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The Epidemiological Basis of Communicable Disease Control in Relation to the Global Public Goods for Health

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THE EPIDEMIOLOGICAL BASIS OF COMMUNICABLE DISEASE CONTROL IN RELATION TO GLOBAL PUBLIC GOODS FOR HEALTH

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Introduction

This paper sets out to explore how far the concept of Global Public Goods is relevant and useful in considering the control of communicable diseases in an international development context. The analysis is deliberately focused on the diseases themselves and uses the standard defining criteria of global public goods. The aim is to see where this takes us. A specific effort has been made to avoid taking the development consequences as a starting point: the hazard of starting from a political goal and reading this back into scientific analysis has to be avoided if concepts are not simply to become transient slogans to encourage funding agencies.

It should be noted that the term 'communicable disease' can be used in either a strict sense (to cover infections that are not contagious) or more loosely to cover infections as a whole, in American usage particularly (Chin, 2000). Similarly the term 'infectious disease', is in Europe generally used to mean communicable disease in the broad sense (Christie, 1980). In this paper the terms 'communicable disease' and 'infectious disease' are both used in the broad sense and interchangeably. The term ‘contagious’ is used for diseases spread directly from one person to another, and the term ‘transmissible’ for those communicable diseases that are not contagious.

It has been apparent for centuries that the communicable diseases of one country can be transferred to other countries with devastating effect. This clear example of a 'Global Public Bad' carries the implication that if the original donor country of the pathogen were to control that infection effectively the other countries would not suffer, or would suffer less, from the introduced infection. Thus the control of the infection in the ‘donor’ country would be a global public good. The introduction of quarantine and similar measures was an attempt to prevent the spread of these global public ‘bads’.

The concept of globalisation has been developed to summarise a large group of phenomena. Some of these are the almost inevitable consequence of improvements in communications technology while others are the result of a deliberate policy of facilitating free trade internationally. Some follow from the increase in international travel. Yet others are global environmental changes resulting from the scale of resource utilisation in some countries. All, though diverse in nature, fall conveniently under the umbrella of ‘globalisation’. Recently some have sought to apply globalisation thinking to trying to understand the role of international aid and to selectively justify some forms of it (Kaul, Grunberg and Stern, 1999). Within a nation the market handles many personal and private transactions, but the state is

expected to provide what are known as public goods: items and conditions that can benefit all, and without people having to compete since there is not a finite limit on the number who can share the benefit. In formal terms such public goods are non-rivalrous (you don't have to compete for your share) and nonexcludable (it's very hard to stop anyone from accessing the benefits). That is why the market is not good at providing them. This concept is now being extended globally, in terms of 'Global Public Goods', corresponding to the public goods described earlier at a national level. World peace is perhaps the clearest global public good.

The question has then been raised of what aspects of communicable disease control can be rightly considered 'global public goods'. Two extreme cases fit well: the global eradication of an infection is such a public good, because all in the world benefit. So too is communicable disease surveillance, as information benefits almost all countries, in enabling them to take suitable preventive measures. Conversely, the reduction by one country of a cosmopolitan infection to perhaps half the number of cases usually suffered by that country will generally have negligible external benefits to other nations. Outside these extremes, what about public health control of infections? Where there are abundant numbers of the particular pathogen in all countries, then public health control in one of the countries will provide little benefit to the others. Similarly, control of a vector-borne disease in a country will have little benefit for another country that does not have the vector present or where the temperature is inappropriate. However, what a neighbour does to control an infection matters greatly to a country that is attempting control itself and which has a large amount of migration across its borders. The key determinant of whether control of a disease is a global public good will be the degree of migration of infected people, or vectors, or reservoir hosts, or the pathogens themselves or their genes. The theory of this process will be developed and specific examples explored.

A broad consideration of communicable disease control suggests that there are four aspects of this that are clear global public goods; beyond these there is a complex situation with regard to actual control in countries. This requires more detailed analysis. The paper is therefore divided into two unequal parts.

Four unequivocal Global Public Goods

Four areas of disease control where many of the activities are unequivocal global public goods are eradication, research, developing expertise, and surveillance and information.

Eradication

Global eradication of an infection is a global public good in the strict sense. Once a pathogen is eradicated from the world the stream of benefits is indefinitely long, available to all inhabitants of the world without further cost, and in the case of the one success so far, smallpox eradication, the benefits have been massive in relation to the costs.

It is also clear that in the late stages of eradication, when the goal is in sight and appears attainable to those best qualified to judge, getting rid of the residual cases of infection is a process which merits general support. Most countries, probably including all the most prosperous ones, have a huge stake in avoiding re-introductions of the infection, and the few, usually poor and stressed countries - often with problems of complex emergencies or more conventional war - will merit and probably receive help from the others both for selfish and for altruistic reasons. Guinea-worm eradication is at this stage, with most residual cases in one country, Sudan, and polio eradication is moving towards the same position. Much less

clear is the point at which the possible eradication of an infection could legitimately be stated as an aim. If the statement of something as a global public good were seen to unlock resources not readily available otherwise, the incentive to declare eradication as a goal would be much increased, with unfortunate consequences in the long term. The lessons of the failure to eradicate malaria in the 1970's were well learned, in that there has had to be very widespread control of an infection before eradication is considered as a possible goal. Large sums were wasted in the failed areas of malaria eradication, with consequent adverse effects on control. By the nature of the task to be undertaken, those advocating eradication of a given infection will tend to overstate their case to a substantial degree.

Eradication as a strategy can only be defined *post hoc*, since there is a world of difference between attempted eradication and successful eradication. The former, if it then fails, is a qualified disaster: it results in collapse of morale and motivation for control programme staff, both the waste of a huge sum spent on eradication and the subsequent impoverishment of the control programme, as well as a discouragement to other countries which may have different circumstances that might in reality be more favourable for eradication attempts.

It is right that, as at present, great debate and caution be exercised before a goal of eradication is stated for a particular infection: unsuccessful attempts at eradication cannot be considered as global public goods.

Research

Research leading to better methods of disease control is another global public good, certainly if the new intervention remains in the public sector. It can be argued that more applied and operational research is country- or place- specific and therefore cannot be described as a global public good; however the methodology of such work is often widely, even if less than globally, applicable.

Poor countries may be excluded from the benefits of new control interventions in practice because they cannot afford to implement them, and it can be argued that the greater the cost of a specific intervention, the less it qualifies as a global public good. On the other hand, the prices of drugs fall as the royalties pay off the development costs. International and societal pressures may successfully force down prices or the formation of national programmes may enable cheap bulk purchase, and in any case until a drug has been discovered and developed it is not possible to haggle about price. (That is not to deny that it is possible and desirable to select compounds for development that are likely to lead to lower cost medicines for diseases prevalent amongst the poor). Thus the research leading to an inexpensive antimalarial drug, that can be applied on a large scale by most countries, approaches closer to a global public good than one which is so expensive to make (or which is likely to be so highly priced by the manufacturer) that most people in the affected population are excluded from the benefits of the research. However it might have an important role as a tertiary care or third-line drug. Medicines and vaccines against communicable diseases that are widespread in occurrence or are, more particularly, readily transportable to other countries where they would give rise to outbreaks or an extension of their endemic areas, have a greater potential for being considered as global public goods than other drugs against infections confined to more circumscribed areas. However, the latter are more likely, *ceteris paribus,* to be eradicable.

Surveillance and Information

The role of international disease surveillance as a global public good has been reviewed thoroughly by Zacker (Zacker, 1999) and would be generally agreed, though there are some difficult areas, described by Zacker. Information about some communicable diseases is largely of local or national relevance; some countries are unable to benefit from information received from other countries, because they either are too poor to take the preventive action required or lack the expertise for a measured and effective response. A further serious problem is that other countries may over-react to information about disease in a particular place with resulting great economic hardship to the reporting country. The plague outbreak in Surat caused immense economic loss to India even though no cases occurred outside the country.

Whilst there is a need for surveillance systems to be rationally developed in order to collect relevant data (many are not, and collect large amounts of data that are not only useless for operational and policy purposes but dilute out the available expertise so that there is little guidance of action by information), it is not possible – especially for the detection of newly emerging infections – to confine surveillance to a very narrow field, and it is the overall quality of the work which will have the best ability to contribute as a global public good.

These issues all point to the fourth of the global public goods, developing expertise for surveillance and control in all countries.

Developing Expertise

Optimising the response of countries to the hazard presented by communicable diseases requires good surveillance data, efficient use of the resources available for control, and prudent responses to external information. All these are crucially dependent on having enough, or at least some, skilled epidemiological staff in each country. In the absence of such staff, not only does the country suffer but also other countries will lack reliable information and trustworthy assessments of new problems, and of progress in control on longstanding infections, and consequently react in expensive and less than optimal ways. The huge sums which may be lost by trade restrictions, limitations on travel, and various forms of quarantine can be mitigated if communicable disease control authorities have confidence in the information coming from the affected country and the measures put in place locally.

It follows that training of able people as communicable disease control staff, and ensuring stable and reasonably remunerated employment thereafter, are global public goods, both as a necessary step towards good surveillance and to provide the global network that is essential for optimal control activities.

Analytical Framework for Specific Disease Control

Structure of Transmission

The basic structure of communicable disease transmission comprises several interacting populations. At the simplest, there are two such populations: people and the pathogen being considered. If the pathogen is vector-borne, as with malaria or with yellow fever, there is also a population (or several populations if several species are involved) of insect or other invertebrate vectors. Where the infection has a reservoir in other vertebrates there will be one or more populations of reservoir hosts. In the case of parasitic worm infection transmitted by invertebrates, these latter are more correctly called intermediate hosts but for our purposes may be considered as vectors too (Webber, 1996).

The simplest pattern of transmission is by airborne contagion. This applies to the respiratory viruses and many of the common diseases of childhood. The child developing the symptoms of measles has a time early in the infection when he or she will pass on the virus to other non-immune people around. Hence the great epidemics when it was first introduced to parts of the Pacific islands. The disease will tend then to die out in small communities as susceptibles are exhausted. Use of measles vaccine to control and then eradicate the infection, as is being attempted in parts of the world, will leave a largely immune human population in the short run. However, if national eradication were achieved, the tendency would be to let vaccination also die out, thus gradually creating a large population of non-immune people. Introduction of even a single infectious case from another country could undo the whole of the recipient country's control and eradication programme.

Migration Processes

The effects of control of communicable disease in one country upon others is of necessity dependent on the movement of components of the life cycle, in the broadest sense, from one country to another. In a completely closed country, where nothing entered or left the country, the state of its communicable diseases would have no impact upon such infections elsewhere in the world.

Several types of movement across borders, or 'migration' as it will be called here, in the broad sense, are relevant to communicable disease epidemiology. The categories of migrant are:

1. Pathogens in people, reservoir hosts or vectors moving to a country from which they were previously absent.
2. Pathogens migrating, in people, vectors or reservoir hosts, in sufficient numbers, between two countries in both of which the pathogen is already present. The effect is quantitative. It will occupy much of our attention here.
3. A special case: non-immune people entering a highly endemic country for the pathogen cycle being considered, are liable to heavier or more lethal infections than the indigenous inhabitants.
4. Vector species reaching new habitat countries.
5. Vector migration between countries in which they are found.
6. Transfer of potential reservoir hosts to new countries.
7. Transfer of genes and alleles to countries from which they were previously absent.

The zoonoses (Western usage: diseases transmissible between other vertebrates and people, in the broad sense) complicate the situation. There are many epidemiological possibilities; that grade into each other. At one extreme are those diseases of animals where man is a dead-end host who does not pass on the disease under normal circumstances. If two countries have such a zoonosis and one takes steps to control the disease effectively, the immigration to that country of infected people will not affect transmission there. A transfer of infected reservoir hosts would have a potentially large effect. There is also the potential for transmission by unusual routes from infected migrant people. For example, the human hazard from new variant CJD to those living outside the UK was from exported livestock or meat; the risk from neurosurgery on a preclinical case of CJD travelling overseas and transfer by surgical instruments was remote.

From the viewpoint of a recipient country (**b**) that has undertaken control measures against an anthropozoonosis (Russian usage; Pavlovsky, 1966), a disease transmissible between people

and between animals and across the people/animal reservoir boundary, the benefit from control measures undertaken also in country (**a**) may be limited, if there is a persisting reservoir of the pathogen in (**b**)'s animals as well as in human visitors from (**a**).

Migratory Activities

One aspect of globalisation that is always referred to is migration - the physical interconnectedness that mirrors the more novel internet and other forms of intercommunication. The most obvious health aspect of migration in the short run is its potential to change the epidemiological patterns of infections and communicable diseases. BSE/CJD is a clear and devastating example of an infection immensely affected by the migration of livestock, of food products and people. We shall pursue three linked hypotheses more widely: that the scale and types of migration are increasing, that this is a major determinant of the current epidemiology of communicable diseases and it is crucial to this discussion of the nature and implications of communicable disease control as a global public good.

The pattern of migration is changing in many ways. The scale of migration has greatly increased. Over four generations in the family of the author, the linear distance between the extreme points of the lifetime track (a trace of all the movements taking place during life) has increased by a factor of 10 per generation and the area over which each person has roamed has shown an increase of the order of 100 times per generation. While this may be extreme, all the data show increasing numbers of people on the move and over greater distances.

The facility of travel has also much increased so that the number of times that individuals go to far-off places has gone up, even though the total time spent at the distant place visited has probably fallen. (This was written prior to the recent events that will probably reverse the former trend, at any rate for a time). The scale of travel globally is vast: 625 million tourists cross international boundaries each year, and ten times that number move around within their own countries (Handszuh and Waters, 1997). In addition - and from a health viewpoint still more important, are labour migrants and over 20 million refugees. Perhaps *Homo sapiens* should be renamed *Homo vagans* (the wandering human).

A consequence of this is that the boundaries of local and global are increasingly blurred. Local processes when replicated worldwide can create a global effect. This has implications for the way we look at the population biology of pathogenic organisms - bacteria, viruses, and other parasites that cause disease. Parasites have always been the key examples of meta-population biology (Hanski and Gilpin, 1997; Hanski, 1999): that is, where the organisms are separated into discrete subpopulations which only interact to a limited extent. Even if three of us have typhoid fever at the same time, the populations of *Salmonella typhi* inside each of us remain largely separate from each other. That is the case regardless of the presence or absence of globalisation. However, many disease-causing organisms also form a higher order of meta-populations. The schistosome worm parasites of people who live near village X and contract the disease in the ponds of X may be relatively isolated from the schistosome populations of the people in nearby village Y. Gene flow between them may be rare. But if infected people are migrating at a great rate these separate village gene pools may receive so many migrants passing on the infections that they may behave as one large, relatively homogenous, gene pool and also as a continuous huge population of the pathogenic organism. The dynamics of infection spread in a network of rarely intercommunicating villages is very different from that in a large city whose inhabitants are intermingling.

The consequence of transferring infections from one country to another depend not only upon the initial state of infection in each of the two countries but also on the potential for transmission in the receptive country. If we consider the transfer of a vector-borne infection from an endemic country to one that is non-endemic, then the cost to the recipient that lacks a vector will be the care of the imported cases, the economic loss to the cases and the cost of preventive measures taken by its citizens when travelling in the endemic country. If circumstances allow limited secondary transmission, the costs will include those related to the introduced and consequential cases and to control of the outbreak. If effective vectors are present and the disease becomes newly endemic in the recipient country the costs will become very high indeed whether assessed in terms of human disease or economic costs.

Where an infection is already present in a country, there will be a sense of the local value of R_o (the basic case reproductive number; Anderson and May, 1991) and consequent rate of spread, and in many circumstances an imported case will behave similarly to an indigenous case. However, this is not so in several circumstances, which will depend on the specific infection being considered. Three such situations are as follows. Where the imported case is from a highly endemic country for a disease such as malaria where the chance of prolonged symptomless carriage of the infection is much greater in holoendemic areas, so the imported case may be epidemiologically infectious to local vectors for much longer. The variants on this theme are described in the malaria section. Secondly, the imported case may be in a specific social or ethnic group whose pattern of social behaviour may be less or more conducive to continued transmission than that of most of the indigenous inhabitants. Thirdly, if the imported case has a different pattern of drug resistance than the local strains this may have a different set of consequences than would result from simply adding another case of local infection. These three examples reflect that subsequent differences occur when the imported case shows heterogeneity of human host immunity, host behaviour or parasite genotype as compared with indigenous cases.

The traditional view (indeed, the basis of quarantine) is that of travellers bringing epidemic diseases which then spread rapidly in a non-immune population. Cholera and plague are the classical examples. But today the transfer of genes rather than organisms may be the aspect of greater public health importance. Staphylococci are present in most, if not all, countries but migrants from one country with antibiotic resistant genes in their staphylococci may carry them into the country they visit, and subsequently those genes may spread through the resident staphylococci. Where antibiotic resistance is carried on plasmids, there may be subsequent horizontal transfer of the antibiotic resistance across species barriers in bacteria. Here, if you like, is an epidemic of genes in a population of microbes.
We believe that migration has a profound and often underestimated role in the epidemiology of infections, that the newer ways of measuring gene flow combined with more sophisticated detailed quantitative measures of migration will move our understanding of infectious disease forwards, and that this will have implications for how to control these diseases in a globalising world.

The Migrating Organisms: Pathogens, Vectors, Reservoir Hosts and Genes

Whilst migration is usually thought of chiefly in this context as a pathogen travelling inside an infected person, there are other migrations liable to prevent communicable disease control. The increase in range and distribution of potential vectors of pathogens is important and well illustrated by the spread of *Aedes albopictus,* an important vector of dengue, far beyond its previous range as a result of moving tyres across the world (it is a container-breeding mosquito), possibly assisted by climate change. Earlier incursions of the most efficient vector

of malaria, *Anopheles gambiae (sensu stricto)*, into both Brazil and Egypt were followed by major outbreaks of falciparum malaria and it was clearly of interest to many countries to limit any further extension of its range; it was successfully pushed out of both countries. Much concern has been expressed that an effect of global climate change will be both a spread of the range of vector species and temperatures facilitating the vectorial capacity of such insects as are present already.

Reservoir hosts for human pathogens migrate less readily than insects; they tend to increase their local role in response to agricultural and ecological alterations. Genetic mutations affecting drug susceptibility of pathogens (and insecticide resistance in vectors) may arise polyphyletically but the occurrence of some, especially that for chloroquine resistance in malaria parasites, is best explained as spread outwards from two sites where the initial mutation occurred.

Descriptive Section: Particular Diseases

This section explores relevant aspects of the control of several major infectious disease problems. It covers a diverse range of infections to illuminate issues, rather than aiming at completeness. There is an emphasis on the more difficult epidemiological situations in order to define the criteria against which any classificatory scheme is to be tested.

Smallpox

As the one major disease to have been eradicated, it is easy to see how immense global funds would have been made available to deal with the last few cases of the disease in the Horn of Africa. Smallpox also provides an illustration of the relative protection against reintroduction of the infection provided by vaccination three decades ago as compared with vulnerability at present. Maintained immunization is a costly but more stable state for a population than the loss of immunity that will tend to follow successful elimination of a contagious disease.

Trachoma

Among the chlamydial infections, *Chlamydia trachomatis* is complex and raises theoretical issues in relation to global public goods, though these are more straightforward in practice. The organism can infect the eyes, genital tract, and less frequently other organs. Eye infection is the most important, as it is the main infectious cause of blindness in Africa (north and south of the Sahara) as well as in some parts of Asia and Latin America. Some 150 million people are infected and over 5 million are blind.

Infection spreads, particularly within families, by contact with fingers that have picked up infection from already infected eyes or genital tract. The initial infection is an acute conjunctivitis - inflammation of the membranes of the eye - which gradually heals. Long-term damage to the eye results from repeated infections so that the inner eyelids become scarred and eventually contract, bringing the eyelashes to become turned inwards and gradually destroy vision in the eye. There is good evidence that infections may be carried between people's eyes by the fly *Musca sorbens*, and suggestive evidence that in the presence of ample domestic water supplies, used for personal washing, the active trachoma infection is unlikely to progress to permanent damage.

Treatment of the infection is by tetracycline eye ointment applied meticulously twice daily for many weeks, or by oral azithromycin given on three occasions. The latter can achieve a high cure rate with only gradual reinfection. Determined campaigns are being undertaken to eliminate trachomatous blindness, using chemotherapy.

Meanwhile the same organism in the genital tract is the most common sexually transmitted disease of Western countries and also is frequent in developing countries.

What then is the position following successful anti-trachoma campaigns in an endemic country that has had a high trachomatous blindness rate? The heavy eye infections are a disease of the poor who are less likely to travel great distances. Nor is it likely that the levels of genital infection (often asymptomatic) will be much reduced in the long term. So although the disease is contagious it is unlikely that migrant cases will have a substantial effect. Moreover the blinding infections that are the object of public health action, once reduced by chemotherapy, are also dependent on environmental factors of a local nature. I believe this means that the likelihood of reducing levels of infection to that at which migration plays the determining role in transmission is low; and a resurgence of major eye disease after strong chemotherapeutic campaigns is likely to be due to local rather than global factors. The case for action against blinding trachoma appears overwhelming. But this case is not best argued in terms of global public good in a narrow sense

Malaria

The control of malaria has been more fully explored and documented than for any other communicable disease, because of its importance, the diversity of control methods, epidemiological complexity, and above all the attempts at eradication during the 1950-1970 period. These were only locally successful but furnish much information on the interaction between differing levels of control in nearby countries. The transmission of malaria is from person to person chiefly by way of anopheline mosquitoes in which development of the parasites (four species of the genus *Plasmodium*) that cause the disease take place. There are many vector species of *Anopheles*. The female mosquitoes both acquire the infection and pass it on to others subsequently in the course of feeding on human blood. There is no animal reservoir other than man.

Malaria is of particular interest for our topic it was the first disease whose eradication was attempted as a global public good (Pampana, 1969). Antimalarial drug resistance illustrates many further issues (Peters, 1987). Diverse vector ecology and insecticide resistance add complexity, and concern about the consequences of global environmental change for the biogeography of malaria add a further global dimension to the discussion. Several methods of control have different implications for resurgence and for spread of malaria. No vaccine is available for public health use as yet.

Malaria illustrates first the interaction of migration and transmission control. Where two adjacent countries with comparable anopheline environments favourable to transmission have very different levels of malaria control implemented, the more effective country can be severely disadvantaged. A clear example has been Nepal as described below.

Even in situations where one might expect migration to be very limited, especially on a short time span, the results have indicated migration on a substantial scale. In a study in rural Yunnan, China, in the Red River Basin and not near any international boundary, such results were found. The study was hoping to identify, by satellite remote sensing, locational prediction of malaria incidence. But in the "gold standard" ground survey it was found that 126 of the 220 falciparum malaria cases were imported from elsewhere. More interestingly, even among the apparently local cases, the relative risk of infection in the 29 cases who had travelled in the previous few months was 9 times higher than in those who had not travelled,

so they too had probably acquired them elsewhere. In other words, 70% of cases here had been contracted outside the area of residence.

In the UK, which has an imported malaria problem that is tiny by Asian standards but is still the second largest in Europe, the pattern of migration determining the infection has changed from a preponderance of holiday-makers and immigrants some decades ago to a situation in which those who settled in the UK long ago and are now visiting friends and relations in the tropics comprise the largest single group of imported malaria cases. Incidentally, it also shows one of the limits on globalisation: settled groups from South Asia and from West Africa in the UK not only have their distinctive malaria risk patterns but also they tend to have different use of preventive measures and ways of responding to the disease. They each retain separate 'malaria cultures' as named by Dr. Yumiko Doi, who has shown similar distinctive patterns in immigrants from the Kenya lowlands to highland areas. The different tribal groups retain different malaria cultures even decades after moving.

Migration has been related to malaria in several ways, as has been understood for over a century (Wernsdorfer and McGregor, 1988). It was noticed in workers and had the specific name 'malaria of the tropical migration of labour', where it had two aspects. The chief one involved movement of workers from the overpopulated highland areas to work at a lower and more malarious altitude. This might or might not involve crossing national borders. The workers suffered greatly from clinical malaria because they were without acquired immunity. Mortality could be very heavy, sufficient to stop development projects and render areas uninhabitable by non-immunes. Paradoxically, such workers were often accused of importing malaria, since they were seen to suffer more than the local people, whereas the latter were semi-immune and less aware of their own malaria. The other situation was where workers converged on a new site (for a dam or irrigation project) and some were from a malarious area. These infected the local anophelines and created a local malaria outbreak involving many of the workers. One or both of these processes has affected new immigration schemes such as the Mahaveli in Sri Lanka, transmigration programmes in Indonesia (within-country, but so great is the area and dispersed are the islands comprising it that it forms a good illustration), and many migration patterns of workers in Africa to some degree.

Because there is a great range of transmission encountered in endemic areas for malaria, from a basic case reproduction number R_o=1 (any smaller value and the malaria would die out) up to the extremely high levels of the African savannah and sahel where R_o can even exceed 1,000 locally and temporarily, it is not rare for contiguous national boundaries with different levels of malaria endemicity to occur (Bradley, 1991). More important today are countries with marked differences in the effort devoted to malaria control. A clear recent example is the border between Nepal and the state of Bihar in India. Nepal had a good control programme which had several decades ago almost removed *Anopheles minimus* from the highly malarious Inner Terai zone, and which had applied control measures effectively to the Outer Terai zone where less efficient malaria vectors are found. But this control could not be taken closer to eradication because of the migration of large numbers of malaria cases across the uncontrolled border with Bihar where control was poor. At one stage half the 40,000 malaria cases recorded in Nepal each year were imported. Because the migrants from the area with high transmission were more likely to be asymptomatic, they were also more important, person for person, than the indigenous cases for transmission (although the local Tharu tribal group from the Inner Terai had also been subject to greater transmission and were semi-immunes at an earlier stage).

A more common situation is importation of malaria into places from which it has been eradicated. Europe is now free of indigenous malaria because in the north (including the UK) transmission died out with land use changes, while in the Mediterranean basin determined eradication efforts were successful Bruce-Chwatt and de Zulueta, 1980). With the increase of international travel and the immigration of sizeable populations from highly malarious areas of Africa and South Asia imported malaria is a problem in most European countries with, for example, over 2,000 cases annually being reported from the UK over the past decade. The risk of restarting indigenous transmission varies by country. For example, the UK has anophelines which are able to transmit *P.vivax* but appear to be refractory to *P.falciparum* of African origin, which would be a much more hazardous parasite. Moreover, anopheline populations are localized and not often dense. The temperatures are marginal for plasmodial development. Clearly, if temperatures continue to rise as they have done for several decades, the potential for *P. vivax* transmission will increase and the country could become more comparable in malaria risk with that affecting Southern Europe at present.

The southern Europe countries, such as Italy, eradicated malaria by a combination of agricultural 'bonification' and specific campaigns. The latter having ceased after eradication had been achieved, some parts of country have the potential vectors in adequate numbers and a recent introduced case (locally contracted, secondarily to an imported case) demonstrates this. Prompt action is able to terminate the risk of a substantial outbreak, but the burden of this is clearly greater than simply treating imported cases. The third scenario is where imported cases give rise to an endemic situation, with massive consequences for the recipient country. For malaria this may have happened for some central Asian countries but resurgence has usually followed incomplete eradication, where local cases have persisted and given rise to outbreaks and then renewed endemicity, so the global public good argument has had less force in this case.

The spread of resistance to antimalarials by *Plasmodium falciparum* is more relevant. Resistance to the antifolate antimalarials such as pyrimethamine and proguanil arises regularly when the drug is used on a large or uncontrolled scale in a locality. The relevant genetic guide alleles may be present already, or relatively common mutations give rise to resistance. This contrasts with the more important emergence of resistance to choloroquine. The mechanisms of choloroquine resistance are only now becoming clearer, but historically the striking aspect has been its relatively slow emergence as compared with the huge amounts of chloroquine in uncontrolled use throughout malarious areas. Yet the origins of choloroquine resistance can be most readily ascribed to emergence on the Thai-Cambodian border and in Colombia around 1960. Resistance then spread out from the former source throughout south-east Asia, and reached Africa, where resistance has had devastating consequences. It appears to have arrived on the East African coast in the 1980's in an infected seaman (or several) from Southern Asia and spread out from there. The subsequent mutations that transformed the situation to one of high-grade resistance may have occurred locally, but the initial step does seem to have occurred at a few sites and been transferred in parasites inside infected people. This is another example of where prevention of gene transfer might have been a greater public good than preventing introduction of malaria as such.

Viral Haemorrhagic Fevers

The viral haemorrhagic fevers are among the most feared infections both locally and as imported infections. This is mainly due to a high case-fatality rate for some of these infections, usually the absence of a vaccine and very little in the way of dramatic treatment.

They are also perceived as extremely infectious though this is only the case under specific circumstances. In fact, the viral haemorrhagic fevers are diverse in their causative agents and still more so in their epidemiology. They include many of the most important of emerging diseases (Greenwood and De Cock, 1997).

Many of these are zoonoses, with reservoirs in rodents, birds or primates. Outbreaks involving people may follow ecological changes, invasion by people of their habitats or changes in agricultural practice. Specific hunting activities and subsequent close contact with an infected animal may lead to human infections. Secondary spread from person to person may follow, as contact with the blood of the patient is likely to lead to infection. Since a prominent feature of severe disease from these viruses is haemorrhage from the nose or mouth, many further cases are especially liable to occur among the staff of the health care facilities where patients are taken. Thus various outbreaks of Ebola fever in tropical Africa, in Uganda, Zaire, Sudan, have involved frightening mortality among hospital staff. Once the diagnosis was made, and stringent barrier nursing procedures observed, the incidence fell dramatically.

The hazard for distant countries has chiefly been from imported cases. The cost of special evacuation procedures to get the sick person back to a temperate home country may be massive. Secondary cases of, for example, Ebola fever are likely to be few and contracted prior to diagnosis. A more substantial outbreak of the closely related Marburg virus occurred in vaccine laboratory workers who contracted it from infected vervet monkey kidney cells, used for tissue culture, that had been derived from a monkey imported from East Africa. Expatriate nursing and medical staff have been among the victims of Ebola outbreaks. Control of outbreaks once they have occurred involve accurate diagnosis and barrier nursing to a high standard. We do not know enough to be able to completely prevent outbreaks in the tropics but understanding of public health management of cases will minimise both local and exported cases - further evidence of the value of expertise and trained staff as a global as well as local public good.
Lassa fever, endemic in Sierra Leone and neighbouring countries, is another lethal viral fever, but one which causes substantial morbidity and mortality locally, and with a rodent reservoir. Public health control is difficult, but rather more tractable than for Ebola so far as affected populations are concerned, since the reservoir is known. The exorbitant costs of coping with evacuation and imported cases might suggest some reasons for wider support for local control activities.
There are many other specific viruses, each with its particular epidemiological features and where control is a matter of local changes in behaviour or environment, with a very limited but relatively frightening risk elsewhere. It is clear that good surveillance and availability of information on the epidemiological situation, research leading to better understanding of the epidemiological processes, and well-trained local control and surveillance staff are the main relevant global public health goods.

African Trypanosomiasis

The trypanosomiases of Africa illustrate a complex zoo-anthroponotic situation. There are two main trypanosomes that infect people - *gambiense* and *rhodesiense*. Both are transmitted between people by tsetse flies. *T. rhodesiense* has a reservoir in wild and domestic ungulates and is zoonotic to a substantial degree, whilst the primarily West African *T. gambiense* is primarily transmitted from person to person although a degree of reservoir in pigs has been detected though it is of doubtful importance. Sleeping sickness, the usually fatal disease due to African trypanosome infections, is notoriously related to the migration of infected people

in the *gambiense* form, since the disease is only slowly lethal over a period of years and people remain infective to tsetse over this period. The movements of explorers and their followers, and of military forces, across Africa were responsible for the great outbreaks of sleeping sickness throughout Africa in the early 20th Century. More recently the linkage has been with complex emergencies.

Tuberculosis

Human tuberculosis is not only one of the greatest single causes of adult death among infectious diseases on the global scale, it is also today closely related to poverty and to HIV infection (Porter and McAdam, 1994). Its spread is facilitated by migration, particularly forced migration of the poor, not only because those groups have a high prevalence of infection and come from situations with poor health services but also because the long duration of chemotherapy needed for cure is particularly difficult to achieve in migrant groups, and may not even be attempted.

While the refugees and other migrant poor populations may introduce many cases of tuberculosis into richer countries which have low levels of indigenous tuberculosis, the occurrence of tuberculosis in rich countries among those immunosuppressed due to HIV infection had led to other problems. In some of these countries the rarity of the indigenous tuberculosis had led to the control programmes to wither away. Treating the new epidemics in the immunosuppressed had favoured emergence of multidrug resistant strains of the causative mycobacteria. So while there has been concern about spread of infection from high prevalence areas there is also a concern about reverse spread of drug resistance genes in the mycobacteria from more affluent to highly endemic countries.

Problems of control of tuberculosis in rich countries with communities of settled immigrant groups living in relative poverty and a high incidence of the infection, combined with the cost and poor efficacy of screening at the point of entry, have led industrial countries to actively, (and for self-centred practical reasons) consider assisting tuberculosis control in the areas of origin of their ethnic minorities. It is noteworthy that tuberculosis is one of the three infections specifically singled out for major attention in what has been referred to as the 'Global Fund', reflecting a broad feeling that this disease is of concern to many countries and that its control would indeed be a global public good. The persisting high levels of regular travel between settled ethnic minorities and their original homeland communities illustrate an aspect of globalisation that makes tuberculosis control a global public good.

The sources of infection are going to tend to be in high incidence and prevalence communities that are also migrant. Most infections are more prevalent amongst the poor. However, genes for chemotherapy resistance will tend to emerge in communities affluent enough to afford the newest and more expensive antibiotics and chemotherapeutic medicines but either unable to complete proper curative regimens or so immunosuppressed as to have a low cure rate or both.

Indirect Global Drivers of Communicable Disease Epidemiology

An analysis of which aspects of communicable disease control are global public goods today is deficient, as by the time any action resulted from such an analysis, the world would have changed and moved on. A series of processes linked to globalisation and global environmental charges are tending to increase the globally public bad results of taking no

action over current levels of communicable disease and ignoring changes that are already perceptible.

Global Environmental Changes

The global climate changes, in particular temperature increase, will tend to increase the areas in which it is warm enough for vector-borne infections to be transmitted (Houghton. Meira Filho, Callander et al. 1996; McMichael and Haines, 1997; McMichael, Haines, Sloof and Kovats, 1996). Because the countries which will become more suitable for this are in more temperate, and richer, regions they are able to take adequate preventive measures so that spread of such diseases as malaria and dengue in the short term is unlikely. There is greater likelihood of transmission reaching densely populated highland areas in the tropics, but though this has the potential to greatly increase malaria incidence, for example, the effects will be within highly endemic countries and the control benefits will be more local than of relevance beyond.
However, the risk of imported infections giving rise to further cases will be increased, provided susceptible vectors are present. In the medium term a greater concern is likely to be that altered climate will make areas suitable for new species of vector and create a much more receptive ecological situation where introduced pathogens can gain a foothold.

Globalisation

The diverse phenomena grouped together under the general heading of globalisation may also affect the degree to which communicable disease control in one country may affect another. The clearest issue is increased travel, in frequency, range and especially speed, so that people with imported diseases to non-endemic areas can arrive, spread out over a large area and become hard to trace. The fall of trade restrictions globally may make it hard to control overuse of inappropriate antibiotics and other chemicals such as insecticides, so putting strong evolutionary pressures for selection of resistance, an unequivocal 'global public bad' (McMichael and Beaglehole, 2000)..

Globalisation, like many another transiently popular - one might almost say fashionable - term is open to considerable hazard. In some respects it is so broad as to either act as a way to describe a rather arbitrary collection of phenomena or else to become so all-embracing as to lose much useful meaning. Moreover, because it is fashionable, there is a temptation for all manner of topics to get linked to the word in the hope of augmented funding. In the midst of all the many processes occurring on a global scale there are many links to be found to the present topic.

Complex Emergencies

Whether the occurrence of complex emergencies falls strictly under definitions of globalisation, these prolonged wars appear to have become more prevalent with the ready availability of weapons and by other aspects of globalisation. Several epidemic diseases are closely linked to the occurrence of complex emergencies, of which the most relevant are the African trypanosomiases. Major epidemics are occurring in Congo (formerly Zaire), Angola and N. Uganda. Eradication of dracunculiasis (guinea worm) is primarily held up by the civil war in Sudan. Such areas provide major sources of infection that can be exported to other countries to which refugees flee or to which mercenaries, foreign military missions or aid workers return. The numbers of holiday travellers who might become imported cases of infection will however be extremely low. Because of the notoriously protracted duration of

these emergencies - the Ugandan one lasted over 20 years and many still continue - they are likely to provide the main reasons for delay in global eradication of other infections.

Integration of Processes and Diseases

Whilst a crude taxonomy of diseases in relation to their control as a global public good is possible, they in reality come nearer to forming a multi-dimensional continuum. However, some understanding of the variables and processes involved has hopefully shown that the boundaries between local and global determinants of communicable diseases and their control are increasingly blurred. Mutual co-operation in their control is often essential, always helpful, and that for a mixture of both altruistic and selfish reasons. A situation in which patches of largely uncontrolled high prevalence infections co-exist with many areas where the same infections are well controlled, is usually both risky and unstable for neighbouring countries and often a threat to inhabitants of more distant lands, as well as causing much preventable suffering in the affected patches.

In the case of a contagious disease (D_1) viewed in very simple terms, with migrants passing from country A to country B, then at any given moment the public health importance of immigrant cases of D_1 to country A will be in the ratio of the number of prevalent infectious cases that are in migrants who brought in their infections to the number of prevalent infectious cases in the indigenous population. Thus if the prevalence of measles at a certain instant in people from country B is 20 and the simultaneous prevalence in the indigenous population is 7,000, the imported cases pose little relative threat to the public health. However, if an immensely successful anti-measles campaign had reduced the number of indigenous cases to 4, then the immigrant cases would pose a relatively major problem. To assess the overall threat of imported D_1 it would be necessary to sum the prevalences over all source countries of visitors to B. To go further to all contagious diseases, one would further sum across all countries as hosts. The matter would be further complicated insofar as the indigenous cases in BA or any other country had derived from earlier in-migrant infections.

Caution is required in leaping straight into building simplistic models of this overall process, because of marked heterogeneities at every step of the process, in particular the lack of homogenous mixing, so that high prevalence infected people from a source country will mainly encounter a particular subset of the host country population. This will still of course cause great harm but the hazards to the overall public health of country A's entire population may be less than with homogenous mixing.

Those who travel may be unrepresentative of the source country population : if they are business travellers they may belong to an elite group with low incidence of infectious disease. If they are holiday travellers they are unlikely to have been acutely ill when the journey was begun, and if refugees, they may well have been liable to an increased risk of contracting infections. Similar heterogeneities will affect those who begin in A, visit B, and may import infection back to A on their return. Some such travellers may be exposed to a high risk of infection, others on a short visit will have a far lower rate of infection; moreover as non-immunes they will get ill and are likely to have markedly reduced opportunities to spread the infection, though this will be very much a disease-specific variable. There will be a health service cost of these imported cases even if they do not give rise to further incident cases, but that has not been the focus of the above discussion.

Imported Outbreak Risk

With those caveats we may explore a general model. The risk of an outbreak of a specific disease in country B as a result of imported infection from country A is proportional to the product of the A→B rate of migratory activity times the prevalence rate of the disease in those migrants times the potential for spread, conveniently viewed as the basic case reproduction number (R_B) in B, and divided by the prevalence of infection (rate times population) in the indigenous inhabitants of country B

$M_{A \rightarrow B}$ consists usually of at least two components with different prevalence rates: the indigenous inhabitants of A who seek to travel to B and whose home is in B but who have travelled to A and are now returning home. Further subdivisions are possible.

The ratio of the point prevalences (not prevalence rates) between those from A on B and the indigenous B inhabitants is clearly crucial. If the disease is of comparable prevalence rates in A and B, then unless the cross-border migration rate is very high indeed, action in A will have little effect on B. However, as B controls its indigenous infection (unless it be by high coverage immunization) the risk of imported outbreaks will rise, until when the local prevalence is 0 (i.e. local eradication has been achieved) the entire disease risk will depend imported cases and the global public goods value of control in A, in terms of its benefit to B, will reach a very high level.

Screening of immigrants and returning travellers will only be attempted in B if the level of indigenous cases is low relative to that in arrivals. Once introduced, such screening/ focused surveillance will have a cost related to the scale of immigration rather than of the risk. Classically, this is the situation for immigrants to temperate countries who are suspected of a high prevalence of open tuberculosis.

The preceding sections apply to genetic variants as well as microbes, particularly for resistance to chemotherapy. So even if two countries have comparable levels of, say, malaria transmission, importation of a rare drug resistance mutation into B where it did not previously occur will be subject to the same considerations as 'whole' infections.

Treatment and case management costs will be proportional to the number of imported cases unless they be left to pass on the infection, when the augmented number of cases will require treatment.

Prophylactic costs are proportional to the number of travellers in the reverse direction, from B to A and the preventive measures taken.

The degree of pubic good realized in country B as a result of control of a disease in country A will therefore be, to a first approximation, the sum of those four functions of migration:

(i) the ratio of imported to indigenous cases prevalent in B, multiplied by the local potential for transmission, that is, the outbreak potential from imported cases of the disease from A plus
(ii) the cost of screening arrivals from A in B for preventing importation of cases, differentially for immigrants and returning visitors plus
(iii) the cost of managing imported cases of the disease from A to B plus
(iv) the cost of specific protection (including advice) against the disease for prospective travellers to A from B.

These processes may be summed across all endemic countries outside B to get a measure of the total public good that may result from a given level of global control of that disease to B,

though the calculation may not be straightforward since prophylaxis against the risks of visiting one country (or staying at home) may, if a vaccine, protect against visits elsewhere. Similarly for combining all diseases in contact between A and B, or looking at the global benefits from control of disease in country A, and, by extrapolation, the total external benefits, global public goods, from control of a particular disease in many countries.

Because the contagious infections are those for which vaccines have been particularly developed, the risk of introduction of infection will be much reduced if the host population has been largely immunized against the infection being introduced. Where the infection is not directly contagious from person to person the situation will be much more complicated.

But to summarise for the contagious infections: the importance of the situation as a global public health 'bad', and of its control as a good, will be dependent on the ratio of imported infectious cases to indigenous ones. Where the ratio is high, then control of disease in the source country will be a relative global public good and where the host countries have eradicated the infection so that the ratio is infinite, control of that infection in places where it remains is indeed a clear global public good.

With the increasing diversity and frequency of antimicrobial resistance genes, and the strong positive selection pressure to which they are exposed in many countries, the risks from spread of resistance genes, even between otherwise comparably endemic countries, may be as great a risk or, in my view, even greater, and contributes to the importance of control of communicable disease since the spread of rare antimicrobial resistance mutations is a clear global public bad.

In practical terms, the greatest threat to country B from A is from an infection common in A and absent in B but for whose transmission B is a very suitable place. This could best apply to an untreatable contagious disease for which no vaccine was readily available. The history of the early spread of HIV infection bears that out, as does global concern about microbiological warfare.

A feature of the whole concept of global public goods is that for disease control the global benefits are greatest to a country that has already reduced its level of the disease in question to a low level. Such countries are likely to be more rather than less prosperous. However, it can be argued that once they have good local control it is incumbent on them to assist poorer and higher incidence countries to implement control also, to switch from local to international expenditure for control rather than simply reducing their control budget and criticising their neighbours.

Can one categorize disease control in relation to the global public goods concept in an exploratory taxonomic approach? Enough has been presented in the descriptive part of this chapter to show the complexity displayed by each particular disease. An attempt is made in Table 1 to list some major infections and some of the relevant criteria for assessing relevance to 'global public goods' of their control. The number of plus signs is either a measure of the degree to which the criterion applies to that disease category or else of the proportion of the elements within that disease category to which the criterion applies. When the situation is a clear-cut yes or no, the letters Y or N are used. Numbers are avoided lest the reader yield to the misguided temptation to add them together to produce an 'index'! This table is a tentative first attempt and will be revised.

A few generalisations are possible. If the primary means of protection is by immunization and good coverage be maintained, the frequency of the disease in other countries is of much reduced concern to the public health worker, to a first approximation. Where an invertebrate vector or intermediate host is an essential stage in the life history of the pathogen causing an infection, then the disease prevalence elsewhere will be of limited public health interest to countries that either lack vectors or have too cold a climate for the pathogen to develop in the vector. Where an intractable animal reservoir of an infection exists in a country, then efforts to eliminate the infection from neighbouring countries will be of limited interest to the first country.

There are several caveats to such an analysis. One is that it ignores the clinical risk to travellers from the country under consideration, and the consequent harm to its travelling citizens who then suffer from the disease they import, regardless of the presence or absence of public health hazards. The second is that, were the global public goods paradigm be the only criterion for health aid, countries that were cold or vector-free would lose interest in such major problems as malaria. There are diseases whose control is a global public good for epidemiological reasons, as discussed in this chapter, but there are other major diseases such as malaria and many diarrhoeal diseases which need control if poor countries are to escape from poverty, regardless of the disease risk to rich temperate countries. One can argue that national health budgets should contribute to the control of such diseases as are 'global public bads' but not at the expense of aid budgets designed to meet the primary health needs of the poorest countries.

It is seen that it is possible, to a first approximation, to categorize aspects of the control of communicable diseases according to the degree to which they fit the definitions of global public goods as currently discussed, but such tabulation is less useful than analysing the issues. The analysis sheds some new light on thinking about CD control, giving rise to what may be thought of as a series of concentric circles, around any given country, of decreasing influence of that country's control status upon others. It appears that the conclusions, if treated too logically, may lead to odd decisions if viewed from alternative positions than that of global public goods. In other words, the latter concept has some utility but will not solve all our conceptual problems. One cannot fit complicated systems into simple categories except by Procrustean means. However, there are some activities that clearly fall into the category of global public goods: global eradication of specific infections, much research on control tools, development of expertise, and provision of much information about CDs: surveillance. However, care must be taken, particularly in relation to poorer countries, before rating all these above more modest control measures of common diseases in considering priority health goals. More particularly, a narrowly global public goods approach might see no reason for assistance to a poor country seeking to get rid of its malaria, from a rich country which just happened to contain no relevant anopheline vectors.

Conclusions

In conclusion, this exploration of the concept of global public goods in relation to communicable disease control has emphasized the increasing interdependence and vulnerability of the world's countries to each others' pathogens, vectors, reservoir hosts, and the genes that assist the spread, lethality or resistance to chemotherapy of the pathogens. The global public goods issues emerge when there is wide disparity in prevalence rates between any pair of countries with migratory interchange of their populations. All have very much to lose from new infections, as the spread of the HIV pandemic has demonstrated. With

widespread endemics now under control in more affluent countries, the latter have much to lose from re-emergence of these diseases. They therefore in their own self interest have much to gain from funding the collective reduction of such infections and surveillance to guard against more. We may, for communicable diseases, apply not only to individuals but also to communities, up to the scale of nations and regions, the words of John Donne:

No man is an island, entire of itself
Every man is a piece of the continent, a part of the main…
And therefore never send to know for whom the bell tolls,
It tolls for thee.

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					Vector		Animal Reservoir			Human	Overall	
Table 1				Feasibility						Asymptom-	Endemic	
	Endemic	Drug		of					Temp.	atic	need for	
Diseases	Importance	Resistance	Vaccine	Eradication	Needed?	Localised?	Exists?	Essential?	dependent	reservoir	Control	Risk
Diarrhoea overall	++++						±	-		+	++++	+
Specific Viral Diarrhoeas	++	+								+		+
Tuberculosis	++++	+++	+	±			+	-		+	++++	+++
Malaria	++++	+++		±	Y	+	0		Y	++	++++	++
Meningococcal Disease	++	++	++							+		+
Pneumococcal Disease	++	++	++							+		-
Schistosomiasis	++			±	Y	+++	+	-	Y	+		
Dengue	++				Y	+			Y			
Viral Haemorrhagic Fevers	++				±	?+						
Influenza	+++		+++				+	±				
Acute Respiratory Infections	++++	++					-				+++	
HIV/AIDS	++++	+++					0				++++	++++
Measles	+++		++++	++			0					++
Tetanus	+		++++				++					
Polio	++		+++	+++						+		++
Pertussis	+		++									
Diptheria	++		+++							+		+
Geohelminths	+		++			+	±		Y			-
Onchocerciasis	++				Y	++			Y	+		-
Guinea Worm	++			+++	Y	++			Y			-
CJD	++						Y	Y				++
Salmonelloses	++	++					Y	+				++
Leishmaniasis	++	++			Y	++	+	±	Y			+
Emergent Viruses	-	-	-	+	±	±	+	±	±		+++	+++