

## PERSPECTIVE

## Threats to Global Health and Survival: The Growing Crises of Tropical Infectious Diseases—Our “Unfinished Agenda”

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Health, one of our most unassailable human values, transcends all geographic, political, and cultural boundaries. The health problems of the rapidly growing 80% of the world's population that live in the tropical developing countries of Asia, Africa, and Latin America pose major threats to industrialized as well as developing regions. These threats can be divided into three areas, or three “E”s: (1) emerging, reemerging, and antimicrobial-resistant infections; (2) exploding populations without improved health; and (3) erosion of our humanity or leadership if we ignore the growing health problems of the poor. Our assessment of current trends in global population distribution and resource consumption; DALY calculations, causes, and distribution of global mortality and morbidity; and the misperceptions about and maldistribution of resources for health point to the critical importance of addressing tropical infectious diseases and global health for preservation of democracy and civilization as we know it.

We begin this monograph by emphasizing the importance of health as a universal human value (section 1) and review three ways that tropical infectious diseases among the growing majority who reside in the tropics threaten us all (section 2). We then address the current and future trends in global population distribution and resource consumption (section 3); calculations, causes, and distribution of global morbidity and mortality (section 4); and the misperceptions about and maldistribution of global resources for health in sections 5–7. Finally, in section 8, we summarize the reasons that change is essential and outline the needs for education about the critical importance of global health for us all.

### Section 1: Background, Principles, Agenda, and Goal

#### Health as a Universal Value

Health is one of our most unassailable human values. It transcends all geographic, political, economic, and cultural barriers.

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Good health is linked to voluntary population control, as well as to productivity and national and international security. At the end of this millennium, health, like education, has become largely attainable with existing resources. We shall argue that addressing health crises of the poor in the tropics is imperative both for our self-interest and for our survival as a civilization.

The major threats to health for the rapidly growing majority of the world's population (>80% now live in the developing countries of Asia, Africa, and Latin America [1]) are tropical infectious diseases. Not only are these diseases the leading causes of mortality and morbidity globally, but the huge unmeasured impact of malnutrition and impaired development associated with widespread intestinal and other infections (often without overt illness such as diarrhea or pneumonia) is not even included in the morbidity calculation of disability adjusted life years (DALYs) lost as a result of infectious diseases. In addition, we must now include >35 new and emerging infectious diseases [2, 3] and antibiotic-resistant pathogens that have become evident in the last 2 decades alone [4], as well as diseases such as peptic ulcers, stomach and hepatic cancer, and possibly coronary artery disease and others, which are increasingly recognized as resulting from chronic infections due to organisms such as *Helicobacter pylori*, hepatitis B virus, or *Chlamydia* species, rather than the results of stress or other factors. In addition, given the increasing evidence of the intentional use by desperate terrorists of infectious agents associated with life-threatening disease [5, 6], one can begin to understand the basis for the focus of this monograph: the threats of tropical infectious diseases to global survival.

#### The Three Es That Threaten Us

As detailed in section 2, we have divided the global threats from tropical infectious diseases into three areas (or three Es):

emerging infections, exploding population without improved health, and erosion of our humanity and leadership if we ignore the readily addressable health problems related to tropical infectious diseases experienced by a growing majority of disadvantaged people on our planet.

#### **For Whom Do the Warning Bells Toll?**

When addressing the threats from tropical infectious diseases, one quickly realizes that the use and control of resources lie not with the growing majority, but instead in the hands of a shrinking minority. Less than 18% of the world's population live in industrialized countries and consume >60% of global nonrenewable resources [7]. Unfortunately, our perceptions of resources that are directed to addressing global health problems are often far greater than the worrisomely inadequate reality.

#### **Basis for Hope: The Dawning of Realization?**

Although the task of educating the affluent to address the health problems of the disadvantaged may seem overwhelming, we may be entering an era of awareness of infectious diseases threats. Outbreaks of Ebola virus infections in Africa and infections due to hantavirus, *Cyclospora*, and *Escherichia coli* in the United States and elsewhere, as well as popular documentary books and movies, now make it clear to the average citizen that we cannot live in a world of isolation. Increasingly worrisome emerging infectious diseases caused by microbes such as multi-drug-resistant *Mycobacterium tuberculosis*; streptococcal, staphylococcal, or *E. coli* bacteria; malarial or cryptosporidial parasites; and dengue virus, hantavirus, HIV, or influenza viruses threaten us all.

During the 1950s, supermarkets in the United States had only 300 items on their shelves, whereas currently they have >30,000 items, including fresh fruits and other produce items from around the world throughout the year. In 1996, Guatemalan raspberries that contained *Cyclospora* parasites infected >2,000 people throughout the United States and Canada [8]. Popular fast food chains enable the remarkably rapid distribution of dangerous *E. coli* strains across a country (as has happened repeatedly in the United States, Japan, and Europe in recent years) [9]. Sharing of the world's most dangerous pathogens is clearly unavoidable in an era when rapid international air travel, the existence of resistant microbes in hospitals and institutions, and globalization of the food supply are all commonplace and are only going to continue to increase.

#### **The Survival Advantage to Caring: The Next Stage of Human Evolution?**

When coupled with threats of the exploding population and erosion of our humanity (if we turn our backs), emerging tropical infectious diseases threats may (along with the nuclear threat) uncover the next critical phase of human evolution: an

evolutionary survival advantage to being concerned about other individuals. In addition, the issue of health might well help form a broad-based core of human values to be taught worldwide: respect for human dignity (of self and others) and the importance of helping those beyond just ourselves, thereby giving life its meaning (not to mention giving civilization its survival). That is, our survival and that of our children and grandchildren will be determined increasingly by our ability to genuinely and effectively address the growing health crises of the exploding numbers of disadvantaged individuals around the world and in our midst [10–13].

#### **Agenda and Goal**

Hence, the purpose of this monograph is to educate each one of us about the nature of the worsening health problems of the growing majority of impoverished people and how these problems threaten everyone. For it is only with such an awareness that we can hope to address these threats to our future. To paraphrase our great political mentor, Thomas Jefferson (from a letter written to William C. Jarvis in 1820):

The power of society belongs in the hands of the people. If the people should ever seem inadequately enlightened to exercise this power, the solution is not to remove the power from the people, but, the hard way, to educate them. [14]

This is a tall order, but nothing else will suffice.

#### **Section 2: The Three Es That Threaten Us**

Tropical infectious diseases not only constitute the leading threats to health for the growing majority of the world's population who live in tropical developing areas, but these diseases pose some of the greatest threats to us all [13]. We have divided these threats into three areas (or three Es): (1) emerging and reemerging infections, (2) exploding population without improved health; and (3) erosion of our humanity and leadership should we ignore the health crises of the growing numbers of disadvantaged in our midst and around the world.

#### **Emerging Infections: The Importance of Emerging Infectious Diseases and Biological Warfare**

In his 1970 Nobel Prize acceptance speech, Solzhenitsyn said:

What seems to us more important, more painful, and more unendurable is not really what is more important, more painful, and more unendurable but merely that which is closer to home. Everything distant which for all its important moans and muffled cries, its ruined lives and millions of victims, that does not threaten to come rolling up to our threshold today we consider endurable and of tolerable dimensions.

The message from emerging infections is that as we approach the twenty-first century, given the rapidly increasing globaliza-

tion of international travel and trade, "everything distant" now does threaten to come rolling up to our threshold. Tourism has now replaced agriculture as the largest industry in the world [15]. Of 500 million international travelers each year, 50 million (including 27 million from the United States and Canada) travel from Europe, the United States, Canada, Japan, Australia, and New Zealand to Asia, Africa, Latin America, the South Pacific islands, and parts of Eastern Europe where food, water, and vector-borne infections pose significant health risks [15–17]. To deal with the health of the disadvantaged (abroad and in our midst) and also to protect ourselves, we must apply the best of modern medicine, research, and public health to the understanding and control of the tropical infectious diseases that remain the leading causes of disability and mortality around the world.

*Examples of emerging infectious diseases.* Probably more from frightening accidents of nature (such as *Cyclospora*, *Cryptosporidium*, *E. coli*, hantavirus, and Ebola outbreaks) and from popular documentary books like *The Coming Plague* or *The Hot Zone*, or from works of fiction and movies such as Dustin Hoffman's "Outbreak," than from public health education, the average American is now beginning to realize (perhaps for the first time) that we cannot, even if we desired, live in a world of isolation.

Emerging infectious diseases were brought to our attention by the National Institutes of Health (NIH) and the Centers for Disease Control and Prevention (CDC), and the list now includes >35 emerging and reemerging infectious diseases threats from the last 2 decades of the twentieth century alone (table 1) [2, 3, 18]. These include viral, parasitic, bacterial, and fungal infections that pose growing threats, not only to tropical developing populations, but to the entire world. Infections due to streptococcal or *E. coli* bacteria; malarial or cryptosporidial parasites; or dengue virus, influenza virus, hantavirus, or HIV threaten us all. Malaria cases in the United States between 1991 and 1995 totaled 5,100; 12 of these cases were locally acquired. The problems are further compounded by increasing drug resistance, and many diseases once thought to have been under control (such as malaria, cholera, diphtheria, and tuberculosis) are now reemerging, often with a vengeance.

Although infectious diseases occur predominantly in the tropics, even in the United States there has been a 58% increase in infectious diseases–related mortality between 1980 and 1992, with only half of this increase being the result of the impact of AIDS [19].

*Dengue.* As an example, dengue hemorrhagic fever was practically eradicated before 1981 in the Americas. However, it has returned throughout much of Central and South America since that time, and is now blanketing southern Asia. Fewer than 30,000 cases were reported from 1956 through 1980, >137,000 cases from 1981 through 1985, and >267,000 cases from 1986 through 1990, illustrating the dramatic increase in reported cases of dengue hemorrhagic fever worldwide [20–22]. Burgeoning populations in the tropics, as well as urbanization, social unrest, increasing travel, and possible climatic

changes, all influence emerging and reemerging infectious diseases.

*Cholera and other diarrheal diseases.* Cholera, another example, which was probably contained in southern Asia for centuries, if not millennia, spread in several pandemics across Asia, Europe, and the Americas during the last century [23]. It then disappeared from the Western Hemisphere for nearly a century until it erupted in Peru in 1991, and it has since spread throughout nearly every country in South and Central America. In late 1992, an entirely new strain erupted that has since become endemic throughout southern Asia, posing fresh challenges to new vaccines. This dramatic disease produces devastating dehydration and is associated with a high mortality rate, approaching 50%, as seen among the refugees in Rwanda a couple of years ago.

Not only has cholera toxin, like *E. coli* heat stable toxin (STa), enabled us to understand basic cell signaling [24], but some have said that "the most important medical advance this century" is the finding that glucose, sugars, or simple starches can drive absorption of water and electrolytes and reduce the associated mortality rate to <1% [25]. We are now excited about the possibility of glutamine, and its new more stable derivatives, as new oral rehydration and nutrition therapies (ORNT) for acute or persistent diarrhea, performing even better at rehydration while also rebuilding the damaged gut mucosa [26, 27]. Even with the highest cholera-related mortality rate ever recorded, this disease still constitutes <1% of the global mortality rate associated with diarrhea, and even less of the associated morbidity.

*Impact of persistent diarrhea and "asymptomatic" enteric infections on nutrition and development.* We work with a number of colleagues in Fortaleza, in northeastern Brazil, where among the poor, diarrhea constitutes the leading cause of death, often exceeding all other causes combined when years of potential life lost are taken into account. However, when J. McAuliffe met each week with the coveiro (grave digger) to review child deaths over a year in a township in northeastern Brazil, he found that persistent diarrheal illnesses are now emerging as a major cause of death [28]. It should be noted that the etiologies are somewhat different from the toxigenic *E. coli* and rotaviruses that cause acute dehydrating diarrhea. Instead, enteroaggregative *E. coli*, *Cryptosporidium* species, and possibly toroviruses are among the major etiologies of persistent diarrhea [29, 30].

Even more important, however, than the staggering mortality (reaching as high as 1 in 4 children dying in poor areas before their fifth birthday) may well be the impact on the other three children who survive, but who live through repeated or persistent malnourishing and dehydrating enteric infections during their most formative first 2 years of life [31, 32], a long-term impact not even included in the popular DALY calculations. For example, Leslie et al. have calculated that diarrhea illnesses in the second year of life alone account for >5 cm of growth shortfall among children in our collaborative studies in northeastern Brazil [32a]. We and others are now finding that malnu-

**Table 1.** Emerging and reemerging infectious diseases threats, 1980–1997.

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Viral
Bolivian hemorrhagic fever—1994, Latin America
Bovine spongiform encephalopathy—1986, United Kingdom
Creutzfeldt-Jakob disease (new variant V-CJD)/mad cow disease—1995–96, United Kingdom/France
Dengue fever—1994–97, Africa/Asia/Latin America/United States
Ebola virus—1994, Gabon; 1995, Zaire; 1996, United States (monkey)
Hantavirus—1993, United States; 1997, Argentina
HIV subtype O—1994, Africa
Influenza A/Beijing/32/92, A/Wuhan/359/95, H5:N1—1993, United States; 1995, China; 1997, Hong Kong
Japanese encephalitis—1995, Australia
Lassa fever—1992, Nigeria
Measles—1997, Brazil
Monkey pox—1997, Congo
Morbillivirus—1994, Australia
O'nyong-nyong fever—1996, Uganda
Polio—1996, Albania
Rift Valley fever—1993, Sudan
Venezuelan equine encephalitis—1995–65, Venezuela/Colombia
West Nile fever—1996, Romania
Yellow fever—1993, Kenya; 1995, Peru
Parasitic
African trypanosomiasis—1997, Sudan
<i>Ancylostoma caninum</i> (eosinophilic enteritis)—1990s, Australia
Cryptosporidiosis—1993+, United States
Cyclosporiasis—1995–1997, United States/Canada
Malaria—1995–1997, Africa/Asia/Latin America/United States
Metorchis—1996, Canada
Microsporidiosis—Worldwide
Bacterial
Anthrax—1993, Caribbean
Cat scratch disease/bacillary angiomatosis ( <i>Bartonella henselae</i> )—1990s, United States
<i>Chlamydia pneumoniae</i> (pneumonia/coronary artery disease?)—1990s, United States (discovered 1983)
Cholera—1991, Latin America
Diphtheria—1993, former Soviet Union
<i>Ehrlichia chaffeensis</i> , human monocytic ehrlichiosis (HME)—United States
<i>Ehrlichia phagocytophilia</i> , human granulocytic ehrlichia (HGE)—United States
<i>Escherichia coli</i> O157—1982–1997, United States; 1996, Japan
Gonorrhea (drug resistant)—1995, United States
<i>Helicobacter pylori</i> (ulcers/cancer)—Worldwide (discovered 1983)
Leptospirosis—1995, Nicaragua
Lyme disease ( <i>Borrelia burgdorferi</i> )—1990s, United States
Meningococcal meningitis (serogroup A)—1995–1997, West Africa
Pertussis—1994, United Kingdom/Netherlands; 1996, United States
Plague—1994, India
<i>Salmonella typhimurium</i> DT104 (drug resistant)—1995, United States
<i>Staphylococcus aureus</i> (drug resistant)—1997, United States/Japan
Toxic strep—United States
Trench fever ( <i>Bartonella quintana</i> )—1990s, United States
Tuberculosis (highly transmissible)—1995, United States
<i>Vibrio cholerae</i> 0139—1992, southern Asia
Fungal
Coccidioidomycosis—1993, United States
<i>Penicillium marneffi</i>

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Adapted from [13].

trition may be the greatest of all emerging enteric infections (often without overt diarrhea as reported in association with *Cryptosporidium* and *Giardia* species, and enteroaggregative *E. coli* [33–36]) with profound implications for Christopher

Murray's DALY calculations and his "unfinished agenda," to which we shall return [37, 38].

*Emerging enteric protozoa (Cryptosporidium, Cyclospora, and Microsporidium species).* The emerging enteric proto-

zoa, long recognized by veterinarians, have been brought to the attention of infectious diseases specialists by the AIDS epidemic. These enteric protozoa now hold additional lessons for developed, as well as developing, countries [39].

The largest waterborne outbreak in U.S. history occurred in Milwaukee in 1993. More than 52% of people in the distribution area of the South Milwaukee Water Works plant were stricken with diarrhea. There was only a slight increase in turbidity, well within the then Environmental Protection Agency (EPA) standards [40]. Although many people became ill, it was the impact on professional basketball (when Milwaukee lost to Miami because of cryptosporidial diarrhea) that awakened many people to the outbreak through the national attention these players received. It was only later that the profound impact, with a >59% mortality rate among the 82 HIV-positive individuals with cases of cryptosporidiosis occurring in Milwaukee's waterborne outbreak, was fully appreciated [41]. Because it is highly resistant to chlorine, surviving even full-strength household bleach, *Cryptosporidium* thus threatens not only the world's water supply, but that in the United States as well [42–44].

Perhaps one of the best recent examples of how infectious diseases abroad can have an impact in the United States is the *Cyclospora* outbreak caused by raspberries from Guatemala. There were >2,200 victims who experienced diarrheal illnesses, often after eating fresh raspberries from Guatemala at country club events throughout the United States and Canada in 1996 and 1997 [8, 45–47]. This year, in addition to raspberries, mesclun lettuce and basil in pesto pasta have brought *Cyclospora* to 240 people who attended catered events in the Washington, D.C. area, once again demonstrating the irretrievably increasing impact of the globalization of our food supply [48, 49]. During the 1950s, supermarkets in the United States had only 300 items on their shelves; they now have >30,000 items, including fresh fruits and other produce items from around the world throughout the year [50, 51].

*Threats from our industrialized food supply (enterohemorrhagic E. coli).* Yet another example (like *Cyclospora*) of the extraordinary capacity of the food industry in industrialized countries to distribute emerging pathogens lies in the increasing numbers of episodes of infections due to strains of enterohemorrhagic *E. coli* (EHEC). In 1982, when EHEC first appeared in outbreaks several months apart in Oregon and then in Michigan, it was McDonald's stock that dropped only transiently when *E. coli* O157:H7 was first traced to the "specialty burger at hamburger chain A" [52]. Well known are the subsequent Jack-in-the-Box and many other outbreaks of potentially devastating hemolytic-uremic syndrome (HUS), as well as hemorrhagic colitis, seen with EHEC infections. In 1997, it was Hudson's hamburger [9] and alfalfa sprouts [53] that made headlines; radish sprouts infected >9,000 schoolchildren in Japan in 1996 [54].

Furthermore, we may not prevent the complications of HUS or thrombotic thrombocytopenic purpura (TTP) with antibiot-

ics. Similar to the difficulty of eradicating *Cyclospora* or *Cryptosporidium* species with chlorination, EHEC reminds us yet again of our vulnerability to emerging infectious diseases, not to mention the threats of increasingly resistant organisms and the growing list of diseases such as gastric and hepatic cancer, malnutrition, and even coronary artery disease that are now being linked to infections [33–36, 55–63].

*The potential for biological warfare.* In addition to the problems represented by emerging and reemerging infectious diseases, we only now add to these threats the unspeakable nightmare of the potential use of infectious agents as weapons, as noted in Richard Preston's latest book *The Cobra Event*, and *The New Yorker* article "Annals of Warfare: The Bioweaponers" [6, 64].

It was in late 1969 and early 1970 that President Nixon terminated the United States' offensive biological weapons program by executive order [65]. Subsequently, the Biological and Toxin Weapons Convention (BWC) was signed by 158 countries and ratified by 140. The BWC prohibits the development, production, and stockpiling of microbial or other biological agents or toxins of types and quantities where there is no justification for prophylactic, protective, or other peaceful purposes, as well as the weapons, equipment, or means of delivery designed to use such agents or toxins for hostile purposes or in armed conflict [66].

The United States and allied countries have a clear strategic interest in outlawing biological weapons programs [65]. Potential effects from a biological warfare attack could be far greater than those from a chemical warfare attack. Unlike a nuclear attack, biological agents typically leave the physical infrastructure intact [67]. In addition, costs associated with the production of biological weapons are minimal because of advances in microbiology and biotechnology. For this reason, biological weapons are sometimes referred to as the "poor man's atomic bomb" [67]. Furthermore, given the small quantities needed and the ease with which they can be concealed, transported, and disseminated, biological weapons present an attractive option for terrorists [68]. Agents of potential consequence are listed in [69].

The presence of the BWC has not (and will not) stop governments or political groups from producing biological weapons. In addition, there are no means available to accurately detect violations of the BWC [66]. We have in fact witnessed several instances of "bioterrorism," such as the 1984 infection of 751 individuals (of the 10,500 residents of The Dalles, Oregon) with *Salmonella typhimurium*, which was intentionally placed in the salad bars of several restaurants by the followers of Bhagwan Shree Rajneesh in order to influence the outcome of a community-wide election [70]. Perhaps most frightening is the example of Iraq. The fact that Iraq developed and maintained a standby biological weapons capability under the constant scrutiny of United Nations routine and no-notice inspections confirms a global inability to control proliferation through conventional means [66].

Until now, the U.S. government has responded to this growing threat by funding programs aimed at defending against and coping with biological warfare. The Defense Advanced Research Projects Agency (DARPA) funds research for the development of software (to manage an emergency), sensors, diagnostic technology, and novel ways to prevent infection or shore up the body's ability to block the effects of pathogens and toxins, whereas the primary interest of the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) is protecting troops from biological agents and toxins [65, 71].

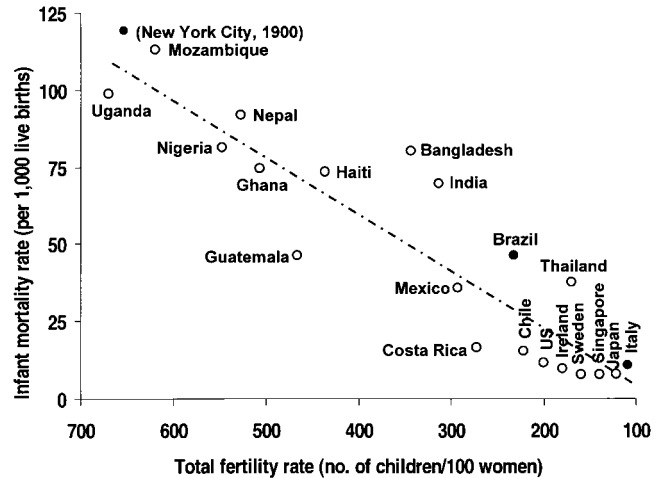
Although response mechanisms are essential, the necessity for preventing biological attacks compels us to explore more unconventional methods and ideas. First, as suggested in a recent article by Joshua Lederberg in the *Journal of the American Medical Association*, is the need for scrupulous adherence to the BWC by the United States. This will build a "moral platform" on which to stand [72]. However, further action is warranted. Those willing to use methods such as biological terrorism are those with little or nothing to lose: persons living with conditions of poor health, poverty, and overpopulation. As is suggested throughout this monograph, improving the current plight of the disadvantaged by addressing the growing threats of emerging and reemerging infectious diseases and improving health where poverty exists is key to controlling population growth and improving the conditions that lead to economic and political stability. Such improvements are critical for reducing the impetus behind political ideologies that call for the use of extreme measures such as biological agents and toxins against countries such as the United States, Japan, or those of Europe.

**Exploding Population**

Our Malthusian thinking is dangerously backward—disease and poverty do not control, but are associated with population overgrowth [12].

*Implications for population growth.* Around the world and even within most countries, closely linked to high infant mortality rates in impoverished, developing areas, is the problem of uncontrolled population overgrowth. Several experiences support the concept that high infant mortality rates contribute to rather than control population growth.

The brilliant and insightful eighteenth-century political essayist Sir Thomas Malthus predicted sharp limitations on geometric population increases by lesser (arithmetic) increases in food production and subsistence and by war, disease, and famine [73]. Although in his later writings Malthus acknowledged that an improved capacity for voluntary birth control might alter his predictions, he did not foresee the impressive degree to which economic development can result in a quality and security of life that is consistently associated with a reduction in population growth, largely on a voluntary basis in most countries. Instead of limiting population growth, poverty and



**Figure 1.** Correlation of infant mortality and total fertility in selected countries and areas of world. 1995 data updated from [24].

disease are actually associated throughout the world with the greatest population growth rates. Not only is this true of developed and developing countries today (figure 1) [20, 24], but it has been consistently true throughout the history of developed countries as well. We forget that both the infant mortality and population growth rates in New York City in 1900 were higher than those in Bangladesh or Nigeria today. The control of population overgrowth in the last three generations can be readily demonstrated in any educated audience by simply asking how many people have or plan to have more than six children and then asking how many had great grandparents who were from families with more than six children. Some tend to blame the Pope, but population growth in Italy is lower than that in the United States, Japan, or Sweden. In addition, the industrial and green revolutions have greatly extended global population growth potential.

Specific experiences in such areas as northeastern Brazil confirm the contribution of poverty and high infant and childhood mortality rates to population growth. To study the epidemiology of diarrheal diseases, we attempted to obtain approximately comparable sized families in households from "better" and "poor" living conditions in the small rural town of Pacatuba in Ceará in northeastern Brazil. Our goal was to enroll households with two to six children under the age of 12 years in our prospective surveillance. However, we encountered some difficulty in finding two or more children under the age of 12 in the better homes. In contrast, in poor homes there were often six or more children under the age of 12. Furthermore, during the course of 2.5 years of prospective surveillance, 17 of 32 mothers from the poorer homes had an additional child, while only one of 23 mothers from better homes delivered a baby during the period ( $P < .001$ ). While both groups represented essentially similar cultural, racial, and religious (Roman Catholic) backgrounds, the reason for not having more children in the better homes appeared to be primarily economic. Much as

populations that have limited their growth throughout the world have done, individual families with economic means say they “cannot afford to have more children,” since they pay to send their children to a private kindergarten and further schooling and this becomes difficult with more than one to three children per family. Precisely the opposite is true in the poor homes where individuals have not even achieved a level of economic means that allows them to live in a cash-based market economy. The impoverished have only to gain by having more children, particularly male children in some societies, some of whom might survive and provide a source of income on which the remainder of the family might depend in the absence of any form of reliable social security. Consequently, it is the very problem of childhood mortality that contributes to the pressure to have larger and larger families that, despite the high mortality rates and oppressive morbidity, helps sustain continued population overgrowth. As is the history of essentially all developed countries, the rate of population growth has consistently declined with control of the high infant mortality rates, and improved life expectancy and standard of living.

Furthermore, there has been a consistent decrease in the period required for the “demographic transition,” the time over which infant mortality and fertility rates decline. Within 40 years of Malthus’ death in 1834, the infant mortality rate in Western Europe began to decline—a trend that was associated (over the ensuing 60 years) with a steady reduction in birth rates and resulted in an essentially stable population size. This interval has shortened progressively from >60 years for Western Europe (from 1870 through the 1930s), to ~40 years in the early twentieth century in the United States, to <12–20 years in rapidly developing countries like Thailand, Botswana, Kenya, and Zimbabwe (1980 through the 1990s) [12].

The ineffectiveness of even record-breaking natural or political disasters in controlling population overgrowth is evident from the demographic effects of the cyclone and war in Bangladesh in 1970–1971. The huge peak of devastating mortality, with more than a quarter million deaths in each of these disasters within a 4-month period, was more than offset by a “post-disaster baby boom” [74].

Even the devastating impact of AIDS in areas of Uganda with some of the highest rates of HIV-positivity in the world reaches demographic importance only in the most localized parish areas—in part because orphaned children move away. At the district or national level, this slows the staggering 3 1/2% growth rates only slightly [75]. Conversely, one can practically draw a map of the roads traveled from a three-dimensional graph of orphan rates in the Rakai and Masaka districts of Uganda, as reported by Low-Beer et al. in *Nature* [75]. Indeed, as detailed in section 3, it is Sub-Saharan Africa that has the greatest projected overgrowth of population in the world, despite the staggering impact of AIDS!

Finally, the dramatically greater effectiveness of improved health (over high infant mortality) in reducing population overgrowth was demonstrated clearly in the Naraganwal and Jam-

<p><b>Hi IMR (120/1000)</b> <b>Hi BR (40/1000)</b></p> <p><b>1000 population</b> <b>40 births</b> <b>5 deaths</b> <b>35 children</b></p>	<p>Introduction of Primary Health Measures</p> <p>→</p>	<p><b>↓IMR (20/1000)</b> <b>↓BR (23/1000)</b></p> <p><b>1000 population</b> <b>23 births</b> <b>1 deaths</b> <b>22 children</b></p>
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**Figure 2.** Impact of introducing basic health measures on population growth in Naraganwal and Jamkhed Projects, West India. IMR = infant mortality rate; BR = birth rate.

khed projects in western India, as reported by Taylor (figure 2). Before a primary health project, the birth rate was 40 per 1,000 and the infant mortality rate was 120 per 1,000 live births. In other words, of 1,000 people, there were 40 births and five deaths, resulting in an increase of 35 children per year (a typical 3 1/2% growth rate). In contrast, after the introduction of basic health measures (at a cost of <\$2.00 per capita per year, borne by the villagers themselves), the infant mortality rate dropped to only 20 per 1,000 live births, with a reduction in birth rate from 40 to 23 per 1,000. This means that of 1,000 people, 23 children were born and one died; resulting in the addition of only 22 children (now much healthier) to the population each year (a striking 37% reduction in population growth as a result of simple health improvements) [76].

Thus, lest we leave population control to disastrous infectious diseases and famine or to a dangerous removal of human dignity, we must work unceasingly for the improved health (and education and economic development) of all who share our planet—as this is the only way to see the population explosion brought under control. Choosing to improve the health of and opportunities for the poor may well prove to be the greatest test of our democracy.

Consider even the nuclear or biological warfare threats—they much more likely lie in the hands of the enraged disadvantaged person who has nothing to lose, than in the hands of the so-called “powerful” who stand to lose everything they have. The growing ease and unspeakable horror of the use of biological, if not nuclear, weapons have been emphasized by an entire issue of the *Journal of the American Medical Association* [5], as well as by *The Cobra Event*.

#### **Erosion of Our Humanity/Leadership If We Ignore Growing Health Problems Related to Tropical Infectious Diseases**

The third, and some argue the most important threat, is the erosion of our humanity if we ignore the readily addressable health problems of the growing majority on our planet. By turning our backs, we would argue, we become something less than human. The speech writers in Washington indicated that this point was politically incorrect and that its restatement as

erosion of our “world leadership” was believed to be more palatable. So be it—we see our human dignity and our leadership as fundamentally the same!

This has been most eloquently stated by the Bengali writer, Rabindranath Tagore, who in 1893 wrote:

If in this world misery must exist, so be it; but let some little loophole, some glimpse of possibility at least, be left, which may serve the noble portion of humanity to hope and struggle unceasingly for its alleviation. . . .

Who then is the noble portion of humanity? Who and where are our leaders?

Some have suggested that the increasing global inequities of distribution necessitate that we develop a “triage” system and simply not attempt to assist other countries for which conditions are the most hopeless. Such a concept has been called the “lifeboat” ethic, suggesting the analogy of countries being like people after a shipwreck in a stormy sea struggling onto the lifeboat earth. Thus, if we continue to attempt to deal with the “have not” peoples, the lifeboat itself will not sustain the strain. This bold analysis has certainly raised important questions about global distribution of resources as well as considerable controversy. However, there are serious problems with the validity of this analogy. First are the disparate consumption patterns of the majority of nonrenewable and limited resources by a shrinking minority of the population on a global scale. Second, despite the fact that it may reflect our position more often than we wish to admit, this position has been referred to as “morally reprehensible” and “advanced muddlement” [77] by those who maintain that a better analogy would be the earth as a spaceship (without a lifeboat) in which we must work in concert, lest the developed and developing countries, by failing to understand global issues of interdependency, become the world’s “Titanic” [77, 78]. Finally, the validity of the analogy also breaks down when the people who are kept off the lifeboat fail to drown and disappear, but instead actually multiply—faster than those in the lifeboat. Ultimately, no amount of defense or strength by a shrinking minority can prevail over a growing majority of the world’s population. Certainly this disparity of living conditions, most simply reflected in widely disparate infant and childhood mortality rates around the globe, threatens civilization as we know it both physically (with the potential risk of annihilation in a nuclear age where those who have nothing to lose will certainly take risks on a global scale not taken by the more affluent) as well as philosophically (in that, by continually ignoring the plight of the increasingly destitute around us, we become something less than human ourselves).

A perhaps extreme glance at the grim reality facing a growing majority of the poor is reflected in an Indian poem (circa 1970), a reality that may be the result of what Dr. Maurice King has called “entrapment” [79].

Mother decide: who will go without today?  
Will it be Ram who is the strongest,

And does not need it so much?

Or Raj, who is the weakest,

And will not need it so long?

Or Sita, who is a girl anyway?

Decide mother, and kill part of yourself.

Such unthinkable entrapment has had King struggling over whether there exists a potential for increasing suffering if children survive. It led others to the inappropriate analogy of the developed world as a “lifeboat” leaving those outside in the developing world to drown; this analogy is inappropriate for many reasons, among which is that those who are struggling to survive are in fact multiplying the fastest, as we have noted.

Clearly it becomes imperative to avoid this unthinkable entrapment. In subsequent writings, King suggests that the two ways to avoid unthinkable entrapment are to control population growth (necessitating improved health and education) and enhance “connectedness” (that is, the ability to obtain products or migrate) (figure 3) [79]. Regions that have avoided this entrapment include Singapore and Thailand. Countries in which entrapment remains worrisome are those such as Nepal.

### Avoid unthinkable entrapment

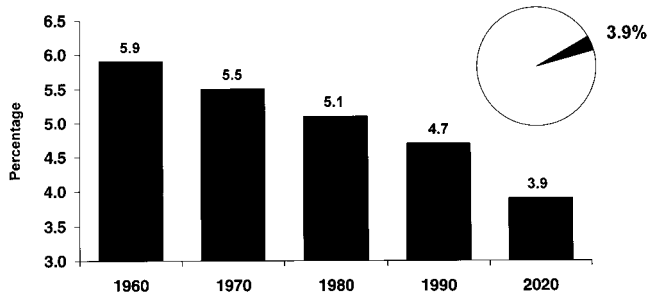
- **Control population growth**
  - necessitates improved health and education
- **Enhance “connectedness”**
  - ability to obtain products or migrate

Figure 3. Avoid unthinkable entrapment.

### Section 3: Current and Future Trends—Population and Resource Consumption

#### Where Are We Now? Population and Urbanization, Resource and Energy Consumption, and Foreign Assistance

Let us begin by examining the current realities and trends with respect to the distribution of population and resources consumed. Consequent to the striking skew in population growth among the poor, we in the United States comprise a shrinking minority of the world’s population, soon to fall below 4% (figure 4). Arguably the world’s strongest and most influential economy at the moment, the United States comprised 5.9% of the world’s population in 1960. However, this level has steadily declined to ~4.5% at present and is projected to be 3.9% by the year 2020 [80]. We often fail to recognize that 96% of the world’s population live outside the United States and will increasingly influence our lives.



**Figure 4.** The United States' shrinking population as a percentage of world population.

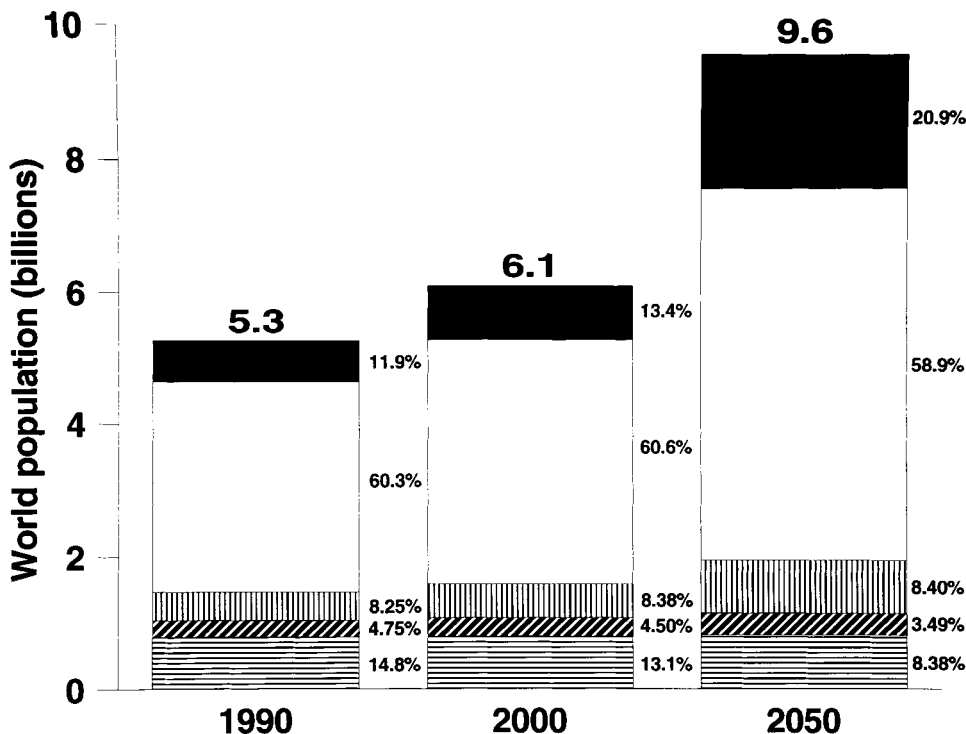
Conversely, there is a striking increase in the global population, but predominantly in developing countries, with a projected 84% of the world's 7.8 billion residing in developing countries by the year 2020 [1]. In fact, Sub-Saharan Africa is the only region in which a relative increase in percentage of the world's population is projected, despite the dire consequences of AIDS and its staggering impact on the orphan rate (figure 5) [81]. In addition, the urban migration even further skews this population distribution, to the extent that by the year 2015 it is projected that of the 10 largest cities in the world, all but Tokyo, Shanghai, and Beijing will be in or border on the tropics [82]. If we do not attend to the major consequences of these trends—increasing economic disparity, increasing numbers of people living in poverty, and increasing

societal challenges from urbanization and AIDS orphans in tropical developing areas—the resulting instability poses severe threats to all.

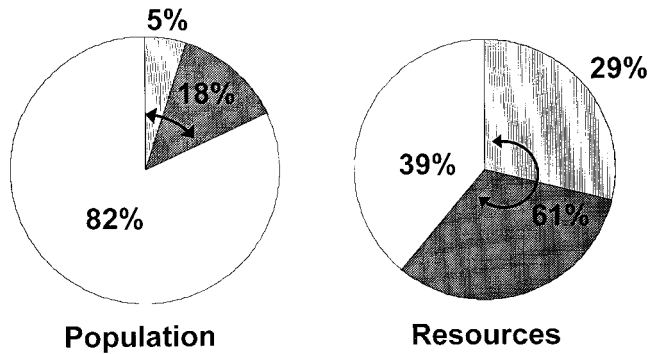
Even if one includes the populations of all high-income countries (Portugal, New Zealand, Spain, Ireland, Israel, Australia, United Kingdom, Finland, Italy, Kuwait, Canada, Hong Kong, Netherlands, Singapore, Belgium, France, Sweden, Austria, Germany, United States, Norway, Denmark, Japan, Switzerland, and the United Arab Emirates), the percentage of the world's population totals only 18%, as shown in figure 6. Yet, this 18% consumes >60% of the global nonrenewable resources such as oil (figure 6), whereas the 82% in lower- and middle-income countries consumes only 39% of global energy resources at a nearly sevenfold lower per capita level of 739 kg/year [7]. This striking disparity in consumption only further magnifies the discrepancies between the shrinking minority in industrialized areas and the increasing numbers of people living in poverty.

**Income Distribution and Increasing Poverty**

Perhaps most alarming is the destabilizing disparity between the rich and the poor (also assessed as the Gini coefficient [7]), illustrated by the percentage share of income for the highest and lowest 20% segments of the population for four representative countries. While this difference is four- to ninefold for Bangladesh and the United States, respectively, it is a striking 15- to 32-fold for Honduras and Brazil [7].



**Figure 5.** Relative population projections for major regions of the world between 1990 and 2050. ■ = Africa; □ = Asia; ▒ = Latin America; ▨ = United States; ▩ = Other (Europe, Oceania, et al). Only Africa shows a substantial relative increase of 3.2-fold. Reprinted with permission from [13].



**Figure 6.** Percentages of world population residing in high- and middle/low-income countries (HIC and L/MIC, respectively) as compared with the percentage of total resources consumed for 1995. ■ HIC (▨ U.S. portion); □ L/MIC. High income countries include Canada, Finland, Germany, Ireland, Italy, Japan, Sweden, Switzerland, New Zealand, United Kingdom, Australia, Austria, Belgium, Denmark, France, Netherlands, Norway, Portugal, Spain, United States, Hong Kong, Israel, Singapore, United Arab Emirates, and Kuwait.

Further, as noted by the World Health Organization (WHO), poverty is increasing [17]. The number of extremely poor doubled between 1970 and 1990; one-fifth of the world's population now lives in extreme poverty, one-third of children are undernourished, and one-half of the world's population lacks regular access to essential medications.

In summary, therefore, current and projected trends in population growth and resource consumption come together to create a powder keg of health and social crises that must be addressed if we are to survive as a civilized society.

**Section 4: Magnitude of Global Morbidity and Mortality—What Are the Threats to Health?**

**The DALY Calculation**

As shown in figure 7, the DALY calculation involves a very thorough analysis of the total “burden” of disease: the number of people affected (N) times the mortality rate (MR) plus N times the probability of a disability occurring (Prob) times the disability weight (Dwt), ranging from 0 for no disability to 1 for death [37, 38]. This burden for a given disease is then multiplied by a “DALY converter,” which is the difference between the total life expectancy at the age of disease onset and the age of onset of the disability or death. Finally, the “value” of life at each age involved is weighted by an age-weight function ( $Cxe^{-\beta x}$ ) and by a “discount function” ( $e^{-r(x-a)}$ ). The age-weight function ( $Cxe^{-\beta x}$ ) places different values on life lived at different ages such that the calculated value of life lost by a death at age 15 years—after societal investments are made to get to that age—is greater than that by a death at age 1 year and reflects decreasing economic productivity or “value” with aging beyond the peak middle years (figure 7). The discount function ( $e^{-r(x-a)}$ ), also used in economics, is a simple rate that weights life or health in the future as being less important than in the present. DALYs thus represent the sum of the years of life lost (YLL) and the years lost to disability (YLD).

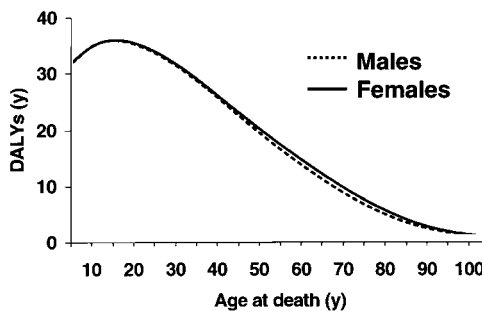
**Global Mortality and Morbidity (DALYs)**

What, then are the health threats on a global scale? Whether one examines the global mortality or Christopher Murray's

$$\begin{aligned}
 & \text{DALY} = \text{burden} \cdot \text{DALY converter} \cdot [ 1 + 2^\circ / 1^\circ \text{ DALYs} ] \\
 & \quad \downarrow \\
 & [ N \cdot \text{MR} + N \cdot \text{Prob} \cdot \text{Dwt} ] \\
 & \quad \downarrow \\
 & (0 \text{ to } 1)
 \end{aligned}$$

$$[ (\text{LifeExp} - \text{AgeD} / \text{D}) \cdot \text{AgeWt} \cdot \text{discount fun} ]$$

$$Cxe^{-\beta x} \cdot e^{-r(x-a)}$$



$$\begin{aligned}
 C &= 0.16243 & e &= 2.712 \\
 x &= \text{age} & \beta &= 0.04 \\
 a &= \text{age of onset} & r &= 0.03
 \end{aligned}$$

$$\text{DALY} = \text{YLL} + \text{YLD}$$

**Figure 7.** The disability adjusted life year (DALY) calculation. N = number affected; MR = mortality rate; Prob = probability of a disability occurring; Dwt = disability weight; LifeExp = total life expectancy at; AgeD/D = age of onset of the disability or death; AgeWt = age weight function; discount fun = discount function; YLL = years of life lost; YLD = years lost to disability.

**Table 2.** Global mortality (total and percentage of total) and global morbidity as percentage of total disability adjusted life years (DALYs).

	Mortality	Morbidity (% DALYs)
1. Infectious Diseases	16.5 (32.0)	36.4
2. Cancer	6.1 (11.8)	5.9
3. Heart Diseases	5.0 (9.7)	3.1
4. Cerebrovascular Disease	4.0 (7.8)	3.2
5. Chronic Lung Disease	3.0 (5.8)	3.5

Reprinted with permission from [13].

DALY calculations that include morbidity, infectious diseases account for 1–3 times the mortality and morbidity caused by heart disease, cancer, and strokes combined (tables 2, 3) [37, 83]. Infectious diseases by decreasing DALY count are respiratory infections, diarrheal diseases, tuberculosis, malaria, and measles followed by others (table 4) [17, 21, 37, 38, 84]. Stated differently, 12.2 million children under the age of 5 die each year (that is >33,000 children dying each day) in developing countries, largely of respiratory illnesses, diarrheal diseases, measles and malaria, with more than one-half of these childhood deaths also associated with malnutrition [1, 85].

#### Important for Whom? Where the DALYs Are

This devastating mortality (and, we would argue of even greater significance, the underestimated morbidity) affects primarily the poor. Davidson Gwatkin has pointed out that while communicable diseases cause only 8% of deaths among the wealthy, they account for 56% of deaths among the poor [86]. Of the global DALYs, 89% occur in the lower- and middle-income regions of Asia, Africa, and Latin America [38]. When the DALY rates are assessed according to region, the rates for Latin America, Asia, and Sub-Saharan Africa tower over those of the higher income countries [38].

#### Challenges for the “Unfinished Agenda”

Thus, as Murray largely acknowledges, huge challenges remain to address his “unfinished agenda” (figure 8) [37]. First of these challenges is the disproportionate effect on the poor, whose numbers are growing the fastest. Second, socioeconomic development and the availability of effective antimicrobials are assumed and are far from certain. Indeed, alarming increases in antibiotic resistance were reviewed in section 2. Third, the increasingly appreciated impact of infectious diseases on ulcers, cancer, malnutrition, and possibly coronary artery disease is overlooked.

Finally, and perhaps most important of all, sequelae of childhood illnesses, helminths, and malnutrition are not adequately quantified or even counted. For example, the DALY for diar-

rhea includes only the slight disability for a few days of overt illness, but overlooks the likely far more devastating, but poorly quantified, impact of repeated or persistent illnesses and enteric infections without overt diarrhea on long-term child and human development. When Bundy included these calculations for intestinal helminths, for example, their DALY impact more than doubled [87, 88].

Thus, one of the greatest challenges for Murray’s “unfinished agenda” is including adequate information to enable a more accurate estimation of the total, long-term disability impact of the repeated illnesses and, as noted below, even “asymptomatic” infections that so devastate children living in poverty in the tropics. Unless these challenges are addressed by our best science and resources, the growth of these infections in exploding populations threaten us all.

#### The Need for Accurate Data and Better Understanding

One of the greatest challenges for obtaining accurate DALY calculations is the need for valid data and the understanding of not only the effect of the disease on mortality, but also on morbidity. Murray and Lopez have made truly heroic strides in identifying and quantifying the mortality and especially the morbidity of communicable and noncommunicable diseases and injuries [37]. Their analyses have resulted in an appropriately increased recognition of the tremendous importance of such disabling problems as tobacco-related and neuropsychiatric diseases.

Shown in table 3 are not only the relative contributions of selected diseases to the global total of 1.4 billion calculated DALYs, but also the relative contributions of the disability portion (percent YLD) of the DALY calculation for each of these diseases. The estimated overall contribution of disability to the global DALY calculation is 34% [37, 38]. However, while the tremendous portions of DALYs due to long-term disability for neuropsychiatric illnesses and rheumatoid arthritis are included and account for 92.8% to 96.4% of the total DALYs for these diseases, respectively, the suspected huge long-term disability for diarrheal and other childhood diseases has not been quantified or included. Instead, 95% of the DALY calculations for diarrheal and respiratory diseases is based on mortality only.

Some have argued that even in areas where as many as one in every four children die of diarrhea and other childhood diseases, morbidity of as many as five to  $\geq 12$  dehydrating, malnourishing diarrheal illnesses in the most critical developmental first 2 years of life may be of far greater impact than even this staggering mortality [11, 89]. Even if one conservatively estimates a 2% to 5% lifelong impairment in physical activity, physical fitness, and cognitive function due to diarrhea and enteric infections from only 10 diarrheal illnesses from 6 to 24 months of age, the DALY calculation that currently includes a 0.1 disability for 7 days for each diarrheal illness goes from  $0.1 \times 70$  (for those 10 illnesses) to  $0.02$  to  $0.05 \times 25,550$

**Table 3.** Percentage of total disability adjusted life years (DALYs) and percentage of total years lost to disability (YLD) according to group and cause.

	Percentage of total DALYs	Percentage of total YLD
Group I. Communicable, maternal, perinatal, and nutritional conditions		
Diarrhea	7.2	5.2
Malnutrition	3.7	64.2
Respiratory	8.5	4.9
Childhood-cluster*	5.2	5.7
Tuberculosis	2.8	10.7
Malaria	2.3	11.6
Tropical-cluster†	0.8	67.7
Intestinal nematodes	0.4	85.0
Group I total	43.9	19.0
Total for infectious diseases and malnutrition	30.9	15.8
Group II. Noncommunicable diseases		
Neuropsychiatric conditions	10.5	92.8
Cancers	5.1	8.1
Ischemic heart disease	3.4	10.9
Cerebrovascular disease	2.8	16.6
Chronic obstructive pulmonary disease	2.1	50.4
Rheumatoid arthritis	0.2	96.4
Group II total	40.9	49.8
Group III. Injury (Group III total)	15.1	36.5

NOTE. YLD = years lost to disability. Of 1.4 billion total world DALYs (35% of which = YLD).

\* Childhood cluster—pertussis, poliomyelitis, diphtheria, measles, and tetanus.

† Tropical cluster—trypanosomiasis, Chagas' disease, schistosomiasis, and leishmaniasis.

days of lifelong disability, a calculation that would increase the current 5.2% YLD calculation by 73- to 183-fold to 380% to 952% of the current DALY calculation for diarrhea. This would result in an increase by three- to ninefold to well over one quarter (27% to 68%) of total global DALYs. Although this calculation does not include age-weighting or discount functions, the potentially great impact of early childhood illnesses on disability is likely to be substantial. Undoubtedly some, but by no means all, of this long-term impact from enteric infections is included in the malnutrition DALY calculation, which was estimated to account for 3.7% of total global DALYs, 64.2% of which is years lived with disability (YLD).

*The example of DALYs from intestinal helminths.* It was just such a calculation that enabled Bundy and Chan to more accurately determine the calculated DALY burden, which more than doubled from 18 to 39 million DALYs for intestinal helminths [87, 88], based on improvements in physical growth, physical activity, physical fitness, school attendance, and several measures of cognitive function [90–99] several months after a reduction of intestinal worm burdens by use of a single oral dose or brief course of the anthelmintic drug albendazole.

**Malnutrition as an Emerging Infectious Disease**

When fully understood in terms of its potential causation and long-term DALY impact, malnutrition may well be the most devastating of all of the new or newly recognized “emerging infectious diseases.” For example, we have found that persistent diarrheal illnesses not only identify a high-risk child (for heavy diarrhea burdens), but that they predispose to a subsequent tripling of diarrhea burdens for many months thereafter [27]. Indeed, infections due to *Cryptosporidium* species (one of the leading causes of persistent diarrhea) predispose to a doubling of diarrhea burdens and to growth shortfalls for >1 year after the infection, even when controlling for increased previous diarrhea burdens [100]. On the basis of our prospective surveillance studies in northeastern Brazil, we have just calculated that each persistent diarrheal illness can account for a 2-cm growth shortfall and that diarrheal illnesses in the first 2 years of life alone may account for a 4-cm growth shortfall at 5 years of age. Furthermore, malnutrition predisposes to more frequent and more prolonged diarrheal illnesses, thus compounding this “vicious cycle” of diarrhea and malnutrition.

As shown in figure 9 [33–36], not only do symptomatic diarrheal illnesses (defined by liquid stools) predispose to malnutrition, but even asymptomatic enteric infections (i.e., bowel infections that impair absorption without causing overt watery diarrhea) caused by *Cryptosporidium* species, enteroaggregative *E. coli*, or perhaps even *Giardia* species result in important growth shortfalls [13, 27, 33, 34]. Because they are often much more common than overtly symptomatic infections caused by

**Table 4.** Global mortality and disability adjusted life years (DALYs) lost from specific infectious diseases, 1990.

Infectious disease(s)	Global mortality (millions/year)	Percentage of total global mortality	Percentage of total DALYs lost
Acute respiratory infections	4.3	8.2	8.5
Diarrheal disease	3.1	5.9	7.2
Tuberculosis	2.9	5.6	2.8
Malaria	2.1	4.0	2.3
Measles	1.2	2.2	2.6
Hepatitis B	1.2	2.1	0.2*
HIV/AIDS	1.1	2.1	0.8
Other STDs	Leishmaniasis	Polio	
Tetanus	Yellow fever	Chagas' disease	
Pertussis	Dengue	Trachoma	
Meningitis	Japanese encephalitis	Intestinal helminths	
Schistosomiasis	Cholera	Other	
All infectious diseases	16.5	32	30.9†
All deaths	51.6	100	100

NOTE. DALYs = disability adjusted life years. Adapted from [13].

\* Includes both hepatitis B and C.

† Malnutrition included.

### Challenges for the “Unfinished Agenda”:

- Disproportionate impact on poor (growing numbers);
- Socioeconomic development and effective antimicrobials assumed;
- Impact of infectious diseases on ulcers, cancer, malnutrition, coronary diseases overlooked; and
- No sequelae of childhood illnesses, helminths or malnutrition. (Example: Only 0.1 disability per day counted for diarrheal diseases and only for 7 days; helminth DALYs increased from 18 to 39 million when disability was included.)

Figure 8. Challenges for the “unfinished agenda.”

these agents, these “asymptomatic” infections may be even more important in terms of their long-term (i.e., DALY) impact.

The basis for the profound nutritional (and likely developmental) impact of these common infections is clear when one understands the loss of absorptive villi that occurs with many prolonged gut infections [39, 101]. Indeed, given the rapid renewal of the normal intestinal mucosa every 3 to 5 days, the potential for substantial improvement (perhaps with a combination of micronutrients like vitamin A and zinc and major enterocyte energy sources of glutamine) is on the horizon.

Only when these long-term impacts are quantified and recognized will these silently devastating early childhood infections

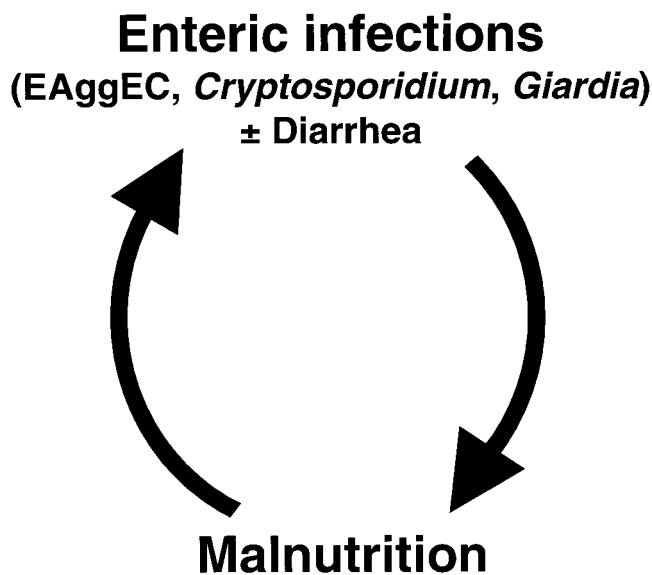


Figure 9. The vicious cycle between enteric infections and malnutrition. Enteric infections may well be a major cause of malnutrition and other developmental shortfalls in children. Enterotoaggregative *Escherichia coli* (EAggEC) and *Cryptosporidium* infections have been shown to impair growth, even in the absence of overt diarrhea. Furthermore, malnutrition predisposes to increased diarrheal illnesses to complete this vicious cycle—interventions at any point are therefore important. Reprinted with permission from [13].

(resulting from crowding, poverty, and inadequate water and sanitation) achieve the headline attention they deserve, because their impact is far greater than the lesser crises on which we routinely focus.

## Section 5: American Misperceptions About Overseas Development Assistance

### Public Perceptions Versus Reality

So, how are we doing at improving the poor health, population overgrowth, and connectedness of the world’s poor that threaten us all?

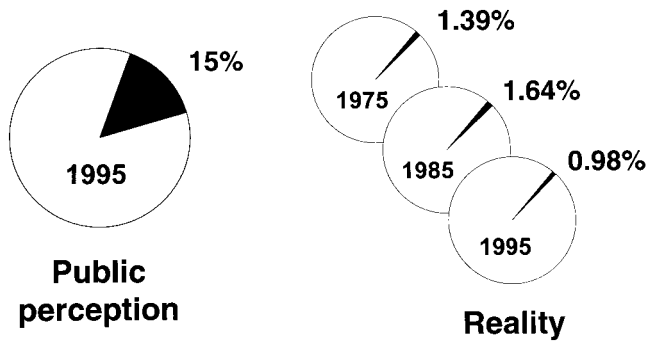
Very disturbing discrepancies between the American public’s perceptions regarding U.S. foreign aid and the worsening realities have been documented by the University of Maryland Center for the Study of Policy Attitudes. The American public believes that we are spending 15% of our Federal budget on foreign assistance (figure 10), and that we should be spending at least 5% to 8% [102, 103]. This genuine concern is reflected in the way the public eulogized and nearly idolized the selfless caring demonstrated by such people as Princess Diana and Mother Teresa.

However, the harsh reality is that we spend a shrinking percentage (now <1%) of our national budget (figure 10) [104–107]—barely one tenth of 1% of our gross national product (GNP)—on foreign assistance, and only a small fraction of that goes toward health care. This places the United States at its lowest point for foreign assistance since 1950, and for the first time ever (in absolute amounts of foreign aid) behind Japan, France, and Germany (figure 11A) [103].

Despite Ted Turner’s high-profile and insightful gift of \$1 billion to the United Nations (UN), among the top 21 industrialized countries, in foreign aid as percentage of GNP, the United States comes in last (figure 11B) [103]!

Focusing exclusively on government grants, as defined by the Organisation for Economic Co-operation and Development (OECD), the U.S. percentage of the total amount going to developing countries from OECD member countries has progressively fallen from 32.6% to only 17.7%, reflecting a steady decline in our leadership in this area [106]. In 1996 alone, the United States slashed bilateral and multilateral aid by more than \$1 billion, reflecting a further 15% decrease from the 1995 amount [108]. In addition, much of the U.S. bilateral aid goes to higher income countries such as Israel as well as countries in Eastern Europe and the former Soviet Union. Although bilateral aid was increased in 1997, as compared with 1995 levels, for Asian and Latin American countries by 7% and 6%, respectively, it was reduced by 5% for African countries [108].

The complexity of effective and lasting assistance likely involves difficult challenges such as more favorable trade agreements and understanding of economic motivations, in addition to the application of biomedical advances.



**Figure 10.** The public’s perception of the percentage of the United States’ budget that goes towards official development assistance (ODA) as compared with reality, for years 1975, 1985, and 1995. Total ODA is total net ODA plus grants as defined by the Organisation for Economic Co-operation and Development (OECD). Reprinted with permission from [13].

**Section 6: Are Organizations Accomplishing Their Missions?**

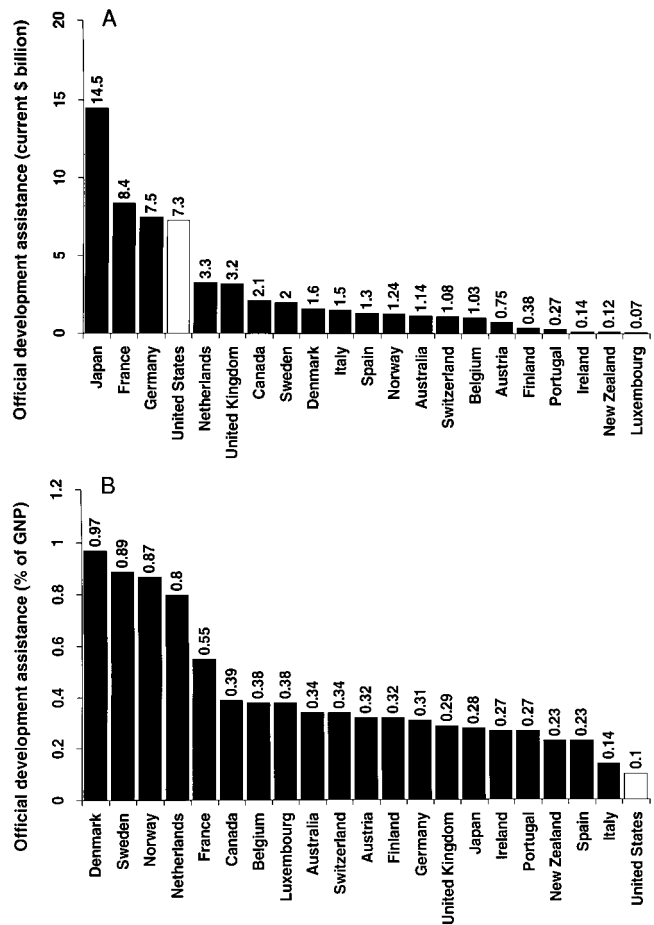
Before addressing the resources allocated for health, let us first examine the missions of selected major organizations involved in health and the current realities that determine their effectiveness. The 1990s have been a decade of reflection and reform for many international agencies involved in health issues. Examples of such organizations include the UN, the WHO, and the World Bank. Reform and/or reorganization within these agencies has included an examination of their missions or mandates.

Missions (or mandates) function at two levels [109]. First, the formal mission or mandate for an organization is the agreed statement of the overall purpose, or *raison d’etre*, usually encapsulated in a constitution, charter, or articles of agreement. There also exists what have been termed effective mandates. These mandates result from the interpretation of the formal mandate over time, as the purpose and functions of the organization change and specific activities and policies are implemented. It is, therefore, the effective mandates that reflect the current initiatives within an organization.

It has been suggested that the evolutionary nature of effective mandates, resulting from broad interpretations of the formal mission statement or mandate, has been problematic for some international organizations involved in global health initiatives [109]. For example, some critics of the UN system argue that the mission statements for the different special agencies, funds, and programs working on global health issues have become so broadly interpreted that their respective roles are now confused—despite the plausibility of the ultimate goal of improving international security by providing an adequate standard of health that preserves fundamental human dignity for all peoples. The confusion, it is argued, has in turn led to increased duplication of efforts, inconsistencies in policies and interventions, poor coordination, and inefficiency within the system.

Additionally, a lack of central vision and organization and too much independence have prevented coordinated efforts, division of labor, and the development of a master plan. Such criticism has given some countries, such as the United States, cause for suspending their dues.

Developed countries, like the United States, have also been forced to reflect on what future role the government will need to play in addressing global health issues. The increasingly apparent threats of emerging and reemerging infectious diseases have called international health policy and its woefully inadequate funding into question. Distinctions between domestic and international health problems are becoming useless, irrelevant, and often misleading. The recent report published by the Institute of Medicine (IoM) entitled “America’s Vital Interest in Global Health” states that “all countries have a responsibility to protect their citizens—residents, soldiers, and travelers” [103]. This same report argues that improving health abroad can produce economic benefits here at home. We would add that improved health abroad is key to controlling emerging



**Figure 11.** A. Official development assistance in billions of dollars as recently reported by the Institute of Medicine. B. Official development assistance as a percentage of the gross national product (GNP) from 21 top countries; the United States comes in last.

infections and exploding population, and to retaining the leadership of free democracies in addressing threats resulting from economic growing disparity. The IoM report then concludes that strategies and priorities developed by industrialized nations must recognize the importance of global health surveillance and communication networks, the value of sharing information for better health services, and the value of acquiring knowledge from international research and clinical trials.

Potential solutions to these problems may lie in current discourse. One framework for addressing the problem of effective mandates—which could also facilitate national policy and funding involvement—has been put forth recently in *The Lancet* by Jamison, Frenk, and Knaul [110, 111]. They suggest that international health efforts be categorized as core or supportive functions. Core functions are defined as those that transcend the sovereignty of any one nation state and include promotion of international public goods (research and development) and surveillance and control of international externalities (environmental risks and spread of infectious diseases). Core functions serve all countries and would address “global market failures.” Supportive functions, on the other hand, deal with problems that occur within individual countries, but which may justify collective action at an international level as a result of shortcomings in national health systems. Categories identified as supportive include helping the dispossessed as well as technical cooperation and development financing. Supportive functions are aimed at assisting countries with greater needs [110]. Framing international involvement in health in this manner could provide a much needed organizational structure in which individual organizations or agencies could more easily define the role for which they are best suited and secure their niche within the framework.

Examples of agencies that could help support the core functions in research and development include foundations, governmental agencies (such as the United States’ National Institutes of Health [NIH], British Medical Research Council [MRC], Brazilian National Council for Scientific and Technological Development [CNPq]), universities, and corporations. Core functions of surveillance and control of externalities include the UN, the WHO, and the CDC. Supportive functions for technical support and development could come from foundations and governmental agencies, while development financing is best taken on by the World Bank. Relief organizations and UN funds such as the United Nations Children’s Fund (UNICEF) could be charged with helping the dispossessed, and it could prove essential for the UN to adopt such a framework. The UN and its specialized agencies, funds, and programs might play a major role in providing core and supportive functions globally. In addition, such a role might give the UN the credibility it needs in order to demand that countries—such as the United States, which would benefit greatly from core and supportive functions, as argued above—pay funds that are now past due, and much needed.

Finally, it would be important for an independent organization to monitor which core and supportive functions are being

fulfilled and by whom, and which functions are lacking much needed funding and support. Further, the results could be published in a report aimed at informing those involved in international health, in an effort to eliminate the duplication, competition, and inefficiency that exist in the current system. One example of such concerted efforts includes “Malaria Research: An Audit of International Activity” funded and published by the Wellcome Trust [112]. Such reporting would also be invaluable for governments interested in issues of national security, economic stability and prosperity, and the health of its citizens.

### **Section 7: Distribution of Resources—Woefully Inadequate for Tropical Infectious Diseases**

At the Earth Summit in 1992, developed countries reaffirmed their commitment to achieving the UN target of 0.7% of the GNP for international aid. Since that time, the total amount of aid for developing countries has fallen by almost 17%. In 1996, the 21 OECD members gave a total of \$55 billion, which amounts to 0.25% of their total GNP. This represented a record 30-year low for aid as a percentage of GNP, and reflects a great inconsistency in the donors’ commitment to end absolute poverty [108].

#### **Global Health Resources**

Where, then, do global health resources go? Of the \$1.7 trillion spent on health care globally (8% of the gross world product), 90% is allocated to the 15% of people living in high-income countries (\$1,500 per capita, per year), while 10% goes to the remaining 85% of the world’s population (~\$41 per capita, per year) [20]. Parenthetically, 41% of all global health resources are allocated for health expenditures for the 4% of the world’s population living in the United States (\$3,291 per capita, per year).

Even within the United States, the annual cost of intestinal infections, influenza, and other infectious diseases totals >\$63 billion per year (table 5) [2, 103].

#### **Infectious Diseases and International Health Spending**

Despite the exciting and important new initiatives and global leadership at the NIH, the CDC, and World Bank, the \$2.9 billion in expenditures (even including the U.S. Agency for International Development [USAID], Foundation and Department of Defense [DoD] funds) for all of infectious diseases or international health constitute <0.3% of the U.S. health budget (0.04% of our GNP). Even when including World Bank lending and the WHO expenditures, spending for international health comes to only \$3.8 billion per year (table 6). This means that a small number of sources represents a major portion of the total global external assistance for health of \$4.8 billion per year! But these global totals come to <\$3 per DALY for measles, <\$1.31 per DALY for malaria, and <\$.60 per DALY

**Table 5.** Annual cost of selected infectious diseases to the United States.

Infectious disease(s)	Cost (billions of U.S. dollars)
Intestinal infections	23
Influenza	17
Nosocomial infections	10
STDs	5
Drug-resistant infections	4
HIV/AIDS	3
Tuberculosis	1

NOTE. STD = sexually transmitted disease.

for enteric and respiratory infections that kill >30,000 children each day and leave far more children developmentally scarred for life [38].

### The Improving Bargain of Buying Health

These limitations exist, despite the improving bargain of buying health. The total U.S. investment of \$32 million for smallpox eradication is estimated to be returned to the United States every 26 days; polio eradication will save \$500 million by the year 2000 and \$3 billion by 2015; each dollar spent for measles-mumps-rubella (MMR) immunizations saves \$21, while each dollar spent for diphtheria–tetanus toxoid–pertussis (DTP) immunizations saves \$29. Furthermore, the major improvements in life expectancy can be accomplished with a fairly modest income. Chile has attained its current life expectancy of 75 years with a per capita income of only \$5,000, an income equivalent to that in the United States in 1900, when we achieved only 40 years of life expectancy [103].

Despite the unprecedented opportunities and the extraordinary “bargain” that health represents, however, it is clear that we have fallen far behind where the American public thinks we are in showing the leadership that is so urgently needed in global health.

### Section 8: Why Change Is Essential—Evolving Global Civilization

As is illustrated repeatedly throughout this monograph, much of the data and information needed to assess current policy and conditions are available. However, as noted in section 2, it is when diseases “threaten to come rolling up to our threshold today,” as is happening through increased interdependence and globalization of the food supply, trade, and travel, that we take notice and start to understand the importance of these diseases. What now affects them, affects us. We are unaware of the skewed distribution of population and global resources—our privileged standard of living and overconsumption of resources (section 3). We do not realize that our perceptions are inaccurate,

and that in reality our nation grossly underfunds work in international health on which our future depends (section 5). We are unaware of the skewed distribution of DALYs and the dangerous implications that misinformation has for policy formation and redirection of critical resources for infectious diseases in developing areas (section 4). We do not realize that the opportunity to improve health through prevention is in actuality a bargain (section 6). In summation, we are unaware of the immediate threats posed by emerging infectious diseases, exploding population, and the erosion of humanity (section 2). When confronted with current realities and future prospects, the need for change becomes apparent. We have the resources, we now need the will.

### Toward a Global Civilization: The Urgent Evolutionary Survival Advantage of Caring

It has been suggested by Houston Smith that three civilizations have each made unique major contributions toward our present global civilization. Further, the evolution and survival of a global civilization are dependent on everyone learning from the unique contributions of all three civilizations. The three civilizations he lists and their contributions are: (1) “Western civilization” that contributed scientific technology, (2) the “Indian subcontinent civilization” that contributed individual introspection, and (3) the “Oriental civilization” that has traditionally contributed a system of social order. Despite our economic strength and technological advances in Western civilizations, we remain in need of a strong societal structure and commitment to community (family, neighborhood, city, etc.), as well as the ability to introspectively retain our individual dignity and sanity, without which social disorder develops as often reflected in our dysfunctional families and cities, our neuroses, and our high suicide and crime rates. Likewise it is readily apparent that the other civilizations are dependent on technological advances for modernization and development.

With respect to community, we must learn that a full understanding of “self” includes the community of which we are a part. It is the “non-self” toward which violent acts (of epidemic proportions) are typically directed. Hopefully, this community of “self” can increasingly be broadened to include the entire human family, so that we are not content until basic human needs are met for all.

Achieving development in tropical areas around the globe is certainly a complex and challenging goal. Yet the major problems of high infant and childhood mortality—that reflect basic underdevelopment, poverty, and high population growth rates—tend to occur predominantly in tropical areas in Asia, Africa, and Latin America. While battling tropical heat and humidity or drought may not be much easier than battling blizzards or subfreezing temperatures in temperate areas, the lack of brutal winters in tropical areas may allow impoverished, homeless peoples to survive and multiply more readily. In addition, however, tropical areas have the tremendous potential

**Table 6.** Direct and indirect resources for international health in millions of U.S. dollars—United States Government and selected nongovernmental organizations and private foundations.

Source of resources	1995	1996	1997
United States Government			
National Science Foundation*			3,270
International Cooperative Scientific Activities <sup>†</sup>			18
Centers for Disease Control and Prevention <sup>‡</sup>			2,302
Infectious Diseases—Non-HIV/HIV			88/617
National Institutes of Health <sup>§</sup>			12,740
NIAID (excluding HIV)			1,257 [609]
Fogarty International Center			27
USAID <sup>  </sup> (Population and Health, Africa/non-Africa)			6,725 [228/343]
Defense <sup>#</sup>			
Military branch			254,300
Total health budget**			41
International health spending <sup>††</sup>			7
Nongovernmental organizations			
World Bank <sup>‡‡</sup> /Population, Health & Nutrition <sup>§§</sup>			19,147/940
World Health Organization <sup>   </sup>			421
UNICEF—Total expenditures <sup>###</sup>		936	
Direct program assistance and support costs <sup>***</sup>		824	
Expenditures for child health <sup>†††</sup>		222	
United Nations Development Programme—total field program expenditures <sup>†††</sup>		1,036	
Field program expenditures for health, education, and employment <sup>§§§</sup>		141	
Foundations <sup>    </sup>			
Burroughs Wellcome	1.80		
Carnegie Corporation	4.00		
China Medical Board	6.40		
Clark Foundation	4.10		
Ford Foundation	20.00		
Gilman Foundation	0.05		
Health Foundation	1.50		
Howard Hughes Medical Institute	0.50		
Kaiser Family Foundation	5.00		
W. K. Kellogg Foundation	36.00		
MacArthur Foundation	14.00		
Pew Charitable Trusts	4.15		
Rockefeller Foundation	20.31		
Thrasher Research Fund	1.50		

NOTE. CDC = Centers for Disease Control and Prevention; NIAID = National Institute of Allergy and Infectious Diseases; UNICEF = United Nations Children's Fund; USAID = U.S. Agency for International Development.

\* Source—National Science Foundation, Overview of FY 1998 Request.

<sup>†</sup> Portion designated for International Cooperative Scientific Activities (ICSA), Source—National Science Foundation, Overview of FY 1998 Request.

<sup>‡</sup> Funds listed for international health may overlap with funds listed for infectious diseases and HIV categories, Sources—Office of Global Health, CDC, and Budget of the U.S. Government, 1998.

<sup>§</sup> Funds listed for international programs may overlap with funds listed for Fogarty International Center and NIAID categories. Also note that funds listed for the Office of AIDS Research may overlap with funds listed for NIAID. Sources—NIH and Budget of the U.S. Government, 1998.

<sup>||</sup> Source—USAID Congressional Presentation FY 1997, 1998.

<sup>#</sup> Source—Department of Defense and Budget of the U.S. Government, 1998.

\*\* Department of Defense total health budget equals \$15.8 million (basic + 6.2 million applied + 6.3 million transitional) and 25.5 million for biodefense research.

<sup>††</sup> Department of Defense international health spending equals \$7 million for six overseas labs (three Army and three Navy), Source—Department of Defense.

<sup>‡‡</sup> Total for the World Bank is International Bank for Reconstruction and Development (IBRD) and International Development Association (IDA) lending for a given fiscal year, Source—World Bank Annual Report 1997.

<sup>§§</sup> International health spending for the World Bank is the portion of total in <sup>‡‡</sup> going for population, health, and nutrition, Source—World Bank Annual Report 1997.

<sup>|||</sup> Based on biennial budget figure divided by 2 for 1996–1997, Source—Resolutions of the 48th World Health Assembly Relating to the Programme Budget for the Financial Period 1996–1997.

<sup>###</sup> Source—1996 and 1997 Annual Reports.

<sup>\*\*\*</sup> Source—1996 and 1997 Annual Reports.

<sup>†††</sup> 1995 amount based on actual dollar figure, while 1996 amount arrived at using percentage of expenditure on programs as reported in <sup>||</sup> by sector, Source—1996 and 1997 Annual Reports.

<sup>††††</sup> Source—1995 Annual Report.

<sup>§§§</sup> Source—1995 Annual Report. Private Foundations

<sup>||||</sup> Source—Dr. Joseph Cook, EM Clark Foundation, 1995

to provide the vegetative growth on which we all depend. Not only is the rich Delta region of Bangladesh one of the most fertile in the world (with the potential of being the “Bread Basket” of southern Asia), but the Amazon, African, and Asian jungles provide most of the world’s oxygen supply. We are, thus, far more interdependent on a global scale than is generally appreciated.

In conclusion, the high infant and childhood mortality rates that often approach 25% in the first 5 years of life in the poorest areas not only help to define the health problems in greatest need of attention, but also reflect and magnify the basic problems of disparate development. The specific causes of death, led by diarrheal disease, respiratory and parasitic infections, and associated malnutrition, can account for more life lost than all other causes combined. Furthermore, this staggering mortality (and the even greater morbidity) does not control but likely contributes to uncontrolled population growth. Thus, it is imperative that growing populations with high infant and childhood mortality rates be improved with the provision of basic human necessities including food, homes, and reasonable health not only for them, but for the very survival of all who share the planet.

#### **Reasons for Despair and Fear**

As detailed throughout this monograph, there are many valid reasons for grave concern in the face of imposing threats from emerging and reemerging infectious diseases and antibiotic resistance, the exploding population, and the erosion of our humanity. The potential for human depravity is indeed worrisome. From Hitler’s Nazism and presumption of supremacy to the brutal tribal conflicts in Bosnia, Africa, the Middle East, and Ireland, it is clear that we have the potential to exercise the worst forms of denial of human dignity. All that is required for this disturbing “rationalization” to gain authority is for the proverbial “good people (for whom individual dignity and rights are unswervingly unalienable) to do nothing.”

#### **Reasons for Hope**

The very clarity with which the above threats are increasingly evident may in fact be the greatest basis for hope. Clearly the awareness of some (if not all or even the most important) of these risks, as noted in the opening paragraphs of this monograph, are increasingly on the minds of the general public. Whether, as noted, because of frightening epidemics or because of popularized, barely fictional accounts, the public is perhaps open to the awareness of our interdependence like never before.

While we have lived through times of great fear and despair during the twentieth century—from the wars that repeatedly engulfed the entire world to fears of nuclear disasters in the 1960s through the 1980s—we now realize that the opportuni-

ties for progress (as well as destruction) are greater than ever before. It is imperative that we think creatively about such possibilities as genetic engineering, with its potential for affording nonpolluting solutions to global energy and food supply needs by using microorganisms that could produce hydrocarbons, carbohydrates, or proteins using solar energy. Indeed, the benefits of applying the best of modern science to tropical infectious diseases include not only potential solutions to real human needs but also the very “laboratories” of human diseases elucidate some of the most profound and novel concepts in basic biology.

Some have lamented that our rudderless, post-cold war society appears to have lost its bearings (figure 12). Global health (now an achievable imperative for our survival) may well provide the missing compass. The opportunities are greater than ever before. The genetic sequences for entire genomes are known. We must think creatively about new vaccines, simple-but-elegant diagnostics and therapeutics, and molecular approaches to prevention or control for the major health threats in the tropics.

As noted at the outset, is it just possible that we may be entering an era when we can begin to realize, perhaps for the first time, and act upon the dawning recognition of the survival and evolutionary advantage of concern about the “other” person. We have seen how emerging and reemerging infections threaten us all, and how the staggering mortality and even greater morbidity rates in the poorest areas led by tropical infectious diseases do not control but are associated with exploding population overgrowth, and how growing disparity threatens us all. We suspect that only such a realization will move those in authority to respond as necessary. If they are convinced, we have no doubt about the potential for coping with the major health threats from tropical infectious diseases. We have or could likely acquire the means—we lack only the will. Improved health education and opportunity for all may well prove to be the greatest test for the survival of a free democratic society (figure 13). Of one thing we are certain, the plight of the disadvantaged will be what determines the destiny of us all.

**For our rudderless, post-cold war society**  
**without “bearings”**  
**Global Health**  
**(now an achievable imperative for our survival)**  
**may well provide the missing “compass”**

Figure 12.

**The future of a free and democratic society depends on our ability to direct adequate resources to address the growing global health threats to us all.**

Figure 13.

### Acknowledgments

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