REFERENCES

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Early effects of climate change: do they include changes in vector-borne disease?

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The world's climate appears now to be changing at an unprecedented rate. Shifts in the distribution and behaviour of insect and bird species indicate that biological systems are already responding to this change. It is well established that climate is an important determinant of the spatial and temporal distribution of vectors and pathogens. In theory, a change in climate would be expected to cause changes in the geographical range, seasonality (intra-annual variability), and in the incidence rate (with or without changes in geographical or seasonal patterns). The detection and then attribution of such changes to climate change is an emerging task for scientists. We discuss the evidence required to attribute changes in disease and vectors to the early effects of anthropogenic climate change. The literature to date indicates that there is a lack of strong evidence of the impact of climate change on vector-borne diseases (i.e. malaria, dengue, leishmaniasis, tick-borne diseases). New approaches to monitoring, such as frequent and long-term sampling along transects to monitor the full latitudinal and altitudinal range of specific vector species, are necessary in order to provide convincing direct evidence of climate change effects. There is a need to reassess the appropriate levels of evidence, including dealing with the uncertainties attached to detecting the health impacts of global change.

Keywords: climate change; early effects; vector-borne disease; highland malaria; desert fringe malaria

1. INTRODUCTION

Natural ecosystems become adapted to the prevailing climate conditions, as these normally change only slowly over time. Rapid climate change, for example the sustained global warming of 0.2 °C per decade since the 1970s, however, raises questions about how natural ecosystems and species will respond. Vector-borne diseases are one of the major contributors to the global burden of disease (WHO 2000), and are highly sensitive to climate conditions. Climate change may be irreversible, and is predicted to become more extreme in the future (IPCC 2001*a*). It is therefore important to determine whether, and how, climate change is affecting vector-borne diseases. This paper will examine the criteria for the detection and attribution of observed (i.e. past) changes in vector-borne diseases to observed changes in climate. Very little quantitative work has been done that specifically addresses that question. In contrast, there has been a great deal of public and scientific debate about the role of climate change in recent disease emergence and re-emergence. For reasons that will be discussed, it is likely that it will be very difficult to attribute unequivocally a change in disease patterns to climate change. Therefore, we will consider two further important questions. (i) Where and how should we be looking for evidence? (ii) Considering the paucity of data, what do we accept as evidence within this context?

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(a) *Climate change: detection and attribution*

It is important to distinguish between climate change and climate variability. Climate change is defined as a statistically significant variation in either the mean state of the climate or in its variability, persisting for an extended period (typically decades or longer) (IPCC 2001*a*). Climate change may be due to natural internal processes or external forces. The latter include anthropogenic changes in the composition of the atmosphere or in land use.

Detection of climate change is difficult because any climate change 'signal' is superimposed on the background 'noise' of natural climate variability. Nevertheless, there is now good evidence that the climate is changing. The global average land and sea surface temperature has increased by 0.6 ± 0.2 °C since the mid-19th century (IPCC 2001*a*). Nearly all of this increase has occurred in two periods: 1910–1945 and since 1976 (figure 1). At the regional scale, warming has been observed in all continents, with the greatest temperature changes occurring at middle and high latitudes in the Northern

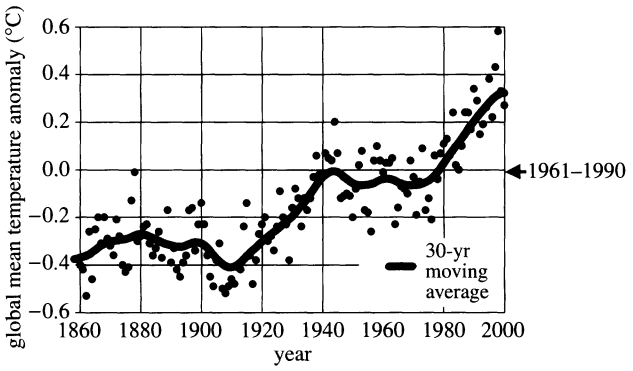

Figure 1. Observed global average land- and sea-surface temperatures from 1860 to 2000. Source, Climatic Research Unit, Norwich, UK.

Hemisphere. Significantly, in the context of vector-borne disease transmission, minimum temperatures have been rising faster than maximum temperatures, resulting in a narrowing of the diurnal temperature range in most parts of the world (Easterling 1997). Patterns of precipitation have also changed (Hulme *et al.* 1998). It appears that arid and semi-arid areas are becoming dryer while other areas, especially mid-to-high latitudes, are becoming wetter. There is also evidence that where precipitation has increased, there has been a disproportionate increase in the frequency of the heaviest precipitation events (Karl & Knight 1998).

The Intergovernmental Panel on Climate Change (IPCC) Third Assessment Report states that 'most of the warming observed over the last 50 years is likely to be attributable to human activities' (IPCC 2001*a*). For this type of attribution, climatologists rely on the following types of evidence: (i) comparison of climate-model-simulated patterns of greenhouse gas-induced change ('fingerprints') with observed changes; (ii) evaluation of changes in time and space and by season, which can distinguish non-anthropogenic causes such as solar and volcanic activity; and (iii) more emphasis being placed on climate changes in areas of low natural variability.

Climate variability can be expressed at various temporal scales (by day, season and year) and is an inherent characteristic of climate, whether the climate system is subject to change or not. Climate 'exposures' can be described in three broad temporal categories (Smit *et al.* 2001): (i) long-term changes in mean temperatures, and other climate 'norms' (e.g. global climate change); (ii) climate variability about norms over periods ranging from a few years to several decades, including shifts in the frequency distributions of climate variables and recurring climate phenomena such as the El Niño Southern Oscillation (ENSO); and (iii) isolated extreme events (either simple extremes, e.g. temperature and precipitation extremes, or complex events such as tropical cyclones, floods or droughts).

These types of 'exposures' are clearly not independent. Assuming a normal distribution of daily temperature, for example, a shift in the mean will entail a nonlinear response in the frequency of extreme events defined according to fixed criteria. There is some evidence for changes in frequency of extremes over recent decades (IPCC 2001*a*; Easterling *et al.* 2000). Many health outcomes are sensitive to isolated extreme events (e.g. heavy rainfall, high temperatures) but are not likely to be significantly affected by long-term, incremental climate change, unless these same meteorological extremes also change in frequency or character.

ENSO is a strong determinant of interannual variability in many parts of the world and has been associated with changes in vector-borne disease transmission (see Kovats (2000) for a review). Weather patterns associated with an El Niño (warm) event are concentrated around the Pacific and include regional land and sea surface warming, changes in storm tracks, and changes in rainfall patterns (particularly heavy rain or prolonged drought). The change in precipitation is the principal mechanism by which El Niño affects mosquito-borne disease. Individual El Niño events should not be confused with long-term climate change. In reality, these fluctuations introduce more noise into the long-term trends, which makes it more difficult to detect the climate change signal. To add further complication, climate change is anticipated to affect the frequency and/or intensity of El Niño (and La Niña) events in the future (IPCC 2001*a*). In the last two decades of the 20th century, there were an unusually high number of El Niño events, including major events in 1982–1983 and 1997–1998. Therefore, in many regions, the warming trends in the 1980s and 1990s were heavily influenced by ENSO.

Alternative explanations for observed warming at the regional scale therefore include 'natural' interannual (e.g. during El Niño) or decadal climate variability. (Although it is now arguable whether current climate variability can be considered completely natural.) At the local scale, it may not be appropriate to attribute changes in climate to global anthropogenic climate change. Local environmental factors, such as deforestation, are thought to increase local temperatures and this complicates the attribution of local effects to global climate change (Reiter 1998).

(b) *Early evidence of climate change in biological systems*

The evidence on biological effects of observed climate change has been categorized in four ways (Hughes 2000): (i) effects on physiology—metabolic or development rates of animals, and plant processes; (ii) effects on distributions—response to shifts in mean temperature and precipitation conditions; (iii) effects on phenology—the timing of life-cycle events, e.g. budding of flowers or egg laying; and (iv) adaptation—species with short generation times and rapid population growth rates may undergo some micro-evolution.

Published studies that support these effects include Poleward shifts in the distribution of particular insect and bird species (Parmesan *et al.* 1999; Thomas & Lennon 1999) and altitude shifts of alpine plant communities (Grabherr *et al.* 1994). The annual average growing season in Europe has lengthened by about 11 days since the early 1960s (Menzel & Fabian 1999). At least 20 different UK bird species are showing a trend of earlier egg laying (Crick & Sparks 1999). Figure 2 presents a summary of the literature of long-term studies (20 years or more) of changes in biological or physical systems that are correlated with regional changes in temperature (IPCC 2001*b*). A formal review of

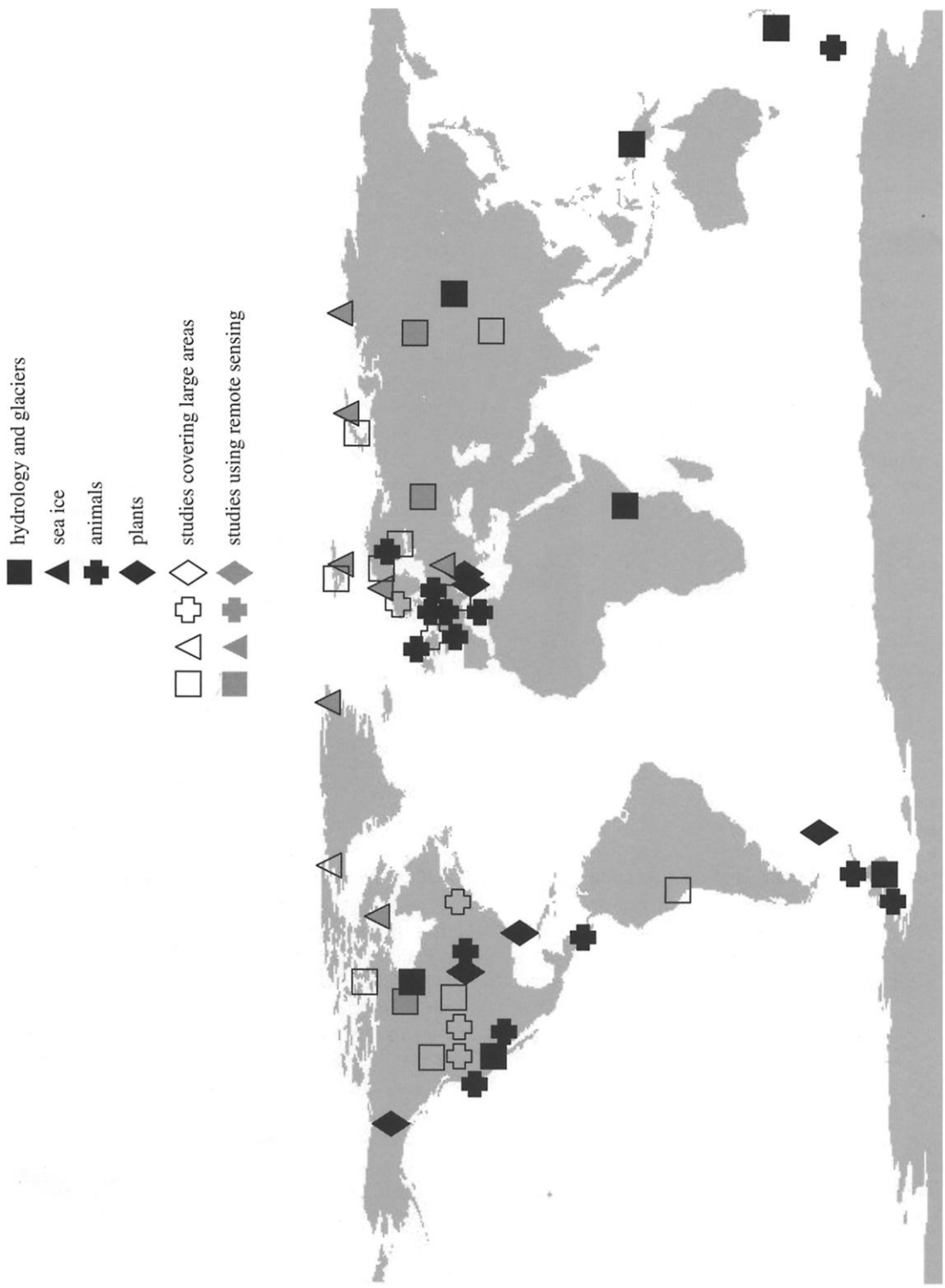

Figure 2. Locations at which systematic long-term studies meet stringent criteria documenting recent temperature-related climate change impacts on physical and biological systems. Hydrology, glacial retreat, and sea-ice data represent decadal-to-century trends. Terrestrial and marine ecosystems data represent trends of at least two decades. Remote-sensing studies cover large areas. Data are for single and multiple impacts that are consistent with known physical and biophysical system responses to observed regional temperature-related changes. For reported impacts spanning large areas, a representative location on the map was selected. Source, IPCC (2001*b*).

such studies emphasizing the pattern and plausibility of these diverse observations will be published in the IPCC Third Assessment Report (IPCC 2001*c*).

Although there is a strong demand for information on the early impacts of climate change on health, there is very little equivalent information on health and health-related outcomes. A clearer understanding about the current role of climate change in disease patterns will enable scientists to improve forecasts of future potential impacts of projected climate change and support action to reduce such impacts. Further, confirmed effects on humans are likely to have a larger impact on the international policy debate over mitigation of greenhouse gas emissions than effects on butterflies.

2. CLIMATE CHANGE AND VECTOR-BORNE DISEASE

Accumulated laboratory and field evidence on the sensitivity of pathogens and vectors to environmental conditions suggests that climate change (particularly the global trend towards warmer temperatures) is likely to act on both individual organisms and potentially, over time, the genetic characteristics of populations. With respect to disease transmission, changes to the following properties will be most important: (i) survival and reproduction rates of vectors, in turn determining their distribution and abundance; (ii) intensity and temporal pattern of vector activity (particularly biting rates) throughout the year; and (iii) rates of development, survival and reproduction of pathogens within vectors.

The relationship between these characteristics and the potential of vector populations to transmit disease can be summarized as the vectorial capacity (VC) (Garrett-Jones 1964), the number of future infections resulting from the bites taken on one infected person in one day. For anthroponotic diseases such as malaria, this can be expressed as $VC = (ma^2p^n)/-\mathrm{Ln}p$, where m is the density of vectors in relation to man, a is the number of bites on humans per vector per day, p is the daily survival probability, and n is the days required for development of the parasite in the vector. As all of the individual components of VC are highly sensitive to climate (particularly temperature), and two are represented as squared or exponential terms, it seems likely that even small alterations in global climate may cause significant changes in the following properties of the vector-borne disease transmission. (i) The overall incidence, and the duration of the transmission season in particular sites. Small changes in seasonality may be very important, as transmission rates tend to increase exponentially rather than linearly through the transmission season. (ii) The geographical distribution of disease transmission, as climate-driven changes in VC cause transmission to become unsustainable in previously endemic areas, or sustainable in previously non-endemic areas. Even small increases in disease distributions may expose new populations which lack acquired immunity, often resulting in more serious clinical disease.

As rapid climate change is a new problem little research effort has yet been directed at measuring effects of long-term climate change on vectors and disease. Some progress has been made in developing criteria for non-human systems (see Parmesan 1996; Ahmad & Warrick 2001). However, the criteria for assessing the evidence for climate change effects in the recent past and in the future on health have not been well defined. We suggest that the minimum requirements to be met before accepting 'causal' relationship between climate change and changes in human health outcomes are as follows.

(i) Evidence of biological sensitivity to climate: this is straightforward for most vector-borne diseases, as there is usually strong laboratory and field evidence that major components of the transmission cycles are sensitive to temperature, humidity and rainfall.
(ii) Meteorological evidence of climate change. Although there is now clear evidence of a global change in climate, there is significant geographical variation in the pattern of change. In interpreting health changes in any one particular region, meteorological measurements must be carried out for a sufficient period, and with enough site replicates, to determine whether a long-term trend in meteorological conditions has occurred. Data from a single site or from a short time-period should be interpreted with caution.
(iii) Evidence of entomological and/or epidemiological change in association with climate change. In order to show that vectors and diseases are indeed changing in association with any observed change in meteorological conditions, it is necessary to carry out standardized monitoring of changes in disease patterns. The degree of any response attributed to climate change should be consistent with the known climate sensitivity of the vector.

The observation that climate change is associated with changes in vectors or disease does not, of itself, prove a causative relationship, since it is usually not possible to completely exclude all alternative explanations for any change in disease patterns. This is true of all observational studies. Studies constitute more convincing evidence, however, if they fulfil the following criteria.

(i) To detect changes in distribution or phenology or seasonality, sample sizes should be maximized by studying multiple species, diseases and populations.
(ii) To detect Poleward or altitudinal shifts in vector or disease distributions, studies should extend across the full range (Parmesan 1996), or at least the extremes of the range (Parmesan *et al.* 2000), so as to exclude simple expansions or contractions.
(iii) Given the natural variability in both climate and biological responses, long data series are needed (most studies on biological systems have used data series longer than 20 years).
(iv) Variability in the climate series (e.g. year to year) should correspond to variability in the health time-series.
(v) If a continuous series is not available, studies that rely on comparison of specific points in time should ensure that the studies from the two (or more) time-slices are sufficiently comparable.
(vi) Both time-series and spatial analyses of correlations between climate and health outcomes should make adjustments for autocorrelation. Failure to do so will tend to overestimate the effect of climate variables.

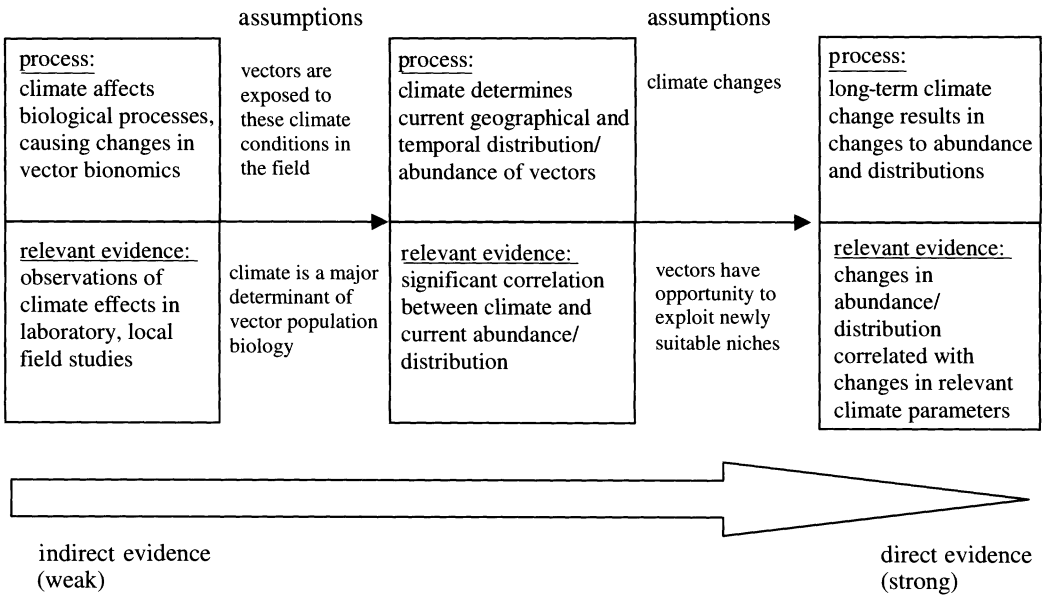

Figure 3. The processes through which climate change may be expected to affect vectors. Source, Kovats *et al.* (2000).

(vii) Quoted statistical significance values for the association between temporal variation in climate and health outcomes should clearly distinguish between the effects of (in increasing order or relevance) seasonal variation, interannual variation, and long-term trends in climate.

(viii) Analyses should take into account, as far as possible, other changes that have occurred over the same time-period which could plausibly account for any observed association with climate.

These criteria are suggested as guidelines to produce stronger studies, rather than as a definitive checklist. This is particularly true of the last two criteria. The most direct evidence would be a trend in disease over many years which is significantly correlated with a change in climate, but not with any other potential driving mechanism. As this situation will be almost impossible to achieve with complex natural systems, the degree to which a particular study is judged as evidence of climate change effects will ultimately require a judgement of the plausibility of alternative causative mechanisms.

3. DISEASE VECTORS

Ideally, climate effects on vector-borne disease should take into account the transmission system as a whole and combine climate data with concurrent measurements of the vectorial capacity and infection rate of vectors, abundance and infection rate of reservoir hosts (if any), and the infection rate and eventual health impacts on humans. It is often more practicable, however, to carry out separate analyses of climate effects on vectors as information on vectors may be collected separately from disease data, often by different bodies (e.g. entomological researchers rather than public health personnel). In addition, such studies have the advantage that they may detect responses in vector populations before they cause changes in health, and may avoid some confounding factors, such as changes in treatment regimes or public awareness of disease.

Figure 3 describes a framework for assessing climate change effects on disease vectors. Earlier processes in the chain are necessary for later processes to occur. It is clear, however, that proximal changes may not always be sufficient to produce disease, as one or more of the intervening assumptions may not hold true. For example, even vectors that are highly sensitive to temperature (and sometimes humidity) in the laboratory may survive outside their supposed climatic range by exploiting microhabitats with more amenable conditions. This is likely to be particularly true of vectors that live in close association with humans, whose houses are usually more climatically stable than the outside environment (e.g. Lazzari *et al.* (1998) for domestic vectors of Chagas disease). Alternatively, factors other than climate (e.g. control programmes, availability of suitable habitats) may prevent vectors from exploiting all of their climatically suitable range.

At the next level, even if climate is important in determining current distributions, climate change will only be reflected in altered vector distributions if they are able to expand into newly suitable areas. This will depend on the ability of the vector to actively or passively disperse into newly suitable ranges before their current range becomes unsuitable, when faced with the challenges of interspecies competition or other possible limiting factors (Jenkinson *et al.* 1996) (table 1).

(a) *Detection of climate-driven changes*

Demonstrations of climate effects on the abundance and distributions of vectors, either now or in the recent past, constitute stronger evidence for attribution to climate change than laboratory studies. The recent increase in affordable computing power and the advent of geographical information systems (GIS) software has facilitated the mapping of available data on vector abundance and distributions (e.g. Coetzee *et al.* 2000). New ground and satellite-based sensors (e.g. Hay *et al.* 1996)

Table 1. Potential vector responses to climate change.

vector	major diseases	active dispersal	passive dispersal
mosquitoes	malaria, filariasis, dengue fever, yellow fever	able to disperse and reproduce relatively rapidly to exploit newly suitable areas	common and wide ranging: often transported by human transportation, including intercontinental aircraft and cargo, e.g. *Aedes albopictus* in used car tyres
sandflies	leishmaniasis	limited flight ranges	highly unlikely: breed, and usually rest, away from human habitations
triatomines	Chagas disease	able to fly considerable distances	common and wide ranging: often transported by humans in luggage
Ixodes ticks	Lyme disease, tick-borne encephalitis	very limited powers of active dispersal	common and wide ranging, due to long periods of feeding attachment to birds and large mammals
tsetse flies	African trypanosomiasis	able to fly considerable distances	rare: some dispersal of adult flies in vehicles
blackflies	onchocerciasis	can travel hundreds of kilometres on wind currents; new habitats are quickly colonized by blackflies	highly unlikely: breed, and usually rest, away from human habitations

have allowed these data to be matched against increasingly accurate climate measurements.

Collections of many vectors are made using a variety of different trapping methods, applied with varying effort over time and space, so that it is often difficult to obtain standardized measurements of abundance. With some notable exceptions, the majority of studies therefore centre on analysis of patterns of presence versus absence (i.e. distributions), which are relatively more robust and less data-intensive. The correlation between climate variables and the distribution of vectors may be analysed either using explicitly statistical techniques (e.g. Rogers & Randolph 1991), or through semi-quantitative climate-matching methods such as the CLIMEX model of Sutherst (1998). Factors other than climate may exert a significant influence on distribution patterns (e.g. variation in natural vegetation, land-use, natural or artificial barriers to species dispersal) and as far as possible, the effects of such factors should be tested and included in multivariate models exploring climate effects.

In general, the mapping studies that have so far been carried out confirm the importance of climate as a limiting factor in the distribution of many important insect and tick vectors (Kovats *et al.* 2000). These findings suggest that vector distributions are likely to change as climate change progresses. Statistical models describing the climatic limits of distribution for particular vector species have been coupled to models of predicted future climate change. These produce quantitative predictions of the new geographical limits of particular vectors under various climate scenarios (e.g. Rogers (1996) for tsetse, mosquitoes and ticks in southern Africa).

Predictions of the outcomes of future climate change are, however, quite separate from the gathering of direct evidence of an observed impact of climate change. Given the powerful GIS and analytical tools now available, it should in principle be possible to carry out such direct tests, by mapping changing climate conditions as they occur and correlating them with changes in vector distributions. However, as most vector surveys are carried out for purposes other than climate change studies, available data covering all of a species range usually consist of composite summaries of multiple surveys collected over long periods of time, and are therefore often uninformative about any changes over time. Surveys more closely reflect the distribution of entomologists than the insects they are studying, and some countries have not reported any surveys at all. Entomological studies are expensive and are not seen as a high priority for disease surveillance.

In addition to these logistic limitations, direct tests of climate-change-driven effects on vectors face other severe difficulties.

(i) The lack of standardization and short-term nature of most vector-monitoring efforts hampers detection of changes in distribution and abundance.
(ii) The high sensitivity of many vectors to climate parameters means that unless monitoring is carried out frequently, interobservation changes caused by interannual climate variability may be misinterpreted as long-term trends.
(iii) Many non-climate factors that have a powerful influence on vector distribution (including control interventions (e.g. Schofield & Dias 1999)) may change over time, so that it is difficult to attribute observed changes to climate effects.
(iv) Vector-monitoring effort is generally concentrated where disease is most prevalent; i.e. the centre of distributions, rather than the boundaries of either vector or disease distributions.
(v) Detection of the edge of distributions usually relies on passive reporting of apparent changes in altitudinal or latitudinal limits. This is subject to severe biases, as only expansions, rather than contractions, are likely to be detected, and changes in vector abundance or

distribution that correlate with climate change are more likely to be reported than those which do not, creating a substantial reporting bias. This is a particular problem given the increasing interest in climate change effects in recent years.

It therefore seems that current methods of data collection fail to fulfil several of the criteria outlined above (§ 3a), and will only tend to detect extreme responses by vectors to climate changes. More standardized monitoring in sensitive areas (e.g. at the altitude and latitude limits of current distributions) may need to be implemented in order to detect more subtle responses. Until such methods are implemented, however, it is necessary to carry out the most careful analysis possible of currently available data.

(b) *Case study: northward expansion of ixodid tick populations in Sweden*

Over the past two decades marked increases have been reported in the abundance of ticks and in the incidence of tick-borne disease in both North America and Europe. In North America, these changes have been attributed to (i) an increase in awareness of tick-borne diseases; and (ii) increased abundance of wild tick hosts (principally deer), as reforestation has expanded areas of suitable habitat. Studies of the altitude and latitude limits of ticks and tick-borne diseases have not been carried out in this region. In Europe, climate change has been proposed as an explanation for recent changes in the distribution of *Ixodes* ticks and tick-borne disease. Talleklint & Jaenson (1998) and Lindgren *et al.* (2000) showed that respondents to a 1994 questionnaire in central northern Sweden reported a greater occurrence of ticks throughout the survey area in the early 1990s compared with the early 1980s, indicating a northward shift in the latitudinal limit for reported tick occurrence. Further, there have been observed changes in human disease. The incidence of tick-borne encephalitis (TBE) in Sweden approximately doubled for the period 1984–1994, compared with 1960–1983. Annual TBE incidence is positively correlated with increasing temperatures in the summer and preceding winter (Lindgren 1998). Climate data from 1979 to 1981 and from 1991 to 1993 showed milder winters (more days with temperatures of more than −12 °C) and a cooler spring–summer–autumn season (more days with temperatures 5–8 °C and fewer days with temperatures of more than 8 °C) in the latter period (Lindgren 1998).

These studies use the best available data, and are clearly consistent with climate-driven change. However, they illustrate the challenges involved in proving that climate change is responsible for apparent changes in vector or disease data. Because the comparisons of tick distributions are based on passive retrospective reporting at two time-points, it is difficult to test alternative explanations such as better recollection of more recent sightings of ticks, or the acknowledged increase in roe deer populations in Sweden from the mid-1980s. Similarly, the fact that all TBE cases in Stockholm county have been laboratory confirmed since the 1950s is strongly supportive of a real increase in cases, but does not exclude the possibility that doctors or patients may have gradually become more likely to detect and report encephalitis cases for laboratory confirmation of TBE (i.e. a reduction in false negatives). As stated above, it remains necessary to judge whether such alternative hypotheses are more or less plausible than climate change.

4. CHANGES IN HUMAN DISEASE

Many of the same principles and problems (variability in monitoring and surveillance, necessity for long datasets to overcome statistical 'noise', confounding variables, publication bias, etc.) apply to the detection of changes in human disease. However, there are significant additional challenges, mainly involved with differentiating climate influences from the other multiple determinants of vector-borne disease transmission. Therefore, field-based epidemiological research on climate influences on disease causation requires even greater emphasis on differentiation between the effects of coexistent climate and non-climate factors. Many environmental or socio-economic factors have affected the distribution and seasonality of vector-borne diseases in recent decades (Morse 1995; Gubler 1997) (table 2). This is a major stumbling block, as it is difficult to get adequate time-series data on many of these factors. Methods of surveillance and case ascertainment can change dramatically from one year to the next. Sometimes, reports are aggregated for administrative purposes and information is lost. Vector-borne disease monitoring and surveillance varies widely depending on the locality, the country and the disease. Many developing countries have poorly developed surveillance systems. Detecting the effect of climate change is not a priority for disease surveillance in any country at present.

(a) *Changes in disease distribution, transmission intensity and seasonality*

To detect change, one needs to define a 'baseline' distribution before climate change. Mapping efforts have received new impetus in recent decades from the advent of remote sensing and GIS technology. Mapping can be conducted at various geographical scales from village to continental scale and on temporal scales varying from the duration of an outbreak to multiyear models (Kitron 2000). The choice of scale is important, and is determined by the purpose of the map. At the continental scale, climate may be a good predictor of disease distribution: large-scale (continental–national) maps have been produced for malaria in Africa (Craig *et al.* 1999) and for Lyme disease in the USA (Glass *et al.* 1995). However, at the 'local scale', other environmental factors are likely to be more important. Despite the new technology and its application, it is very difficult to obtain accurate and reliable information on current or previous distributions of disease. Maps can sometimes be misleading where they are based on insufficient data, use artificially drawn boundaries, or are used for purposes other than those originally intended. Another consideration in interpreting data is that meta-analyses of multiple studies can be associated with a bias towards publication of positive results and multiple publications with the same data.

As for studies of vectors, the principal current limitation is the lack of data on potential confounders. These problems may be partially overcome by careful study design. Taking a different environmental health example,

Table 2. Possible precipitating factors for malaria epidemics (based on Molineaux 1988).

(Factors are also categorised as to whether they are temporary and reversible triggers of an epidemic, or whether they cause a sustained change in malaria transmission dynamics (including a shift to more stable transmission patterns).)

factor	cause	evidence rating[a]	temporary or reversible	long-term or sustained
increase in vectorial capacity through:				
importation of a more potent vector	anthropogenic	+	no	yes
increased emergence through:				
increased availability of breeding places through:				
abnormal rainfall	natural	+	yes	no
errors in water management; irrigation, drainage, flooding	anthropogenic	+	yes	yes
deforestation	anthropogenic	?	no	yes
increased temperature; accelerated development	mixed[c]	?	yes	yes
deterioration of larval control through:				
operational failure	anthropogenic	?	yes	yes
resistance to larvicides	mixed	?	yes[b]	yes
increased survival of adult vectors through:				
favourable meteorological conditions; humidity, temperature	natural	+	yes	yes
deterioration of adult control through:				
operational failure	anthropogenic	+	yes	yes
physiological insecticide resistance	mixed	+	yes[b]	yes
behavioural insecticide resistance	mixed	?	?	yes
increased feeding frequency through increased temperature	mixed[c]	?	yes	yes
increased human–vector contact through destruction of cattle or houses	either	+	no	yes
decreased incubation period in vector through increased temperature	mixed[c]	?	yes	yes
immigration of infective person	anthropogenic	+	yes	no
immigration of non-immunes	anthropogenic	+	yes	no
drug resistance	mixed	+	yes[b]	yes

[a] Proven or very probable precipitating factor of some past epidemics; the question mark denotes a possible factor; not clearly documented.

[b] Only temporary if a new, effective intervention is subsequently used.

[c] Assumes that climate variability in the last 50 years is no longer completely natural.

much anecdotal evidence has accumulated that the building of dams has changed local transmission dynamics of infectious diseases, but because many other changes occur at the same time, there was little or no proof that dams caused ill-health. A recent study in Ethiopia, however, used a case-control design at the village level to show that microdams increased malaria incidence (Ghebreyesus *et al.* 1999). The influence of factors may be reduced by conducting studies in areas that have stayed relatively constant with respect to non-climate variables. Even with careful monitoring and analysis, however, it will always be both difficult and time-consuming to provide strong direct evidence of climate change effects on disease transmission. The fact that several monotonic changes are occurring simultaneously (e.g. increases in population movement and temperature, decreases in vector control) ensures that describing the contribution of a single factor will remain difficult.

5. HIGHLAND MALARIA

Within the wider field of malaria epidemiology much recent interest has focused on transmission patterns in highland regions (Mouchet *et al.* 1998; Lindsay & Martens 1998; Epstein *et al.* 1997; Reiter 1998, 2001). This interest appears to stem largely from reported increases in the occurrence of malaria epidemics in certain highland areas since the late 1980s. Given the absence of malaria outbreaks in similar areas during the 1960s and 1970s, debate has centred on the possible contributory role that climate change may have played within this apparent shift in epidemiology. Highlands have long been seen as a 'natural laboratory' for studying the effects of climate on the epidemiology of vector-borne diseases, primarily because variations in climate (and particularly temperature) occur over relatively small distances and are associated with steep gradations of disease endemicity (Epstein *et al.* 1997). As temperatures are negatively correlated with altitude, there will come a point at which the transmission of a particular disease will become impossible due to the constraints of climate (that is providing that the highlands in question are sufficiently high). It has therefore proven tempting to define historical disease baselines in terms of specified altitude limits (e.g. Schwetz 1942; Lindsay & Martens 1998). By logical extension it should be possible to evaluate the effect of climate change by monitoring any shifts in the altitudinal range of disease occurrence. But this type of analysis is complicated by a variety of factors.

(i) Altitude may not be a reliable guide to climate. The relationship between altitude and temperature, for example, will be affected by aspect, continentality and (most significantly) latitude. The correlation

between elevation and rainfall, which has been shown to be a significant risk factor for disease outbreaks in highland areas (e.g. Lindsay *et al.* 2000), is highly variable and somewhat weak. Comparison of disease patterns at different sites with similar altitudes should therefore be carried out with caution unless accompanied by local climate data.

(ii) Despite the common assumption that the transmission of vector-borne diseases in highland areas is constrained by temperature, in reality a number of other important factors may play a role, and may buffer the disease system against any potential impact of climate change. The altitudinal limits of malaria transmission, for example, are in many localities far below what would be expected on the basis of temperature alone. In some cases this might be a product of insufficient rainfall, but in many instances it appears that the dominant factor is the presence or otherwise of suitable breeding sites for efficient malaria vectors (Cox *et al.* 1999).

(iii) It is probable that quoted historical baselines are unreliable. In many cases altitudinal cut-offs are nothing more than stated expert opinion. Where parasitological or entomological surveys have been carried out these may also be subject to bias. For example, in Colombia it was assumed historically that *Aedes aegypti*, a vector of dengue, was absent from all areas above 1500 m. This view was perpetuated by the fact that surveys for this vector deliberately avoided areas above this threshold—and it was not until the work of Suarez & Nelson (1981) that this notion was discounted (P. Reiter, personal communication, 1998).

(iv) Neither vectors nor vector-borne disease conform to any simple notion of thresholds or cut-offs. Taking the example of malaria, variations in transmission intensity due to altitude will follow a continuum of increasing instability as altitude increases. Within this continuum there will be a significant amount of seasonal and interannual variation (i.e. any arbitrary stratum of malaria endemicity will move up- and down-slope), which makes the detection of subtle shifts in transmission intensity difficult to detect, particularly over small distances.

Despite these analytical constraints, it should be noted that the vast majority of anecdotal evidence suggests that climate parameters play a dominant role in the occurrence of malaria epidemics in highland regions. These include seasonal or annual anomalies (temperature or precipitation well above or below the long-term average) rather than long-term changes in climate. Precipitation is an important limiting factor of transmission in many highland areas (Cox *et al.* 2001). For example, in eastern Africa, ENSO-related rains of 1997–1998 were implicated as the cause of serious malaria epidemics in a number of highland and desert fringe localities (Kilian *et al.* 1999; Lindsay *et al.* 2000). But while the importance of extreme climate events is well accepted (table 2), analyses of climate as a factor in longer-term shifts in malaria transmission have been less convincing (Mouchet *et al.* 1998). Many significant changes have been occurring in highland regions, such as population movement, decreases in vector control activity, and spreading drug and insecticide resistance (Reiter 1998). Drug resistance is increasing and in such circumstances a rise in morbidity or mortality may not necessarily reflect an increase in transmission (Cox *et al.* 2001). As previously discussed, the absence of reliable longitudinal datasets for malaria and other vector-borne diseases impedes our ability to detect long-term trends. Where reliable data do exist, it is not always possible to identify, or obtain data for, factors likely to confound any disease–climate interaction.

A few studies have looked in detail at changes in highland malaria and changes in climate over time. A selection of these are summarized below in order to illustrate some of the main findings and caveats.

Tulu (1996) examined trends in malaria transmission around Debre Zeit, Ethiopia, situated at 1900 m above sea level (ASL). Data from health facilities and seasonal blood surveys spanning the period 1968–1993 were analysed, and results indicated a strong upward trend in malaria incidence, hospital admissions and deaths, particularly since 1988. Data from epidemic reports also suggested that the incidence of malaria outbreaks rose markedly in the period 1981–1993, as did their altitudinal range. Climate data showed that from the mid-1980s Debre Zeit experienced an increase in daytime and nighttime temperatures, a decrease in mean monthly rainfall and an upward trend in relative humidity. Tulu found a strong positive correlation between minimum temperatures and (monthly) malaria incidence and attributed the rapid increase in malaria transmission in the period 1988–1993 in part to observed climate change. Tulu accepted, however, that this relationship may be confounded by the effects of non-climate factors. Between 1972 and 1985, for example, the amount of DDT (dichlorodiphenyltrichloroethane) used for house spraying in Debre Zeit sector fell by over 95%. Local studies *in vivo* also suggested that by the 1990s the increasing resistance of *Plasmodium falciparum* to chloroquine had made a contribution to increasing hospitalization and mortality (Tulu 1996; Tulu *et al.* 1996). The importance of drug resistance has also been highlighted in the Kenyan highlands. An analysis of clinical data for tea estates near Kericho over the period 1965–1997 led Shanks *et al.* (2000) to the conclusion that changes in drug sensitivity, rather than climate or environmental change, were the key factor behind the dramatic increases in the numbers of malaria admissions and case fatality rates among highland residents.

Loevinsohn (1994) analysed malaria data from Gikonko Health Centre near Butare, Rwanda, for the period 1975–1990 and described a large upsurge in cases in 1987 and 1988. Using local station data for rainfall and temperature, Loevinsohn was able to model the variability in malaria cases on a monthly basis and so demonstrate the strong (seasonal) association that exists between malaria and meteorological conditions. In the highlands of eastern Africa the association between exceptionally wet and/or warm years and high levels of malaria transmission has long been known (e.g. Campbell 1929). The key question in Gikonko is whether increased rates of malaria transmission associated with the wet El Niño conditions of 1987–1988 were subsequently sustained beyond the duration of that event. Given that

Loevensohn's malaria series ends in 1990 more data are required for this question to be answered satisfactorily.

Beyond Africa, Bouma *et al.* (1996) studied the role of climate in malaria transmission in 13 districts in the North West Frontier Province (NWFP) in Pakistan, the northern limit of current seasonal malaria transmission in Asia. The altitude of the region varies from 150 m to over 3000 m ASL in the Hindu Kush. A previous study in this area had found that mean November temperature was significantly correlated with percentage of slides examined that were positive for *P. falciparum* (Bouma *et al.* 1994). The two main outcomes in this study were: annual proportion of *P. falciparum* infections to all malaria infections (1978–1993) and the proportion of all slides examined by passive case detection in health centres that were positive for *P. falciparum* (1981–1993). Both series were converted to monthly time-series using malaria case report data from the whole province. The data were analysed in a multivariate regression model with a variety of monthly climate variables (precipitation, temperature, relative humidity) and by district. Monthly average rainfall in September and October, mean monthly temperature in November and December, and humidity in December accounted for 82% of the observed variation in malaria over the approximately 10-year period. Longer-term trends in nearly all the malaria-relevant climate variables were detected in the climate data series (1878–1993), in particular an increase in winter (November and December) temperatures, and an increase in October precipitation. The authors therefore cautiously suggest that the significant increase in *P. falciparum* in NWFP in the 1980s may be related to the favourable climate conditions. Late season temperatures were exceptionally high with years of high precipitation in critical months. Further, the contribution of temperature was more significant in the cooler districts, at higher altitudes. The malaria data series (1978–1993) was selected because insecticide spraying strategy did not change during this period. By eliminating data on refugees, this study attempted to exclude the possibility of human population movement explaining the change in malaria rates. An observed increase in chloroquine resistance is consistent with the increase in *P. falciparum* observed up to 1990 but not with the observed decreases in 1991 and 1993. This paper is an example of a thorough investigation of the role of climate in malaria transmission in a highland region. It is strongly suggestive of the observed trends in climate contributing to an increase in malaria. However, it can be argued that the contribution of chloroquine resistance and the role of refugees (which may have increased transmission to the resident population) have not been sufficiently resolved. Further, the short time-series may also have been affected by El Niño-related climate anomalies in 1987–1988 and 1991–1993 (Bouma *et al.* 1994).

The studies described above have made important advances in describing the causative factors of highland malaria. They are highly suggestive of a significant role of temperature and precipitation in increasing malaria transmission and burden of disease, although this is not a new finding. They are also suggestive that global climate change has contributed to increases in highland malaria. The studies illustrate how well confounding factors can be quantitatively addressed if data are available. Two of the studies described above, however, do not have time-series of sufficient duration to show a long-term trend rather than seasonal and/or interannual variations. These two caveats are some of the considerations with which to weigh the evidence for climate change attribution. Expert judgement must be made about the consistency of such results across multiple studies in highland areas.

6. CLIMATE CHANGE, DROUGHT AND MALARIA RETREAT

Precipitation and/or low humidity is an important limiting factor for mosquito-borne disease transmission in many arid and semi-arid areas (Cox *et al.* 2001). The minimum monthly rainfall thought to be essential for endemic malaria transmission ranges from 50 to 80 mm and needs to be sustained for a number of consecutive months (Craig *et al.* 1999). However, stable seasonal transmission can occur in drier climate regimes where oasis or irrigation schemes have provided breeding sites. Relative humidity of 60% or more has also been deemed necessary for effective malaria transmission (Molineaux 1988). In Africa, the Sahel is a band of savannah lining the southern limit of the Sahara desert and representing the northern limit of malaria distribution in many countries (Senegal, Mali, Niger, Chad, Sudan and Ethiopia). Beyond the very fringes of malaria distribution (the unstable 'epidemic zone') there is a region where stable transmission occurs every year following the seasonal rains. It is in this region that there is some evidence from studies in Senegal and Niger that malaria has decreased in association with the observed decline in annual rainfall (Mouchet *et al.* 1996).

On average, the Sahel region has experienced a decrease in annual precipitation since the 1970s; major droughts occurred in 1983 and 1984, and in the early 1990s. The region has large interannual variability in rainfall, as well as substantial multidecadal variability, and the role of anthropogenic climate change in the prolonged dry period remains uncertain (Hulme *et al.* 2001). A study by Faye *et al.* (1995) in the Niayes area of Senegal compared entomological and parasitological surveys in 1991–1992 with what the authors considered to be data from comparable surveys undertaken in 1967–1968. A reduction in malaria transmission was indicated by a significant decline in the parasite index in children from 40–80% in 1967 to *ca.* 10% in 1991 and 1992. Julvez *et al.* (1997) also reported lower-than-expected parasite rates in the Sahelian eastern region of the Niger Republic (Niger Valley, Zinder and Diffa).

The reduction in malaria transmission is attributed to a major reduction in the abundance of the predominant vector *Anopheles funestus*. In both Senegal and the Niger Republic, entomological surveys in the early 1990s were unable to capture any of this species (Mouchet *et al.* 1996), which likes to breed in pools with emergent vegetation that appears following the rains. A combination of human activities (such as deforestation and agriculture) and the decline in rainfall are likely to be responsible for the loss of breeding habitat. In recent years, the Sahel rainfall has been quite stable around the 1961–1990 annual average (Hulme *et al.* 2001). However, *A. funestus*

did not return following rains in 1995 because larval habitats were not restored (Mouchet *et al.* 1996).

In summary, changes in climate have contributed to an observed shift in the malaria epidemiology in this region. Populations that previously have experienced seasonal transmission are now within an expanded epidemic risk zone of 'desert fringe' malaria. This example also illustrates the difficulty in attributing climate changes at the subregional level to anthropogenic climate change.

7. DISCUSSION AND CONCLUSIONS

A very limited number of studies present evidence for effects of observed climate change on vector-borne disease. In our judgement, the literature to date does not include strong evidence of an impact of climate change on vector-borne diseases. This must be seen as 'absence of evidence', rather than 'evidence of absence' of an effect. There is a lack of long-term (more than 10 years') quality data on disease and vector distributions in areas where climate change has been observed and where a response is most likely to have occurred. While several studies are highly suggestive, alternative explanations such as 'background' socio-economic, demographic and environmental effects remain plausible enough to cast some doubt on the role of climate change. New approaches need to be developed in order to assess the pattern and plausibility of these diverse studies of health impacts.

There has been a tendency to oversimplify the mechanisms by which climate change may affect disease transmission. For example, discussions of highland malaria have relied on assumptions of shifts in mean temperatures and a simple threshold effect or 'altitude limit'. Many studies have clearly demonstrated the importance of precipitation (and humidity) in limiting malaria transmission in highland and desert fringe areas. Decreases in precipitation are a feature of climate change and these may have beneficial effects by reducing malaria transmission. However, changes in precipitation patterns are complex to describe and project under climate change.

Frequent and long-term sampling along transects to monitor the full longitudinal and altitudinal range of specific vector species, and their seasonal patterns, would provide stronger evidence of any changes in vector or disease distribution. Such studies may be the most cost-effective and robust methods of directly detecting the first health-relevant effects of this predicted climate change. Unfortunately, current vector-monitoring systems are often unable to provide reliable measurement of changes in even the limited number of parameters suggested.

Most climate models, however, predict that climate change will increase rapidly in coming decades (IPCC 2001*a*). The rate of warming already observed is unprecedented in human history. Careful consideration should therefore be given to maximizing the chances of detection of the effects of these changes on vector-borne diseases. It is difficult to detect and attribute climate change effects using data collected for other purposes. Consideration should be given to setting up long-term surveillance programmes to specifically monitor sensitive aspects of climate change effects on vector-borne disease (and possible confounders) over the coming decades. There is a need to identify areas where populations are vulnerable to the health impacts of climate change. There are areas where diseases are likely to respond to a change in climate and where the population at risk is large with limited capacity to respond to emerging disease threats.

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