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EDITORIAL

Epidemic infections and their relevance to the Gulf and other Arabian Peninsula countries

Euan M. Scrimgeour

ألإلتهابات الوبائية وأهميتها لدول الخليج وشبه الجزيرة العربية

إيوان سكريمجر

The strategic location of the Arabian Peninsula between Africa, Asia and Europe, has since early historical times drawn travellers, seafarers, and merchants to this part of the Middle East. It is inevitable that importation of communicable diseases should be a feature of such population movements. In Saudi Arabia, this has been demonstrated repeatedly over past decades, with epidemics occurring during the annual *Hajj*, when over a million pilgrims from more than 80 countries congregate together with a similar number of local worshippers for a week in Mecca and Medina. Plague used to break out almost every year until 1918,[1] and other frequent outbreaks have included smallpox,[2] cholera,[3] and meningococcal infection.[3,4] The latter has continued to pose a problem despite the use of bivalent (A,C) vaccination for intending pilgrims, and two recent meningococcal outbreaks in 2000 and 2001 caused by new serogroups required planning to introduce quadrivalent (A,C,Y, W135) vaccination in the future.[5]

All Arabian Peninsula countries have been subject to outbreaks of introduced communicable diseases caused by various micro-organisms, although these have not always been so well documented as the Saudi epidemics.

Parasitic infections have not posed a significant threat in recent decades except perhaps, falciparum malaria. It likely that malaria was introduced to the western region of Saudi Arabia and the United Arab Emirates in the very remote past since a large proportion of inhabitants of oases have one or more red cell markers which confer resistance, e.g., thalassaemia or the sickle cell trait.[3] Suitable *Anopheles* mosquito vectors are present in all countries in the region. Although effective malaria-control programmes have been implemented in most countries in the region, the emergence of chloroquine-resistant falciparum malaria contracted overseas has created a new concern, and this has been noted in Saudi Arabia,[3] Kuwait,[6] Oman,[7] and the United Arab Emirates.[8]

Leishmaniasis occurs widely in the Middle East. The cutaneous form causes minor morbidity in a relatively immune population, but the occasional complication of systemic infection, especially in the non-immune, became significant during Operation Desert Storm when eight American servicemen stationed in the Eastern Province of Saudi Arabia developed visceral leishmaniasis after *Leishmania tropica* infection.[9] The usual species causing visceral leishmaniasis or kala azar in the Middle East is *L. infantum*. (This is the probable cause of kala azar in Oman.[10]) As a result of exposure of overseas troops to sandfly vectors of leishmaniasis during the recent war in Iraq, thousands of potential blood donors among the American troops were excluded as future donors.

It is probable that schistosomiasis mansoni and haematobium which are widely prevalent in the Middle East, were introduced from the Nile Valley of Egypt in prehistoric times to Saudi Arabia, Yemen and probably Oman.[11] Snail vector control programmes in most countries have limited transmission, but the need to implement vector control indefinitely was demonstrated recently in Dhofar province in Oman, when suspension of regular molluscicide resulted in a new epidemic of schistosomiasis mansoni.[12]

Bacterial infections of potential epidemic significance to the Arabian Peninsula other than meningococcus infection, are few. Small outbreaks of typhoid fever are not infrequent, but do not pose a major community threat. Cholera has been introduced sporadically, e.g. by illegal immigrants from Pakistan and Afghanistan in Oman in 2000, and occasionally in other countries. In

Department of Medicine, College of Medicine and Health Sciences, Sultan Qaboos University, PO Box 35, Al-Khod-123, Sultanate of Oman. Email: scrim@squ.edu.om

the Iraqi war, the breakdown in communicable disease control programmes led to epidemic cholera affecting 94 patients.[13] There has been one documented outbreak of plague which spread from affected rodents on the Saudi Arabian-Yemen border in 1969 with 10 deaths.[14] Anthrax is rare in the region,[3] but its use as a possible biological weapon has lately received notorious publicity. A second agent with potential as a biological weapon is the rickettsial infection Q fever, caused by *Coxiella burnetii*. This would have limited impact in the Middle East where it is widely endemic, and there is widespread immunity, such as in Saudi Arabia[3] and in Oman.[15]

Viruses are currently the most likely source of significant epidemic infections in the Arabian Peninsula. The era of air travel has increased the opportunities for introduction of viral infections with short incubation periods from distant locations. Among these, viral haemorrhagic fevers (VHF) are regarded as one of the most serious risks. Many of these are arbovirus infections (spread by arthropod vectors). There is always the possibility of importing Ebola and Marburg disease (caused by *Filoviridae* viruses) from Africa, Lassa virus (an arenavirus) from West Africa, or Kyasanur Forest disease (caused by a flavivirus) from India, but fortunately, these have never been reported. Sources of infection of VHFs include rodent urine (Lassa fever), Hantaan virus disease (caused by a hantavirus, a genus of the *Bunyaviridae* which is widely prevalent in neighbouring regions), vector ticks (Kyasanur Forest disease and Crimean-Congo haemorrhagic fever (which is caused by a Nairovirus), possibly monkeys, (Ebola) or aerosol spread (Ebola, Marburg disease, Lassa fever, Crimean Congo haemorrhagic fever). Accordingly all major hospitals in the region should have an admission policy for suspected VHF.[16]

Crimean Congo haemorrhagic fever is widely prevalent in the Middle East wherever suitable vector idoxid (hard) ticks (especially *Hyalomma* spp.) are present. The disease can also be spread from contact with blood or meat from an infected animal, or by aerosol. It was almost certainly already indigenous to the Western Province of Saudi Arabia,[17] when over a decade ago, there was evidence of new introduction through Jeddah seaport by imported small Sudanese ruminants.[18] Similarly, because the vector ticks for CCHF were already indigenous to Oman,[19] and no doubt also present in the United Arab Emirates, the first diagnoses of disease in a man in Buraimi, northern Oman, and at the same time in a patient in Muscat, merely confirmed that the disease was present.[20] Luckily epidemiological studies elsewhere have shown that even when this zoonosis is prevalent in a country, human cases are infrequent and sporadic. Alkhurma virus (family *Flaviviridae*, genus Flavivirus) is another emerging VHF in the Middle East. It was reported to have caused haemorrhagic fever in Saudi patients in 1995,[21] infection being contracted from viraemic vertebrates by tick bite, parenteral exposure to their blood, or drinking unpasteurised milk.

Other VHFs include the arbovirus infections yellow fever and dengue fever which cannot be spread directly from person to person but require a mosquito vector. Arbovirus infections occupy a special category of communicable disease epidemiology. The majority are zoonoses which immediately poses a problem in control. When suitable vectors such as mosquitoes or ticks are already present in a region, there is always the risk of importation of a new virus infection. Although dengue fever (which is strictly anthroponotic) had never occurred in Saudi Arabia, the presence of indigenous *Aedes aegypti* mosquitoes in Jeddah allowed dengue type 2 to become established in 1994. (The first patient, a Saudi, who died from dengue haemorrhagic fever, was under the care of the author). It was suspected that a viraemic Indonesian visitor to Jeddah had infected local mosquitoes which then infected the Saudi population. It proved to be impossible to eliminate the vector mosquitoes, and surveillance thereafter showed that two other serotypes, 1 and 3 had become established in the community.[22] Fortunately, Oman has so far escaped an epidemic of dengue fever despite its diagnosis in several patients who had visited India, possibly because the *Aedes* spp. in northern Oman is not a suitable vector. It is only in Dhofar that *A. aegypti* is present (D. Roberts, personal communication).

Rift Valley fever, another arbovirus infection, has become of concern to the Arabian Peninsula. The responsible virus is a member of the Phlebovirus genus, one of the five genera of *Bunyaviridae.* Its first detection on the Arabian Peninsula was southern Saudi Arabia and Yemen in September, 2000. Genetic analysis supported the belief that this zoonosis originated in East Africa and was probably imported to Saudi Arabia and/or Yemen in livestock.[23] The natural hosts include birds and animals including cattle, sheep, goats and camels, and the vectors include *A. aegypti* and other mosquitoes including *Anopheles* and *Culex*, as well as ticks. Transovarian virus infection results in the new generation of infected arthopods, perpetuating infection in the community. Infected mosquito eggs may survive several years in dry conditions. The disease causes haemorrhagic fever and necrotising retinitis with blindness, in a small percentage of patients. In livestock, it causes

abortions and mortality among young animals. In Saudi Arabia, a total of 884 hospitalized cases occurred with 124 deaths, whereas in Yemen, it was estimated that 1,087 cases occurred with 121 deaths.[23] A major control programme in Saudi Arabia and Yemen, was implemented with advice from international experts from WHO, the United States Naval Medical Research Unit (NAMRU-2) based in Egypt, experts form Oman, and the Food and Agriculture Organisation. Measures included limiting population movements in affected areas, wholesale slaughtering of potentially infected livestock, and control of arthropod vectors, and a limited vaccination programme. (An animal vaccine is routinely used to protect susceptible livestock, but supplies of an experimental inactivated vaccine for man are not commercially available.) The measures.appear to have been successful in localising the infection and preventing its spread elsewhere in the Peninsula. At the time of writing (October 2003), cases have not been reported in Oman.

West Nile virus a Flavivirus spread from birds by *Culex* mosquitoes to man, horses, and other mammals, occurs in the Nile Valley and around the Mediterranean basin. It may well have been indigenous to the Arabian Peninsula as well, although it had never been detected here The virus has shown an ability to spread and become established wherever suitable mosquito vectors are present e.g. it became widespread in the USA following its accidental introduction to New York in 1999. It was first reported in Israel several years ago, and appeared to have been spread from geese and migrating storks.[24] It has also been of concern in Lebanon and Jordan[25,26] and poses a definite risk to Gulf countries including Oman. The virus has become more neuropathic in recent years with a higher rate of encephalitis.

Viruses other than arboviruses pose a threat of epidemic infection in the Arabian Peninsula. Outbreaks of human-strain influenza A in Jeddah regularly follow the *Hajj*, presumably having been introduced by pilgrims.[3] Avian influenza is an important source of epidemic influenza in man. It is believed that the 1918 pandemic of Spanish influenza,[27] and certain that the last three pandemic strains of influenza A virus-Asian/57, Hong Kong/68, and Russian/77, which originated in China, arose from interspecies transmission of viruses, from avian and other sources.[28] Reassortment of human and avian virus genes in a permissive host e.g. the pig has been proposed as an amplifying source of virus.[29] Genetic analysis of avian influenza viruses allows tracking of subtypes which may be associated with human infection.

Severe acute respiratory syndrome (SARS), a newly identified epidemic disease, appeared for the first time in February, 2003 in Hanoi, Vietnam. The causal virus was later identified as a previously unrecognized species from the coronavirus family.[30] (Coronaviruses cause about one third of common colds.) The new virus spread locally and cases were confirmed in Canada, China, Hong Kong, Singapore and Taiwan. The source of the virus was unknown, but later, it was reported to be similar to a coronavirus in civet cats (popular as food in South China). It became apparent that person-to-person spread was responsible for its rapid dissemination and a number of health workers contracted the disease, with fatalities in some cases. In Oman, as in other Arabian Peninsula countries, the Ministry of Health implemented a comprehensive, extensive (and expensive) public health project to prevent introduction of SARS. Similar preventative measures were in force in other Gulf countries. A large team of health personnel was at hand with 24 hour airport surveillance of visitors who may have been in contact with the infection, to evaluate and treat suspected cases. After many weeks of surveillance, the epidemic waned in the Far East, and as no cases were encountered in Oman, the project was concluded.

There are other conditions apart from those mentioned, which could cause epidemic disease in the Arabian Peninsula. The bovine spongiform encephalopathy (BSE) epidemic in the United Kingdom, caused by a variant prion (an infectious amyloid protein) derived from the scrapie prion (which causes spongiform encephalopathy in sheep), and its passage into the food chain, resulted in the emergence of variant Creutzfeldt-Jakob disease (v-CJD). In 1990s BSE was identified in Oman in two cattle imported from the UK.[31] The report that sporadic, endemic CJD occurred in Oman[32] gave further impetus to the decision to ban the importation of British beef into Oman. Similar bans were imposed in other Gulf counries. Surveillance for possible cases of v-CJD in Omanis continues, but until now, no case has been diagnosed. Nevertheless, prior to the ban, beef imports both fresh, frozen, and canned, may have been infected in some cases, and v-CJD may yet appear in Oman and perhaps other Gulf countries. This disease has an incubation period of several years, possibly decades. The evidence to date indicates that a major epidemic is unlikely, but the median incubation period has not yet been ascertained.

The evidence suggests all countries of the Arabian Peninsula will have to remain constantly vigilant to the importation of recognised as well as new epidemic infectious diseases in the future. Most of these countries have a well-established public health programme

of surveillance of diseases, and an effective system of preventing introduction of infections. The ministries of health and veterinary services within the Gulf and neighbouring countries can collaborate to mutual advantage, sharing expertise in this field where many infections are zoonotic.

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