PRESIDENTIAL ADDRESS

DISEASES WITHOUT BORDERS: GLOBALIZATION’S CHALLENGE TO THE AMERICAN SOCIETY OF TROPICAL MEDICINE AND HYGIENE:
A CALL FOR PUBLIC ADVOCACY AND ACTIVISM*

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First, I want to thank the American Society of Tropical Medicine and Hygiene (ASTMH) membership for having the courage and/or folly to elect a woman clinician to the Presidency. It has been an honor and a privilege to represent the Society in this somewhat tumultuous year post September 11th. I want to share this podium and acknowledge my co-workers of the executive committee; Peter Weller, Stephen Hoffman, Ed Ryan, William Petri, Kevin Hacke, and Judy DeAcetis.

As Dr. Stansfield mentioned, it was 21 years ago that I attended the Puerto Rico ASTMH meeting; I have been a faithful attendee ever since. In preparing for this special occasion I have tried to reflect upon why I have been so faithful to this Society, rather than to one of the infectious disease, public health, bioethics, or even rheumatology societies, since I have interests in those areas too. I believe the reason is that the ASTMH offers a unique setting for fostering intense, collaborative relations between clinicians and basic scientists, whether in universities, foundations, private practice, or government service. This unusual blurring of usually rigid boundaries stimulates projects, cross-pollinates ideas, and makes for unusual bed fellows. In a non-biblical sense, of course.

For example, after a late night conversation with Peter Schantz of the Centers for Disease Control and Prevention (CDC) at an annual meeting several years ago, I began a collaborative sabbatical project on neurocysticercosis in Ecuador. Secondary to relationships formed at ASTMH, I have had the pleasure of rounding at the Armed Forces Research Institute Medical Units in Bangkok, Manila, and Cairo. Various CDC laboratories have hosted Yale students on Wilbur Downs fellowships. A project on dracunculiasis was completed by one of my students under the guidance of Don Hopkins at the Carter Center. Innumerable clinical consultations and referrals have transpired between myself, my partner Frank Bia, and Jay Keystone, Marty Wolfe, Barbara Hervaldt, and other members of the clinical group. Diagnostic support to unravel particularly perplexing cases has been provided by Tom Nutman, Diane McMahon-Pratt, Rebecca Rico-Hesse, and other basic scientists. Thanks to the arbovirologist experts so accessible in our Society, such as Tom Monath, Charles Calisher, Bob Shope, and Jim LeDuc, it has been possible to dissect enigmatic tropical fevers. I will never forget C. J. Peters’ words to me the unfortunate night I diagnosed one of our ASTMH members with a lethal arenavirus (Sabia). With great anticipation I asked for patient evacuation to a CDC or Fort Detrick mobile hospital: C. J. replied: “Hell, Michele, we don’t do that anymore. We’ll just have to chew on this together.” Membership in the ASTMH permits access to a company of scholars and collaborators and more distinctly, a Society of friends.

Clinical tropical diseases became my dominant career pathway in part for political reasons. They gave a chance to offer some skills unique to underserved populations, both in the United States and in developing countries. Presidential speeches are usually devoted to “The State of Our Union,” at this meeting Society reflections. Tonight, instead, I would like to deviate from the norm and devote the rest of my remarks to what I view as the moral challenges for the future of this Society as it enters its 100th year: the challenge to become activist, and more of a public advocate for tackling the global health disparities that have widened dramatically during the era of globalization. Dick Guerrant presciently argued in his Presidential address that our post-cold war society appears to have lost its bearings; emerging diseases, growing health disparities, and exploding population growth without health threaten us all.1

The benefits of globalization are potentially enormous and include increased sharing of ideas, cultures, life-saving technologies, infrastructures, and resources to breach disparities and lessen the threat. Yet according to the United Nations Development Program, over the past 30 years the gap in per income capita between wealthy and poor countries has tripled (Table 1). More than 1.2 billion of the world’s people live on less than one dollar a day.2 Life expectancy in the 48 least developed countries is just 51 years and infant mortality rate (IMR) averages 100/1,000.3 By comparison, in high income countries life expectancy is 78 and the IMR is 6/1,000. There are several areas where globalization itself has helped widen these gaps and directly affected the health and security of the world. The unprecedented interconnection and interdependency among human populations introduces newly shared risks of communicable diseases and accelerates global spread of antibiotic resistance and emerging environmental health hazards.

Our Society has been on the early frontline of one of the most predictable accompaniments to globalization: the emergence of new diseases and re-emergence of old ones. In 1865, it took 365 days to circumnavigate the globe; now it takes 36 hours.4 In the year 2000, 90,000 people were given refugee status in the United States, 900,000 received permanent immigrant status, and there were 60 million foreign visitors.5 The number of foreign born residents living in the United States has tripled over the past 30 years to 28 million.6 Disease migrates as well: the share of foreign-born tuberculosis cases increased from 30% of all U.S. tuberculosis cases in 1992 to 46% in 2000.6 While the overall number of tuberculosis cases in the United States that exhibited multidrug resistance decreased from 3% in 1992 to 1% in 2000, the share

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of multidrug-resistant cases occurring in foreign-born U.S. population increased from 31% to 72%.6

The potential for transportation of infected individuals, pathogens, and antibiotic resistance is staggering; borders are crossed with impunity. Unfortunately, due to national interests or constituency priorities, often research, teaching, surveillance, public health infrastructure, and institutions are not as globally efficient at crossing these borders. This creates what I have loosely termed egregious globalization gaps (EGGs), of which I will try to address four major areas (Figure 1). The EGGs that affect eradication of tropical diseases are 1) a Research 10/90 Gap, 2) a Pharmaceutical Research and Development (R & D) Neglected Diseases Gap, 3) an Internet Gap, and 4) a Gender Gap. My challenge to the ASTMH membership is to take the U.S. lead in trying to breach these gaps.

Egregious Globlization Gaps (EGGs)

1) Research 10/90 Gap

2) Pharmaceutical R & D Neglected Diseases Gap

3) Internet Gap

4) Gender Gap

FIGURE 1. Egregious globalization gaps that affect eradication of tropical diseases. R & D = Research and Development.

RESEARCH 10/90 GAP

The Research 10/90 Gap is a term that emphasizes the fact that only 10% of the biomedical research funding is targeted to the diseases that account for 90% of the global disease burden.7 These data come from the Global Forum for Health Research, which was created in 1996 to support public and private sector partnerships to focus research on the heaviest burden of disease in the world. Although research in high income countries may not always be transferable or appropriate for use in low or middle income countries, globalization has intensified the problem of lack of qualified researchers to set appropriate priorities to conduct relevant research for lower income countries. It is estimated that in the case of 20 African countries more than 35% of nationals with a university degree are now living abroad, mostly in the United States, Canada, or Europe.8 As Africa struggles with the dearth of scientists and doctors, high income countries continue to attract and recruit the best and the brightest with monetary inducements and visa preference.

The Commission on Macroeconomics and Health has found it helpful to distinguish between three types of diseases to identify R & D activities. As one can see, our Society is mostly involved with the study of the very neglected diseases.9 The Commission drew attention to the high burden and low investment in research of these diseases. According to their economic analysis, at least $3 billion per year should be allocated to the R & D of health priorities of the poor.9 Half of this three billion is proposed to go to a newly created international version of the National Institutes of Health (NIH) called the “Global Health Research Fund” with a key goal to build long-term research capacity in developing countries themselves. For comparison, the entire budget of tropical disease research at the World Health Organization (WHO) directed at the eight major tropical diseases is only $30 million.7 For further comparison, it is estimated that worldwide, countries spend more than $800 billion on weapons and military resources. The economists on this panel estimated that the cost to a donor country would be 0.1% of the donor gross national product (GNP) or approximately $34 per person.9 Currently, the United States musters approximately $5 per person in donor aid.9

HOW THE ASTMH HAS PLAYED A ROLE AND CAN HELP REDUCE THE 10/90 GAP

Our society remains the outstanding voice for tropical medicine research within this country. Our constituency includes the premier collection of scientists staffing collaborative field sites, gathering data on very neglected diseases. However, excellent science does not always translate into solutions. A Nobel Prize was awarded in 1902 to Sir Ronald Ross for unraveling that the transmission of malaria is via mosquitoes. Despite this stunning achievement, a century later there remain more than 300 million cases of malaria within the world each year with 1–2 million deaths. A Nobel Prize was awarded in 1905 to Robert Koch for the discovery of the bacterium that causes tuberculosis and a second was given almost 50 years later to Selman Waksman for the development of antibiotic chemotherapy; however, 50 years still later the incidence of tuberculosis is eight million cases per year and it kills two million people annually.6 In 1951, Max Thieler won a Nobel Prize for the development of the yellow fever vaccine, yet the developing world carries most of the burden of tuberculosis and yellow fever is more deadly a half century later. Science needs money and infrastructure to translate scholarship into egalitarian solutions. Clinicians and researchers, like those in our Society, who can stand at the interface between the laboratory bench and global public health issues, are vital to this process.
Our Society can and has supported Fogarty and NIH budgets for research in neglected diseases by lobbying Congress with our legislative initiatives via Capitol Associates. Hopefully, most of you received the e-mails I sent with copies of advocacy letters for increased NIH-Fogarty budget, reorganization of study section guidelines, and reorganization of bioterrorism research. At The Fogarty Center, ASTMH members Gerry Keush and Joe Bremen have spearheaded initiatives such as “GRIIP” (Global Health Research Initiative Program for Foreign Investigators) to combat brain drain and fund young scientists from developing countries to return to their indigenous countries with financial and institutional support. I urge our members to host such overseas scientists and create collaborative field sites to enhance research capacity around the world.

The ASTMH has developed specific awards (with support by Pfizer, Burroughs-Wellcome, and The Gorgas Institute) that offer seed money to young investigators to study and collaborate in overseas settings. We need to find more serious and sustainable funding streams for these initiatives. The Ben Kean Fund initiated by Stephen Hoffman sends young clinicians to overseas settings. We need to nurture this fund to spark interest in neglected disease research and foster cultural understanding and overseas partnerships. Reviewing our first 15 years experience of the Yale International Health Program, a colleague of mine, Dr. Anu Gupta, found that the 192 resident physicians who spent even a small amount of time overseas were more likely to work with the underserved in the United States, patients infected with human immunodeficiency virus, or in a public health arena than their stay-at-home colleagues. For sure, selection bias plays a role. However, many of us in this room were inspired to go into tropical disease study by a hands-on experience in the developing world. Certainly, my early clinical exposure at the Hôpital Albert Schweitzer in Haiti and at the Kilimanjaro Christian Medical Center in Tanzania helped direct my career choice. In the end, though, these are minuscule assaults on a huge and intractable burden of disparity.

PHARMACEUTICAL R & D GAP

Parallel to the 10/90 research gap is the effect globalization and the World Trade Organization (WTO) agreements have had on access to drugs and development of new drugs for tropical diseases. The small part of the globe accounting for 15% of the earth’s population provides nearly all of the world’s technology innovations, with one-third of the population completely technologically disconnected. Heavy reliance on an increasingly consolidated and competitive multinational drug industry has left the development of life-saving drugs to the whimsies of a market economy. North America, Europe, and Japan will account for 80% of the world pharmaceutical market in 2002 (total value projected $406 billion) while Africa, Asia, Latin American, and the Middle East will account for 20% of the market, despite representing 80% of the world’s population. It is no surprise then that of the 1,393 new drugs approved worldwide between 1975 and 1999 only 1% (16 drugs) were specifically developed for a tropical disease or tuberculosis. A recent survey of the world’s pharmaceutical companies, to assess the level of R & D in neglected diseases compiled by one of our past Presidents, Dy-ann Wirth, reveals that the pipeline of new drugs for tropical diseases is virtually empty. At last year’s annual meeting a plenary session was devoted to eflornithine, an effective drug for African sleeping sickness that was discontinued as a parenteral preparation, only later to be marketed in the United States as a depilatory for women’s facial hair. Even when effective drugs are available, patent protection, access to drugs, and the WTO agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPs) can hinder availability to those with the most need (a well-named agreement = TRIPs).

Although many multinational pharmaceutical companies have initiated drug donations to overcome access problems and to combat specific diseases, economic analysis of the donation model reveals that the cost of such programs to the donor country (after tax gains and tax incentives to the pharmaceutical company) exceeds by four-fold other suggested models, such as purchasing and distributing low-quality generics or differential prices of a branded drug for a needy country. It is obvious one cannot expect a market-driven pharmaceutical industry to invest in non-profitable research or R & D. Donated drugs cannot be the primary solution to the vast inequities in global drug access.

HOW THE ASTMH HAS PLAYED A ROLE AND CAN HELP BREACH THE PHARMACEUTICAL R & D GAP

Our Society can play a role as a sentinel voice, a unique group that has specialized expertise in diagnosis and treatment of tropical diseases. It already has. Two years ago, when manufacturing of praziquantel, the preferred treatment for schistosomiasis, was discontinued for lack of a profitable market, the clinical group sounded an early alarm via an e-mail list-serve and a letter-writing campaign. Our lobby of this particular pharmaceutical company led to successful reinstatement of production.

Earlier this year, I had the pleasure of representing this Society at an international conference in New York sponsored by Medecin Sans Frontieres on the Crisis of Neglected Diseases, Developing Treatments and Ensuring Access. I was able to offer our membership’s support for their new needs-driven drug development network, the Drugs for Neglected Diseases Initiative (DNDi) that seeks to correct the R & D gap for neglected diseases. I e-mailed you the proposal accepted this year by Council offering our assistance to the Medecin Sans Frontieres initiative. Many members have already gotten involved; for members who want to get more active in the initiative, the website is www.neglecteddiseases.org. We have many active Society members who are leaders within the pharmaceutical industry. I invite any member to offer suggestions to our newly formed corporate industry liaison group spearheaded by Tom Monath, Adel Mahmoud, Brad Connor, and Phil Coyne. Clearly, radical and innovative incentives need to be built into the R & D of treatment for tropical diseases. Existing capabilities of indigenous countries need to be expanded and creative partnerships in drug research and trials need to be fostered, while maintaining high cross-cultural ethical standards. Who better than our Society membership can advocate for these changes?
GLOBALIZATION AND THE INTERNET GAP: HOW THE ASTMH CAN ASSIST

The past two decades have seen dramatic advances in independent media and global communication with the development and dramatic expansion of the Internet. In August 2000 in the United States, 54 million households (51%) had one or more computers, with four of five of these computer households accessing the Internet.\(^{18}\) Although radio, television, and newspapers have dramatically expanded in the developing world, it has been the Internet that offers the best potential for scientific exchange, management of scientific data, and unfettered access to information. Yet in 2001, although 440 million people were Internet users, this represented activity by less than 7% of the world’s population\(^{18}\) (Figure 2). In Africa, with a population of 700 million, fewer than three and a half million have access to the Internet and most of those are in South Africa.\(^{19}\) Over time this division between developed countries and developing countries is increasing. Internet usage is even larger than the spread of gross domestic product between the world’s rich and poor countries and larger than disparities in other technologies such as television and telephones.\(^{18}\) Access to the Internet is often gauged by the number of registered online computers. In April 2001, there were more than 77 million computers registered online in the United States and almost six million in Japan, but a number of countries had less than 10 (Bangladesh, Angola, Chad, and Iraq) or even zero (Burundi, Benin, and Syria) computers registered under their country code.\(^{18}\)

Members of our Society (in particular Jack Woodall and Charlie Calisher) have played a dramatic role in trying to reach developing countries with the development of ProMED, offering daily free electronic dissemination of worldwide disease outbreaks and facilitating scientific discussions by email. In eight years ProMED has grown from 40 subscribers in seven countries to more than 27,000 in more than 155 countries (33% outside the United States) (Woodall J, personal communication). When Ebola broke out in Gabon in October 1996, ProMED posted the news four days before WHO’s own outbreak reporting system disseminated information. The diagnosis of the Nipah virus outbreak was aided by electronic challenge of the original diagnosis of Japanese encephalitis. During the bioterrorism anthrax outbreak, daily bulletins aided participants in diagnosis and treatment operations. In August 2002 alone, the Web site received almost 180,000 hits (6,000/day) from 13,000 different addresses (Woodall J, personal Communication). However, the majority of ProMED users are still from developed countries. Clearly, barriers such as literacy and language, lack of modems and computers, and financial barriers to Internet access are considerable in the developing world. Yet cyber cafes, library nodal points, low-orbit satellites, and cell phones with Internet capabilities will hopefully soon enhance access and bridge the digital divide. A proposal was recently floated that non-governmental organizations act as local intermediaries on the web or on the ground; staging posts to read, translate, and convert information into culturally relevant content.\(^{19}\)

We will soon be going on-line electronically with our journal now that a new contract was finally negotiated. I propose that we as a Society either donate free access of our journal to targeted countries with a low GNP or consider offering free full text access of certain relevant articles selected by our editorial staff or by our cyber space committee led by David Freedman. Precedents have been set by the British Medical Journal, which offers free access to all scientists on-line and the Lancet, which offers access to selected full text. (see the Web site freejournals.com). Even if there is a large gap to electronic access in developing countries, at the very least the ASTMH can offer its journal free to institutions and libraries in developing countries.

GENDER GAP IN TROPICAL DISEASES AND HOW THE ASTMH HAS AND CAN BREACH THE GAP

Lastly, as one of your few female presidents, I want to raise the issue of gender gap in the field of tropical infectious diseases. Until recently, researchers have paid little attention to sex or gender differences in disease acquisition. Now this has become the standard for all NIH research into disease development. In the field of tropical diseases even less attention has been directed towards gender differences, yet diagnosis and effectiveness of treatment of tropical diseases may also be affected by gender. For example, recent studies of malaria have demonstrated that biological immunity is compromised in pregnancy and the early post-partum period.\(^{20}\) Pregnant women have been shown to be more susceptible to mosquito/vector transmission than men or non-pregnant women.\(^{21}\) A recent study in Nigeria showed that the prevalence of schistosomiasis in girls is highest at age 15 when they are maximally involved in water-related domestic work. While the rate decreases in males after late adolescence, that of females remains stable, reflecting women’s continued exposure to domestic duties and male lack of exposure to play at the river as they age.\(^{22}\) Access to hospitalization and drugs for tropical diseases often is limited to the male child in developing countries where land ownership and inheritance patterns are patriarchal.

Members of the ASTMH are now encouraged to incorporate sex and gender into research design by funding agencies, yet more awareness of gender differences in disease acquisition and treatment is needed. Women scientists need to be recruited into tropical medicine (35% of our membership is female) and more women need to be nurtured to ensure professional success. Women’s voices need to be heard in negotiations for funds at the International Monetary Fund, the
World Bank, the NIH, on the Internet, and most importantly, in the field to highlight gender issues to disease patterns. Given how progressive the ASTMH has been in the last eight years in its election of four women presidents, why not be a Society in the forefront of advocacy for women’s issues in the tropics?

In conclusion, I would like to return to where I began, with the title Diseases Without Borders and the contribution that our special expertise in tropical medicine can make. In the medical condition of the world’s poorest people, we can see the incubators of political and social pathology as well as medical ones, and as events of the past year have pointed out, the borders of the advanced industrial countries are permeable to all three. Tropical medicine specialists are a kind of distant early-warning system of public health. We see problems in their early stages. We have seen the acquired immuno-deficiency syndrome catastrophe building in Africa for 20 years. Yet only now does it occur to some of our most powerful politicians that a threat to a continent is not only a human tragedy for the continent of Africa, but a threat to the world. Priorities must be chosen carefully, we cannot be issuing orange or red alerts all the time, but we should make sure that our voices are heard. Globalization means a threat to any of the world’s peoples is a threat to all the world’s peoples. Advocating for resources to bridge the egregious globalization gapes I have referred to is no longer a moral imperative, but an imperative for the health of all. It is also an imperative for the ASTMH as it enters its next century.

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Editor's note: The full text of Dr. Barry’s Presidential Address with slides can be found on the ASTMH website at http://www.astmh.org/q&a/pp/index.htm.

REFERENCES