Parasites, People and Policy: Infectious Diseases and the Millennium Development Goals

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特別講演

**寄生動物、国民及び政策：
感染症とミレニアム開発目標**

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本稿は、平成18年10月3日、日本学術会議講堂で開催された日本学術会議第149回総会における特別講演の原稿である。

講演要旨●本講演では、生態系の相互作用に関する過去の研究をレビューし、先進国及び発展途上国における、寄生動物（ここでは、原生動物、ぜん虫や節足動物の寄生虫とともに、ウィルスやバクテリアも含むよう広く定義している。）と人間集団の間の相互作用のパターンについて述べている。これらを背景として、国レベル及び国際レベルで現在行われている公衆衛生に関するイニシアチブについて、特にMDGに関連して、いくつかの考えを提示している。

Abstract

This paper briefly reviews past history and present patterns in the interactions between parasites (defined broadly to include viruses and bacteria along with protozoan, helminth and arthropod parasites) and human populations, in developed and developing countries. Against this background I shall offer some thoughts on current public health initiatives, at national and international levels, with particular reference to the Millennium Development Goals.

Introduction

In this paper, I define parasites broadly to include both microparasites and macroparasites, in the sense defined by Anderson and May (1979, 1991). That is, I include viruses and bacteria along with the protozoan, arthropod and helminth agents of conventionally-defined parasitology. Thus defined, parasitic infections relate directly to 3 of the 8 UN Millennium Development Goals or MDG (namely, numbers 4, 5, 6 in the list in Box 1), and also are very much involved in two others (namely, the leading numbers 1 and 2).

In what follows, I will first sketch some past and present patterns in the interactions between humans and parasites. The general trend here could be called “Good News”. I then turn to the Bad News—the persisting distinction between diseases of the rich and diseases of the poor. Against this background, I discuss possible actions to achieve a fairer world: this discussion covers research priorities (basic knowledge); economic impediments to developing medical products for diseases of the poor, and ideas for new incentives; and other things. I conclude with some worries about new or re-emerging infectious diseases.

Box1: UN MILLENNIUM DEVELOPMENT GOALS

1. Eradicate extreme poverty and hunger
2. Achieve universal primary education
3. Promote gender equality and empower women
4. Reduce child mortality
5. Improve maternal health
6. Combat HIV/AIDS, malaria and other diseases
7. Ensure environmental sustainability
8. Develop a global partnership for development

Good News: The Past 50 Years and the Present

Figure 1 shows survivorship curves (probability of surviving to age a for a typical developed country, and for a typical developing country, 50 years ago). The developing countries curve is better, but not much better, than those inferred for our hunter-gatherer ancestors, before the dawn of agriculture.

As a global average, life expectancy at birth on our planet 50 years ago was 46 years, with an average difference of 26 years between developed and developing countries. Today, as a result of much better understanding of the transmission dynamics of infectious diseases and of methods for their treatment and control (better hygiene, vaccination, control of vectors, simple rehydration procedures for infant diarrhea, etc), average life expectancy at birth is 64 years. In India, for example, in 1950 average life expectancy was 39.4 and 38.0 years for males and females, respectively. The corresponding figures in 1998 were 62.1 and 63.7. This change is primarily because the average gap between developed and developing countries has diminished to a still-distressing 12 years.

Figure 1
Typical age-specific survivorship curves for human populations in developed and developing countries 50 years ago
(after Bradley, 1972)

It is, however, interesting to compare Figure 1 with Figure 2, which shows the survivorship curve in mid-nineteenth century Liverpool, which is fairly typical of early industrial centres in the West. In the nineteenth and early twentieth century slums in Western cities, mortality rates were appalling. A child born in Liverpool in 1860 had only a 50% chance of living beyond 5 years. In contrast, last year roughly 130 million children were born, and although some 10 million will not survive the first 5 years (for a mortality rate of around 8%), the odds are much better than for the developed world's past.

Interestingly, recent studies indicate that the improvements in public health which have resulted in today's developing, low-income countries being much healthier than OECD countries were at comparably levels of development come mainly from scientific and technological

advances, rather than simply from "income growth" (as some economists have rather mystically suggested). One such study finds income growth explains only 10–25% of increasing life expectancy (Preston, 1975). Another finds decline in infant mortality owing 5% to income growth, as against 21% to better education (Jamieson, 2001).

Bad News: Diseases of the Rich and Diseases of the Poor

These encouraging trends must, however, be set against the still-wide gap in life expectancy, and general health, between the developed and developing worlds. A

Figure 2

Age-specific survivorship curves for Liverpool in 1860 and for England in the 1990s
(from Richard Peto, Private Communication)

Figure 3

Disease burden (in DALYs) for High-Income Countries
(after Kremer and Glennerster, 2004 p.8)

Figure 4

Disease burden (DALYs) for Low-Income Countries
(after Kremer and Glennerster, 2004 p.8)

more meaningful measure of disease burden goes beyond life expectancy, to assess Disability Adjusted Life Years (DALY; Murray and Lopez, 1996). This quantitative measure combines premature mortality with years of productive life lost owing to morbidity or disability. One DALY equals one year of healthy life lost.

The pie-charts in Figures 3 and 4 contrast the causes of DALY in High-Income (developed) with those in Low-Income (developing) countries, respectively (Kremer and Glennerster, 2004). In the rich world, communicable infections account for only around 7% of DALY. The corresponding fraction for poor countries is an order-of-magnitude higher at 57%. Table 1 reinforces this contrast between Figs 3 and 4, giving a catalogue of infectious diseases for which 99% of the global burden falls on the developing world.

Some facts associated with these differences in DALY between rich and poor countries are worth noting.

(1) *Health Care Infrastructure.* In Europe, there are on average 3.9 physicians per 1,000 people. In the USA, 2.7. In sub-Saharan Africa, 0.1, and the problem is compounded by patterns of absenteeism, assessed at around 40% in one recent study (Kremer and Glennerster, 2004).

Table 1

Diseases for Which at Least 99 Percent of the Global Burden Fell on Low-and-Middle-Income Countries in 1990

Disease	Deaths per Year	DALYs(thousands)
Diarrheal diseases	2,124,032	62,227
Malaria	1,079,877	40,213
Measles	776,626	27,549
Pertussis	296,099	12,768
Tetanus	308,662	9,766
Syphilis	196,533	5,574
Lymphatic filariasis	404	5,549
Ancylostomiasis and necatoriasis(hookworm)	5,650	1,829
Leishmaniasis	40,913	1,810
Schistosomiasis	11,473	1,713
Trichuriasis	2,123	1,640
Trypanosomiasis	49,668	1,585
Trachoma	14	1,181
Onchocerciasis(river blindness)	—	951
Chagas disease	21,299	680
Dengue	12,037	433
Japanese encephalitis	3,502	426
Poliomyelitis	675	184
Leprosy	2,268	141
Diphtheria	3,394	114

Note: Diarrheal diseases differ from the other diseases in this list because they are actually a variety of diseases, caused by different pathogens.

Source: Global Burden from WHO(1996a), cited in Lanjouw and Cockburn(2001), table 1.

(2) *Basic Research on Diseases of the Poor.* Table 2 shows the results of a study of research papers published in four leading medical journals in 2002 and 2003 (Raja and Singer, 2004). The study assessed the overall proportion of papers relating to diseases of importance to developing countries. Given that such papers include those on HIV/AIDS and on TB (which are also significant problems in OECD countries), the small fraction is surprising, as well as lamentable.

Table2

Proportion of papers in four leading medical journals which relate (defined in accordance with the UN Global Forum on Health Research) to developing countries (Raja and Singer, 2004)

Jornal	proportion of Articles			
	Jan2002		Jan2003	
USA : New England Journal of Medicine Journal of the American Medical Association	7%	(7/29)	3%	(3/118)
	7%	(12/180)	4%	(5/138)
UK : Lancet	21%	(50/234)	23%	(52/227)
BMJ (British Medical Journal)	24%	(66/273)	18%	(44/242)
Overall :	15%		12%	

(3) *Drug Development.* In a study by Pecoul et al (1999), of 1,233 pharmaceutical drugs licensed (worldwide) in 1995-1997, only 13 (or 1%) were for tropical diseases. Moreover, of these 13, five came from veterinary research and two from modifications of existing medicines. Another two were developed by the USA military, an only four were developed by pharmaceutical companies specifically for tropical diseases of humans.

(4) *Pharmaceutical Sales.* Figure 5 shows world sales of pharmaceutical drugs, broken down by regions. Note that North America, Europe and Japan account for 82% of sales, Africa for 1%.

(5) *Disease Burdens and Research Efforts.* Table 3 shows the global burden of disease, measured in DALY, for several major afflictions, along with R&D expenditure. This R&D

Figure 5
The world pharmaceutical market: sales by region in 1998
(PhRMA, 2000).

Table3
Disease Burden and Funding Comparison
(after Cohen, 2006, p.164)

Condition	Global Disease Burden (million) DALYs	R&D Funding (\$Millions)	R&D Funding per DALY (\$)
Cardiovascular	148.190	9402	63.45
HIV/AIDS	84.458	2049	24.26
Malaria	46.486	288	6.20
Tuberculosis	34.736	378	10.88
Diabetes	16.194	1653	102.07
Dengue	0.616	58	94.16

expenditure in relation to DALY shows great variation, with malaria—by this comparative measure—getting less than one-tenth the attention given to cardiovascular problems.

Actions for a Fairer World

(1) *Private Benefactors.* No account of “actions for a fairer world” can be complete without acknowledging the example and inspiration provided by individual actions, of which those of the Rockefeller Foundation over the years, and the Bill & Melinda Gates Foundation more recently (selflessly enlarged very recently by Buffet), are particularly notable.

(2) *Public Incentives for Private Sector Drug Development.* One major fact, which underlies many of the above-mentioned problems, is the understandable failure of free-market mechanisms to deliver pharmaceutical products for diseases of the poor. Pharmaceutical companies, quite properly, have a responsibility to deliver both useful drugs and profits to shareholders. For many things, this works very well—better than public “command and control” mechanisms. But the research and development that leads to safe and effective pharmaceutical drugs is an expensive and unpredictable process. No matter how good the intentions, it does not make sense for a well-managed company to make a large investment in developing a drug whose potential beneficiaries are, in aggregate, too poor to pay the true costs (direct and indirect) that are involved.

One possible way out of this dilemma is for Governments or other agencies to help pay for the delivery of the drug, once it is developed. But the costs of producing and delivering a drug are typically small compared with the basic costs of research, development, and clinical trials. Public bodies have generally been unsympathetic to pharmaceutical company’s needs, once the drug exists; once their money has been spent, and an effective product achieved, the pharmaceutical companies’ negotiating position in respect to *ex post facto* subsidy for delivery tends understandably to be weak.

An important study by Kremer and Glennerster (2004) suggests a possible way forward, of benefit both to pharmaceutical companies and disease-afflicted poor people. The basis of the idea is that the threshold for privately financed investment in R&D toward a new drug is

higher than the corresponding “social threshold” which takes account of the public (economic) benefit of reducing DALY. The proposal thus is that Governments, individually or collectively (e.g. via the UN), in advance guarantee purchase of the drug at a price that makes BOTH producers and consumers better off: the producers, knowing the pay-off for a successful product in advance, can take more risks than they would if worried about the pay-off; society benefits from a healthier population and work-force. The essential idea is not new, but this particular application is both new and potentially hugely important.

(3) *Opposing Bureaucracy or Ideology Masquerading as Accountability.* Figure 6 gives an impression of the mind-boggling proliferation of different agencies and “stakeholders” that jostle to do good things in the developing world. There is arguably a need for egos and administrative structures to be subjugated to disciplined, coordinated and effective actions.

This need is even more important when some of the organizations involved seek to impose inappropriate “moral values” — for example, opposing condom distribution (or even disseminating lies about their being ineffective) in relation to HIV transmission.

Figure 6

A confusing cluster of agencies aims to help Tanzania with its HIV/AIDS epidemic
(after Cohen, 2006, p.166).

Relationships Between Various Stakeholders in Tanzania

(4) *Avoiding Priorities Set by Fashion.*

Most current activity on “diseases of the poor” focuses on the Big Three: HIV/AIDS, malaria, TB. However, as Molyneux (2004) and others have emphasised, the burden of other, relatively neglected, tropical diseases is roughly 1/4 the global disease burden of HIV/AIDS, 1/3 TB, and 1/2 malaria (all as measured in DALY). Table 4 sets out 13 such “Neglected Tropical Diseases”, which in total cause roughly half a million deaths annually.

Despite the availability of cost-effective, stable, and successful agents for the control or elimination of each of these 13, large numbers of the world's poor remain afflicted or at risk

Table4

Thirteen "**Neglected Tropical Diseases**"
(Which cause roughly 500,000 deaths annually)
and their etiologic agents (Molyneux *et al*,2005)

Protozoan Infections

African trypanosomiasis	<i>Trypanosoma gambiense, T. rhodesiense</i>
Kala-azar (visceral leishmaniasis)	<i>Leishmania donovani</i>

Helminth Infections

STH Infections

Ascariasis	<i>Ascaris lumbricoides</i>
Trichuriasis	<i>Trichuris trichiura</i>
Hookworm infection	<i>Necator americanus</i>

Schistosomiasis

Urinary schistosomiasis	<i>Schistosoma haematobium</i>
Hepatobiliary schistosomiasis	<i>Schistosoma mansoni</i>

Lymphatic filariasis

Onchocerciasis	<i>Onchocerca volvulus</i>
Dracunculiasis	<i>Dracunculus medinensis</i>

Bacterial Infections

Trachoma	<i>Chlamydia trachomatis</i>
Leprosy	<i>Mycobacterium leprae</i>
Buruli ulcer	<i>Mycobacterium ulcerans</i>

from this group of parasitic infections. Molyneux *et al* (2005) urge that “The low costs [for already-available integrated control of neglected tropical diseases] represent compelling figures to advocate for a pro-poor, proactive public health strategy of preventive chemotherapy to be delivered to all affected populations of Africa” . We need to look at our priorities in a more objective, analytic way, free from the understandable inertia of yesterday’s activities and fashions.

The Future

Reader (2004), in his book *Cities*, reminds us that “Bacterial and viral diseases are the price humanity has paid to live in large and densely populated cities. Virtually all the familiar infectious diseases have evolved only since the advent of agriculture, permanent settlement and the growth of cities. Most were transferred to humans from animals —especially domestic animals. Measles, for instance, is akin to rinderpest in cattle; influenza came from pigs; smallpox is related to cowpox. Humans share 296 diseases with domestic animals.” And the world’s cities become daily more crowded. Three hundred years ago, they contained 10% of the planet’s population; a century ago, 25%; today, 50%; by 2050, almost 70%.

The resulting high aggregations, coupled with increasing patterns of movements of peoples, present ideal conditions for new infectious agents to emerge, or old ones to re-appear. These opportunities are further enhanced by the increasing volume— amounting virtually to globalization— of the bushmeat trade, which previously was confined to small-scale, local operations. We do well to remember HIV/AIDS, in effect, came from bushmeat: HIV-1 from chimpanzees, HIV-2 from monkeys. We were luckier with SARS, which came from the

internationalization of bushmeat trade in “exotic animals” (specifically civets) to serve suburban restaurants in South East Asia. Table 5 hints at the growing volume of this trade.

Quite apart from the implications for Conservation Biology, we should be seriously worried about the likely epidemiological consequences of this rapidly growing trade.

Table5
HUMAN POPULATION DENSITY AND BUSHMEAT HARVESTS
(Bell *et al*, 2004)

Region	Density (people/Km ²)	Bushmeat Harvest (tonnes/yr)
Asia (S and SE Asia)	522	Unquantified
Africa (Congo Basin)	99	1—4 million
South America (Brazilian Amazon)	46	ca.100,000

Hikari to Kage

In short, the world today is a healthier place than it has ever been, both in developed and developing countries. But serious inequalities remain, even though they are less marked than 50 years ago. There are encouraging signs that these problems are being addressed, but problems remain. And we should be giving more forward-looking thought to reducing the probability of new infectious diseases appearing, and to being alert and prepared if they do.

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