ISBT Science Series (2009) **4**, 87–94

ORIGINAL PAPER **3A-S16-01**

Climate change and vector-borne viral diseases potentially transmitted by transfusion

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Vector-borne diseases occur when infectious agents (virus, protozoa, bacteria, or helminthes) are transmitted to their hosts by a carrier organism. Climate conditions and their changes play a role in the inter-relationship between these agents, the vectors and the host (or hosts). This review is focused on arthropod-borne viruses (Arboviruses). These viruses are transmitted between susceptible vertebrate hosts by blood-feeding arthropods, and may be transmitted by blood transfusion, tissue and organ transplantation and breast feeding. The lifecycle of arboviruses is influenced by changes in temperature, rainfall, humidity, length of day, average daily solar radiation and/or storm patterns, as well as changes in the frequency of rare events such as floods or droughts. A plethora of studies have suggested that climate changes, particularly temperature changes, are likely to be induced by increase in the amount of greenhouse gases, such as methane, carbon dioxide (CO_2) and chlorofluorocarbons, which deplete ozone in the atmosphere leading to an increase in ultraviolet radiation. Current models predict that ambient temperature will increase by 3–5°C on average with a doubling in CO_2 concentration in the atmosphere. Vectors, pathogens and hosts each survive and reproduce within a range of optimal climatic conditions: temperature and precipitation being most important, while sea level elevation, wind and daylight duration are also important. Climate changes may affect important determinants of vector-borne disease transmission including (i) vector survival and reproduction, (ii) the vector's biting rate, and (iii) the pathogen's incubation rate within the vector organism. Droughts can increase the dissemination of arboviral diseases in urban areas by allowing a boost in the population of mosquitoes in foul water concentrated in catch basins where they breed. Furthermore, eggs can be vertically infected with arboviruses and heat waves speed up the maturation of the mosquitoes and of the viruses within mosquitoes. Droughts also cause a decline in mosquito predators like frogs, darning needles and dragonflies. In addition, birds congregate around shrinking water sites, enhancing circulation of viruses among birds and mosquitoes. In conclusion, the seriousness of some of the recent epidemics like West Nile virus and Dengue appear to has been influenced by climate change. As most of the arboviral infections are asymptomatic in humans, there is an increased opportunity for blood, organ and tissue donations by infected individuals during the viraemic period, resulting in an increased risk of transmission of arboviruses.

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Conflicts of interest: The author declares no conflicts of interest.

Vector-borne diseases occur when infectious agents (virus, protozoa, bacteria or helminthes) are transmitted to their hosts by a carrier organism. Climate conditions and changes play a role in the inter-relationship between these agents, the vectors and the host (or hosts). This review is focused on arthropod-borne viruses (Arboviruses). These viruses are transmitted between susceptible vertebrate hosts by blood feeding arthropods, and may be transmitted by blood transfusion, tissue and organ transplantation and breast feeding. The lifecycle of arboviruses is influenced by changes in temperature, rainfall, humidity, length of day, average daily solar radiation and/or storm patterns, as well as changes in the frequency of rare events such as floods or droughts. A large number of studies have suggested that climate changes, particularly temperature changes, are likely to be induced by increases in the amount of greenhouse gases, such as methane, carbon dioxide (CO_2) and chlorofluorocarbons (which deplete ozone in atmosphere increasing ultraviolet) and models predict that ambient temperature will increase by 3–5°C on average with a doubling in CO_2 concentration in the atmosphere.

Vectors, pathogens and hosts each survive and reproduce within a range of optimal climatic conditions: temperature and precipitation are the most important, while sea level elevation, wind and daylight duration are also important. Climate changes may affect important determinants of vector-borne disease transmission including (i) the vector survival and reproduction, (ii) the vector's biting rate and (iii) the pathogen's incubation rate within the vector organism.

There are more than 520 viruses registered in the international catalogue of arthropod-borne viruses (Karabatsos N. 1985) of which about 150 infect humans. Many of them also infect animals, can cause disease and are impacted by climatic change, but will not be addressed here.

The lifecycle

Arboviruses are RNA viruses that pass back and forth between hosts as a continual means of survival. Most arbovirus infections are zoonotic (infections that are transmitted between different species of vertebrate hosts including humans). Most are carried by mosquitoes, ticks and flies, do not naturally infect humans and naturally infect wild birds and other animals without causing disease and, in general, are asymptomatic for the natural host. However, they may infect humans and Table 1 shows some arboviruses of human importance.

Table 1 Major arbovirus of human importance

Disease/agent	Host(s)	Transmission route (other)	Incubation	Diseases: range of symptoms	Geographic Distribution/season
Transmission vector: mosquito					
Chikungunya (Alphavirus)	Primate	Possibly by transfusion	2–12 days	Fever, nausea, vomiting, joint pain, photophobia, rash, neuroinvasion	Africa, India, Asia, 2007 Europe. May–July
Dengue (Flavivirus)	Human	Transfusion	4–7 days	Fever, headache, muscle/joint pain, encephalitis, haemorrhagic disease, death	Africa, Asia, Australia, India, North, Central and South America. Summer
Eastern Equine Encephalitis (Alphavirus)	Bird & rodent	Not reported	3–10 days	Malaise, muscle/joint pain, fever, fatal encephalitis	Mostly in the US & also Canada. May–Aug
Japanese Encephalitis (Flavivirus)	Mammal (swine), bird	Possibly by transfusion	5–15 days	Fever, headache, stupor, seizures, fatal encephalitis	Asia, China, India, Japan, Korea; Torres Strait Islands, Au. May–Oct
La cross Encephalitis (Bunyavirus)	Small mammal	Transfusion	4–14 days	Fever, headache, nausea, vomiting, fetal encephalitis	US and Canada
Mayaro (Alphavirus)	Mammal & bird	Not reported	3–11 days	Headache, backache, chills, nausea, rash, muscle/joint pain	South & Central America, West Indies. Rainy season
Murray Valley Encephalitis & Kunjin (Flaviviruses)	Mammal & bird	Possibly transfusion	2–14 days	Fever, headache, vomiting, diarrhea, fatal encephalitis. Kunjin is not fatal	Australia, New Guinea. Jan–Apr
O'Nyong-nyong (Alphavirus)	Human	Not reported	7 days	Fever, rigors, headache, rash, severe joint pain, very debilitating	Africa, Rainy season
Oropouche Fever (Buyavirus)	Mammal & bird	Not reported	4–8 days	Fever, headaches, muscle/joint pain, dizziness, photophobia, nausea, vomiting, diarrhoea	Mainly in Brazil, Jan–Jun
Rift Valley Fever (Phlebovirus)	Mammal (goat, camel)	Contagious by body fluid	2–6 days	Fever, headache, muscle/back pain, anorexia, eye damage, fatal haemorrhagic disease	Sub-Saharan Africa, Egypt, Yemen, Saudi Arabia, Madagascar; Rainy season
Rocio Encephalitis (Flavivirus)	Bird, other animals	Not reported	4–14 days	Headache, fever, vomiting, malaise, anorexia, fatal neurological diseases	Mostly southern Brazil. Mar–May

Table 1 *Continued.*

Disease/agent	Host(s)	Transmission route (other)	Incubation	Diseases: range of symptoms	Geographic Distribution/season
Ross River & Barmah Forest (Alphavirus)	Mammal & bird	Possibly by transfusion	3–21 days	Fever, rush, polyarthritis: ankles, fingers, knees, wrists	Australia, western Pacific Islands. Jan–Mar
Sandfly fever (Naples/ Sicilia/Toscana) (Phlebovirus)	Mammal (rodent)	Possibly by transfusion	2–12 days	Fever, malaise, neuroinvasion	Europe, Middle East, Southeast Asia, Central & South America.
Sindbis & Ockelbo (Alphavirus)	Mammal & bird	Not reported	2–20 days	Fever, headache, weakness, rash, joint pain	Widespread to most Continents
St Louis Encephalitis (Flavivirus)	Mammal & bird	Possibly by transfusion	4–21 days	Headaches, fever, nausea, fatal neuroinvasion	Mainly USA, Jun–Oct
Venezuelan Equine Encephalitis (Alphavirus)	Mammal birds?	Not reported	1–6 days	Fever, malaise, headache, muscle/joint pains, fatal neuroinvasion	Southern, Central and North America.
West Nile fever (Flavivirus)	Mammal & bird	Transfusion, transplantation, mother-to-child	2–14 days	Fever, headache, muscle/joint/eye pain, fatal neuroinvasion	Africa, Europe, Middle East, Americas. May–Oct
Western Equine Encephalitis (Alphavirus)	Mammal & bird	Transfusion	5–10 days	Fever, headache, nausea/vomiting, stiff neck, fatal neuroinvasion	Western North America, South America. Midsummer
Yellow Fever (Flavivirus)	Primate	Possibly by transfusion	3–7 days	Headache, pain, jaundice, haemorrhage, tachycardia, death	Tropical Africa, Central & South America. Rainy season.
Transmission vector: tick					
Colorado tick fever (Coltivirus)	Mammal (rodent)	Transfusion	3–20 days	Fever, rash, children encephalitis	Western North America, Mar–Sept
Crimean-Congo haemorrhagic fever (Nairovirus)	Mammal (rodent), bird	Contagious by contact	4–13 days	Fever, malaise, headache, vomiting, diarrhoea, muscle pain, rash, haemorrhage, death	Russia, Middle East, China Europe, Pakistan, South Africa, May–Sept
Issyk-Kul fever (Bunyaviridae)	Bat, bird, rodent	Not reported	8–14 days	Fever, headache, dizziness, muscle pain, rash, nausea	Russia; Apr–Oct
Kyasanur forest disease & Omsk haemorrhagic fever (Flavivirus)	Rodent	Rodent body fluid and contaminated water	4–10 days	Headache, chills, fever, myalgia, diarrhoea, vomiting & bleeding, 10% fatality rates	India, west Siberia
Powassan Encephalitis (Flavivirus)	Mammal (rodent), birds	Transfusion	7–14 days (34 days?)	Fever, vomiting convulsion, respiratory problem, fatal encephalitis	North America, Russia, China, Southeast Asia. Jun–Sept
Tickborne Encephalitis (Flavivirus)	Birds, mammals	Transfusion/oral with milk	7–14 days	Headaches, fevers and nausea, paralysis, coma, death	Western Europe and former USSR

Alphavirus (Togaviridae family, enveloped, +ssRNA virus); Flavivirus (Flaviviridae family, enveloped, + ssRNA virus); Bunyavirus, Nairovirus and Phlebovirus (Bunyaviridae family; enveloped –ssRNA viruses); Coltivirus (Reoviridae family, non-enveloped, dsRNA virus).

The lifecycle of arboviruses involves the vector (arthropod) where the virus replicates reaching levels that allow transmission to the natural host (vertebrate: birds, mammals and rodents). In the natural host, the virus replicates to levels that can be transferred (infectious) to a non-infected vector. Additionally, several arboviruses can be transferred by vertical/transovarial transmission between generations of the vector through the egg and larvae stage. They survive the winter, and generate infected adults that pass the virus to the natural host during blood meals, reinitiating the replication cycle.

It should also be noted that a large number of arboviruses have birds as natural hosts and climate changes affect bird migration. Altered pattern of bird migration and the presence of susceptible vector have a major role in spreading of arboviruses, as vectors can transfer the agent from infected migratory bird to local susceptible vertebrate host.

The vectors

The following arthropod families are vectors of arboviruses: Ixodidae (hard ticks), Argasidae (soft ticks), Culicidae/Culicinae, Culicidae/Anophelinae (mosquitoes), Psychodidae/Phlebotominae (sand flies) and Ceratopogonidae (gnats). Arboviruses have also been isolated from some other arthropod families (mites, bugs, fleas, blackflies and horseflies); however, it is unclear whether any of those may act as hosts and biological vectors.

Table 2 Arboviruses known to cause neuroinvasion in human infection

Family/virus	Vector	Vertebrate host	Geographic distribution	Ecology	Epidemics
Togaviridae Alphavirus					
Eastern equine encephalitis	Mosquitoes	Birds	Am	Rural	Yes
Western equine encephalitis	Mosquitoes	Birds, rabbits	Am	Rural	Yes
Venezuelan equine encephalitis	Mosquitoes	Rodents, equines	Am	Rural	Yes
Flaviviridae Flavivirus					
Dengue	Mosquito	Non-human primates, human	Af, Am, As, Au, Eu	Rural, urban suburban	Yes
Japanese encephalitis	Mosquitoes	Birds, swine	As, Au	Rural, suburban	Yes
Murray Valley encephalitis	Mosquitoes	Birds	Au	Rural	Yes
St. Louis encephalitis	Mosquitoes	Birds	Am	Rural, urban suburban	Yes
West Nile virus	Mosquitoes Ticks?	Birds	Af, Am, As, Eu	Rural, urban suburban	Yes
Rocio	Mosquitoes	Birds	SA	Rural	Yes
Tick-borne encephalitis	Ticks	Rodents	Worldwide in temperate area	Rural	No
Powassan encephalitis	Ticks	Rodents	NA	Rural	No
Kyasanur forest disease	Ticks	Primates, rodents, camels	In, ME	Rural	No
Bunyaviridae *Bunyavirus*					
Rift Valley fever	Mosquitoes	?	Af, ME	Rural	Yes
LaCrosse encephalitis	Mosquitoes	Rodents	NA	Rural, suburban	No
California encephalitis	Mosquitoes	Rodents	NA	Rural, suburban	No
Jamestown Canyon	Mosquitoes	Rodents	NA	Rural, suburban	No
Reoviridae *Coltivirus*					
Colorado tick fever	Ticks	Rodents	NA	Rural, suburban	No

Af, Africa; Am, Americas; As, Asia; Au, Australia; Eu, Europe; In, India; ME, Middle East; NA, North America; SA, South America.

The agents

Arboviruses are found in different virus families, and can be single-stranded RNA positive and negative sense, double-stranded RNA and double-stranded DNA viruses. Table 1 shows some of the major arboviruses of human importance.

The hosts

Numerous species of vertebrates function as hosts for arboviruses including: non-human primates (monkeys, baboons), domesticated and wild mammals (equines, pigs, goats, sheep, cats, dogs, camels, deer and marsupials, rodents: chipmunks, lagomorphs, mice, rabbits, rats and squirrel), reptiles, amphibians, many birds including water birds and passeriforms, and humans.

Human infection by arbovirus and potential transmission by transfusion

Generally, infected arthropods bite the host and inject the viruses into host tissues where they multiply and within a few days are released into the bloodstream, spreading to various other tissues. Most resulting infections are asymptomatic, subclinical or mild and do not progress. However, several of these viruses may cause serious human disease with symptoms varying from fever, rashes and arthralgia to haemorrhagic fevers with lesions in the blood vessels, kidneys and liver, and infection of the central nervous system with consequent meningitis, encephalitis and meningoencephalitis with focal paralysis, seizures, coma and death. Examples of neuroinvasive arbovirus are shown in Table 2.

The viral replication associated with the majority of human infections with arboviruses is asymptomatic or silent and may result in viraemia (virus circulating in the blood stream), providing an opportunity for transmission from human-to-human by transfusion of blood and components, tissue and organ transplantation, and occasionally, breast-feeding. The transmission of an agent through blood transfusion depends on several factors including length of viraemia and levels of circulating virus during asymptomatic infection, and susceptibility of the blood recipient. For instance, efficiency of West Nile virus transmission has been associated with weakening of the immune system including but not limited to the use immunosuppressant drugs in transplanted patients, which may result in serious outcome of infection. Examples of arboviruses transmitted by transfusion are: West Nile Virus, Dengue Virus, La Crosse virus, tick-borne encephalitis virus and Colorado tick-fever virus. Examples of viruses potentially transmissible by transfusion are Chikungunya virus, Japanese encephalitis virus, St. Louis encephalitis virus and Yellow fever virus.

Climate change and arboviral infections

Vector-borne diseases, including malaria, dengue and viral encephalitides, are among the most sensitive to climate conditions and climate change, particularly changes in temperature and humidity, factors that affect vector population dynamics and disease transmission. Arthropods do not have self-regulated body temperature, which depends on climate variation. Thus, climate conditions affect the development, reproduction and maturation of arthropods and may directly affect disease transmission by shifting a vector's geographical range, increasing reproductive and biting rates or by shortening the pathogen incubation period.

Models used to predict how climate change might affect the distribution of vector-borne diseases consider both direct impacts (such as changes in temperature or rainfall) and indirect impacts (such as changes in hydrology or agriculture) of global warming on the agent, vector, intermediary host and the human host. Each one of the elements involved in the disease process (agent, vector or host) impacts the others elements. For example, increased precipitation results in the increase of the vertebrate host food sources that result in increased survival and reproduction. Increased temperature and moisture facilitates hatching of the vectors that feed on the natural vertebrate host. Extreme climate changes may also lead to the extinction of predators of natural hosts, and thus affect the biological equilibrium that maintains a zoonosis under control, leading to an increase in the susceptible host population and potentially a bigger expansion of the infectious agent.

Vector-borne diseases, including malaria, dengue and viral encephalitis are very sensitive to extreme climate changes that affect the agent itself and the susceptibility and ability of the human host to survive the infection, with consequent changes in morbidity and mortality.

Climate change can affect disease transmission by: (i) shifting vector's geographical range; (ii) affecting arthropod abundance, increasing reproductive, development, maturation and bites rate; (iii) shortening pathogen incubation period; (iv) affecting natural host abundance; (v) promoting extinction of predators of arthropod and of natural vertebrate hosts; and (vi) altering migration of natural vertebrate host.

Climate change and global warming projections

The global average surface temperature of the Earth has increased by 0·6° ± 0·2°C over the last century and globally, 1998 was the warmest year and the decade of the 1990s was the warmest on record until the end of the 20th century. Many areas have experienced increases in rainfall, particularly mid to high latitude countries. The frequency and intensity of droughts in some regions of Asia and Africa have increased in recent decades. Episodes of El Niño have been more frequent, persistent and intense since mid-1970s compared to the previous 100 years.

The third Assessment Report of the Intergovernmental Panel on Climate Change 2001, predicted that the global mean surface temperature will rise by 1·4–5·8°C in next century (by the year 2100). Warming will be greatest over land areas, and at high latitudes. The projected rate of warming is greater than anything humans have experienced in the last 10 000 years. The frequency of weather extremes is likely to increase, leading to an increased risk of floods and droughts. Fewer cold spells but more heat waves are expected. The frequency and intensity of El Niño may be affected. Global mean sea level is projected to rise by 9–88 cm by the year 2100.

Evidence of climate change

Data from the National Aeronautics and Space Administration, from 1880 to 2007, shows significant warming over the past 30 years. The past decade had the eight hottest years on the Goddard Institute for Space Studies records, with 2005 as the hottest recorded year, followed by 2007 and 1998 tied in second place. Figure 1 shows the average global temperature.

These dramatic changes in temperature are thought to impact the reproduction and maturation of arthropods and facilitate the emergence of re-emergence of zoonoses caused either by apparently new agents, or by previously known micro-organisms, appearing in places or in species in which the disease was previously unknown. New animal diseases with an unknown host spectrum are also included in this definition. Natural animal reservoirs represent a more frequent source of new agents of human disease than the sudden appearance of a completely new agent. Factors explaining the emergence of a zoonotic or potentially zoonotic disease are usually complex, involving molecular mechanisms, such as genetic drift and shift, and modification of the immunological status of individuals and populations. Social and ecological conditions influencing population growth and movement, food habits, the environment and many other factors may play a more important role than changes at the molecular level. Most arboviruses are human zoonoses.

A World Health Organization/Food and Agriculture Organization of the United Nations /World Organization for Animal Health joint consultation on emerging zoonotic diseases held in Geneva, 3–5 May 2004, defined an emerging zoonosis as 'a zoonosis that is newly recognized or newly evolved, or that has occurred previously but shows an increase in incidence or expansion in geographical, host or vector range'. They concludes that droughts can increase the dissemination of arboviral diseases in urban areas by allowing a boost in the population of mosquitoes in foul water concentrated in catch basins where they breed. Furthermore, eggs can be vertically infected with arboviruses and heat waves speed up the maturation of the mosquitoes and of the viruses within

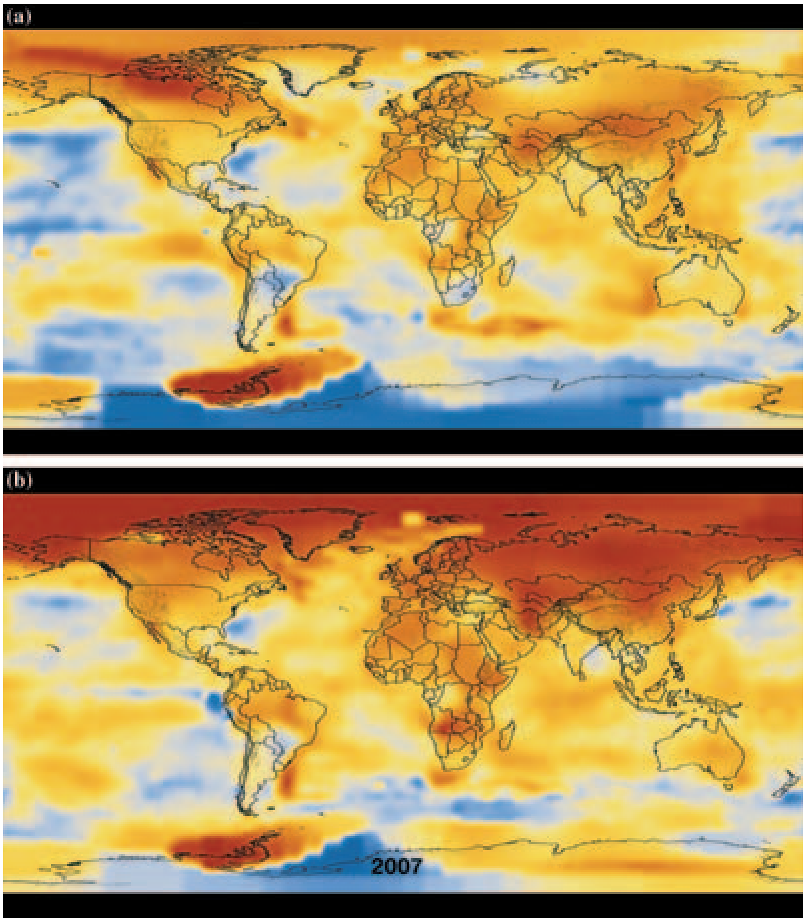

Fig. 1 Average global temperature between 1996 and 2000 (a) and between 2003 and 2007 (b); in red the greatest warming and in blue the greatest cooling. From NASA/Goddard Space Flight Center Scientific Visualization Studio (http://svs.gsfc.nasa.gov/vis/a000000/a003400/a003490/index.html).

mosquitoes. Droughts also cause a decline in mosquito predators like frogs, darning needles and dragonflies. In addition, birds congregate around shrinking water sites, enhancing circulation of viruses among birds and mosquitoes. Altogether these events facilitate circulation of arboviruses and the predisposition for human infection.

Scientists at the National Aeronautics and Space Administration Goddard Institute for Space Studies reported that the global surface temperatures in 1998 set the first new record since the initiating of instrumental measurements (Fig. 2). Surface change anornalies from 1950 through 1998, as of January 19, 2008, are posted at http://svs.gsfc.nasa.gov/goto?391. The 1998 warmth was associated partly with a strong El Niño that warmed the air over the eastern tropical Pacific Ocean in the first half of the year and in turn affected weather around the world. Red and yellow colours indicate warmer temperatures than normal conditions and blue colours indicate cooler temperatures than normal conditions.

In the USA, in spring and summer of 1999, mid-Atlantic states baked under intense drought, until torrential end-of August rains – capped by Hurricane Floyd – drenched the coast. These weather conditions coincided with the beginning of appearance and establishment of West Nile virus in the northeast coast of the USA.

Considering that most human infections with arbovirus are asymptomatic or have some extended incubation period, it is not unreasonable to expect an increased opportunity for blood donations made by asymptomatic infected individuals living or travelling through epidemic/endemic regions where arboviral activity may be high. As an example, 80% of human infections with West Nile virus are asymptomatic, and most of the 20% of the symptomatic infected individuals have only malaise or a flu-like illness that may appear up to 2 weeks after donation of a contaminated unit of blood. In the USA, arboviral encephalitis occurs mostly from June through September, when arthropods are most active. In milder (i.e. warmer) parts of the country, where arthropods are active late into the year, cases can occur into the winter months.

Conclusion

Arboviral infections are affected by climate change. The seriousness of some of the recent epidemics like West Nile virus and Dengue appear to have been influenced by climate

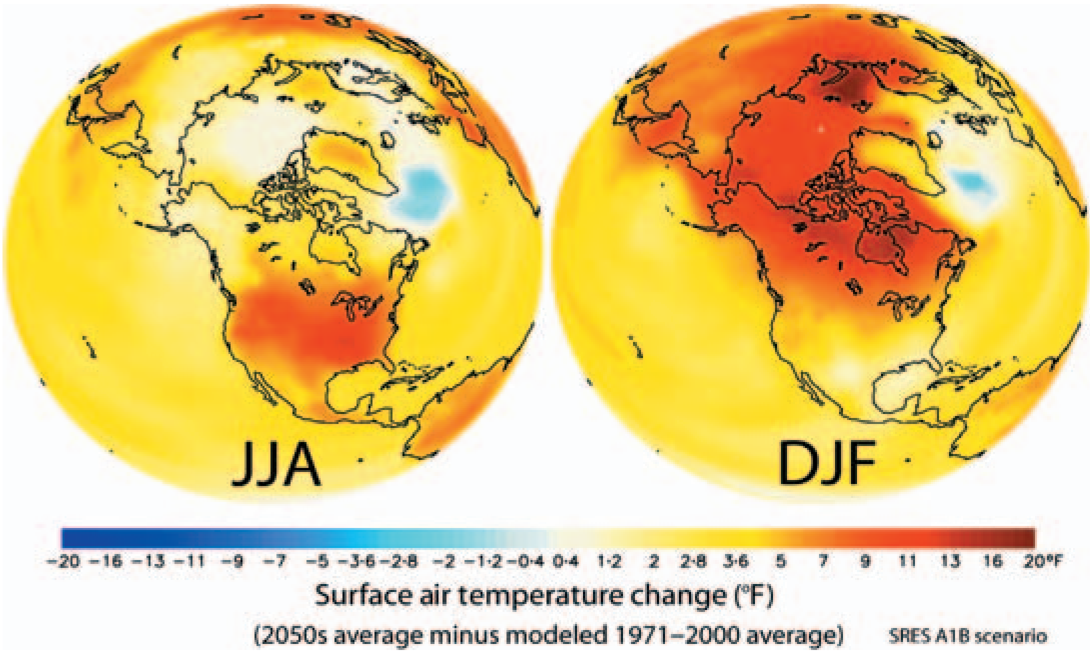

Fig. 2 The predicted temperature by NOAA GFDL CM2·1 Climate Model in the North America and the north pole in 2050 for the summer (months of June, July and August–JJA) and winter (December, January and February DJF).

change. As most of the arboviral infections are asymptomatic in humans, there is an increased opportunity for blood, organ and tissue donations by infected individuals during the viraemic period resulting in an increased risk of transmission of arboviruses.

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