



**Resolving the Global Burden
of Gastrointestinal Illness:
A CALL TO ACTION**

Copyright © 2002
American Academy of Microbiology
1752 N Street, NW
Washington, DC 20036
<http://www.asmtusa.org>

This report is based on a colloquium, "The Global Burden of Infectious Diseases Through the Gastrointestinal Tract: A Critical Scientific Assessment of Exposure," sponsored by the American Academy of Microbiology and held February 15-18, 2002, in Galway, Ireland.

The American Academy of Microbiology is grateful for the generous support of the following organizations:

American Society for Microbiology
Centers for Disease Control and Prevention Foundation (R13/CCR320199.01)
Food Safety and Inspection Service, U.S. Department of Agriculture
Centre for Infectious Diseases Prevention and Control, Health Canada
National Institute of Allergy and Infectious Diseases,
National Institutes of Health
U.S. Environmental Protection Agency

The opinions expressed in this report are those solely of the colloquium participants and do not reflect the official positions of our sponsors.

This report is available in PDF format at: <http://www.asmtusa.org>



**Resolving the Global Burden
of Gastrointestinal Illness:
A CALL TO ACTION**

Pierre Payment and Merry S. Riley

Board of Governors, American Academy of Microbiology

Eugene W. Nester, Ph.D. (Chair), *University of Washington*
Joseph M. Campos, Ph.D., *Children's National Medical Center*
R. John Collier, Ph.D., *Harvard Medical School*
Marie B. Coyle, Ph.D., *University of Washington*
James E. Dahlberg, Ph.D., *University of Wisconsin, Madison*
Julian E. Davies, Ph.D., *Cubist Pharmaceuticals, Inc.*
Arnold L. Demain, Ph.D., *Drew University*
Lucia B. Rothman-Denes, Ph.D., *University of Chicago*
Abraham L. Sonenshein, Ph.D., *Tufts University Medical Center*
David A. Stahl, Ph.D., *University of Washington*
Judy A. Wall, Ph.D., *University of Missouri*

Colloquium Steering Committee

Pierre Payment, Ph.D. (Chair), *University of Quebec, Canada*
Alfred P. Dufour, Ph.D., *U.S. Environmental Protection Agency, Cincinnati, OH*
Timothy Ford, Ph.D., *Montana State University*
Deborah Levy, Ph.D., *Centers for Disease Control and Prevention*
Joan B. Rose, Ph.D., *University of South Florida*
Carol A. Colgan, Director, *American Academy of Microbiology*

Colloquium Participants

Michael Baker, Ph.D., *Kenepuru Science Centre, Wellington, New Zealand*
Jamie Bartram, Ph.D., *World Health Organization, Geneva, Switzerland*
Sandy Cairncross, Ph.D., *London School of Hygiene & Tropical Medicine, London, England*
Rebecca L. Calderon, Ph.D., *U.S. Environmental Protection Agency, Durham, NC*
Rachel Chalmers, Ph.D., *Public Health Laboratory Services, Cardiff, Wales*
John M. Colford, Jr., Ph.D., *University of California, Berkeley*
Martin Cormican, Ph.D., *University College Hospital, Galway, Ireland*
Alfred P. Dufour, Ph.D., *U.S. Environmental Protection Agency, Cincinnati, OH*
Lorna Fewtrell, Ph.D., *Center for Research into Environment and Health, Cheshire, England*
Timothy Ford, Ph.D., *Montana State University*
Roger Glass, M.D., Ph.D., *Centers for Disease Control and Prevention*
Jeffrey K. Griffiths, M.D., *Tufts University School of Medicine*
Arie Havelaar, Ph.D., *RIVM, Bilthoven, The Netherlands*
Allen Hogue, Ph.D., *U.S. Department of Agriculture, Washington, DC*
Paul R. Hunter, Ph.D., *University of East Anglia Medical School, Norwich, England*
Lee-Ann Jaykus, Ph.D., *North Carolina State University*
C. William Keevil, Ph.D., *University of Southampton, Southampton, England*
Dennis Lang, Ph.D., *NIAID, National Institutes of Health, Bethesda, MD*
Elaine Larson, R.N., Ph.D., *Columbia University School of Nursing*
Arthur P. Liang, M.D., *Centers for Disease Control and Prevention*
Deborah Levy, Ph.D., *Centers for Disease Control and Prevention*
Christine L. Moe, Ph.D., *Emory University*
Sarah O'Brien, Ph.D., *Communicable Disease Surveillance Centre, London, England*
Pierre Payment, Ph.D. (Chair), *University of Quebec, Canada*
Paul Sockett, Ph.D., *Health Canada, Ontario, Canada*

Science Writer

Merry S. Riley, Ph.D., *New London, CT*

Executive Summary

The American Academy of Microbiology convened a colloquium to consider the global burden of gastrointestinal disease. The colloquium, held February 14-16, 2002, in Galway, Ireland, brought together an international group of scientists—researchers and public health specialists—to discuss the current state of knowledge in the field and appropriate future directions for the clinical arena, research, education, disease prevention, and communication.

In the next 15 seconds, a child somewhere in the world will die from diarrheal disease. Globally, it is estimated that 6-60 billion cases of gastrointestinal illness occur annually. These illnesses are not limited to minor, uncomfortable cases of stomach upset. They are a scourge of humanity and are largely the result of fecal contamination of the environment.

The sum total of the incidence, severity, and duration of gastrointestinal disease are known as the global burden of these illnesses. Grasping these facts is critical to understanding the threat these diseases pose to public health and to appropriately allocating resources and efforts to curb them. Currently, however, there are a number of obstacles to overcome. They include the use of non-standardized definitions of disease and symptoms; failure to identify a causative agent in many, if not most, cases of disease; failure to report episodes to health authorities; and the existence of incompatible reporting systems. There are a number of modes of transmission that contribute to the burden of gastrointestinal disease, and the relative significance of each changes with economic development.

Colloquium participants discussed the routine clinical data issues central both to the question of global burden of gastrointestinal diseases and to matters of public health. Several key weaknesses in the current systems for collecting and processing clinical data were identified. Recommendations were developed, including a shift from passive reporting systems to active surveillance and reporting systems, epidemiological training for clinicians and environmental health specialists, improved data collection during outbreaks, improved surveillance and specimen collection and laboratory testing for public health purposes, more thorough investigation of the agents responsible for incidents of gastrointestinal disease, and the careful consideration of the employment of new diagnostic techniques for clinical testing. Advances in the clinical setting can lead to more thorough reporting of disease, and hence, to better management of important routes of transmission and the diseases themselves.

Progress in research and education has always been critical to improving public health. In many ways, efforts in these areas can be honed to better address needs related to gastrointestinal disease. Through establishment of standard definitions of the parameters related to gastrointestinal disease, scientists can ensure that their studies can more easily be related to the results of other work. By coordinating funding programs and encouraging interdisciplinary efforts, research programs and collaborations can more effectively address unanswered questions in the field. Improved efforts in systematic data review and peer review in the relevant journals could help synthesize the current body of knowledge and



IN THE NEXT 15 SECONDS, A CHILD SOMEWHERE IN THE WORLD WILL DIE FROM DIARRHEAL DISEASE. GLOBALLY, IT IS ESTIMATED THAT 6-60 BILLION CASES OF GASTROINTESTINAL ILLNESS OCCUR ANNUALLY.

lend more credibility to findings in the field. Finally, three specific areas of research were identified as critical to progress in battling gastrointestinal disease: validation of intervention techniques, quantitative evaluation of gastrointestinal disease, and exploring the role of the host and the dose-response relationship in the development of disease.

In terms of preventing gastrointestinal illness, by far the greatest advances can be made by providing adequate sanitation—or excreta disposal—facilities to poor and developing nations. Worldwide, it is estimated that sanitation, combined with appropriate hygiene practices, could end 90% of gastrointestinal disease. Further inroads could be made by using the results of research to drive successful interventions and training of health professionals in public health, epidemiology, and hygiene promotion. Finally, communicating the risks and priorities related to gastrointestinal disease is critical to gaining recognition of these issues among the public and policy makers. On a related note, there is a great need to adequately educate and train the scientists of tomorrow. These are both key issues in addressing gastrointestinal diseases today and in the future.



IN TERMS OF PREVENTING GASTROINTESTINAL ILLNESS, BY FAR THE GREATEST ADVANCES CAN BE MADE BY PROVIDING ADEQUATE SANITATION—OR EXCRETA DISPOSAL—FACILITIES TO POOR AND DEVELOPING NATIONS.

Introduction

Gastrointestinal illnesses and enteric infections occur everywhere and nowhere at the same time. Although every person on the planet has been afflicted with these illnesses, few recognize them as legitimate health hazards, except when traveling to some countries. For many, incidents of stomach or intestinal disturbance, while extremely uncomfortable when they occur, are simply so common that they are invisible; for most people, these incidents are forgotten as quickly as they came. A large proportion of these illnesses are due to infections by a wide variety of enteric microorganisms, including bacteria, viruses, and intestinal parasites.

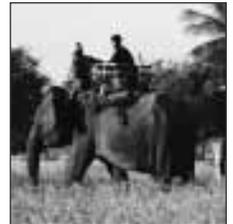
By and large, after multiplying in the gastrointestinal tract, enteric pathogens are introduced to the environment through human and animal waste. Although some of these microorganisms have a limited survival rate outside their host, many have developed means to survive in the environment for days or months. The proximity in which humans have lived for centuries in villages or cities results in almost routine exposure to human and animal feces, and, therefore, to enteric pathogens. This is still true in the 21st century.

Pervasive but disregarded

Every single resident of developed countries is expected to become ill from an enteric infection at least once in the next 18 to 24 months, and yet gastrointestinal illness hardly registers as a major public health problem. The manifestations of these infections are often seen as merely unfortunate or slightly unpleasant events attributable to overindulgence, tainted food, or bad water. However, severe cases of gastrointestinal illness can be permanently crippling or fatal.

Contrary to common belief, diseases associated with enteric infections are not limited to gastrointestinal symptoms. The symptoms of enteric infections depend on the microorganisms responsible and run the gamut of human afflictions, affecting every part of the body. The digestive system, nervous system, respiratory system, muscles, eyes, and skin can all be affected by microorganisms multiplying in the gastrointestinal tract. The most commonly reported symptoms are diarrhea, bloody diarrhea, nausea, vomiting, cramps, headache, muscle pain, and flu-like respiratory symptoms. In some cases, a gastrointestinal infection can lead to more severe symptoms or complications. For example, an infection causing diarrhea and vomiting can lead to severe dehydration; *Campylobacter* infections can lead to the neurological Guillain-Barré syndrome. Infection by *E. coli* O157:H7 may damage the kidneys, leading to hemolytic uremic syndrome and death. In children, some forms of these diseases can be so debilitating that they permanently stunt a child's growth and development. In developing countries, many of these gastrointestinal infections remain untreated and cause premature death in children and adults. In the developed world, there is a tendency to minimize the effects of enteric infections, but in acute cases and in sensitive populations the results of infection can be disastrous.

By and large, after multiplying in the gastrointestinal tract of man or animals, enteric pathogens excreted in the feces are introduced into the environment. Although some of these microorganisms have a limited survival time outside their host, many have developed means to survive in



the environment for days or months. The proximity in which humans live and poor hygiene result in almost routine exposure to human and animal feces, and, therefore, to gastrointestinal pathogens.

Outbreaks

Outbreaks are the public face of infectious enteric disease. Numerous outbreaks in the recent past have highlighted not only our susceptibility to infection, but the potential severity of these diseases.

One outbreak occurred during September and November 2000 when Pennsylvania health authorities identified 51 people who developed acute symptoms following visits to a dairy farm. The agent was a virulent form of a common intestinal bacterium: a strain named *E. coli* O157. Sixteen people were hospitalized and eight developed hemolytic uremic syndrome as a result of their infection.

A large outbreak of foodborne gastrointestinal illness occurred throughout the United States and Canada in 1996 and 1997, when raspberries from Guatemala that were contaminated with the parasite *Cyclospora* sickened approximately 1,400 people. The source of contamination of the raspberries is not known, but it was most likely from fecally contaminated water used to spray crops.

In spring 2000, residents of the small Canadian town of Walkerton, Ontario, were exposed to contaminated drinking water after heavy rainfall compromised the municipal well and the water treatment processes. In that outbreak, *E. coli* O157 and *Campylobacter jejuni* bacteria sickened over 2,300 people and killed seven.

By far the largest documented outbreak of gastrointestinal illness occurred in the spring of 1993 in Milwaukee, Wisconsin, when an apparent failure in water treatment caused an estimated 400,000 cases of diarrheal disease and approximately 100 deaths. The parasite *Cryptosporidium* was responsible for most of the Milwaukee cases.

Outbreaks like these demonstrate serious breaches in public health protective measures, thereby eroding the public's confidence in public health surveillance systems. But these outbreaks still represent only a tiny fraction of the total number of gastrointestinal illnesses every year. Although the publicity surrounding recognized outbreaks is alarming, the public, policy makers, and health care community should be even more distressed by the high baseline rates of infection that continue unabated in communities worldwide. Outbreaks are only the tip of the massive iceberg of gastrointestinal diseases that loom beneath the line of sight of leaders and the public. The high incidence of "background" gastrointestinal disease is a strong indication that gastrointestinal pathogens circulate through the population with ease, and that our environment, our food, and our water are vehicles of transmission for these microorganisms.

Estimates of incidence of gastrointestinal illness worldwide

Very few outside the field of public health fully appreciate the extent to which gastrointestinal illness affects human health across the globe. There are difficulties in deriving a precise number of cases globally, as the symptoms associated with these infections are quite diverse and can be difficult to classify and diagnose. Self-reported or physician-reported



THE BULK OF GASTROINTESTINAL DISEASE STRIKES IN DEVELOPING NATIONS, WHERE FOR MANY MILLIONS OF PEOPLE DRINKING WATER REMAINS CONTAMINATED AND UNTREATED, SANITATION IS UNAVAILABLE, AND HYGIENE PRACTICES DIFFICULT, IF NOT IMPOSSIBLE, TO UPHOLD.

gastrointestinal illnesses have been used as an index of the number of these infections because the numbers are easily collected. Using this index, it is estimated that residents of developed countries experience one episode of gastrointestinal illness every two years, while residents of developing nations may experience between five and ten episodes per year. The rate of gastrointestinal illness is always highest in children between the ages of one and four years (Payment and Hunter 2000). With a current global population of 6.5 billion individuals, this adds up to a staggering 6-60 billion cases of gastrointestinal illness annually.

Every minute, there are over 50,000 cases of gastrointestinal illnesses; some individuals, especially children, will die from these infections. The estimated number of deaths worldwide from diarrheal diseases alone is over 2 million. The estimated number of deaths by gastrointestinal disease does not include mortality from the other manifestations of enteric infections (like hepatitis, encephalitis, hemolytic uremic syndrome, meningitis, etc.), so this number is probably a gross underestimate of the number of deaths from all gastrointestinal illnesses.

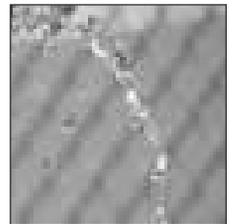
However, even with these staggering estimates we do not have standardized methods with which to estimate the true burden of gastrointestinal diseases. Non-standardized definitions and cultural differences often result in assessments that are extremely difficult to compare even between developed countries. Our understanding of these enteric infections and gastrointestinal diseases remains very incomplete.

Paring down the statistics to a single country may help to demonstrate the point. In the Netherlands, a developed nation of 16 million people, a staggering 4.5 million episodes of gastroenteritis have been reported to occur each year, with very few cases resulting in death (De Wit, 2002). This is particularly disturbing in light of the fact that the Netherlands has a lower rate of gastrointestinal illness than many developed nations.

Furthermore, it is not the developed nations that bear the greatest burden in gastrointestinal illness. The bulk of gastrointestinal disease strikes in developing nations, where for many millions of people drinking water remains contaminated and untreated, sanitation is unavailable, and hygiene practices difficult, if not impossible, to uphold. Since most research and surveillance of gastrointestinal disease takes place in wealthy nations, estimates of incidence and severity for developing countries are difficult to derive. Assuming that the 5.2 billion citizens of low to middle income countries may suffer over five cases of acute gastrointestinal disease each year, more than 26 billion cases are thought to occur every year in the developing world.

Estimating the cost of gastrointestinal illness

Using gastrointestinal illnesses as an index of enteric infections, it becomes possible to estimate the socioeconomic costs of these infections. The costs of gastrointestinal illness are not only felt in the unnecessary loss of human lives and damage to human health, but in the pocketbooks of individual families and in the treasuries of businesses and nations. Every day, millions of individuals who are afflicted with gastrointestinal illness lose productivity and, therefore, lose money



that would otherwise have gone home in their paychecks. The loss in productivity affects business as well; an infected worker experiencing gastrointestinal illness may stay away from work, be less productive, and even contaminate colleagues or customers.

The cost of food-borne illness alone illustrates that the financial loss to gastrointestinal illness can be enormous. Diseases caused by the top seven food-borne pathogens account for only a small portion of the total number of gastrointestinal illnesses in the United States, but they account for between \$6.6 billion and \$37.1 billion in medical costs and productivity losses every year (Crutchfield et al., 1999).

There are also intangible costs to gastrointestinal infections related to reduced quality of life or to lives lost to mortality. Disability Adjusted Life Years (DALYs) are a useful way of expressing these costs, attributable to a given disease or set of diseases. DALYs are the sum of the life years lost due to premature mortality or the years spent with disease, weighted with a factor for the severity of the illness. In the Netherlands, the disease burden of campylobacteriosis has been estimated to be 1,400 DALYs per year (Havelaar, et al., 2000), and the burden of all gastrointestinal infections may range up to 10,000 DALYs per year (De Wit, 2002).

In developed countries, there are currently a large number of actions to reduce the worldwide incidence of enteric infections. However, not enough is being done and the actions that are being undertaken are often poorly coordinated and there is little *a priori* assessment of their anticipated. In the past, efforts were aimed at controlling and reducing the number of outbreaks. This strategy has worked, to a large extent, as evidenced by the relatively low annual number of reported outbreaks in these nations (Payment and Hunter, 2001). However, the high endemic rate of gastrointestinal disease in both developed and developing countries still receives little attention.

Estimating the global burden of gastrointestinal illness

In order to control enteric infections and gastrointestinal disease worldwide, an understanding of the incidence, severity, and duration of these illnesses is crucial. This is known as the *global burden* of gastrointestinal illness.

Humans are chiefly exposed to gastrointestinal pathogens through direct or indirect exposure to human and animal fecal waste, and, with the increasing density of the global population, fecal contamination is pervasive. In light of this, how can regulators, scientists, and health care professionals protect public health from gastrointestinal disease? The answer to this pressing question is not clear.

Controlling global enteric disease partly lies in fully grasping the problem at hand. In order to curb these diseases, we must fully understand exposure to the contaminants, their routes of transmission, their severity, and their impact on society. This synthesis of information should lead to an estimate of the overall burden of gastrointestinal illness including the loss of lives, well-being, productivity, and wealth that results from current incidence of these diseases. Policy makers and regulators in search of cost-effective measures for controlling these diseases will need thorough analyses of burden on regional, national, or global scales.



GASTROINTESTINAL PATHOGENS CAN BE CARRIED FROM REGION-TO-REGION AND COUNTRY-TO-COUNTRY IN THE GUT OF HUMANS AND ANIMALS AND IN THE WATERWAYS, FOOD, AND DRINK THOSE NATIONS SHARE.

Knowing how a nation's citizens fall ill can lead to improved management of those risks and improved quality of life.

In today's global community, infectious agents have unprecedented mobility. Gastrointestinal pathogens do not need a visa to enter the country; they hide within infected individuals. They do not need to pass through customs or satisfactorily answer a list of questions from a public official. They travel at the speed of flight; gastrointestinal pathogens can be carried from region-to-region and country-to-country in the gut of humans and animals and in the waterways, food, and drink those nations share. In the 21st century, people, livestock, produce, and water are truly international, and the infectious agents carried by each of these burden all countries. In light of this, individual nations, even those with sophisticated food and public water infrastructures, cannot ignore the problem of gastrointestinal infections and gastrointestinal disease without potentially grave repercussions.

Understanding the global burden of gastrointestinal disease is within reach, but integration of current knowledge, technology, and labor is required. The same type of integration is needed to assess effectiveness of the steps currently employed to curb these diseases. Many well-intentioned interventions to halt gastrointestinal illness have not been thoroughly evaluated and remain easily challenged. The information needed to understand the true burden of these illnesses and to accomplish effective interventions is available to us. If gastrointestinal illness is to be overcome, the medical and scientific communities must begin to weave these facts into fabric.

Obstacles to estimating the global burden

There are a number of obstacles to understanding the global burden of gastrointestinal disease. These include:

- Non-standardized definitions of gastrointestinal infections and their symptoms.
- Unknown causes of illness due in part to lack of appropriate testing.
- Failure of sufferers and healthcare professionals to report episodes or outbreaks of gastrointestinal infections and gastrointestinal illness.
- Incompatible reporting systems.

These are significant challenges to better understanding the extent of these diseases worldwide, and they must be addressed.

Non-standardized definitions

What, precisely, comprises an episode of gastrointestinal illness? A single bout of vomiting or diarrhea? A sustained hour of stomach cramps? The range of symptoms associated with infections of the gastrointestinal tract is much larger than diarrheal illness and gastroenteritis.

The most severe cases are easily defined and recognized. However, agreeing on the boundaries of what can be called enteric infection or gastrointestinal disease has proven difficult for the scientific and healthcare communities. For this reason, determining the number of cases, even in a single town, is quite complicated. Moreover, comparing or summing the incidence in one area with that of another area requires an agreement on these boundaries, which seldom occurs. Even defining



the symptoms of these diseases is complex. Diarrhea is one example; it is a seemingly simple word, which conveys many different meanings. Is a case of diarrhea defined by a single watery stool or by two or three such incidences? How is diarrhea defined in areas where sanitation is inadequate and loose stool is the norm? Researchers have shown that rate of disease can vary by a factor of four if different criteria are used.

Standardized definitions of the symptoms and syndromes related to enteric infections are elusive. Illnesses that are caused by gastrointestinal pathogens but have manifestations in other areas of the body serve as another example of the complications involved. How can respiratory symptoms often observed with enteric viruses be associated to a gastrointestinal infection? Most would simply call it a “cold.”

Failure to identify a causal agent

Assuming it is agreed that a patient is suffering from gastrointestinal illness due to an infection, identifying the pathogen causing the illness can be difficult, if not impossible, given the technologies and resources available to most hospitals and clinics. This is especially true for viral infections for which diagnosis is often costly and for which the physician has no antimicrobials for treatment.

In addition, the list of suspects in a case of gastrointestinal illness is staggering. Other pathogens still elude identification by scientists, complicating the search for associated agents. Moreover, non-infectious causes, including chemical exposure, oral antibiotics, stress, food allergies, or dietary indiscretion, may be responsible for a significant small percentage of gastrointestinal symptoms.

Identifying the microorganism associated with a bout of gastroenteritis that will most likely disappear in 24 hours is not always feasible or cost-effective in the eyes of the patient or of a health care delivery system. In cases of foodborne illness in the U.S., for example, as many as 81% of all cases and 64% of deaths are due to unknown or unidentified agents (Mead, et al., 1999). The problem of pinpointing an associated organism is difficult, even in outbreaks of gastrointestinal illness. A pathogen is not identified in as many as 50% of recognized outbreaks. Even if the associated agent is recognized, identifying the source of the infection, the drinking water, recreational water, food, animal, or object that was contaminated, is not possible in many situations. Given these problems, it is clearly very difficult to derive a reliable global estimate of the number of cases of any given gastrointestinal infection.

Failure to report gastrointestinal illness

Accumulating the worldwide incidence of reported cases of gastrointestinal disease is informative to a point, but it is evident that those that are reported do not use standardized definitions and that the vast majority of cases are currently unreported. The breakdown in reporting often occurs between the sufferer and healthcare providers; in developed nations, over 98% of cases are never reported to a physician. This failure to report may occur because of the mildness of the episode, or, as is the case with the poor and in many developing areas, the sufferer may lack access to health care. Alternatively, because of unsanitary conditions in some developing countries, gastrointestinal infections may be so pervasive as to become a baseline health condition and,



SWIMMING, BATHING OR RECREATIONAL ACTIVITIES IN CONTAMINATED SURFACE WATERS HAS REPEATEDLY BEEN SHOWN TO BE ASSOCIATED WITH A HIGHER RISK OF GASTROINTESTINAL DISEASE.

therefore, would not be considered significant enough to warrant reporting or treatment.

Although reporting cases of gastrointestinal disease to a health provider is important for accumulating data on these diseases, it is not a guarantee that the case will be reported to a health agency and tallied appropriately. For example, the numerical coding that is used to categorize diagnoses in regional databases can interfere with the process. Because these coding methods may be incompatible with other modes of recording, illnesses frequently go unreported. In order to accurately tally these diseases, consistent reporting routes must be made available to clinicians.

Figure 1 illustrates a conceptual pyramid of gastrointestinal illness. The majority of cases, outside of outbreaks, are relatively mild, and the sufferer does not seek treatment. Therefore, the case goes unreported. The next most common reporting result is the more severe case in which a physician is consulted but clinical samples are not requested or examined. As a result, information on the agent associated with the illness is not obtained. Moving up the pyramid, few of the physician-consulted cases are examined to determine the associated organism, and finally, very few cases are “solved” by identifying the associated agent.

Incompatible reporting methods

Due to difficulties associated with directly measuring all incidences of gastrointestinal disease, health studies are frequently used as a basis for extrapolating regional or worldwide incidence or risk of these diseases. However, there are problems associated with this approach as well. Different reporting techniques are used in different studies, and not all techniques record incidences of illness with the same accuracy. Self-reporting studies will produce different results from objective studies; hence, the incidence of gastrointestinal illnesses will differ depending on the study design. Combining studies that use different techniques to assess the same population can also be problematic. For example, combining the risk estimates derived from a prospective study, in which a group of individuals is tracked over time, with estimates from a retrospective study, in which a group of sick individuals is contrasted with a group of healthy ones, may give spurious results. Consequently, employing study results in extrapolating global burden requires careful consideration.

Significant modes of transmission

The fecal-oral route of infection is at the root of most gastrointestinal infections, but there are a number of modes of transmission or vehicles along this route that lead to exposure. These include human-to-human contact, consumption of contaminated food or water; recreational activities in contaminated water; contact with inanimate surfaces, and contact with animals or their feces. (See Figure 2 next page.)

Human-to-human contact

Human-to-human contact can result in the spread of enteric infections under any of a number of circumstances, including failures in personal hygiene and over-crowding at home or at work. Social activities with numerous contacts, such as parties and family gatherings, are

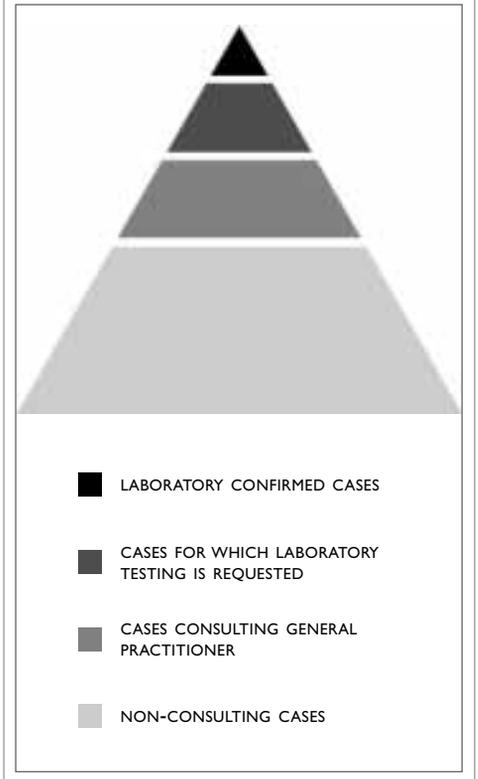


FIGURE 1.
PYRAMID OF SOURCES
FOR SURVEILLANCE OF
GASTROENTERITIS.

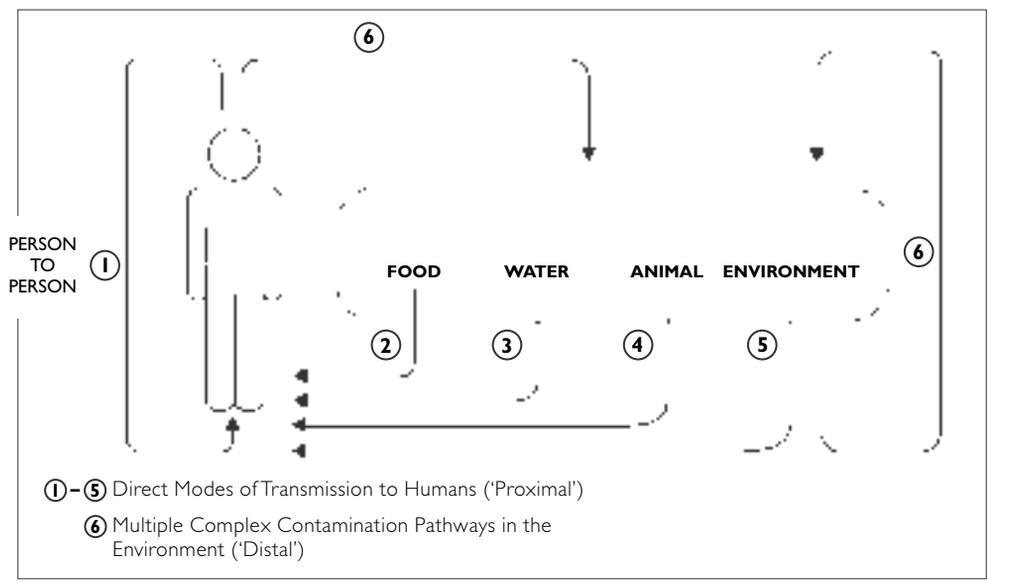


FIGURE 2.
ENTERIC DISEASE MODES
OF TRANSMISSION AS A
BASIS FOR IDENTIFYING
INTERVENTION POINTS.

highly favorable for the transmission of these pathogens and high levels of exposure. Human-to-human contact is thought to be a significant mode of transmission, but statistics on transmission by this mode are difficult to derive. However, person-to-person contacts do not sustain epidemics, making interventions in the transmission cycle potentially effective.

Foodborne

The food we consume can become tainted in any of a number of ways. Contamination may occur during cultivation of food crops, for example, by exposure of crops to composted night soil, human or animal feces, or exposure to contaminated irrigation water. Alternatively, contamination may take place during mechanized processing. Contamination can also occur during human handling of crops or preparation of food on the household level. In the developed world, reports suggest that the majority of foodborne gastrointestinal illness occurs as a result of unhygienic handling during food preparation.

Several well-publicized outbreaks have been attributed to the foodborne transmission mode, often implicating undercooked ground beef. These include a deadly outbreak of *E. coli* O157:H7 traced to tainted hamburger served at Jack-in-the-Box restaurants in the western United States. Over 700 people fell ill, and four children died. Poultry is often contaminated by pathogenic bacteria and has caused numerous cases of infection when the meat has been undercooked, improperly stored, or has come in contact with other foods consumed raw.

Waterborne

Exposure to contaminated water, through ingestion as drinking water or through recreational activities, is a significant mode of transmission of gastrointestinal pathogens. Swimming, bathing, and recreational activities in contaminated surface waters have repeatedly been shown to be associated with a higher risk of gastrointestinal disease. Sources of contamination of surface water include urban and farm runoff, discharges

from wastewater treatment facilities, failing septic systems, wildlife, farm animals, and direct fecal contamination by humans and pets.

Drinking water can easily become contaminated by enteric pathogens if proper source protection measures and treatment facilities are not in place. Groundwater may not undergo disinfection when it is assumed that the subsurface is a protected environment. For public health protection, source water protection is a key element. However, groundwater can be impacted by contaminants from the surface during heavy rains, and improperly constructed wells could allow the infiltration of pathogen-laden surface water. This is what happened and resulted the *E. coli* O157:H7 outbreak in Walkerton, Ontario (Canada) in 2000 that sickened more than 2,300 people.

Drinking water prepared from surface waters (i.e., lakes or rivers) invariably needs to be treated, as it can be impacted by wastewater treatment discharges or by wild or domestic animals. Heavy precipitation can overwhelm previously effective wastewater treatment facilities, rendering them episodically ineffectual and contaminating the surface water used by drinking water treatment plants. The resulting load of pathogens can overcome the treatment barriers in place and significantly increase the risk to the receiving population. Breakdown in treatment and failure to protecting source water are thought to have been responsible for the 1993 *Cryptosporidium* outbreak in Milwaukee, Wisconsin that sickened approximately 400,000 people.

Environmental

Environmental exposure to gastrointestinal pathogens can also occur during handling of contaminated soil, use of contaminated utensils, and, in some cases, through aerosol transmission. The contamination of inanimate surfaces by fecal material remains an important source of contamination. Day-care centers and households with young children offer numerous examples of such contamination and subsequent infection. Some pathogens can survive for relatively long periods on the surfaces of tables, toys, doorknobs, telephone handles, and all the other surfaces encountered in daily life.

Animals

A number of exposure scenarios can result in the transmission of gastrointestinal pathogens from an animal to a human, including direct contact with livestock, handling livestock waste, visiting petting zoos, or handling household pets. In some cases, infected animals can carry one or more pathogens without suffering ill effects, but they remain a consistent pool of pathogens by which some individuals can become infected. Animal-to-human transmission is likely to be a more significant mode of infection in agrarian societies, where humans and livestock live in close proximity and hygiene practices are less developed. In developed countries, little data is available on the level of transmission of gastrointestinal infections from animals.

Burden of gastrointestinal illness

Clearly, the relative contributions of the various modes of transmission to the total of gastrointestinal infections and illness vary regionally and seasonally. The most significant defining characteristic that can predict the relative contributions of the modes of transmission is the



DEVELOPED COUNTRIES MAY BE AT AN INCREASED RISK FROM "IMPORTED" PATHOGENS, EITHER CARRIED BY IMPORTED GOODS AND FOOD OR TRANSMITTED BY HUMAN-TO-HUMAN CONTACT.

state of economic development a particular nation has achieved. The wealth of a country determines what role human-to-human, water-borne, foodborne, environmental, and animal-borne enteric infections play in the lives of its citizens. The burden of gastrointestinal illness has multiple factors and does not simply decrease linearly with increased development. Instead, the relative importance of the aforementioned modes of transmission shift, new pathogens emerge, and unforeseen hazards are uncovered. The result is a trade-off between decreased gastrointestinal infection by some modes and agents in favor of increased infection by others. Moreover, as exposure decreases and infections are controlled, immunity to these diseases decreases, rendering the population more susceptible to the development of large-scale outbreaks.

Comparative burdens

The breadth of knowledge about developed and developing countries is not equal; less is known about the burden of gastrointestinal illness in developing nations. With development, most nations will experience a decrease in the overall incidence of gastrointestinal illness, including a significant drop in each of the categories depicted. However, each of the categories may not be entirely equivalent. It is highly likely that non-reported cases of gastrointestinal illness are more severe in less-developed nations because of lower overall access to health care and differences in health systems. The WHO estimates that 65% of gastrointestinal infections in developing nations could be eradicated with the provision of seemingly simple amenities available in developed nations: basic water improvement, sanitation, and hygiene interventions (WHO website).

When examining different modes of transmission, the comparisons of the burden between developed and developing countries are less clear. Foodborne transmission is a good example of the trade-offs that may accompany development. In terms of household food preparation, economic development is expected to bring about little decrease in foodborne infections except at the highest hygiene levels. The picture is different for foodborne gastrointestinal infections arising from commercially handled food, where the increased retail activity that accompanies development will likely result in a rise in foodborne infections at intermediate stages of development, followed by a drop-off with increased regulation of the food industry.

There are other trade-offs in the modes of gastrointestinal infections transmission. Economic development may lead to different niches for pathogens, new pathogenic opportunities, and new distribution possibilities. For example, developed countries may be at an increased risk from “imported” pathogens, either carried by goods and food or transmitted by human-to-human contact. Increased population densities in urban centers may increase pressure on water resources and infringe on water quality. An increase in meat consumption leading to higher numbers of livestock per capita could also result in greater exposure through the animal-human route.

Another effect of development is a shift in the pathogens responsible for gastrointestinal infections. The more common and highly preventable agents of disease are the most frequent in less-developed nations, while robust, unusual pathogens are more often detected in developed nations.



IT IS HIGHLY LIKELY THAT NON-REPORTED CASES OF GASTRO-INTESTINAL ILLNESS ARE MORE SEVERE IN LESS-DEVELOPED NATIONS BECAUSE OF LOWER OVERALL ACCESS TO HEALTH CARE AND DIFFERENCES IN HEALTH SYSTEMS.

Routine clinical data acquisition issues

Understanding the different facets of the global burden of gastrointestinal illness should lead to a wider recognition of societal costs of these ailments, in terms of human lives and quality of life. This recognition is necessary to drive public policy and funding to effectively control gastrointestinal infections and improve the quality of life for people throughout the world.

The primary obstacle to estimating the global burden of enteric disease and gastrointestinal illness is lack of sufficient consistent, comprehensive, and objective clinical data. It is critical to establish standards for scientists, clinicians, and regulators to apply to the collection, management, and interpretation of data on gastrointestinal disease. For this reason, colloquium participants discussed data issues and identified several important caveats and made recommendations for the clinical arena.

Passive reporting systems

Overall, current strategies for reporting and assessing enteric diseases and gastrointestinal infections are passive, requiring the sufferer or family physician to report incidences of illness. As a result, health organizations and regulators are forced to rely upon the trickle of information that works up the ladder. These data are strongly influenced by the process of selection of patients for specimen collection, by laboratory methods used to identify pathogens, and by the description of symptoms used by the reporting unit. As a result, the information available by this route is often murky and incomplete and may disguise pervasive biases. Such passive reporting systems are not the most efficient means of getting relevant and reliable information to responsible parties.

Health organizations that collect clinical data on gastrointestinal illness from physicians and hospitals should move toward more active collection systems in which standardized methods are specified and followed, including more structured selection of patients for specimen collection and examination of specimens submitted by standardized methods. This type of system would ensure that the information these organizations need is collected and reported systematically.

There is a need to link the data that is collected on gastrointestinal illnesses through an international standardized database. Again, standardized methods should be established in order to ensure consistency. This type of system would prove invaluable in integrating relevant information on gastrointestinal disease into global estimates of total incidence, severity, mortality, risk factors, and cost. Such a database could be established at a modest cost to the global health community and could return great rewards in moving the current state of knowledge forward.

False Outbreaks

It is likely that some reported outbreaks of gastrointestinal illness may not be outbreaks at all, but are actually an apparent increase in cases due to heightened observation. A high endemic level of gastrointestinal illness exists in most communities, and once the interest of the public and health organizations is triggered, surveillance and reporting of gastrointestinal illness is intensified. The surveillance thereby detects the



large number of gastrointestinal illness cases that happen on a day-to-day basis in the community that otherwise remains undetected.

This over-reporting of outbreaks is unnecessary. In order to stem the problem, authorities should consider providing epidemiological training to physicians and local health officials. Through education and training about the incidence of gastrointestinal illness, health authorities would be better qualified to separate the cases from the same exposure route from cases that are part of the endemic level of illness. On the other hand, many true outbreaks go unrecognized, and encouraging epidemiological thinking and inquiry at the front lines of public health could result in more sensitive detection. In the long run, this approach could save money and resources and provide more reliable information for estimating the true global burden.

Data Collection During Outbreaks

Outbreaks can be rich sources of data on gastrointestinal disease. Qualitative information on routes of transmission, identification of previously unknown pathogens, quantification of exposure levels, and identification of effective interventions can all be gleaned from the cases of gastrointestinal disease involved in an outbreak. Clinicians are the primary source for early outbreak data, a critical element in controlling the outbreak. This real-time central data acquisition is one of the efficient means of detecting a developing outbreak; inter-center collaboration and standardization of data are keys to this result. This and public health alertness remain keys to public health protection.

In order to gain the maximum amount of information on future outbreaks, outbreak investigations should be thorough, focused, and well planned. To take full advantage of the opportunities outbreaks offer to health organizations, data acquisition planning should be conducted well beforehand by establishing standard questionnaires that will fulfill the required information gaps. Because an agent is not identified in many outbreaks, there is often reluctance among scientists and health authorities to report and study these “imperfect” stories in which a complete scenario has not been established. These outbreaks can potentially be more informative than those that have a coherent story. Furthermore, authorities should consider the collection of clinical samples for archiving very early in the investigation.

Samples from these incoherent outbreaks may bring to light important gastrointestinal pathogens that have not yet been identified. Alternatively, if a new pathogen is identified in future outbreaks, archived samples can be tested for the presence of the newly identified agent, and it may be possible to determine the agent well after the outbreak. By considering data acquisition and sample needs for outbreaks before they occur, health organizations can ensure that the process goes smoothly and that all necessary information is gathered at the appropriate times.

An Outbreak Rapid Response (ORR) team is a promising tool in handling outbreaks and collecting relevant data. An ORR team is a rapid intervention unit composed of health professionals, sanitarians, environmental specialists, and laboratorians equipped with epidemiological tools and access to expertise in multiple fields. These units would be mobilized at the first signs of an outbreak of enteric infections. Upon



**CLINICIANS ARE THE
PRIMARY SOURCE FOR
EARLY OUTBREAK
DATA, A CRITICAL
ELEMENT IN
CONTROLLING
THE OUTBREAK.**

arrival at the scene, the ORR team would direct interventions to minimize the effects of the outbreak and conduct a thorough collection of data through the aid of pre-prepared standard questionnaires. Having an ORR team ready to go at the first signs of an outbreak may reduce the need for exhaustive outbreak management training for local health workers. These teams could also play a powerful role in unearthing the causes of outbreaks and, in turn, lead the way toward prevention.

Surveillance

Collecting clinical samples from non-outbreak related cases is important not only to the health of the individual (by ensuring appropriate treatment), but also to public health at large, as such testing may lead to ways of preventing dissemination of the pathogen. Obtaining stool samples from diseased individuals can mean the difference between identifying significant infectious agents in the community and struggling on in ignorance. The vast majority of gastrointestinal infections occurs outside recognized outbreaks, and the infectious agents associated with these infections need to be recognized. Health care providers must be made aware of this necessity, and they must be given access to skilled clinical laboratories for accurate analysis.

It should be noted, however, that detection of enteric pathogens in the gut or stool of an individual does not necessarily indicate that he or she is suffering from a gastrointestinal disorder associated with this particular organism. Some individuals may be colonized with potentially pathogenic organisms while they have no associated illness. Treatment of these carriers can be ill advised. The overuse of antimicrobials can result in the generation of antimicrobial-resistant strains. In addition, many individuals have adverse reactions to these chemicals. Similarly, detection of pathogens in water or food is not necessarily an indication of risk. Infection and disease is the result of a set of complex interactions, and the outcome is determined by an intricate dose-response relationship. Hence, although low-level exposure may be associated with a risk of infection, it does not imply infection.

Specimens for Evaluation

Most countries are in need of a more structured approach to identify when clinical specimens require diagnostic evaluation. This determination is often left up to the judgment of the physician or to the financial resources of the patient. Considering that sample analysis plays a pivotal role in public health considerations, physicians should be provided with guidance in identifying the cases that merit further investigation. Sampling should also be associated with the collection of a minimum data set regarding exposures, risk factors, etc. Organizations, like the United Nations Educational, Scientific, and Cultural Organization (UNESCO), the World Health Organization (WHO), or the Centers for Disease Control and Prevention (CDC), could take responsibility for this structuring and make recommendations to individual nations. Currently, the collection and analysis of samples from episodes of gastrointestinal infections for public health purposes is somewhat arbitrary and uninformative. The available resources for public health would be better spent on comprehensive laboratory and epidemiological analysis of a limited number of cases that are selected in a well-structured manner.





RELEVANT FUNDING AGENCIES SHOULD WORK TOGETHER TO FUND RESEARCH THAT ADDRESSES THEIR COMMON GOAL: REDUCING THE GLOBAL INCIDENCE OF GASTROINTESTINAL INFECTIONS AND GASTROINTESTINAL ILLNESS.

Unknown Causes of Gastrointestinal Illness

Another shortcoming of the current system of data collection in gastrointestinal illness is the identification of associated agents. Current approaches to detect infectious agents fail to identify a pathogen in many, if not most, cases reported to a physician. As previously noted, as many as 81% of food-related illnesses and 64% of food-related deaths in the U.S. are due to undetected agents (Mead, et al., 1999). Failure to identify a pathogen may occur because the associated pathogen has not yet been recognized or because limitations in laboratory testing methods allow a recognized pathogen to go undetected. Rates of identification of the causative agents in gastrointestinal illness must be improved for an accurate estimate of global burden.

The location or source of exposure from which an individual was infected is also rarely identified. Clearly, effective interventions cannot be put in place unless the incidence and the sources of exposure of these diseases are known. Each occurrence of disease must be evaluated on a case-by-case basis, so the burden for more aggressive follow-up of the etiology of illness is with the individual health professionals who treat these cases.

Strategies for reducing this diagnostic shortcoming include improving detection of known pathogens and allowing identification of previously unknown pathogens. More sensitive methods for detecting known agents are available or being developed and may be used. PCR methods, immunological tests, and DNA microarrays are being added to the arsenal of culturing methods available to clinicians. There are only a limited number of methods that allow for detection of unknown pathogens. Most efforts are undertaken by researchers outside the public health arena.

New Techniques

Advancements in diagnostic techniques offer exciting new opportunities to reach public health objectives, such as for the surveillance of gastrointestinal infection, but they are not the whole answer to the problem of diagnosing and collecting data on gastrointestinal illness. Newer, faster, better techniques will have the greatest impact in developed nations. In these countries, relatively high levels of sanitation, hygiene, and drinking water treatment prevent infection by the traditional pathogens that are vulnerable to these strategies. By and large, it is the robust, obscure diseases that survive these regimens. Viral diseases, which are often difficult to diagnose conclusively, are especially relevant in developed nations.

In less developed countries, on the other hand, the main agents of gastrointestinal infections are the more common, well-described pathogens, particularly bacteria. These are sensitive organisms that could easily be managed by the same strategies that have worked in developed nations: sanitation, hygiene, and improved drinking water treatment.

New diagnostic techniques are generally aimed at identifying new pathogens or those that are difficult to grow in the laboratory, and for the reasons described above, new and unusual pathogens are most significant to developed nations. Moreover, developed nations are more likely to have the available funding for cutting-edge testing procedures.

For less-developed countries, which carry the greatest burden of gastrointestinal illness, improved diagnosis of new and exotic diseases is not going to help the majority or sufferers. Instead, development of more cost-effective diagnostic techniques for the common diseases in these countries is much more likely to serve the greater good. Diagnostic efforts in developing countries should, of course, be coupled to sanitation, hygiene, and the improvement of the microbiological quality of drinking water and food.

Applying New Diagnostic Tools

In nations where sophisticated diagnostic techniques have been used to analyze gastrointestinal diseases, there is a need to assess the practicality of making these tools widely accessible. There are three main considerations to broader accessibility: cost, interpretation, and applicability. The issue of cost is self-explanatory. The expense of exploiting a particular technique must be balanced by the expected return in the improvement of the current knowledge of gastrointestinal illness and the expectation that it will lead to the application of a treatment to cure the diseased individual. Second, the interpretation of any diagnostic tool requires a certain level of skill. In applying a new technique, it must be determined whether the required level of expertise is available in the community. If not, the feasibility of putting that expertise in place should be weighed. The final consideration is the range of applicability that the technique allows. Few techniques are applicable to the detection of pathogens in a variety of potential sources: food, water, air, surfaces, etc. Most techniques are more limited, which may hinder their usefulness under certain circumstances.

Research and Education

Health research has always been the key to easing the effects of disease, and research into gastrointestinal illness is no different. From Dr. John Snow's groundbreaking work in pinpointing the sources of cholera outbreaks in late 19th century London to current efforts to develop vaccines for ubiquitous gastrointestinal viruses, scientific research has opened new paths for reducing the burden of gastrointestinal illness. Progress in this arena has brought us far, but there are many avenues for improvement, especially in the developing world.

Recommendations

Colloquium participants are expert scientists who are familiar with the current state of research, funding, and peer-reviewed reporting and review. They discussed these topics and identified a number of recommendations for the field.

Standardized Definitions

One of the biggest hurdles in studying enteric infections is the problem of defining the relevant parameters of gastrointestinal disease in ways that will be uniform and commonly understood. These parameters include the commonly observed symptoms and health outcomes associated with these illnesses. Universal definitions of diarrhea, loose stool, meningitis, gastroenteritis, enteritis, and many other syndromes continue to elude professionals in the field. This poses a serious obstacle, confounding efforts to compare studies and derive meaningful estimates of regional, national, and global incidence.



Researchers should take a leadership role in resolving the dilemma of non-standardized definitions by launching an international, multidisciplinary consensus conference to establish definitions that are acceptable to stakeholders worldwide. Developing standardized definitions of the key terms would help international efforts estimate the global burden of gastrointestinal diseases.

Coordinate Research Funding Programs

There is currently a lack of coordination between the public health agencies responsible for data collection and funding research on gastrointestinal diseases. In general, agencies are responsible for promoting investigation of a particular mode of transmission, and they allocate funds accordingly. In the United States, for example, waterborne transmission is managed by the Environmental Protection Agency (EPA), foodborne transmission is managed by the Food and Drug Administration (FDA), animal to human and foodborne transmission are managed by the U.S. Department of Agriculture (USDA), and disease in general is managed by the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH). This division of responsibilities is the norm in most developed countries. Under this system, research priorities are separately established by several different entities, and agencies rarely collaborate in funding research, creating a disjointed and inefficient system for directing research efforts and data collection. In the interest of furthering only the research directly related to the agency's charter, funding agencies may limit the kind of comprehensive work that is necessary to address gastrointestinal disease.

Enteric infections and gastrointestinal disease must be addressed holistically by coordinating research on multiple routes of exposure with the efforts of professionals in a range of relevant fields. In cases of gastrointestinal illness, the pathogens responsible are the same; only the vehicles and exposure routes differ. The relevant funding agencies should work together to fund research that addresses their common goal: reducing the global incidence of gastrointestinal infections and gastrointestinal illness. Through multi-agency coordination of available funds and grant opportunities or by focusing the multiple opportunities available in separate agencies, scientists and researchers will be better able to accomplish significant strides in the control of these pathogens.

Interdisciplinary Research

The most productive research programs frequently involve diverse, multidisciplinary groups of researchers. Pathogens are not limited to functioning within the boundaries of the traditional disciplinary fields of food science, hydrology, bacteriology, virology, veterinary science, epidemiology, etc. Scientists must also work across departmental boundaries if research on enteric pathogens and gastrointestinal diseases is to lead to effective interventions.

Collaborations among researchers in the disciplines pertinent to gastrointestinal pathogens should be encouraged. By establishing grant opportunities that favor collaboration and forming inter-departmental initiatives focused on broad research objectives on gastrointestinal pathogens, progress can advance at an unprecedented rate. The expertise in each of the separate fields related to enteric diseases has already



THE CURRENT BURDEN OF GASTROINTESTINAL DISEASE, PARTICULARLY IN THE DEVELOPING WORLD, IS INTOLERABLE AND OFTENTIMES OVERLOOKED.

been developed. What is now needed are programs that will bring researchers from the different scientific disciplines together to better understand the pathogens and their diseases.

Colloquium participants propose establishment of a network of centers, staffed by skilled specialists, to collect and analyze data from various sources and provide expert knowledge. In many countries, the World Health Organization has established this kind of collaborative center. There is a critical need for integration of data from all sources related to enteric infections and gastrointestinal disease, and collaborative centers could play an important role in this data integration.

Validation of Intervention Techniques

One specific area of research that requires emphasis is validation of intervention techniques used in curbing gastrointestinal disease. Currently, intervention techniques are often put into practice without being thoroughly tested. Educational methods, in particular, have seldom been substantiated as an effective means for managing gastrointestinal diseases, especially their long-term effects. There are a number of social factors that play into the effectiveness of intervention techniques that are seldom taken into account, such as religious and cultural differences. These differences are often barriers to applying programs that have worked elsewhere to new, untested regions.

Hygiene interventions serve to illustrate how a fragmented approach and cultural barriers can come into play. While hygiene behavior has been identified as a key variable in the exposure of individuals to gastrointestinal pathogens, little is known about the effectiveness of specific hygiene interventions and education. This is because interventions and education are often implemented as multifaceted programs, making it difficult to sort out the contributions of individual components. Research in this area could potentially lead to proven techniques for improving hygienic behavior on a sustained basis. Intervention techniques require evaluation prior to their utilization in communities of men, women, children, and elders. The current use of non-validated techniques that are based on untested hypotheses really constitutes a medical experiment—one that may be conducted at the expense of those being helped. The scientific community must dissect and test the old assumptions about hygiene interventions to arrive at reliable, proven approaches. This is a research priority of the first order.

Quantitative Scaling

Another important priority is shifting from strictly descriptive research to the quantitative scaling of gastrointestinal infections. An extensive body of work exists that describes known pathogens, known risks, and commonly accepted interventions in the developed world. Now that a thorough understanding of these phenomena has been achieved, it is time to move forward and apply what we know to quantitatively describe the current circumstances, especially in developing countries. This work will require synthesis of the current knowledge of exposure routes and health effects into useful models and quantification of the enteric disease risks. Work in the area of quantitative scaling is expected to generate important new questions for the field, opening up original and previously unexplored topics for research. Quantitative scaling can also lead to effective prioritization of research



goals and appropriate allocation of public health funding to curb gastrointestinal disease.

Role of the Host and Dose-Response

One of the key variables that determine the outcome of an exposure to gastrointestinal pathogens is the role of the host in the development of disease. This role, however critical, is poorly understood. Clearly, several factors come into play. Immune status, nutritional status, and genetic factors, for example, all affect the ability of an individual to overcome exposure, but the relative contribution of each of these influences is unknown. Moreover, the relationship between the presence and numbers of a gastrointestinal pathogen and development of disease, the dose-response association, also constitutes a vast gap in our understanding of health, and it needs to be explored in research and in public health surveillance.

To better understand the role of the host and the dose-response relationship, researchers need to develop ways to quantify exposure. Quantitative microbial risk assessment, an approach that seeks to link the quantitative aspects of exposure with the development of disease, is quickly becoming an important tool to assess microbial exposure. There is a need to assess the health effects of pathogens at lower doses than currently applied and dynamic models of the host-pathogen interaction.

In future research to quantify exposure to gastrointestinal pathogens, colloquium participants recommend that a broad effort be made to genetically “fingerprint” pathogens detected in clinical and environmental samples. By developing profiles of pathogens found in diseased individuals and those found in the patient’s surroundings, researchers and public health officials can potentially link diseases with their sources. This would not only yield a better understanding of the sources of gastrointestinal infection, but would also allow quantification of the relative importance of the various modes of infection. Better understanding the role of the host and the dose-response relationship potentially could lead to more effective techniques for preventing gastrointestinal infections.

Formalized Data Review

There is a conspicuous need for formalized, systematic evaluations of current data on gastrointestinal illness and enteric disease. Statistically sound review of existing descriptive data and small-scale quantitative data can better inform directions for future research, focusing efforts on the most critical pathways, exposure routes, and interventions.

Systematic review is critical to development of quantitative models and improving our knowledge of the scale of gastrointestinal disease. Regulatory agencies, particularly those in developed countries, have begun to favor quantitative risk assessment as a tool for determining priorities and allotting funding. If enteric infections are to be addressed, available data need to be synthesized into forms that allow scientists to determine the need for action in terms of numbers and lives and convey those to public health authorities. Quantitative models of the causes, effects, and burden of gastrointestinal disease are needed to ensure that resources are properly allocated and that gastrointestinal



CLEARLY, THERE IS A NEED TO TRAIN HEALTH PROFESSIONALS IN THE FIELD HOW TO IDENTIFY THE EARLY WARNING SIGNS THAT POINT TO AN OUTBREAK OF ENTERIC DISEASE AND GASTROINTESTINAL ILLNESS.

disease concerns are addressed in proportion to the seriousness of the problem.

Preventive Strategies

The current burden of gastrointestinal disease, particularly in the developing world, is intolerable and oftentimes overlooked. In both developed and developing countries, this burden falls disproportionately on the children of the poor. The UNICEF estimates that in the 10 years between 1990 and 2000, more children died from diarrheal diseases than all the people killed in armed conflicts since World War II (UNICEF, 2000). The burden is not limited to those living in poverty. Even in developed countries, the level of gastrointestinal disease due to the fecal-oral route of transmission could be significantly decreased by implementing relatively simple strategies. Basic strategies, such as better wastewater treatment or hygiene education, could alleviate a great deal of unnecessary suffering. Advances can be made to decrease the number of lives lost to these diseases in developed countries, but the most noticeable effects would be seen in huge declines in loss of productivity and health care expenses.

Sanitation

Globally, it is estimated that 40% of the global population lacks access to basic sanitation, specifically access to excreta disposal facilities. There is wide consensus among researchers and professionals in the field that implementing basic sanitation and good hygiene practices could alleviate most of the incidence of gastrointestinal disease throughout the world.

Sanitation is the most logical way to cope with any infectious disease, e.g., to prevent exposure by preventing the release and dispersion of pathogens. This often requires removing political, cultural, and economic obstacles. Making sanitary facilities available would prevent the spread of disease from an individual to his or her community. Prophylaxis at the source, rather than at the exposure level, is the key. Treating disease after infection and the development of symptoms is the least effective method of all, as it does not address the problem of the large number of asymptomatic individuals who can serve as major sources of infection.

Providing basic waste disposal facilities to the world's poor will save millions of lives and the expense of treating the vast majority of gastrointestinal disease. This does not require advanced technology, cutting-edge medical techniques, and years of perfection through clinical research. The knowledge needed to make this work is in place. What is needed is recognition that implementing environmental sanitation and hygiene saves lives.

For the reasons outlined earlier in this report, gastrointestinal pathogens travel internationally and are a burden to all nations. Physical separation will not save the developed world from the diseases of less wealthy countries. Acting to reduce the global burden of gastrointestinal disease by implementing environmental sanitation and hygiene practices in poor areas should be a compelling priority for all international agencies.



Communication of Research Results and Interventions

Researchers are continually uncovering new information about the use of interventions in curbing gastrointestinal disease. However, these findings are slow to arrive at the “front lines” of the war against gastrointestinal pathogens. Research findings must be communicated to health professionals and public health organizations. A major effort must be made to educate all levels of the population on the benefits of controlling the circulation of gastrointestinal pathogens.

Epidemiological Training

Outbreaks of infectious gastrointestinal disease can pose a serious threat to public health, but the signs of an outbreak are not always obvious to health professionals working in the clinics and hospitals that first receive patients. Most clinicians are not trained to recognize the patterns of disease that signify an outbreak of gastrointestinal disease. This recognition can be an important first step in bringing the developing outbreak to an end; early action can save lives. For example, in an outbreak of a waterborne disease, keen observation can lead to a “boil water” advisory or to a recommendation for beach closures. In cases of foodborne disease outbreaks, removal of potentially contaminated food from the market is also an essential step. In all cases, the earlier the action is taken, the more efficient the prevention strategy.



EDUCATION PROGRAMS ON PERSONAL AND ENVIRONMENTAL HYGIENE AS PROTECTION AGAINST GASTROINTESTINAL DISEASE WILL BENEFIT THE WHOLE COMMUNITY BY PROVIDING AN EFFICIENT BARRIER AGAINST PATHOGENS.

Clearly, there is a need to train health professionals in the field how to identify the early warning signs that point to an outbreak of enteric disease and gastrointestinal illness. After the sufferers themselves, these clinicians are the first to observe the effects of an outbreak. Too often, patients are treated with an eye focused on the health of the individual and proper attention is not paid to the significance of individual cases to public health. Training health professionals to think about their cases in terms of epidemiology can go a long way toward ending the cycle of outbreaks.

Communication and Education in Gastrointestinal Disease Issues

Issues surrounding gastrointestinal diseases are not confined to research institutions and health agencies. The relevant facts of prevention and risk must be related to the world’s citizens and policy makers and communicated in such a way that communities can act appropriately to curb disease. Likewise, there is a need to reach out to train the next generation of scientists who will continue the current work to end gastrointestinal disease.

Communication by a Group of Stakeholders

Currently, issues related to gastrointestinal disease are communicated to the public and to policy makers in a haphazard manner. The voices of many different groups can be heard; scientists, physicians, national and international health agencies, and charitable organizations all vie for attention on the topic.

This is an inefficient way to elicit action on gastrointestinal disease. If accurate, relevant health information and risk are to be communicated to the public and policy makers, then the relevant stakeholders must act together to present health messages. This requires an agreement on the associated facts and priorities, and such consensus may be difficult to achieve. However, the alternative, in which each of the separate

groups fight to be heard about the prevention of gastrointestinal disease, is frequently inadequate to invoke change. These groups must come together on the issues and speak with a single voice in order to help the public and encourage appropriate funding for prevention and treatment.

Education and Training of Scientists

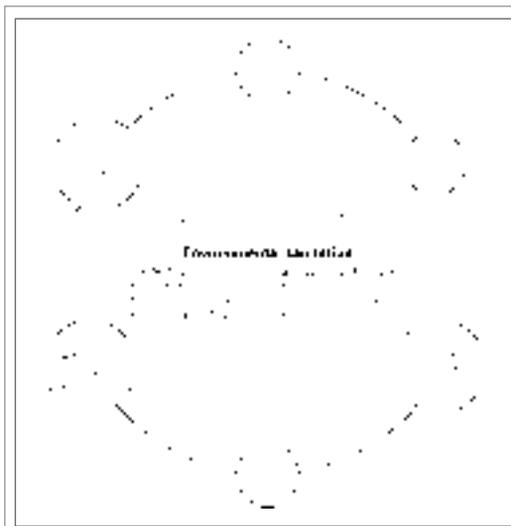
Educating tomorrow's researchers to continue to battle gastrointestinal infections is a priority. Today, interdisciplinary research is recognized as critical to making advances in the field, but the current educational system tends to discourage interdisciplinary training of young scientists. Steps need to be taken to encourage interdisciplinary education and training for young scientists through curriculum development and interdepartmental cooperation.

Since interdisciplinary work is conducted by multidisciplinary teams, the skills necessary to communicate with professionals in other areas of specialty are critical to making these alliances work. There is a distinct need for interdisciplinary communication training for current researchers.

Education and training of the public

Each member of society needs to understand that his or her behavior can lead to personal exposure to gastrointestinal pathogens and, once infected, dissemination of the pathogens can only be stopped through cutting the routes of infection.

The WHO program on Environmental Sanitation emphasizes the importance of sanitation behavior (i.e., personal hygiene, household cleanliness, and community cleanliness). "To allow for transmission of infectious agents, they have to be present in the immediate human environment, exposure has to take place, and transmission has to occur by uptake of the agents through unsafe practices. To interrupt the transmission, environmental sanitation can act on reducing exposure to infectious agents by limiting contact to wastes or polluted media, and by changing hygiene and socio-cultural practices."



[HTTP://WWW.WHO.INT/WATER_SANITATION_HEALTH/
ENVIRONMENTAL_SANIT/ENVINDEX.HTM](http://www.who.int/water_sanitation_health/environmental_sanit/envindex.htm)

Education programs on personal and environmental hygiene as protection against gastrointestinal disease will benefit the whole community by providing an efficient barrier against pathogens.

Conclusions

Colloquium participants agreed that the following recommendations should be adopted:

- The list of enteric pathogens is increasing significantly each year. Newer methods, especially molecular, genetic-based methods, should be employed to detect these pathogens.
- Gastrointestinal diseases should be made reportable and active surveillance implemented, both nationally and internationally.
- Standardized definitions for various health outcomes due to enteric pathogens must be developed internationally.
- Improved risk assessment methodology and database development are needed for gastrointestinal diseases.
- Governments, non-governmental organizations, institutions, and individuals with influence to impact public opinion must be educated about the social and economic burden of gastrointestinal diseases.
- Training, education, technology transfer, and communication with the public through television, radio, and print on subjects relevant to the routes of transmission of enteric pathogens must be undertaken immediately.



EACH MEMBER OF SOCIETY NEEDS TO UNDERSTAND THAT HIS OR HER BEHAVIOR CAN LEAD TO PERSONAL EXPOSURE TO GASTROINTESTINAL PATHOGENS AND, ONCE INFECTED, DISSEMINATION OF THE PATHOGENS CAN ONLY BE STOPPED THROUGH CUTTING THE ROUTES OF INFECTION.

Bibliography

- Colwell, RR, and T Ford. 1995. A global decline in microbiological safety of water: a call for action. A report from the American Academy of Microbiology, Washington, DC.
- Crutchfield, SR, JC Buzby, T Roberts and M Ollinger. 1999. Assessing the costs and benefits of pathogen reduction. *FoodReview*, vol. 22, issue 2. Economic Research Service, USDA.
- De Wit, M. Epidemiology of gastroenteritis in the Netherlands, thesis, University of Amsterdam, 2002.
- Doores, Stephanie. 1999. Food safety: current status and future needs. A report from the American Academy of Microbiology, Washington, DC.
- Mead, PS, L. Slutsker, V Dietz, LF McCaig, JS Bresee, C Shapiro, PM Griffin and RV Tauxe. 1999. Food-related illness and death in the United States. *Emerging Infectious Diseases*, 5(5):607-625.
- Payment, P, and PR Hunter. 2002. Endemic and epidemic infectious intestinal disease and its relation to drinking water. *In Water Quality: Guidelines, Standards and Health. Assessment of risk and risk management for water-related infectious disease.* Fewtrell, L, and J Bartram (Eds). IWA Publishing, London.
- Prüss, AK, L Fewtrell and J Bartram. 2002. Estimating the burden of disease from water, sanitation and hygiene at a global level. *Environmental Health Perspectives*, 110(5):537-542.
- Rose, JB, and DJ Grimes. 2001. Reevaluation of microbial water quality: powerful new tools for detection and risk assessment. A report from the American Academy of Microbiology, Washington, DC.
- Rose, JB, A Huq and EK Lipp. 2001. Health, climate and infectious disease: a global perspective. A report from the American Academy of Microbiology, Washington, DC.
- UNICEF, 2000. Sanitation for all: promoting dignity and human rights. UNICEF, New York.
- World Health Organization (www.who.int).
- World Health Organization, Water and Sanitation Fact Sheet No. 112, 1996. Available online: <http://www.who.int/inf-fs/en/fact112.html>.





AMERICAN
SOCIETY FOR
MICROBIOLOGY