cluster together in a European/Middle East lineage, segregated into 2 distinct branches. The reference method of making a diagnosis of rabies is to demonstrate rabies virus antigen in impression smears of fresh brain by immuno fluorescence.

Table 1 - Important zoonotic viral diseases.

| Virus causing diseases | Pathogen source | Wildlife source | Host/reservoir |
|------------------------|-----------------|----------------|---------------|
| Rabies* | Saliva, CNS | Fox, raccoons, bats | All mammals, dog*, cat*, sheep*, goat*, fox, dromedary*, horse* |
| Influenza* | Aerosols, feces (birds) | Water bird, ducks | Mammaliens, poultry*, houbara bustards*, falcons*, quail*, stone curlew*, pigeon* |
| MERS* | Nasal and eye discharge | - | Dromedaries |
| CCHF* | Blood, ticks, tissue | Rodents | Domestic ruminants (inapparent infection or mild fever and viremia) |
| RVF† | Blood, liver, spleen, midges, mosquitoes | Buffalo, spring buck | Lamb, goat, bovine calves, dromedary† |
| AHF* | Blood, feces, nasal discharge | Ticks | Sheep, dromedary, and others |
| SARS* | Respiratory droplets | Bats, palm civets | Ten mammalian laboratory species |
| Hantavirus | Rodent aerosols, excreta | Rodents, cats, foxes, coyotes | Rodents |
| WNV† | CNS, spinal cord, kidney | Birds, midges | Horse (end host)† |
| Marburg/Ebola | Reuse of unsterile needles and syringes | Green monkey | Human |
| Yellow fever | Mosquito | Monkey | Monkey, human |

* Disease diagnosed in Arabian Peninsula (for Influenza see also Table 2), †serological evidence in Arabia.

Disclosure. The author have no conflict of interests, and the work was not supported or funded by any drug company.
a hunting trip in Mongolia (Wernery U, personal communication, 2005) The virus affected most of the poultry population in Saudi Arabia. Tables 1 and 2 show the many other bird species that can be affected by influenza viruses. However, transmission does not pass easily between avian and humans, but transmission between human and other animal species has been shown, and pigs have been involved in interspecies transmission of influenza viruses, especially the spread of H1N1 to humans.

Table 2 shows in detail which influenza viruses were isolated in the UAE over the last decade from avians. The situation in other countries of the Arabian Peninsula is unknown. Furthermore, in 2009 and 2014, 49 strains of H1N1 were isolated from sick human patients in the United Arab Emirates (unpublished data).

Middle East respiratory syndrome caused by a novel CoV similar to SARS has emerged in 2012 and most human cases were diagnosed in Saudi Arabia. It is now confirmed that the virus can be transmitted by the dromedary (Camelus dromedarius) through nasal and eye secretions to humans. Studies from different Middle Eastern countries have also revealed that dromedaries were infected at high rates with MERS CoV a long time before notification of the first human cases. Dromedaries from USA, Europe, and Australia are free of antibodies against MERS CoV with the exception of some camels from the Canary Islands. It is still obscure if dromedaries act as an intermediate host or if other animal species like bats infected them. Sequence analysis have shown that a MERS CoV isolated from a dromedary was identical to an isolate from a human patient who died from the CoV infection after close contact with one of his camels, which displayed rhinitis.

Severe acute respiratory syndrome, which appeared first in southern China in 2002 and was contained in July 2003 after spreading to 29 countries worldwide was the first serious and readily transmissible disease to emerge in the twenty-first century. Masked palm civets (Paguma larvata) were the intermediate host responsible for passing the virus to humans, but horseshoe bat species (genus Rhinolophus) were the definitive host.

Crimean-Congo hemorrhagic fever (CCHF) is an acute disease of humans caused by a tick-borne virus widely distributed in Asia, Africa, and southern and eastern Europe. The infection is enzootic, but mainly asymptomatic in many animal species such as cattle, sheep, goats, camels as well as small mammals like hares. Thirty species of ticks, particularly the genus Hyalomma act as both reservoir and vector. Humans become infected by tick bites or through close contact with infected animals and humans. Hyalomma ticks were responsible for outbreaks in humans with high fatalities in the UAE, Oman, and Saudi Arabia.

Another viral hemorrhagic disease named Alkhurma hemorrhagic fever (AHF) has emerged in the Kingdom of Saudi Arabia in the mid 1990’s. Alkhurma hemorrhagic fever is a zoonotic disease and human clinical cases have been linked to mainly sheep and camels although the virus has not yet been isolated from livestock. However, AHFV and other arboviruses like Kadam and Quaranfil viruses have been isolated from the camel tick Hyalomma dromedarii in Saudi Arabia, Kuwait, and Yemen. It is important to mention that human movement not only facilitates the transmission of zoonotic diseases into the Arabian Peninsula, but also the introduction into other continents when pilgrims return back to their home countries.
Strikingly, all rift valley fever (RVF) epizootics described to date have followed unusually severe rainy seasons, probably indicating a very large insect population as a vector prerequisite. In 2000, the disease for the first time affected humans and livestock outside Africa, when it was diagnosed in the southern parts of Saudi Arabia\textsuperscript{15} and Yemen.\textsuperscript{16} It is believed that it was introduced into this part of the world by infected ruminants coming from East Africa via the port of Djibouti. For more than 70 years, RVF epidemics have occurred at prolonged intervals in Eastern and Southern Africa.\textsuperscript{5,17} The fatality in the RVF epidemic in southern Saudi Arabia in 2000 reached 14\%.\textsuperscript{18} It is quite obvious that globalization of trade and altered weather patterns are a concern for the future spread of RVF, as the causative agent, the RVF virus is capable of utilizing a wide range of mosquito vectors.

The West Nile virus (WNV) was first isolated in the West Nile district of Uganda in 1937 from the blood of a woman with mild febrile illness. Since then, WNV outbreaks have been reported all over the world. The disease reached the United States in 1999 and has now spread over the entire country as well as Central and South America, and the Caribbean. The genus \textit{Flavivirus}, to which WNV belongs comprises over 70 viruses, many of which may infect humans such as the yellow fever and dengue fever viruses. The genotyping of WNV has demonstrated 2 main lineages with several subtypes. Humans, horses, camelids, and many other mammalian species as well as reptiles and birds can be infected through mosquito bites. However, they are dead-end hosts because they do not produce enough virus particles in their blood to infect biting mosquitoes. The virus can be transmitted only by mosquitoes, which become infected when they take a blood meal from a bird carrying WNV. So far, human infections have been responsible for over 12,000 cases of meningitis and encephalitis and over 1,000 fatalities in the United States as well as several thousand equine fatalities. Antibodies against WNV were found in dromedaries\textsuperscript{19} and horses\textsuperscript{20} in the UAE, but the general situation of WNV on the Arabian Peninsula is unknown and should be more thoroughly investigated in the future.

**Bacterial diseases.** Table 3 shows 10 of the most important zoonotic bacterial diseases of which 9 were diagnosed on the Arabian Peninsula over the last years from samples of dead or diseased animals.

Through intensive health control measures, many industrialized countries have succeeded in eradicating brucellosis. In developing countries, however, brucellosis remains widespread in domesticated and wild animal populations and presents a great economic problem for tropical animal husbandry. In humans, the disease referred to as undulant fever or Malta fever is a very serious public health problem. Human brucellosis remains one of the most common zoonotic diseases worldwide with more than 500,000 new cases annually. Infection prevalence in animal reservoirs determines the incidence of human cases.\textsuperscript{21} \textit{Brucella} spp. are also potential agents of bioterrorism and are classified as a category B bioterrorism agent/disease (second highest priority agent) by the Centers for Disease Control and Prevention, USA. Despite being a notifiable disease in most countries, brucellosis is often unrecognized and unreported. \textit{Brucella melitensis} and \textit{Brucella abortus} are the 2 species most commonly found in human cases, and \textit{Brucella melitensis} is responsible for the most serious infection leading to orchitis and epididymitis.

| Bacteria causing disease | Pathogen source | Wildlife source | Host/reservoir |
|--------------------------|----------------|----------------|---------------|
| Brucellosis* | Milk, after birth, lymph nodes | Bison, elk, gazelles | Ruminants*, camels*, horse |
| Mycobacteriosis* | Aerosols | Badgers, White-tailed deer, gazelle | Ruminants*, camels* other mammals |
| Glanders* | Nasal discharge, lung choanae, skin ulcers | ? | Equids |
| Anthrax* | Animal blood, spores in soil | Mammals | Warm-blooded animals, camels* |
| Chlamydiosis* | Aerosols | Psittacine, falcon, pigeon, other birds | Mammals, sheep, goat*, avian* |
| Q-fever** | Aerosols, raw milk | Rats, pigeon | Livestock, cows, goat*, camels** |
| Salmonellosis* | Feces, blood, tissue | Pigeons, birds | Poultry*, mammalians* |
| Tularemia | Mosquito, ticks, aerosol, drinking water | Rodent, hare, rabbit | Sheep |
| Plague* | Ingestion of poorly cooked food | Rodents, rabbit, rats | Sheep, goat, cattle, camel*, horse, dog |
| Campylobacteriosis* | Chicken meat | Wild birds | Chicken*, cattle, sheep, camels |

\*Disease diagnosed in Arabia, **Serological evidence in Arabia
in men and fetal loss in pregnant women. Infections have been reported to occur in humans, dromedaries, small ruminants, and ruminating wildlife from the Arabian Peninsula. From all these cases different biovars of *Brucella melitensis* have been isolated (Figure 2).

Most human brucellosis cases on the Arabian Peninsula are caused by the consumption of unpasteurized milk. Brucellosis has been recently highlighted in Hajj pilgrims following camel milk consumption. The authors recommend that Hajj pilgrims should not consume unpasteurized dairy products. This recommendation should include all people who consume milk and milk products. In 2003 in Saudi Arabia alone 4534 human brucellosis cases were reported. Radwan et al who examined a large dromedary herd of 2536 animals in Saudi Arabia with a 12% abortion rate and an 8% seroprevalence, diagnosed Malta fever in 30% of camel handlers. *Brucella melitensis* biovars 1, 2, and 3 were isolated from aborted camel fetuses. A similar situation can be expected in other Gulf countries.

Tuberculosis caused by *Mycobacterium tuberculosis* (*M. tuberculosis*) remains one of the major global reportable diseases in humans and a rise in its incidents has caused the World Health Organization (WHO) to declare the disease a global emergency. Tuberculosis has caused more death in humans than all the wars together. Every year, 9 million new cases are reported and 1.7 million people succumb to tuberculosis annually. Many strains have become resistant to medication. However, of great concern is not only *M. tuberculosis*, but also bovine tuberculosis which is a relevant zoonosis that can spread to humans through inhalation of infectious droplets and by ingestion of raw milk. *Mycobacterium bovis* has been isolated from tuberculous granulomas of gazelles and dromedaries as well as domestic ruminants of the Arabian Peninsula (Figure 3).

Glanders is a contagious, life threatening disease of equids and is generally fatal. It is also a very serious zoonotic disease, but extremely rare in human. Human glanders is associated with extensive contact with equids. Susceptibility has been demonstrated in a wide variety of animal species including felines, bears, wolves, and dogs. Dromedaries are also susceptible to glanders as was recently demonstrated for the first time in the Bahrain outbreak. *Burkholderia mallei* is considered a potential biological weapon and is a Centers for Disease Control and Prevention (CDC) category B select agent. Glanders remains endemic in Asian, African, and South American countries, and emerged in the Middle East in 2004, as well as in Pakistan and Brazil in 2008 and 2009. For the first time, the disease was diagnosed in 3 Gulf Cooperative Council (GCC) states of the Arabian Peninsula, namely UAE (2004), Kuwait, and Bahrain.
in 2010 through illegal equine trading from countries such as Syria, Iraq, and Iran. In Bahrain, dromedaries became infected by close contact with positive horses (Figure 4). This was the first reported natural infection of glanders in dromedaries.

In previous centuries, *Yersinia pestis* produced pandemics that killed millions of people. It is said that the ‘Black Death’ killed 40 million Europeans before 1400 AD cutting Europe’s population by one third. At present, the plague is still endemic in many countries, such as those in Africa, India, Vietnam, and some parts of North and South America wherein the natural foci exist. New reports of a plague outbreak in humans caused by the consumption of camel meat, and raw camel liver emerged from different countries including Saudi Arabia. Pharyngeal plague in 4 patients with severe pharyngitis, submandibular lymphadenitis, chills, and malaise and vomiting was observed. All patients had consumed raw liver from a sick camel that was butchered. *Yersinia pestis* was cultured from the bone marrow of the sick camel and from jirds (*Meriones lybicus*), a small rodent as well as fleas (*Xenopsylla cheopis*) captured in the camel coral. The patients reported that several of their camels had died, most probably from plague.

Anthrax remains a threat to livestock in African and Asian countries where control depends on proper vaccination and disposal/decontamination of carcasses. In developed countries, the disease is rare. Animals contact Anthrax by ingesting spores, especially when the grazing animal bites off the pasture grass at ground level during periods of food scarcity. Inhaled contaminated dust can also lead to pulmonary anthrax. Humans become infected via contact with diseased animals or hides or as a consequence of bio terrorism, which was experienced in 2001. Rare cases have been diagnosed in the Arabian Peninsula in ruminating animals including dromedaries (Figure 5).

Q-fever, chlamydiosis, campylobacteriosis, and salmonellosis are zoonotic diseases, which have been diagnosed on the Arabian Peninsula either by antibody detection (Q-fever) in serum or milk or by detection of the pathogen. They do not play a significant role on the Arabian Peninsula.

Parasitic zoonoses. Table 4 shows the most important parasitic zoonoses of which only leishmaniasis and hydatid disease have an important zoonotic impact on the Arabian Peninsula.

Leishmaniasis is a protozoan disease ranging from America and Africa to southern Europe and Asia including the Arabian Peninsula. In many underdeveloped countries, leishmaniasis is a major public health problem but very much neglected. Thirteen of the 15 leishmania protozoa species have zoonotic potential producing the visceral, cutaneous, and mucocutaneous forms. Known vectors are all phlebotomine sand flies which have a wide geographical distribution. Mammal reservoirs are rodents, carnivores, marsupials, edentata, and hyracoidea. In the old world, leishmania is widely distributed in arid and savannah rodents. *Meriones libycus* is the host in the Arabian Peninsula and Central Asia. The viscerotropic strains of *Leishmania infantum* causes the zoonotic visceral leishmaniasis (ZVL). The parasites are transmitted by sand flies, which bite a wide range of warm-blooded animal species including man, and the dog acts as a main reservoir. Zoonotic cutaneous leishmaniasis (ZCL) is caused by *Leishmania major* and sylvatic rodents harbor the parasite. In Saudi Arabia in 2003, 9 visceral and 3466 cutaneous cases were reported.

Cystic echinococcosis or cystic hydatid disease is certainly one of the most wide spread and important
The parasite *Echinococcus granulosus* is found in a wide spectrum of intermediate hosts such as sheep, goats, camels, cattle, pigs and equids. Wild intermediate hosts like cervids (North America), marsupials (Australia), and wild herbivores (East and South Africa) are also known to exist. Canines including hyenas, jackal, and wolves serve as the most important definitive host for the transmission of this parasite. Humans are aberrant intermediate hosts and become accidentally infected by ingestion of the tapeworm eggs. The disease is endemic on the Arabian Peninsula. Typical hydatid cysts have been found in different organs of dromedaries (Figure 6) and small ruminants. Offals containing the cysts and abandoned carcasses may infect canines which start to excrete the infective eggs after a prepatent period of approximately 50 days. Human infections have been recorded in one year old children and in adults more than 80 years of age. The predilection sites of cysts are: liver (63%), lung (25%), muscles (5%), bones (3%), kidney (2%), spleen and brain (1%). However, exact data on the prevalence of this disease in humans is not available although in many countries it is a notifiable disease.

### Conclusion and recommendations.

Numerous zoonotic diseases cause morbidity, mortality, and productivity losses not only in humans, but also in livestock and wildlife populations all over the world including the Arabian Peninsula. These diseases may have large social impacts in endemic areas. Several of these zoonotic diseases have been introduced from other countries into the Arabian Peninsula due to lack of stringent import regulations or lack of implementing them. Typical recent examples are outbreaks of RVF, CCHF, avian influenza, and glanders into the Arabian Peninsula. Mycobacteriosis and brucellosis as well as leishmaniasis are further examples of this situation. Uncontrolled trade of live dromedaries for example from East African countries where a seroprevalence of brucellosis may reach 40% contribute to a rise of zoonotic diseases in the imported countries. Not only zoonotic diseases have been introduced from Africa and Asia into the Arabian Peninsula, but also other diseases such as foot-and-mouth with severe consequences for the livestock industry. Serotypes completely unknown to this region were recently introduced most probably from Egypt.

Therefore, there is an urgent need for interdisciplinary collaboration between health, agricultural, and environmental ministries of all countries of the Arabian Peninsula to avoid the emergence and re-emergence of zoonotic diseases in their territories.

One important step is the establishment of a rapid information system between the responsible ministries of each country as well as the establishment of highly efficient quarantine and veterinary laboratory facilities in each of the GCC countries. The Mediterranean and Middle East Region are known as an important area for concentration of zoonoses; therefore, the WHO has established in 1979 a Mediterranean Zoonoses Control Center operating from Athens, Greece. This zoonotic control center should be widened in the future and include at least all countries of the Arabian Peninsula.

The growth of the human population and the demand for animal protein is constantly rising. Zoonoses are therefore going to continue to be major threats to sustainable development. Veterinary and medical scientists must cooperate and work together across traditional boundaries and share information on the disease outbreaks. This is currently not the case on the Arabian Peninsula. It would include national as well as international surveillance schemes to rapidly detect disease outbreaks and would also detect changes in trend or distribution in order to initiate preventive and control measures.
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