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Influence of climate change on the incidence and impact of arenavirus diseases: a speculative assessment

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Abstract

The current worldwide incidence of viral haemorrhagic fevers caused by arenaviruses is briefly reviewed. The recently published Assessment Report of the Intergovernmental Panel on Climate Change has described the changes in global climate that are expected to occur over the course of the present century and beyond. Climate modelling and forecasting have not yet reached the stage where confident predictions of regional changes at the level of a virus endemic area can be made. However, in the regions where pathogenic arenaviruses now circulate, significant effects are likely to include increases in surface temperature, changes in the extent and distribution of rainfall, the occurrence of extreme weather events, glacier retreat, and coastal flooding as a result of sea level rise. The possible impact of these changes on the geographical location and the incidence of arenavirus diseases and its human impact are discussed.

Keywords: Arenavirus, climate change, global warming, haemorrhagic fever, viral disease
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Introduction

The *Arenaviridae* [1] are a family of 22 enveloped viruses with bisegmented RNA genomes of approximately 10 kb in total length. Each of these RNA segments encodes two viral proteins in an ambisense arrangement. Their principal hosts are members of the mammalian Order *Rodentia*. In terms of human health, they constitute an important family because six of these viruses infect humans and can cause serious and frequently fatal haemorrhagic fevers. With the exception of the type species *Lymphocytic choriomeningitis* virus, which is widely distributed in Europe, Asia and the Americas, each individual arenavirus species is found in a relatively localized area in Africa or in North or South America. The purposes of this review are to outline the general features of the arenaviruses and to consider how currently predicted global climate changes might change the geographic distribution and human impact of these dangerous viral pathogens during the 21st century.

Natural History of Arenaviruses

The arenaviruses are principally viruses of rodents of the family *Muridae*. Each virus is associated primarily with a single rodent species (the reservoir species), although, in several cases, infected animals of another species have been detected from time to time. Viruses are spread among populations through excretion in body fluids, and vertical transmission from mother to offspring also contributes to maintaining infection. Although we have insufficient knowledge of the details of the dynamics of virus–host interactions, the infected rodents show little or no overt disease, and their fitness does not appear to be impaired to any significant extent. It is currently thought that the arenavirus–rodent host associations observed today are the result of the co-evolution of parasites and hosts. It has been a longstanding observation that the geographical range of a host rodent is usually more extensive than that of its associated arenavirus. However, it is likely that such apparent discrepancies may be clarified by molecular approaches to host rodent taxonomy [2,3].

Some members of the arenavirus family are important causes of viral haemorrhagic fevers when humans become infected. These include *Lassa*, *Junín*, *Guanarito* and *Machupo viruses*, which have caused quite large outbreaks, and *Sabiá* and *Chapare viruses*, which are known to have caused disease in a few cases (including laboratory workers). The geographical locations where these viruses have been found are shown in Fig. 1. The haemorrhagic fevers caused by these

FIG. 1. Geographical locations of arenaviruses associated with human haemorrhagic fevers. Map provided by NASA Visible Earth (http://visibleearth.nasa.gov/).

viruses are similar to each other, usually presenting as a non-specific illness, with symptoms including fever, headache, dizziness, asthenia, sore throat, pharyngitis, cough, retrosternal and abdominal pain, and vomiting. In severe cases, facial oedema, haemorrhagic conjunctivitis, moderate bleeding (from nose, gums, vagina, etc.) and exanthema frequently occur. Neurological signs may develop and progress to confusion, convulsion, coma and death. Case fatality rates are in the 5–20% range for hospitalized cases. By contrast, the type species lymphocytic choriomeningitis virus causes aseptic meningitis or meningoencephalitis with an overall case fatality of <1%, but it has also been associated with haemorrhagic fever-like infections in organ transplant recipients [4].

Lassa fever was first recognized in the 1960s and the causative arenavirus was isolated in 1969. It is now known to be present in large areas of both savannah and forest zones of sub-Saharan west Africa. The principal foci are in the west in the border regions of Guinea, Sierra Leone and Liberia, and in the east in Nigeria. The rodent host of Lassa virus is the multimammate rat *Mastomys natalensis*. This often-quoted relationship was recently confirmed, most elegantly, by simultaneous sequence analysis of both the infecting virus and the infected rodent, in Guinea [3]. Lassa virus was found only in *M. natalensis*, and not in another *Mastomys* species, nor in 12 other rodent genera. *Mastomys natalensis* is a peri-domestic rodent that infests houses and foodstores. Infection of humans can occur in the process of catching and preparing the animals for food, as well as by contact with animal excreta or contaminated materials. Another arenavirus, similar to, but not identical with, Lassa virus has recently caused fatal human infections in South Africa [5].

The arenavirus Junín is the causative agent of Argentine haemorrhagic fever, first described in 1955. When first encountered, human cases were limited to an area of 16 000 km^2 in the humid pampas in the north of Buenos Aires province. However, the endemo-epidemic area now extends to over 150 000 km^2, reaching north of Buenos Aires, south of Santa Fe, southeast of Cordoba, and north-east of La Pampa provinces. The human population at risk is estimated to be approximately 5 million. The virus is carried mainly by the vesper mouse *Callomys musculinus*, but other rodents (*Callomys laucha* and *Akodon azarae*) have also been implicated. These rodents mainly infest maize crops, and most human infections are observed in agricultural workers.

Venezuelan haemorrhagic fever is caused by Guanarito virus, which is carried by the cane mouse *Zygodontomys brevicauda*. Those individuals who are most affected are male agricultural workers around the town of Guanarito in Portuguesa State and adjacent parts of Barinas State in Venezuela. The virus was discovered in 1989 and the disease incidence has exhibited cyclical behaviour with a period of 4–5 years.

Machupo virus is the cause of Bolivian haemorrhagic fever, which was first recognized in 1959 in the remote, sparsely populated savannah of Beni state, Bolivia. Ecological studies indicate that the rodent *Callomys callosus* is the principal animal reservoir. Agricultural workers comprise those individuals who are most at risk, especially in fields and houses to which rodents have easy access. There were several local outbreaks of the disease in the 1960s, but the incidence fell markedly in the next decade subsequent to the initiation of rodent control measures.

A small outbreak of viral haemorrhagic disease occurred in 2003–2004 in Cochabamba, Bolivia, as a result of an arenavirus that was distinct from Machupo virus, the causative agent of the previously recognized Bolivian haemorrhagic fever. It was named Chapare virus. As yet, there is no information available about the extent of the public health threat from this virus, nor is there any information concerning the identity of its normal rodent host species.

A single case of haemorrhagic fever caused naturally by the arenavirus Sabiá has been described. It occurred in Sabiá village, near São Paulo, Brazil. No natural rodent host has been identified. Two laboratory infections due to the virus have also occurred.

It is evident that arenavirus-caused disease in humans is an accidental product of their encounters with infected rodents and their excreta and body fluids. Infection of humans can occur through contact with rodent excreta or materials contaminated with them, or via ingestion of contaminated food. Direct contact of broken or abraded skin with rodent excreta is likely to be an important route, and inhalation of small droplets or particles containing rodent urine or saliva is also considered to be a significant mode of infection. The nature of these incidental contacts depends on the living patterns and habits of both the rodent carriers and the human population. Where infected rodents prefer a field habitat, infection is primarily associated with agricultural workers. Where the rodents infest dwellings and other buildings, infection occurs in a domestic setting.

Predicted Climate Changes

This discussion is based on the findings of the Fourth Assessment Report of the Intergovernmental Panel on Climate Change (IPCC), which appeared in 2007. It is now considered to be virtually certain that anthropogenic greenhouse gas (GHG) emission is forcing global warming at a rate quite without precedent in the Earth's climate history [6]. The current rate of warming of approximately 0.2 °C per decade is projected to continue until *c.* 2030, irrespective of whether current greenhouse gas emissions continue at their present rate or whether reductions can be achieved. This implies that mean surface temperatures in the period 2011–2030 will be approximately 0.66 °C higher than in the period 1980–1999. Further into the future, there is greater uncertainty because of increasing differences among the various scenarios modelled. These scenarios cover a range of possibilities for the mitigation of (or lack of) greenhouse gas emissions. For a number of plausible scenarios, the best estimates of the IPCC with respect to the increase in global mean surface temperature for the period 2090–2099 relative to the period 1980–1999 are in the range of 1.8–4.0 °C. Surface temperature increases on land are predicted to be approximately twice this global mean (i.e. in the range of 3.6–8 °C by the end of this century). On the global scale, it is predicted that there will be more frequent and more extreme heat waves, fewer cold periods, and increased and more intense rainfall in regional tropical precipitation maxima. In sub-tropical and mid-latitudes, precipitation will decrease, although intense rainfall events interspersed with long periods of drought will become more common. Sea levels will rise by approximately 0.5 m by the end of the century. Disturbingly, a more recent scientific and economic assessments of the present emission rates and progress in moving towards their reduction indicates that it is increasingly unlikely that any prospective global agreement can stabilize atmospheric GHGs at 450 p.p.m. or even at 650 p.p.m. CO_2 equivalent [7–11]. Hence, the scenarios proposed by the IPCC are very likely to significantly underestimate the degree of climate change in the future.

For the purpose of this review, two principal geographical regions need to be considered. These are the locations where Lassa fever is currently endemic (i.e. sub-Saharan west Africa) and the broader region where South American haemorrhagic fevers are found (i.e. South America). Unfortunately, there are major difficulties in moving from global-scale climate change predictions towards more detailed descriptions of future outcomes at a regional level. These are particularly acute in west Africa because of the relatively sparse data that exist with respect to past and current weather conditions, the complex nature of the terrain and the influence of ocean basins. It is predicted [12] that Africa as a whole will warm more than the global annual mean throughout the year. Drier regions will warm more than the moister tropics. Changes in rainfall in the Sahel, on the Guinean coast and in the southern Sahara in this century remain very difficult to predict because of shortcomings in the current models, which result in systematic errors, disagreements among different climate models and an inability to simulate correctly 20th century conditions. Key features such as the frequency and spatial distribution of tropical cyclones affecting Africa cannot be reliably assessed. Nonetheless, the frequency of extremely wet seasons is likely to rise markedly, as is also the case in east Africa. The west African coast and the Gulf of Guinea are considered to be at high risk of flooding as a result of a rise in sea levels [13].

In South America, the increase in annual surface temperature will be similar to the global mean [12]. This represents an increase in the range of 3–4 °C by the end of the century. Systematic differences among different models, together with large variations in predictions of changes in the amplitude of El Niño, as well as in the height and sharpness of the Andes mountains, make assessments on a regional scale over much of Central and South America very unreliable. Rainfall changes show that regional differences are likely to occur;

most models suggest a wetter climate around the Rio de la Plata but reduced precipitation in parts of northern South America. Extremes of weather and climate are likely to occur more frequently. Water stress will increase as a result of glacier retreat or disappearance in the Andes, leading to highly adverse effects on agriculture.

Arenaviral Diseases and Climate Change

The main factors that can affect the burden of infectious diseases in humans are (i) changes in abundance, virulence or transmissibility of infectious agents, (ii) an increase in probability of exposure of humans and (iii) an increase in the susceptibility of humans to infection and to the consequences of infection. A wide range of biological, physicochemical, behavioural and social drivers can influence one or more of these factors [14]. In particular, alterations in the environment, brought about by currently predicted climate changes, clearly have the potential to affect, to a greater or lesser extent, all three of these factors. We need to consider the possible effects of climate changes within the currently known endemic areas of each arenavirus disease, and also the extent to which such changes may influence the transfer and persistence of arenavirus diseases to hitherto unaffected regions. However, it must be appreciated that the reliability of any such predictions is quite low, not only because of the relatively coarse scale of the available climate change predictions, but also because of our lack of reliable data on the current incidence of these diseases. This applies particularly to the prevalence of Lassa fever and other possible arenavirus diseases in Africa.

When we examine how these factors could affect arenavirus-caused disease, all three are likely to exert significant influence. In the first category, there are likely to be changes in the abundance of arenaviruses, in the sense that the reservoir host rodent populations are likely to be affected one way or another by changes in climate. Thus, prolonged drought in a particular region may lead to a reduction in population size, whereas increased seasonal rain may lead to a population explosion. Such events have been observed for other rodent-borne zoonoses, as documented in the IPCC Report [15]. In the case of another rodent-borne virus disease, hantavirus pulmonary syndrome (HPS), there is evidence that El Niño Southern Oscillation-induced increases in rainfall in the Four Corners region of the south-western USA led to increases in the population of the rodent reservoir *Peromyscus maniculatus* and the subsequent emergence of the disease in the human population [16]. There may be a similar explanation for the emergence of HPS in Panama in 2000, subsequent to increases in the peri-domestic rodent population after heavy rainfall and flooding in the surrounding areas [17].

In west Africa, a recent detailed study [18] of the distribution of human Lassa fever outbreaks and cases in the period 1951–1989 revealed that areas of medium risk had an annual rainfall in the range of 1200–1500 mm, whereas rainfall in the range of 1500–3000 mm was associated with a high risk of disease. Regions with <1200 mm (or more than 3000 mm) of rainfall had no recorded occurrence of Lassa fever. Rainfall thus appears to be a major risk factor in the incidence of Lassa fever. These data also clearly imply that modifications in precipitation quantity and geographical distribution brought about by climate change are very likely to lead to concomitant changes in the burden and geographical distribution of Lassa fever. In Venezuela, Bolivia and Argentina, climate change may lead to changes in agricultural land use, with relocalization of crop-growing areas that are becoming unsuitable for agricultural use to others with more favourable climates. Where arenaviral diseases are carried by rodents infesting crops, as is the case with Venezuelan, Bolivian and Argentine haemorrhagic fevers, there will be corresponding changes in the geographical location of rodents and thus disease.

It is unlikely that changes in virus virulence will result directly from climatic changes, although it is conceivable that virus transmissibility could be influenced. Arenaviruses are enveloped viruses that are not particularly robust when exposed to high temperatures or low humidity. Thus, some climatic factors may be expected to influence the survival of the viruses in the environment, either negatively or positively. This kind of effect may underlie the dependence of Lassa fever distribution in west Africa on rainfall, as noted above [18].

It is very likely that, in some environments, climate change will increase the probability of human exposure to arenavirus infections, whereas, in others, it will decrease the probability. Such effects are likely to be mediated through changes in the probability of encounters with reservoir rodents and contact with their excreta or contaminated materials. We can envisage the direct effects of climate on the size and behaviour of virus-carrying rodent populations, as discussed above, as well as on the human populations themselves, through changing land use (e.g. irrigation) triggered by increasing temperatures, fluctuating weather conditions and the resultant disturbance of local landscapes. Climate change is likely to lead to mass migration and movement of populations, with consequent stresses associated with inadequate shelter and overcrowding. Such considerations are likely to be more significant with respect to Lassa fever compared with the South American arenaviral haemorrhagic fevers as a result of the much larger human population in the endemic areas. As well as possible changes in areas favourable for food production, flooding along the west African coast as a result of storm surges and a rise in sea levels could drive large-scale population movements in the area. It has been projected that the 500 km of coast between Accra and the Niger delta will be a continuous urban megalopolis of some 50 million people by 2020 [13,19]. It has already been demonstrated that Lassa fever can be a significant risk in refugee camps in Guinea [20,21]. There is an increased risk in areas where there are higher numbers of infected rodents [21], as well as in areas with poor-quality housing and in households with reduced levels of hygiene [20]. Thus, populations driven onto higher ground by coastal flooding may be at increased risk of Lassa fever (among other diseases) unless sufficiently adequate housing and rodent control measures can be provided. It should be noted that rodent control is the key measure in any programme to mitigate arenavirus disease in humans. However, authorities in the Lassa fever endemic regions, which include some of the most under-developed countries in the world, do not have an impressive track record with respect to mounting effective healthcare or disease prevention programmes.

Finally, it is possible that predicted climate change may lead to the more frequent transfer of arenavirus-infected patients to regions of the world without any experience of these diseases. Although natural rodent vectors almost certainly will be absent, it is important that infected individuals are swiftly recognized and diagnosed so that further transmission during patient care can be avoided. This can readily be achieved through careful barrier nursing techniques, although the fear engendered by viral haemorrhagic fevers, including those caused by arenaviruses, can place a heavy burden on hospital systems. It would be prudent if such considerations were included in healthcare planning to meet the challenges of global climate change.

Transparency Declaration

The author has no financial interests or connections related to the matters discussed in this review.

References

1. Salvato MS, Clegg JCS, Buchmeier MJ *et al.* Arenaviridae. In: Fauquet CM, Mayo MA, Maniloff J, Desselberger U, Ball LA, eds, *Virus taxonomy, VIIIth report of the ICTV*. London: Elsevier/Academic Press, 2004; 725–733.
2. Salazar-Bravo J, Dragoo JW, Bowen MD, Peters CJ, Ksiazek TG, Yates TL. Natural nidality in Bolivian hemorrhagic fever and the systematics of the reservoir species. *Infect Genet Evol* 2002; 1: 191–199.
3. Lecompte E, Fichet-Calvet E, Daffis S *et al. Mastomys natalensis* and Lassa fever, west Africa. *Emerg Infect Dis* 2006; 12: 1971–1974.
4. Fischer SA, Graham MB, Kuehnert MJ *et al*; LCMV in Transplant Recipients Investigation Team Transmission of lymphocytic choriomeningitis virus by organ transplantation. *N Engl J Med* 2006; 354: 2235–2249.
5. Zeller H, Leitmeyer K, Varela Santos C, Coulombier D. Unknown disease in South Africa identified as arenavirus infection. *Euro Surveill* 2008; 13: pii: 19008. Available at: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19008.
6. Meehl GA, Stocker TF, Collins WD *et al.* Global climate projections. In: Solomon S, Qin D, Manning M, Chen Z, Marquis M, Averyt KB, Tignor M, Miller HL, eds, *Climate change 2007: the physical science basis*. Contribution of Working Group I to the Fourth Assessment Report of the Intergovernmental Panel on Climate Change. Cambridge, UK, and New York, NY: Cambridge University Press, 2007: 747–845. Available at: http://www.ipcc.ch/pdf/assessment-report/ar4/wg1/ar4-wg1-chapter10.pdf.
7. Anderson K, Bows A. Reframing the climate change challenge in light of post-2000 emission trends. *Phil Trans Roy Soc A* 2008; 366: 3863–3882.
8. Anderson K, Bows A, Mander S. From long-term targets to cumulative emission pathways: reframing UK climate policy. *Energy Policy* 2008; 36: 3714–3722.
9. Clark PU, Weaver AJ, Brook E, Cook ER, Delworth TL, Steffen K. *Abrupt climate change*. A report by the US Climate Change Science Program and the Subcommittee on Global Change Research. Reston, VA: US Geological Survey, 2008. Available at: http://www.climatescience.gov/Library/sap/sap3-4/final-report/default.htm#finalreport.
10. Garnaut R, Howes S, Jotzo F, Sheehan P. Emissions in the Platinum Age: the implications of rapid development for climate-change mitigation. *Oxford Rev Econ Policy* 2008; 24: 377–401.
11. Hansen J, Sato M, Kharecha P *et al.* Target atmospheric CO_2: where should humanity aim? *Open Atmos Sci J* 2008; 2: 217–231.
12. Christensen JH, Hewitson B, Busuioc A *et al.* Regional climate projections. In: Solomon S, Qin D, Manning M, Chen Z, Marquis M, Averyt KB, Tignor M, Miller HL, eds, *Climate change 2007: the physical science basis*. Contribution of Working Group I to the Fourth Assessment Report of the Intergovernmental Panel on Climate Change. Cambridge, UK, and New York, NY: Cambridge University Press, 2007: 848–940. Available at: http://www.ipcc.ch/pdf/assessment-report/ar4/wg1/ar4-wg1-chapter11.pdf.
13. Boko M, Niang I, Nyong A *et al.* Africa. In: Parry ML, Canziani OF, Palutikof JP, van der Linden PJ, Hanson CE, eds, *Climate change 2007: impacts, adaptation and vulnerability*. Contribution of Working Group II to the Fourth Assessment Report of the Intergovernmental Panel on Climate Change. Cambridge, UK, and New York, NY: Cambridge University Press, 2007: 433–467. Available at: http://www.ipcc.ch/pdf/assessment-report/ar4/wg2/ar4-wg2-chapter9.pdf.
14. Wilson ME. Infectious diseases: an ecological perspective. *BMJ* 1995; 311: 1681–1684.
15. Confalonieri U, Menne B, Akhtar R *et al.* Human health. In: Parry ML, Canziani OF, Palutikof JP, van der Linden PJ, Hanson CE, eds, *Climate change 2007: impacts, adaptation and vulnerability*. Contribution of Working Group II to the Fourth Assessment Report of the Intergovernmental Panel on Climate Change. Cambridge, UK, and New York, NY: Cambridge University Press, 2007; 391–431. Available at: http://www.ipcc.ch/pdf/assessment-report/ar4/wg2/ar4-wg2-chapter8.pdf.
16. Glass GE, Yates TL, Fine JB *et al.* Satellite imagery characterizes local animal reservoir populations of Sin Nombre virus in the southwestern United States. *Proc Natl Acad Sci USA* 2002; 99: 16817–16822.
17. Bayard V, Kitsutani PT, Barria EO *et al.* Outbreak of hantavirus pulmonary syndrome, Los Santos, Panama, 1999–2000. *Emerg Infect Dis*

2004; 10: 1635–1642. Available at: http://www.cdc.gov/ncidod/EID/vol10no9/04-0143.htm.
18. Fichet-Calvet E, Rogers DJ. Risk maps of Lassa fever in west Africa. *PLoS Negl Trop Dis* 2009; 3: e388. doi: 10.1371/journal.pntd.0000388. Available at: http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pubmed&pubmedid=19255625.
19. Hewawasam I. *Managing the marine and coastal environment of sub-Saharan Africa: strategic directions for sustainable development*. Washington, DC: World Bank, 2002.
20. Bonner PC, Schmidt WP, Belmain SR, Oshin B, Baglole D, Borchert M. Poor housing quality increases risk of rodent infestation and Lassa fever in refugee camps of Sierra Leone. *Am J Trop Med Hyg* 2007; 77: 169–175.
21. Fair J, Jentes E, Inapogui A *et al.* Lassa virus-infected rodents in refugee camps in Guinea: a looming threat to public health in a politically unstable region. *Vector Borne Zoonotic Dis* 2007; 7: 167–171.